during which time eclamptic attacks are most frequent. It then falls till the fifth year, to rise again as puberty approaches. During these years, from six to sixteen, most cases of epilepsy develop. Convulsibility then gradually declines, and few cases of the convulsive neuroses arise after the age of thirty. Convulsibility is somewhat more pronounced in girls and women; and is heightened at the menstrual periods and climacteric. It is, as a rule, lessened during pregnancy, and is increased by sterility in women, and by sexual excesses or depletions in both sexes. The convulsive diathesis may be inherited, connate, or acquired. It is inherited in about one-third of the cases from ancestors of a neuropathic or tuberculous constitution. It is connate as the result of frights, injuries, or nutrition disturbances received by the pregnant mother; perhaps also as the result of intoxication of the father during the sexual act. Convulsibility is acquired, in the young, by infectious fevers, bad food and air, chronic diarrhœa, hemorrhages, and especially by rickets. As the child grows older convulsibility may occasionally be developed by bad systems of domestic and school training, and over-indulgence in emotion. At the time of puberty the abuse of the sexual function, great excess in the use of alcohol, tobacco, and absinthe, worry, fright, and mental strain, come into play. After manhood or womanhood is fully reached, it is only by the powerful and persistent action of depressant and disturbing forces that a convulsive temperament is acquired. Latent tendencies may, however, be brought out at this period.

Climate and season have a slight influence over convulsibility. Tetanus occurs oftener in cold weather; epileptic and choreic attacks occur oftener in the spring and autumn, and on wet, cloudy days, and these diseases are more frequent in temperate climates.

Race is undoubtedly a factor in predisposing to convulsions.

Exciting Causes.—These are very numerous, but vary in character chiefly with age. For details on this point the reader is referred to the special articles. Here it can only be said that in infancy the most frequent exciting causes are: pressure on the brain from meningeal, hydrocephalic, or hemorrhagic effusions, and depressed occiput; blows, acute diseases, fright, and dental or gastro-intestinal irritations. At an older age we find scrofulous tumors, uræmic poisoning, sunstroke, sexual irritations, intemperance, syphilis, the puerperal state, as active factors. Still later, cerebral tumors or hemorrhages, and injuries to the skull are potent. At all ages there is a large class of drugs which can excite convulsions; among these are lead, strychnine, thebaine, papaverine, and narcotine.

Physiopathology.—For the special pathology of the convulsive neuroses, the reader is referred to the special articles on these diseases. There are certain facts in the mechanism of their production, however, which are common to all. In a convulsive attack there are brought into functional activity—

1. A nerve centre, which is discharging its force with excessive violence.
2. Outgoing or efferent neuraxones.
3. Their peripheral end plates, and the muscle or end organ.

In reflex convulsions we must add—

4. Afferent excito-reflex neurones, carrying excitations to the irritable centre.

In order that a convulsion may occur, the nerve centre (1) must be unduly irritable or unduly stimulated, until it is made unstable; the other factors in the mechanism, (2) and (3), must be intact, and the convulsion will be favored by their being in an over-irritable state.

The agents which affect the nerve centre (1), making it over-irritable and explosive, are:

(*a*) Some inherent defect in cell nutrition, as in essential convulsions.

(*b*) Some direct chemical or mechanical irritation, as in toxic and sympathetic convulsions, and in those caused by organic disease.

(*c*) Powerful excito-reflex impulses.

Local and limited convulsive movements may be caused by irritation or interference in the regular conduction of the efferent nerves (2).

To the machinery thus described modern physiology adds another factor, viz.: 5. An inhibitory mechanism. Certain parts of the cerebral nerve centres have an inhibitory action over the function of other parts, rendering the motor cells more stable and less liable to part unduly with their energy. A convulsion may result from a too great weakening or entire loss of this inhibitory force. In the developing and undeveloped nervous system of the child, the inhibitory powers are imperfect; hence a greater convulsibility at this age.

