residue. It is neutral to litmus paper. A simple test is to add a cold saturated aqueous solution to ferric-chloride test solution; the color of the latter should not be changed, indicating an absence of aniline salts.

Acetanilid exercises a depressing action upon the gray matter of the nervous system, and a destructive action upon the constituents of the blood. Upon the former depends its therapeutic properties, while the latter is an altogether undesirable effect.

Its action on the nervous system is most marked upon the gray matter of the spinal cord, by which the power of conducting painful impressions is greatly reduced, and at the same time it lessens the receptivity of the brain. The brain retains its clearness, but motive power and conduction are affected in a slight degree.

Its effect upon the medullary centres is to reduce the frequency and force of the pulse, depress respiration, and by relaxing the blood-vessels to promote the flow of blood to the surface and lessen blood pressure. In very large doses these effects are intensified, and upon animals the drug has caused anæsthesia, loss of reflex action, weakened circulation, convulsions, coma, and general paralysis.

In ordinary doses its action upon the blood is not noticeable, but if its use is persisted in it leads to anæmia. In over-doses it acts directly upon the hæmoglobin, producing methæmoglobin and lessening the oxidizing power of the blood. The blood may become of a dirty-brown color and hæmoglobinuria may be present.

When toxic symptoms arise there is generally a sudden sense of weakness and oppression, with a rapid lowering of temperature and bluing of finger nails and lips; this is accompanied or followed by vertigo, giddiness, noises in the ears, dilated pupils, cold extremities, subnormal temperature, shallow breathing, feeble pulse, nervous twitchings, convulsions, and coma. It is after large doses, or during the prolonged use of the drug, that these symptoms of poisoning are met with, but many instances are reported in which an ordinary therapeutic dose has produced an alarming condition.

In the administration of the drug there are many points to be considered which influence its action. As the effect of the dose is continued for two or three hours, the dose should not be repeated until that interval has elapsed. When the use of the drug is persisted in for some time, a day of freedom from its use should occasionally be allowed to intervene, as it undoubtedly possesses a cumulative action. Many instances are reported in which severe toxic symptoms have followed the same dose that had been given for some days with only beneficial effects. When the patient is anæmic, and in the debilitated and aged, the toxic symptoms more readily supervene, and in women, during the few days previous to menstruation, the condition of the blood is supposed to favor the decomposition of the drug and increase its action. The time of the dose, in relation to the natural rise or decline of temperature, is of importance; when given with the increase of fever, its action is slower and within control; but if its effect coincides with the decline, the fall will be rapid and probably in excess of what is expected.

The tendency to cause profuse sweating and cyanosis has unfortunately engendered in many a sense of dread which has restricted its use. This toxicity is greatly over-estimated and should not be feared if the dose and mode of administering are attended to. It is rather a danger-signal far in advance of any serious consequences.

The cyanosis and depression are not of long duration and are rapidly overcome. Fatal cases are rare, and very large quantities of the drug have been taken without causing death. A case is reported in which teaspoonful doses were taken at short intervals until one ounce was disposed of, and in another instance seven and a half drachms were taken with suicidal intent. In both cases recovery followed.

Kahn and Hepp in their original papers stated that one-fourth of a gramme (3.85 grains) was a sufficient dose, and subsequent writers have insisted on the efficacy of even smaller quantities.

Instead of the seven or ten grains so frequently given, the consensus of opinion now points to three or four grains as a more proper initial dose in every case in which its use is begun, to be increased as the individual susceptibility is learned.

During the past few years it has become evident that, when applied to raw surfaces, acetanilid may be absorbed and produce its physiological effect. In some instances acute poisoning has followed this use of the drug in infants and children. In one case the umbilical cord was dressed with about sixty grains of the crystals. On the second day prostration and cyanosis were marked, and continued for three days. In another case between twenty and forty grains were applied to a burned surface. When used for two successive days the same toxic symptoms arose. Many other cases have been reported. In one, an infant four days old, death resulted in four hours.

A distressing itchiness and burning of the skin, accompanied by a varying degree of erythema, has occasionally been noticed. It is not so common as during the use of other coal-tar products, but many cases have been recorded.

To counteract the poisoning, stimulating treatment is indicated. Warmth to the extremities and surface; alcohol, ether, and camphor by the mouth or hypodermically; belladonna is particularly recommended, four drops of the tincture every half-hour for four doses, afterward at longer intervals, having proved of service. Strychnine is also useful. The inhalation of oxygen is indicated. In extreme prostration the transfusion of saline solution has been adopted with benefit.

Acetanilid in fever is used solely as an antipyretic, and as such it has been classed as one of the best we possess. It is utilized in typhoid fever, pneumonia, phthisis, erysipelas, acute rheumatism, and in all conditions in which hyperpyrexia is present. It was thought by some to have specific properties in acute rheumatism, but such a view is no longer tenable; the duration of the disease is not affected, complications are not prevented, nor does it guard the patient against relapses. It reduces the high temperature and relieves the discomfort and distress that are present, and its sedative action on the nervous system adds to its calming and refreshing effect. Its continuous administration is not advised, but only its use when the temperature is such as to require interference.

In phthisis it proves particularly soothing. In the hyperpyrexia of pneumonia it is used with advantage, but in this condition, as well as in advanced phthisis, where the respiratory tissue is reduced, it must be given with caution.

In acute rheumatism it relieves the painful and swollen joints and reduces the temperature. When the pains are severe larger doses are required than in other febrile affections. Its action is generally thought not to be so efficacious as that of antipyrin or salicylate of soda.