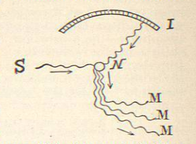

Fig. 1514.—Diagrammatic Illustration of Convulsions. I, controlling centre; N, motor nerve centre, from which neuraxones run to M, groups of muscles, and S, excito-reflex neuraxones. A convulsion may be caused by an over-irritation of N or of S, or by a depression or paralysis of I.

The more localized convulsive movements in chorea and the "tics," or local spasms, have a different origin from the foregoing. Here there is some irregular irritation of the motor cells. Thus, choreic movements are produced by irritation of some parts of the voluntary motor neurones; facial spasm generally by some irritation of the neurones of the seventh nerve. The part that the spinal cord plays in producing convulsions in man is not great and has been exaggerated. Eclampsia infantum, for example, is not the result of the defective inhibition of the brain upon the spinal cord, but rather a defective inhibition of certain higher brain centres upon lower. We see instances of true spinal convulsion (spinal epilepsy, spinal trepidation) in chronic diseases of the spinal cord implicating the pyramidal tracts, at the beginning of the third stage of anæsthesia, and in infants, children, or sensitive adults just as they are dropping off to sleep.

Symptoms.—The general convulsions of eclampsia, epilepsy, hysteria, and hystero-epilepsy have common features. There are often prodromal symptoms, indicating an over-irritable or depressed state of the nervous system. The attacks themselves come on suddenly, sometimes with an immediate prodromal symptom or aura. The muscular movements are irregular and incoördinated, except in some phases of hysterical and hystero-epileptic convulsions. Consciousness is generally abolished, as are also sensibility and the reflexes. Very marked secretory disturbances occur. The vasomotor system is greatly involved, especially that part which controls the blood supply of the brain. The face and probably parts of the brain are at first blanched, but the anæmia is soon followed by pronounced passive hyperæmia. In eclampsia infantum, however, the first sign of the impending attack is sometimes a cerebral hyperæmia, and the convulsion may be arrested by pressure on the carotids. Respiration is disturbed, and the heart beats at first more slowly, then more rapidly than normal.

Diagnosis.—The diagnosis of a convulsion is easy. One has only to differentiate it from malingering. The state of the pupils, of the reflexes, and of the sensibility, and the want of art upon the part of the malingerer, are generally quite sufficient to clear up the case. As to the form of convulsion, the difficulty in diagnosis may lie first in determining whether an attack is one of eclampsia or of epilepsy. Eclampsia occurs oftenest before the age of two years; the attacks are less sudden, more irregular, more prolonged, and less severe than in epilepsy. Usually there is no frothing at the mouth. After the age of two, idiopathic convulsions are most probably epileptic. It is important to distinguish between hysterical, hysteroid, and epileptic convulsions. All that I can say here, however, is that in the two former types the movements are more co-ordinated, consciousness is not entirely lost, sensibility may be present, and hallucinations may develop.

It is very important to determine whether the convulsion is idiopathic, or symptomatic of some general disease, reflex irritation, or organic central affection (see *Chorea*, *Eclampsia*, *Epilepsy*, *Hysteria*).

In some forms of convulsions it is necessary to make an anatomical diagnosis. If the symptoms are in the main bilateral, the cause is to be referred provisionally to the medulla; if they are unilateral, or involve special muscular groups, the convulsion is presumably symptomatic of a lesion in some part of the intracranial pyramidal tract, basal ganglia, or motor cerebral cortex of the opposite side.

There is a certain probability that convulsions in infancy are essential; in childhood are meningitic, febrile, or epileptic; in maturity and old age are symptomatic of syphilis or structural lesions; in women are hysterical.

Prognosis.—As regards the attacks, the danger to life is greatest in infantile and puerperal eclampsia; next in the degree of danger comes a special form of convulsion, viz., laryngismus stridulus; then follow choreic and epileptoid convulsions, epilepsy, hystero-epilepsy, and hysterical convulsions. As regards recurrence and final cure no general comparisons can be profitably made.

Treatment.—The general principles governing the therapeutics of convulsions are nearly the same for all. For the attacks, removal of sources of irritation, the use of chloroform, ether, morphine, amyl, nauseants, bromides, and chloral are indicated. For the disease, removal of all direct or reflex irritants and a treatment calculated to lessen the irritability and increase the tone and nutrition of the nervous system are indicated.

In the convulsions of children the common and effective practice is to place the child in a warm bath. In convulsions of adults, when drugs cannot be given by the mouth, enemas of thirty to forty grains of chloralamid are efficacious. In hysterical convulsions hypodermic injections of apomorphia, gr. $\frac{1}{4}$, or morphia, gr. $\frac{1}{4}$, may be given.

Charles L. Dana.

COOPER'S WELL.—Hinds County, Mississippi.

Location.—Twelve miles east of Jackson (by stage) and 4 miles from Raymond.

This is one of the famous old-time resorts of Mississippi, and the waters of the well have attracted more attention in days gone by than any others in the State. The well is one hundred and seven feet deep and its flow very abundant (Walton). The following analysis was made by Prof. J. Lawrence Smith:

One United States Gallon Contains:

Solids.	Grains.
Potassium sulphate	0.61
Calcium sulphate	32.13
Sodium sulphate	11.71
Aluminum sulphate	6.12
Magnesium sulphate	23.28
Sodium chloride	8.36
Calcium chloride	4.32
Magnesium chloride	3.48
Iron peroxide	3.36
Calcium crenate	0.31
Silicon crenate (?)	1.80
Total	95.48

This is a very valuable mild chalybeate water, containing a certain proportion of purgative salts and bearing considerable resemblance to the waters of Bocklet, near Kissingen, in Bavaria. This combination adapts the waters to numerous conditions in which anæmia is associated with constipation or abdominal plethora. Its effects are found to be very satisfactory in dropsy and in chlorosis. In chronic diarrhœa it has long held a high repute. The water acts as a diuretic or aperient according to the quantity used and the mode of drinking.

James K. Crook.

COPAIBA.—Balsam of Copaiba. "The oleo-resin of *Copaiba Langsdorffii* (Desf.) O. Kuntze, and of other species of Copaiba (fam. *Leguminosæ*)" (U. S. P.). Of the sixteen gigantic trees of this genus, twelve are tropical American, and of these seven are known to contribute to the copaiba of the market, as follows:

C. Langsdorffii (Desf.) Kuntze, *C. confertiflora* (Benth.) Kuntze, *C. coriacea* (Mart.) Kuntze, *C. oblongifolia* (Mart.) Kuntze, all of Brazil, *C. officinalis* Jacq. in the Orinoco valley, and *C. Guyanensis* (Desf.) Kuntze and *C. multijuga* (Hayne) Kuntze of the Amazonian region.

Several species furnish ornamental woods for cabinet work, the so-called "amaranth," or purple wood, being one of them. The timber is also highly prized for boat and wheel making in tropical America, and the seeds are used like vegetable ivory, for small objects.

Collection.—The stems of the copaiba trees contain numerous oil canals and cavities, in which the liquid is accumulated as turpentine is in those of the pine trees. But the copaiba canals are much larger, sometimes even exceeding an inch in diameter, and they traverse the whole length of the stem. Into these the copaiba is freely secreted. Indeed, the pressure of it in them is said to be sometimes so great as to split the trunk itself and to find spontaneous exit, as is also true of one or two other oleiferous trees. As may be supposed, the process of collection is simple enough: a deep gash cut into the trunk, reaching the heart-wood, hollowed and slanting below so as to collect the flow, provided with an improvised spout made from the bark itself, or with a leaf, and a receptacle to contain the oil as it flows in a steady stream, are the essentials. It is carried on mostly by the Indians. The yield is enormous, and may reach from ten to fifteen gallons from a single tree.