Its analgesic properties have proved almost as decided as its power of reducing pyrexia. It is particularly useful in all pains due to irritation of the sensory nerves, or pains of a reflex character, such as those of locomotor ataxia, neuralgia, sciatica, lumbago, pains after operations, ovarian and menstrual irritation; also in migraine, nervous headaches, and the headaches of growing children. In all paroxysmal pains it has proved equally successful.

It has been recommended and tried in epilepsy and chorea, but without much advantage.

Quite recently it has been lauded as a very effective remedy for threatened premature expulsion of the ovum. It is stated that from seven to ten grains will lessen the uterine contraction and pain and check the hemorrhage; the dose to be repeated at intervals of two or three hours.

In the diseases of infancy it has proved of decided usefulness. Its effects are of longer duration and the toxic symptoms are not so liable to follow its use. In scarlet fever, measles, pneumonia, etc., its action has been most gratifying, reducing fever and restlessness and inducing a quiet and refreshing sleep. In whooping-cough it is

also used with success; its action promotes expectoration and reduces the frequency and duration of the paroxysms.

Its non-irritating and antiseptic properties have led to its employment as a dressing after surgical operations, as well as for wounds of every description. It is also recommended as a substitute for iodoform in venereal sores. It may be dusted pure over the parts or mixed with boric acid in varying proportions. A glycerol is made by adding one part to forty of cold sterilized glycerin. If a stronger preparation is desired, a solution of acetanilid in alcohol is prepared, twenty grains to the ounce, and one ounce of this mixed with four of glycerin. It may also be combined with vaseline or collodion.

Beaumont Small.

ACETIC ACID.—Acetic acid, $HC_2H_3O_2$, the well-known acid of vinegar, is a body fluid at ordinary temperatures, and miscible in all proportions with water. Mixtures of the acid and water in different proportions constitute the different grades of the acid in commerce. Strong acetic acid is caustic, largely through its property of dissolving the formed material of the connective tissues to a pultaceous translucent substance. Being caustic, it is of course irritant, and swallowed in concentrated condition operates as a corrosive poison, the effects and symptoms being substantially the same as in poisoning by the strong mineral acids. Two cases of death have been recorded. The treatment is similar to that to be employed in case of poisoning by a mineral acid. In non-corrosive strength of solution (five or six per cent., the equivalent of vinegar), acetic acid produces the usual local effects of the sour acids—exciting the flow of saliva and tending to oppose sour fermentation of the food—and is also distinctly astringent. Inhaled, the fumes are reviving in faintness and may relieve headache.

Acetic acid has many uses in pharmacy. Recently it has been urged strongly by high authority that the Pharmacopœia should substitute acetic acid largely for alcohol as a menstruum for the preparation of extracts, and it is probable that some such course will be followed. It has even been proposed that this class of extracts shall bear the special name "Acetracts." In medicine the strong acid may be employed as a caustic, as to warts or cancers, and the weak acid used to make refreshing acid draughts in fever, or cooling lotions in inflammatory skin affections. Acetic acid is official in the U. S. Pharmacopœia in the following forms:

Acidum Aceticum Glaciale, Glacial Acetic Acid.—This is defined to be "nearly or quite absolute acetic acid." It is "a clear, colorless liquid, of a strong, vinegar-like odor, and a very pungent, purely acid taste. When the acid is cooled to a temperature as near as possible to 15° C. (59° F.), but yet in a liquid form, its specific gravity should not be higher than 1.058, corresponding to at least ninety-nine per cent. of absolute acid. At a temperature somewhat below 15° C. (59° F.), the acid becomes a crystalline solid" (U. S. P.). This grade of the acid is for pharmaceutical uses.

Acidum Aceticum, Acetic Acid.—The grade of acid thus simply named is a "liquid composed of thirty-six per cent., by weight, of absolute acetic acid and sixty-four per cent. of water." It is "a clear, colorless liquid, having a strong, vinegar-like odor, a purely acid taste, and a strongly acid reaction. Specific gravity, about 1.048 at 15° C. (59° F.). Miscible with water and alcohol in all proportions. When heated, the acid is volatilized without leaving a residue" (U. S. P.). This grade of acid is somewhat stronger than the best samples of the commercial so-called "No. 8" acid, these "No. 8" acids rarely being of higher specific gravity than 1.030 and often sinking to 1.025 or less (Squibb). This is the acid that results from the purification of the crude acid—*crude pyroligneous acid*, so called—obtained by the destructive distillation of wood.

Acetic acid of the present quality is sharply irritant and even mildly caustic. Dangerous symptoms have resulted from swallowing it, undiluted, in quantity of two or three ounces. The acid may be used as a mild caustic, but its principal uses under its own form are pharmaceutical.

Acidum Aceticum Dilutum, Diluted Acetic Acid.—This preparation is compounded of one part, by weight, of acetic acid of the foregoing grade and five parts, by weight, of distilled water. It "contains six per cent., by weight, of absolute acetic acid. Specific gravity, about 1.008 at 15° C. (59° F.)" (U. S. P.). This diluted acid is of the strength of the best qualities of vinegar, and is better than vinegar for all the purposes of the same, medicinal or dietetic. Squibb says: "If one part of alcohol be added to about two hundred and fifty-six parts of this diluted acetic acid—that is, about half a fluidounce to the gallon—and the mixture be set aside for a few weeks (the longer the better), enough acetic ether is generated to give it the full, clean aroma of fine vinegar, and then for table use it is very far superior to any vinegar made in the ordinary way by fermenting cider."

Diluted acetic acid is the most convenient grade of the acid for medicinal use, and has also, in the U. S. Pharmacopœia, superseded vinegar for pharmaceutical purposes. For an acid draught a five-per-cent. addition to water is appropriate, and for a lotion a twenty-five-per-cent. addition. The popular notion that the habitual use of vinegar tends to deterioration of nutrition and health is certainly not true of a moderate indulgence, if indeed it be true at all.

Edward Curtis.

ACETIC ETHER.—Under the title *Æther Aceticus*, Acetic Ether, the U. S. Pharmacopœia makes official a preparation consisting of the ethereal salt, *ethyl acetate*, with a little contaminating alcohol and water. Acetic ether is described as "a transparent, colorless liquid, of a fragrant, and refreshing, slightly acetous odor, and a peculiar acetous and burning taste. Specific gravity, 0.893 to 0.895 at 15° C. (59° F.). Boiling point, about 76° C. (168.8° F.). Soluble in about eight parts of water at 15° C. (59° F.); miscible in all proportions with alcohol, ether, fixed and volatile oils. Acetic ether is readily volatilized, even at a low temperature. It is inflammable, burning with a yellowish flame and an acetous odor" (U. S. P.). Acetic ether should be kept in well-stoppered bottles and away from lights or fire.

The effects of acetic ether upon the animal economy are similar, in a general way, to those of common ether, the most important point of difference being that acetic ether is the slower in operation. For this reason this ether is not available as a surgical anæsthetic; but, on the other hand, by reason of its agreeable odor, it makes an excellent and grateful cardiac stimulant, antispasmodic, and carminative, taken internally. Used externally, it may serve to mask disagreeable odors. It may be given internally, in quantities ranging from fifteen to thirty drops, well diluted with water or with some medicinal preparation, to which the ether is added as an adjuvant or corrigent.

Edward Curtis.

ACETONE.—Acetone, C_3H_6O, the ketone of acetic acid, called also *pyroacetic spirit* and *pyroacetic ether*, is a colorless, limpid, and inflammable liquid of pungent quality, miscible in all proportions with water, alcohol, and ether. Its effects upon the animal system are, doubtless, of the general nature of those of the volatile alcohols and ethers, but the substance has never been systematically employed as a medicine.

It is used for chemical purposes in the manufacture of chloroform, and as a solvent for fats and resins.

It occurs normally, in small amounts, as an ingredient of blood, urine, etc.

Edward Curtis.

ACETONURIA.—Definition.—The presence in the urine of a pathological quantity of acetone, $CO(CH_3)_2$.

Historical.—Petters in 1857 discovered acetone in the urine of a patient suffering from diabetic coma, and three years later Kaulich demonstrated its occurrence in ordinary cases of diabetes and added a clinical picture of the condition known as acetonæmia.

Kussmaul in 1874, writing on diabetic coma, first threw doubt on the previously expressed idea that a definite relation existed between diabetic coma and acetonuria, while Gerhardt later on showed the occurrence of diacetic acid in the urine, a substance which has, clinically, even greater importance.

OCCURRENCE.—Physiologically, acetone occurs in the urine in very minute proportions, probably never more than .02 gm. being excreted in twenty-four hours. Pathologically, more than 5 gm. have been in the daily quantity of urine.

The main conditions under which increased acetone is found may be briefly summarized as follows:

1. Alimentary, *i.e.*, according to diet; withdrawal of carbohydrates; this may reach 0.7 gm. after prolonged dieting.
2. Diabetes, especially after some duration of the disease and with proteid diet or increased fats.
3. Fevers (often with diacetic acid and β oxybutyric acid as well); infectious diseases, *e.g.*, enteric fever, sepsis, pneumonia, exanthems, tuberculosis, acute inflammatory rheumatism; in the fevers it occurs only in prolonged cases, probably because of the nature of the diet; acute fevers present no increased acetonuria.
4. Starvation and inanition; cachexia; early carcinoma of stomach.
5. Digestive disturbances with auto-intoxication; peritonitis.
6. Pregnancy with dead fœtus.
7. Nervous lesions and mental disease; tabes; general paralysis; melancholia, etc.
8. Artificially induced general anæsthesia (chloroform).
9. Experimental—after extirpation of the solar plexus or of the pancreas.
10. Medicinal—phlorizin; chronic morphinism.

Source.—There is no doubt that acetone elimination bears a definite relation to the increased destruction of proteids, its occurrence in starvation, fevers, etc., bearing out this theory. It is not yet determined whether the amount excreted depends merely on the quantity of tissue proteid destroyed or upon the total proteid used up by the metabolism. Von Noorden and Honigmann hold that the destruction of tissue proteid is the essential feature. Certainly acetone elimination is not always increased with greater ingestion of proteids; in fact, too much proteid may diminish the degree of acetonuria. Fatty diet seems to increase acetone elimination; indeed, Geelsuyden is of the opinion that disintegration of fat either in the tissues or in the food is the main cause of acetonuria. Again, while increased ingestion of carbohydrates causes decrease of acetone excretion, a diminution of this in the diet is followed by marked acetonuria.

There seems to be no mutual relation between nitrogen elimination and acetonuria.