The principal amount, as well as the finest quality of this drug, is exported from Pará, in Brazil, generally in barrels. Other Brazilian ports, as well as Angostura, Cartagena, Maracaibo, and Trinidad, also export that which is collected in their respective neighborhoods. The products of different countries vary a little in their sensible qualities, and are, in trade, designated by their geographical names; that of Pará is thinner and paler, and rotates the polarized ray to the left; those of Venezuela and Trinidad are thicker and brownish, and rotate to the right. Some species are, moreover, opalescent, others perfectly clear. There is the greatest difference in their medical efficiency.

Copaiba has been known in Europe something more than two hundred and fifty years. Its usefulness was learned from the aborigines of Brazil, among whom it was highly esteemed.

Description.—The consistence and color of this substance, although probably depending in part upon its natural amount of oil, vary also with age and exposure, becoming thicker and darker as the oil evaporates. Fine fresh Pará copaiba is a clear liquid, about as thick as Canada turpentine, and of about the same color. It is often darker, however, and may have a deep golden yellow, or even a sherry tint. Copaiba has a peculiar, aromatic, somewhat terebinthinous odor, and a persistent, bitter, biting, disagreeable taste. Its specific gravity varies from 0.916 to 0.993, and it is soluble in absolute alcohol and in four times its bulk of petroleum spirits. Some varieties, as noted above, are not quite clear, and are sometimes fluorescent. In evaporating a small quantity, there should be no odor of turpentine, and the residue, when cold, should be hard and easily rubbed to powder. It should not boil under 482° F. and should rotate to the left 28° to 34°. Four drops, carefully added to a mixture of half an ounce of glacial acetic acid with four drops of nitric acid, should not afford a reddish or purple color.

Composition.—It contains from forty to sixty, or even eighty per cent., according to its fluidity, of an *essential oil* of the composition $C_{10}H_{16}$, or $C_{20}H_{32}$, of high boiling point, and the odor and taste of the drug itself. A good Surinam article contains seventy-eight per cent. This is also official (*Oleum Copaibæ*, U. S. P.). The crude *resins* left behind in the distillation are also official, under the name Resin of Copaiba (*Resina Copaibæ*, U. S. P.). It is a brownish-yellow, brittle substance, with the appear-

ance of common resin, but having the odor and taste of the oleo-resin. The "resin" of Brazilian (Pará) copaiba is really a natural mixture of at least two substances—an *amorphous indifferent resin*, probably itself compound, and the crystallizable *copaivic acid*, obtained in large, white, nearly odorless prisms. The latter is insoluble in water, and sparingly so in ether, but strong alcohol and the fats dissolve it freely. *Oxycopaivic acid* is an analogous substance, sometimes also met with. "Maracaibo copaiba," that is, the product from the northern coast, yields in a similar way, together with its amorphous resins, crystalline *metacopaivic acid* instead of *copaivic acid*, which dissolves freely in ether as well as in alcohol.

Copaiba is apt to be adulterated; one of the commonest additions is castor or some other fixed oil; Gurjun balsam, oil of turpentine, and other volatile oils are also sometimes added.

Action and Use.—Large doses of copaiba occasion vomiting, purging, and colic, symptoms due to its locally irritant action upon the alimentary canal; they also may cause some difficulty in micturition, with burning pain in the urethra, or even strangury, but the latter is rare. Copaiba is mostly eliminated with the urine, which it increases and changes in odor. According to Brunton, "it forms a conjugate glycuronic acid in the system, and is eliminated in the urine, which with nitric acid gives a precipitate of copaibic acid, easily mistaken for albumen, but distinguished by disappearing on the application of heat. The conjugate acid renders the urine antiseptic, as it is secreted by the kidneys, so that it does not readily decompose, and bacteria either do not appear in it at all or only in very small numbers, even after the surface has become covered with mould." This, if true, may explain at least a part of its usefulness in the urethral and vesical catarrhs, for which it is so much employed. Its elimination products, if sufficiently diluted, appear also to be soothing to the lining membrane of the urinary tract. A portion of the copaiba taken makes its exit from the lungs, as shown by the breath. The principal call for this medicine is in catarrhs of the genito-urinary system, especially of the urethra and bladder. In gonorrhœa and gleet, its employment at one stage or another is almost universal. In chronic vesical catarrh it is also sometimes useful, and more rarely so in chronic bronchitis. Its value in chronic diarrhœa and dysentery, and as a diuretic in cardiac dropsy, is more doubtful. In the acute stage of the above affections, it is not to be advised. An erythematous eruption occasionally appears during the use of the medicine; this, however, departs as soon as the drug is omitted.