In diabetic urine three substances frequently occur together and seem to have some definite relation to one another, though their exact interdependence is not as yet understood. These substances are acetone, diacetic acid, and β oxybutyric acid. We can readily derive one from the other, *e.g.*, β oxybutyric acid from diacetic acid, or again by oxidation β oxybutyric acid forms acetone and carbonic acid. These three exist also together in other conditions than diabetes, *e.g.*, in starvation, severe infections, fevers, etc., and their relative proportions seem to vary without respect to their origin.

Probably, as Naunyn suggests, β oxybutyric acid is usually formed first and is the mother substance for the others, and the amounts of each formed depend on a great variety of conditions; thus, for example, a very marked alkaline state of the blood favors diacetic acid formation, while again acetone forms best in an acid urine, and so on. Certainly the degree of acetonuria does not depend regularly on the amount of β oxybutyric acid.

Clinical Significance.—In all probability the acetone *per se* is harmless and the toxic symptoms are produced by the diacetic and β oxybutyric acids; and possibly also others, *e.g.*, lactic acid or volatile fatty acids, come into action, too, at times. At all events, it is the *acid intoxication* (or excessive acidosis, as it has been called) that induces the serious changes which occur. Patients manifesting this acid intoxication usually get diabetic coma if no intercurrent affection occur to carry them off.

The PROGNOSIS, then, depends rather upon the evidence of acidosis than of acetonuria to a large extent, and Hallervorden has for this reason suggested the importance of frequent estimation of the ammonia eliminated, this giving a fairly accurate idea of the acid intoxication. (More than 3 gm. of NH_3 in twenty-four hours indicates excessive acidosis, while if more than 4 gm. exist, the onset of diabetic coma is almost certain, even though due treatment temporarily diminish the amount of NH_3 elimination.) This theory is proven, too, by Stadelmann's and Minkowski's observations, that diminished CO_2 was in the blood (*i.e.*, less alkalinity), and by the fact, too, that in severe diabetes the sudden restricting to meat diet (*i.e.*, acid) is often followed by coma.

The acetone is to some extent, however, in definite ratio to the intensity of the diabetes, and the presence of a large quantity is of grave import—though not as a prodrome of approaching coma, as Hirschfeldt once supposed. Intercurrent fevers, *e.g.*, pneumonia, may greatly increase the acetone temporarily, and with convalescence the quantity may return to its previous amount. So it was in the case of a diabetic whose urine increased during an intercurrent pneumonia from 0.4 gm. to 4 gm. acetone, daily, and with convalescence the amount returned to 0.4 gm. in the twenty-four hours; coma did not supervene and the patient lived for months afterward, until fatal marasmus came on. It is well, however, to follow the acetone excretion in diabetes, for its increase is so frequent with threatening symptoms;—hence the benefit, at such a time, of judicious administration of carbohydrates.

The DIAGNOSTIC significance of acetonuria lies in the fact that its presence to any extent with glycosuria renders the diagnosis of diabetes certain.

Tests.—Before testing for acetone one should ascertain the possible presence of diacetic acid, which by decomposition often forms acetone. For this, Gerhardt's reaction is to be tried and the following three steps must be taken:

Fifteen cubic centimetres of urine are treated with dilute (not too acid) ferric chloride so long as it gives a precipitate. The precipitate (ferric phosphate) is filtered and more ferric chloride added to the filtrate. In presence of diacetic acid a claret-red color appears. A second portion of the urine is boiled and the same test repeated after cooling. A negative result should follow, because the diacetic acid was decomposed by the boiling. (If a positive result were again obtained it would indicate the presence of acetic or some other acid in the urine.)

A third portion is next acidified with sulphuric acid and shaken with ether. The ether is removed and shaken with a very dilute aqueous solution of ferric chloride, when the watery layer becomes violet red or claret red. The color disappears on warming or after standing twenty-four hours.

In the *absence of diacetic acid* we proceed to test directly for acetone. No single test for acetone is completely satisfactory; hence the necessity of employing several as confirmatory evidence. One may use the urine as it is, although it is more accurate to resort first to distillation. About 250 c.c. of urine are boiled after faintly acidifying with sulphuric acid, and, a good condensation being secured, all the acetone will distil in the first 20 c.c.

When *diacetic acid is present* the urine should first be rendered faintly alkaline and carefully shaken up in a separator funnel with ether (the ether must be free from alcohol and acetone). The removed ether is then shaken up with water, which takes up the acetone, and this watery liquid is tested.

Qualitative Tests.—Lieben's Iodoform Test. Treat a few cubic centimetres of the distilled urine (which should be freshly voided always) with some sodium hydrate and iodine potassic iodide solution and gently warm. With traces of acetone a yellow precipitate of iodoform occurs, and this will be recognized by its odor and by the hexagonal plates or stellate crystals. While this test is delicate enough for acetone, there are many other constituents of the urine and other substances (at least seventeen) which yield a similar reaction. Among them is alcohol; hence the possibility of error from using an alcoholic solution of iodine to make up one of the reagents—which must, of course, be avoided. Gunning modified the test by using an alcoholic solution of iodine and ammonia instead of the mixture mentioned above. A black precipitate of iodide of nitrogen results, and this, in the presence of acetone, gradually disappears, leaving the yellow iodoform behind. The test, though not quite so delicate, is more accurate, neither alcohol nor aldehyde producing a similar result; and, moreover, it is eminently suited for clinical purposes, in view of the temptation to test without the time-absorbing distillation.