Administration.—The oleo-resin itself is generally given. From ♏ x to xx. (a gram = ♏ xv.), three or four times a day, is the usual dose. Dropped upon a lump of sugar, it can be quickly chewed and swallowed, or an emulsion can be made of it with flavored syrup of acacia or yolk of egg. In either case its taste is very disagreeable and persistent. It may be solidified by adding six per cent. of magnesia (Massa Copaibæ, U. S. P.), and made into pills, but the value of this preparation is doubtful. A sort of soap may be made by adding enough *liquor potassæ* to cause it to mix with water. More than by all these methods, it is at present given in gelatin capsules, which are prepared on an extensive scale by numerous manufacturers; they contain from five to ten drops each, and two or three can be taken at a dose, two or three times a day. They are perfectly free from its taste, but the odor will appear in the breath, after an hour or so, as well as when it is taken undisguised. The oil and the resin may be given in similar doses and ways. The action of the oil is not very different from that of the undivided oleo-resin.

Allied Drugs.—Copaiba differs in degree more than in kind from the numerous class of essential oils and resins, being milder than some (turpentine), and more stimulating than others (the carminatives). Cubebs, buchu, and oil of sandalwood have similar action and are employed for similar conditions, but none of them is equal to it. Gurjun balsam has also similar qualities, and has been substituted for copaiba. Uva ursi, and the arbutin and benzoic acid class of remedies may be compared with it, and so may also, in a certain sense, as used for the same disease (gonorrhœa), the vegetable and mineral astringents, hydrastis, and several inert powders used in injections; but the action and characters of these substances are not at all like those of copaiba.

W. P. Bolles.

COPAL.—(Including *Animi* and *Kauri*.)—This name is applied to a number of resins of similar nature, but of widely different origin, both botanically and geographically. As the article is only of mechanical interest, and the different varieties are so similar, they need not be discussed here. It is mostly dug from the ground in a fossil condition, though the trees yielding at least most of the varieties are still in existence. Copal is very hard, of glassy or splintery fracture, of various shades, from light yellow through reddish orange to dark reddish brown, and usually translucent, though sometimes milky or smoky. It may be smooth or dusty or (the best variety of animi) very warty. It occurs in pieces varying from the size of a marble to that of a mass weighing many, in one case several hundred, pounds. It is without odor and taste and the ordinary solvents of resin dissolve it only with difficulty. Its uses are purely for varnish and other mechanical coatings.

Henry H. Rusby.

COPPER.—General Medicinal Properties of Compounds of Copper.—As usual in the case of compounds of the heavy metals, impregnation of the blood with a copper compound tends to affect nutrition. In medicinal doses too small to produce any obvious derangement, the influence tends to the abatement of spasmodic nervous disorders, but not to a sufficient degree to enable copper to compete with zinc and other remedies as a practical antispasmodic. In excess of medicinal dosage copper salts are readily poisonous. Locally, soluble copper salts, such as are alone used in medicine, are powerful irritant astringents. Applied in concentrated form to a moist surface they combine with the albuminous elements of the part, forming a thin, practically invisible slough, and at the same time constringe and irritate. So far as the caustic effect is concerned, it is so superficial as to be of little moment, so that practically the action is simply conjoint astringency and irritation. Such action, however, may determine absorption of easily absorbable tissue, such as granulations, or the healing of indolent ulcers, or the abatement of a catarrhal process. Taken internally, in any beyond quite small dosage, the irritant action of soluble copper salts declares itself by producing at once full and free vomiting. Such vomiting is attended with little nausea or depression, and the emetic dose is itself discharged with the ejecta. Copper salts thus become available medicinally as emetics, and because of their power and promptness of action are peculiarly appropriate for the dislodgment of poisons by vomiting. In considerable single overdose copper salts are irritant poisons.