Legal's Sodium Nitroprusside Test. Treat a few cubic centimetres of the urine with two or three drops of a freshly prepared concentrated solution of sodium nitroprusside and add a thirty-per-cent. solution of caustic potash. A ruby red color appears, which changes to yellow. Any urine may give this reaction. But if acetone be present in pathological amount the addition of acetic acid changes the color to a purple red or violet.

Parakresol and creatinin give somewhat similar reactions. In presence of the former, however, the yellow color changes to pink on addition of acetic acid, while with the latter a *saturation* with acetic acid gives a yellow color, soon changing to green and blue. Acetone, under similar conditions, gives a carmine color. Fehr modifies this test by floating the acetic acid on the urine as the color changes to yellow. A violet is produced at the line of contact, its intensity being proportionate to the amount of acetone present.

Notwithstanding its frequent commendations for clinical purposes, Legal's test is certainly unreliable unless the urine be first distilled.

Le Nobel's test is similar. One adds an alkaline solution of sodium nitroprusside (so dilute as merely to give a faint reddish tint to the solution) to the urine; a ruby red color is obtained, soon changing to yellow. On boiling and adding the acid a greenish blue or violet results.

Penzoldt's Indigo Test. Treat the urine with a warm saturated and then cooled solution of orthonitrobenzaldehyde and add caustic soda. If acetone be present the liquid becomes first yellow, then green, and finally indigo forms, which may be dissolved in chloroform.

Chautard takes fuchsin solution into which a current of sulphurous acid gas has been passed. This decolorizes the liquid and gives it a clear yellow tint. When added to urine containing acetone a deep violet color is produced.

Reynolds' mercuric oxide test depends on the power of acetone to dissolve freshly precipitated mercuric oxide. A mercuric chloride solution is first precipitated by alcoholic caustic potash. The urine is added to this and the mixture well shaken and filtered. If acetone be present the filtrate contains mercury, which may be detected by the black color on adding ammonium sulphide.

Reynolds' and Gunning's tests are particularly recommended for delicacy and reliability combined.

Quantitative Test.—Huppert's modification of Messinger's is that most recommended; Lieben's iodoform test being the method on which it is based.

Acetone forms iodoform when treated in an alkaline solution with iodine. By treating the urine with a known amount of iodine one need simply estimate the quantity unused by the iodoform to know how much has been combined. This can be done by titration with sodium thiosulphate solution. For the details of the method the reader is referred to Huppert's "Analyse des Harns," 1898.

Charles F. Martin.

ACETO-PHENONE-ORTHO-OXY-QUINOLIN, $C_9H_6NO.CH_2.CO.C_6H_5$, is made by the action of an alkali on a solution of acetophenone chloride and orthoquinolin. It is an odorless, tasteless, strongly basic liquid insoluble in water and soluble in alcohol, ether, and chloroform. It forms salts with the acids, and is given in doses of one to three minims as a hypnotic or for neuralgia. Its uses are the same as those of acetophenone (see *Hypnone*), but it lacks the penetrating odor and pungent taste.

W. A. Bastedo.

ACET-ORTHO-TOLUID (Ortho-tolyl-acetamid).
ACET-PARA-TOLUID (Para-tolyl-acetamid), $C_6H_4(CH_3)NH.COCH_3$.

These isomers are produced by the prolonged boiling of glacial acetic acid with orthotoluidin and paratoluidin respectively. They occur in colorless, needle-shaped crystals, almost insoluble in cold water and readily soluble in alcohol and ether. Chemically they differ from phenacetin only by the substitution of a methyl for an oxyethyl group, and they are valuable as antipyretics. The dose is from 5 to 15 grains.

W. A. Bastedo.

ACETYLENE. See *Carbon, Oxids of.*

ACETYL-THYMOL (thymol acetate), $C_{10}H_{13}O.CH_3CO$, is a colorless liquid with an aromatic odor and pungent taste, and is used as an antiseptic.

W. A. Bastedo.

ACIDS.—*Fatty Acid Series,* $C_nH_{2n}O_2$.—Fatty acids are found in the body chiefly in combination with glycerin in the glycerides or neutral fats of adipose tissue. They are also found combined with alkalies, as soaps, and, in small quantities, as free fatty acids. Free fatty acids occur in the intestine as a result of the breaking up of neutral fats in pancreatic digestion. Some of the lower members of the series are found free in blood and sweat. As we ascend the series, the molecules become more complex and the melting and volatilizing points rise. For each acid they vary slightly, according to the mode of preparation. Many fatty acids crystallize in characteristic forms. The following are of most physiological importance:

Formic acid, $H.COOH$, is found combined as salts in minute traces in normal urine, and in increased amount in certain diseases with deranged metabolism, such as leucocythæmia and diabetes. It is present in the stings of certain insects, giving them their irritating qualities. It is a colorless liquid, of strong odor, volatilizing at 100° C.

Acetic acid, $CH_3.COOH$, is found in the intestine and sometimes in the stomach as a result of fermentation processes, occurring in carbohydrates and higher fatty acids. Its salts are present in normal urine in traces, and in increased amount in diabetes and leucocythæmia. In the diseases named, it is also found in the urine combined with acetyl, $CH_3.CO$, to form diacetic acid, $CH_3.CO.CH_2.COOH$. Acetic acid has a characteristic odor like vinegar, a sour taste, and forms transparent crystals which melt at 17° C.

Propionic acid, $CH_3.CH_2.COOH$, occurs occasionally in sweat. It is present in the blood, urine, and vomit of certain diseases. It is the first fatty acid to form a neutral fat with glycerin. It has an odor like acetic acid and volatilizes at 142° C.

Butyric acid, $CH_3.(CH_2)_2.COOH$, is found in the intestines and occasionally in the stomach, as a result of fermentations. It may be formed from the decomposition of proteids, carbohydrates, fatty acids higher in the series, or lactic acid. It is found in sweat, and traces have been demonstrated in blood and urine. It is present in milk and butter, combined with glycerin as butyrin. Butyric acid is an oily liquid, volatilizing at 162.3° C. and solidifying at −19° C.

Isovalerianic acid, $(CH_3)_2.CH.CH_2.COOH$, is found in cheese, the sweat of the foot, and the urine of certain diseases. It is a product of proteid decomposition. It is found combined as a neutral fat in dolphin blubber. It is an oily, colorless liquid, smelling like rotten cheese, and volatilizing at 176.3°.

Caproic acid, $CH_3.(CH_2)_4.COOH$, is found in the fæces and sweat, also in cheese, is formed from putrefaction of proteids, and occurs as a glyceride in butter. It is an oily, colorless liquid, with a faint, unpleasant smell. It volatilizes at 205° C. and solidifies at −18° C.

Caprylic acid, $CH_3,(CH_2)_6,COOH$, and
Capric acid, $CH_3,(CH_2)_8,COOH$, are found in sweat, in cheese, and as glycerides in butter. Caprylic melts at 16.5° C. and volatilizes at 236° C. Capric melts at 30° C. and volatilizes at 270° C.

Lauric acid, $CH_3(CH_2)_{10},COOH$, and
Myristic acid, $CH_3,(CH_2)_{12},COOH$, are present as glycerides in human fat and in butter, also as compound ethers in spermaceti. Lauric acid melts at 43.6° and myristic at 53.8° C.

Palmitic acid, $CH_3,(CH_2)_{14},COOH$, is found as a glyceride in all animal fats and as compound ethers in spermaceti and beeswax; it is also found combined with cholesterin in wool fat (lanolin). It melts at 62° C.

Stearic acid, $CH_3,(CH_2)_{16},COOH$, is found combined like palmitic acid in animal fats and spermaceti. It melts at 69.2° C. Margaric acid is a name sometimes applied to a mixture of palmitic and stearic acids.

Arachidic acid, $CH_3,(CH_2)_{18},COOH$, is found in butter as a glyceride. It melts at 75° C.

Cerotic acid, $CH_3,(CH_2)_{25},COOH$, is found free in beeswax. Combined as cetyl ether, it forms the principal part of Chinese wax. The free acid forms granular crystals, which melt at 78° C.

Acrylic Acid Series, $C_nH_{2n-2}O_2$.—Some of the higher members of this series form compounds with glycerin, resembling the neutral fats. The most important member of this group physiologically is—

Oleic acid, $CH_3,(CH_2)_{14},(CH)_2,COOH$; it is found united with glycerin in all the fats of the body, as a liquid fat, olein, which holds the higher fats of the fatty acid series in solution at the body temperature.

Glycolic Acid Series, $C_nH_{2n}O_3$. — Carbonic acid, $OH,COOH$, is unknown in its free state, being doubtless too unstable to exist. Its salts, however, are present in large quantities in the body, and play an important part in the alkalinity of the tissues and fluids. Its corresponding oxide, CO_2, is the principal form in which carbon leaves the body.

Glycolic acid, $H,CHOH,COOH$, does not occur in the body.

Lactic acid, $CH_3,CHOH,COOH$, exists in three isomeric varieties:

1. Fermentation lactic acid is present in sour milk, and in the stomach and intestines during digestion. It is also found in small quantities in the muscles and brain, and in diabetic urine. It is a colorless or faintly yellow liquid of syrupy consistency, and is distinguished from the two following by being optically inactive.

2. Paralactic or sarcolactic acid is the principal acid of meat extracts and of muscle, and is also found in numerous glands. It is present in the sweat in puerperal fever, and in the urine after severe fatigue, in acute yellow atrophy of the liver, and in phosphorus poisoning. It is dextro-rotatory to polarized light.

3. A third lævo-rotatory lactic acid has been obtained by the fermentation of cane sugar by a special bacillus.

Oxybutyric acid, $CH_3,CH_2,CHOH,COOH$, found along with diacetic acid and acetone in the blood and urine of diabetes, is an odorless syrupy liquid, which mixes freely with water, alcohol, and ether, and rotates polarized light to the left.

Oxalic Acid Series, $C_nH_{2n-2}O_4$.—Oxalic acid, $COOH,COOH$, is found in small quantities in the urine as calcium oxalate, and often occurs in excess after the ingestion of rhubarb or cabbage. It is usually increased where the amount of uric acid is increased. It may be obtained in the laboratory along with urea and carbonic acid gas from the oxidation of uric acid, and it is believed to be formed from the latter in the body to some extent. Oxalic acid is a violent poison. It crystallizes from aqueous solutions in large, transparent prisms, which effloresce when exposed to the air.

Succinic acid, $COOH,(CH_2)_2,COOH$, has occasionally been found in the urine after the ingestion of asparagus and other vegetables and fruits. It has also been detected in the sweat, the intestinal contents, and in the thymus and thyroid glands. It forms large colorless crystals which are unaltered by the air and which fuse at 180° C.

Amido Acids are derived from the fatty acids by replacing one or more hydrogen atoms by amidogen, NH_2. They are formed from proteids and albuminoids (gelatin) during digestion and metabolism, and are considered important precursors of urea.

Carbamic acid, OH,CO,NH_2, amidoformic acid, is not known in the free state. Its ammonium salt has been found in the blood and is believed to be an intermediate substance between proteids and urea.

Leucin, $(CH_3)_2,CH,CH_2,CH,NH_2,COOH$, *a*-amidoisobutylacetic acid, is isomeric with and was formerly considered identical with amidocaproic acid. It is present wherever proteids are being broken up by tryptic digestion, by boiling with dilute acids or by putrefaction. It has been found in certain glands after death, and is found in the urine in acute yellow atrophy of the liver and phosphorus poisoning. There are satisfactory proofs of its being one of the precursors of urea. It crystallizes if pure in shining white plates, but usually forms characteristic round knobs or balls.

Tyrosin, $HO,C_6H_4,C_2H_3,NH_2,COOH$, p-oxyphenylamidopropionic acid, contains a phenyl group, and is consequently a member of the aromatic group of substances as well as an amido acid. It is formed with leucin from the breaking up of proteids in pancreatic digestion, and especially in putrefaction. It crystallizes in colorless, silky, fine needles, which are often grouped into tufts or balls. It has not been definitely proved to be a precursor of urea.

Aspartic acid, $HOOC,C_2H_3,NH_2,COOH$, amidosuccinic acid. It is formed from proteids during pancreatic digestion, and is probably a precursor of urea in the animal body. It crystallizes in rhombic prisms.

Glutamic acid, $HOOC,C_3H_5,NH_2,COOH$, amidopyrotartaric acid. It is formed along with aspartic acid during pancreatic digestion. It crystallizes in rhombic tetrahedra or octahedra or in small leaves.

Lysin, C_6H_{14},N_2O_2, Arginin, C_6H_{14},N_4O_2, and Histidin, C_6H_9,N_3O_2, are probably amido acids, but in their reactions they resemble bases and are grouped together under the name of the hexone bases because they each contain six atoms of carbon. They are among the products of proteid decomposition. Lysatin or lysatinin, which is sometimes given as a separate substance, is probably a mixture of lysin and arginin.

Glycocoll, $NH_2,CH_2,COOH$, amidoacetic acid, is also known as glycocin or glycin. It is formed from the decomposition of proteids and albuminoids, and is found free in the intestine as a result of the breaking up of the bile salts. It is also set free when hippuric acid is boiled with mineral acids or alkalies.

Sarcosin, $NH,CH_3,CH_2,COOH$, methyl glycocoll, is not found in the body.

Creatin, $NH,CNH_2,NCH_3,CH_2,COOH+H_2O$, may be prepared synthetically from cyanamide, CN,NH_2, and sarcosin. It occurs among the extractives of muscle and is regarded as a probable precursor of urea. When injected into the blood, however, it loses the elements of water and appears in the urine as creatinin, $C_4H_7N_3O$.

Taurin, NH_2,C_2H_4,SO_2,OH, amidoisethionic acid, is found combined in the bile salts. It may occur free in small quantities in the intestines. It crystallizes in colorless, shining, four to six sided prisms, often of large size.

Bile Acids.—Glycocholic and taurocholic acids are found in the bile combined with soda to form the bile salts. They consist of cholalic acid in combination with glycocoll and taurin respectively.

Glycocholic acid, $C_{26}H_{43}NO_6$, is found in human and ox bile, but is absent or nearly so from that of carnivora.

Taurocholic acid, $C_{26}H_{45}NSO_7$, is found principally in the bile of the carnivora and man, but is also present in oxen, sheep, and goats.

Cholalic acid, $C_{24}H_{40}O_5$, is found combined in the above-named bile acids. It is insoluble in water, but soluble in alcohol, and slightly so in ether. It crystallizes in rhombic prisms or in large rhombic tetrahedra or

octahedra. Choleic acid, $C_{24}H_{40}O_4$, and fellic acid, $C_{23}H_{40}O_4$, are also present in small quantities in human bile, combined in place of cholalic acid in the bile salts.

Aromatic Acids.—Acids of the benzene series. A number of these are present in the body in small quantities. They are derived partly from the aromatic substances contained in the food, and partly from the breaking up of proteids. Tyrosin has been already described under the amido acids. The following are found principally in the urine:

Hippuric acid, $C_6H_5,CO,NH,CH_2,COOH$. Benzoylamidoacetic acid occurs in large quantities in the urine of herbivora, but only in small quantities in the carnivora and man. The quantity in the urine is increased by vegetable food containing benzoic acid compounds, and by putrefactive processes in the intestine. It may be decomposed into benzoic acid and glycocoll.

Ethereal sulphuric acids include the following four acids, phenol-sulphuric acid, C_6H_5,O,SO_2,OH, cresol-sulphuric acid, C_7H_7,O,SO_2,OH, indoxyl-sulphuric acid or indican, C_8H_6N,O,SO_2,OH, and skatoxyl-sulphuric acid, C_9H_8,N,O,SO_2,OH.

These acids are all found in the urine, and are derived from the phenol, cresol, indol, and skatol which are formed in the intestines as a result of the putrefaction of proteids. Any circumstances favoring the latter process, such as intestinal diseases accompanied by obstruction, increase the amount of these acids in the urine.

Aromatic oxyacids, of which the principal are paraoxyphenyl-acetic acid, $C_6H_4,OH,CH_2,COOH$, and paraoxyphenyl-propionic acid, $C_6H_4,OH,C_2H_4,COOH$, are formed from tyrosin in small quantities in the intestine and pass unchanged into the urine.

Nucleic Acids.—These are acids rich in phosphorus, of complex and variable composition, found among the most characteristic constituents of cell nuclei. They combine with proteids to form numerous varieties of nuclein and nucleoproteid. Among the products of their decomposition, the most important are the alloxuric bodies, also known as the xanthin or still better as the purin bodies.

Uric Acid.—$C_5H_4N_4O_3$, trioxypurin, is found in adult human urine to the extent of from seven to ten grains per day, combined with bases to form urates. In birds and reptiles it replaces urea in the urine as the principal end product of proteid metabolism. In man it is derived principally from the nuclei of broken-down cells and from the purin bodies contained in the food. The extent to which it is formed from proteids in the body cannot be considered settled. For further details about uric acid, see the articles on *Gout* and *Urine*.

Wesley Mills.
William S. Morrow.

ACIDS, MINERAL, TOXICOLOGY OF.—The only mineral acids which require extended consideration at the hands of the toxicologist or physician are sulphuric, nitric, and hydrochloric acids.

I. *Sulphuric Acid.*—A number of different forms of sulphuric acid occur in commerce.

First, the pure acid, colorless and oily, known as *chemically pure sulphuric acid*, having a specific gravity of 1.842, and containing about 99 per cent. of sulphuric acid.

Second, a solution of much the same appearance containing 92.5 per cent. of sulphuric acid, the *Acidum sulphuricum* of the United States Pharmacopœia.

Third, the dilute, watery solution of the acid, also clear and colorless, containing 10 per cent. of sulphuric acid, the *Acidum sulphuricum dilutum* of the United States Pharmacopœia.

Fourth, the *commercial acid* of varying strength, and colored brown to black by organic impurities.

The concentrated acid in all its forms is intensely corrosive, destroying readily any organic tissue with which it may come in contact. Its power in this direction is due to its avidity of water, it being able to extract the elements of water from wood, cloth, or flesh, leaving the residue charred and more or less blackened as a result.

On clothing, if dark colored, the acid produces a brown stain with red edges, and after a time decomposes and softens the fibres of the cloth, so that it easily falls to pieces. The acid spot is always wet, due to absorption of water from the material and from the air. On light-colored cloth the acid produces a brown stain, which after a time turns black and destroys the tissue of the cloth.

Wood is blackened by the action of the acid, and at the same time softened and disintegrated. In damp weather the stain of this acid on wood is moist, unless the acid has been neutralized by an alkali.

On the skin the concentrated acid produces an intense, biting sensation, and soon blisters and destroys the cuticle, and to a greater or less extent corrodes the tissues underneath. If the acid is not removed at once, the spot turns brown; and even when it is washed away immediately, or its action neutralized by alkalies, the cuticle is destroyed and a red scar remains wherever the acid has acted. This acid, because it is so readily obtained, is the favorite of the acid thrower, who attempts to disfigure or blind his victim by throwing the fiery liquid over the face and person. A number of cases are reported yearly in which such attempts have been more or less successful. If the acid gets into the eyes, its corrosive action and the intense inflammation it sets up are almost sure seriously to impair the sight, and certainly to cause the most excruciating suffering.

Fatal results from sulphuric acid introduced into the body are numerous. Yet the acid has never been used in homicidal cases except when the intended victim has been incapable through age or condition of resisting the administration of the acid. For so intensely sour is its taste, and so suddenly corrosive its action, that in the very act of taking it, it is rejected. The results of taking it are therefore to be looked for in cases of suicide or accident. A number of such cases are reported, and some in which there has occurred a curious lack of early symptoms, the action of the acid seeming to be delayed by the presence of food in the stomach. Some cases are reported in which the acid has been taken by the vagina or rectum. In all these instances the corrosive action of the acid has been in evidence sooner or later.

When the concentrated acid is swallowed, there is at once the most intense pain in the mouth and throat. In many instances this sense of pain is so excruciating as to deprive the person of the power of motion, yet cases are recorded in which, after taking it, the person has walked or ridden a considerable distance. The pain quickly extends to the stomach, and there is continued vomiting of a thick, brown material, strongly acid and tinged with blood. The mouth becomes filled with a tough, stringy mucus, so that difficulty of swallowing and loss of speech speedily occur. The mouth and the tongue are greatly swollen and, at times, as though smeared with white paint, though after a time the color changes to gray or brown. The abdomen is very painful when touched, and is generally distended. All food is immediately rejected by the stomach and vomiting is usually incessant. The face is pale and anxious; the pulse is quick and feeble; the body cold and covered with a cold perspiration. There is no delirium. The bowels are constipated; the stools, if any, are more or less black and contain shreds of lining membrane. Death usually occurs within from eighteen to forty-eight hours, though it may occur from the secondary effects of the acid many months after the latter has been taken.

The treatment consists in the administration of dilute alkalies, by preference calcined magnesia, though in an emergency washing soda or even the plaster from the wall may be used to neutralize the acid, and, in case of the lack of all these, water should be given copiously. Mucilaginous and oily drinks should also be administered to aid in recovering the corroded surfaces. The stomach pump should not be used on account of the softened condition of the tissues. In cases of impending suffocation, which sometimes occurs from the swollen condition of the glottis or from the presence of a mass of stringy mucus, tracheotomy must be resorted to.