The therapeutics of copper compounds are comprised in the applications set forth above—locally for an astringent irritant operation, internally to provoke vomiting, or in smaller dosage for an astringent effect in diarrhœas. For the latter purpose, however, other astringents more agreeable than copper compounds are commonly preferred.

A single compound, only, of copper is official in the United States Pharmacopœia, namely, the *sulphate* (cupric sulphate, $CuSO_4,5H_2O$). The salt is entitled *Cupri Sulphas*, Copper Sulphate, and is the one so well known by the common name of *blue vitriol* or *bluestone*. It occurs in "large, transparent, deep blue, triclinic crystals, odorless, of a nauseous, metallic taste; slowly efflorescent in dry air. Soluble, at 15° C. (59° F.), in about 2.6 parts of water, and in 0.5 part of boiling water; almost insoluble in alcohol" (U. S. P.). The salt effloresces slowly on exposure, or on moderate heating, to an opaque, pale blue powder. Cupric sulphate may be used locally in

substance, a smooth crystal, with its edges rounded by a file, being selected, or cylindrical or conical pencils may be made by fusing one part of alum with two of the copper salt and shaping in suitable moulds. Lotions are made by aqueous solution, the strength ranging from one-half to two per cent. As an internal astringent the dose is about 0.015 gm. (gr. ¼); as an emetic from 0.12 to 0.30 gm. (gr. ij.–v.) or more if the stomach be insensitive from narcotic poisoning. But if a full dose is given, and fails to vomit, it must be removed by the stomach pump lest undue gastric irritation result. The salt is best given in powder, mixed with powdered sugar.

Edward Curtis.

COPPER, POISONING BY.—Copper is poisonous to man and the lower animals in any of the forms in which it may be brought into the circulation, and its toxicology is of special interest because of its widespread occurrence in nature and its extensive use in the arts. The commercial compounds of chief medico-legal interest are the sulphate and the acetates. The crystallized sulphate, $CuSO_4,5H_2O$, also known as blue vitriol or bluestone, is extensively used in calico printing, in electro-metallurgy, as a fungicide in agriculture, and to some extent in medicine. There are several acetates used in dyeing and calico printing and as pigments. The several varieties of verdigris are basic acetates of different chemical composition. Other important compounds are the nitrate, chloride, and the arsenical pigments, as Scheele's green and Paris green. Metallic copper as such, and in the form of its numerous alloys, is extensively used in manufacturing industries, and hence many persons are exposed to its influence.

Notwithstanding the toxic character of copper compounds and their ready accessibility, poisoning in man is not common in this country and fatal poisoning may be said to be rare. Copper salts have been used for criminal poisoning, but more frequently for suicide. Usually the poisoning has been accidental.

To understand the present state of the question of poisoning by copper, it is necessary to distinguish clearly between the effects of the corrosive local action in the alimentary canal and the general systemic poisoning due to the metal after its entrance into the circulation. Within a few years the problems have been especially studied from the experimental side (Harnack, Lehmann, Tschirch, Filehne, Brandl).

Physiological Action.—A soluble salt of copper has little or no effect on the sound skin, but acts as a mild caustic to surfaces denuded of cuticle, and on the mucous membranes as an astringent, irritant, or corrosive according to the form in which it is applied. Administered internally it acts as a prompt emetic, but if not thus expelled it produces a more or less severe gastro-enteritis with the local and general symptoms which accompany this condition. Relatively small amounts are absorbed from the stomach and intestines, but enough may be taken into the circulation to produce a general intoxication, especially with animals that do not vomit, and in the case of very large doses. In the latter case it is believed that the local destruction of the integrity of the epithelium favors the absorption. Systemic poisoning has, however, been especially studied by the subcutaneous or intravenous injection of organic salts such as the copper sodium tartrate (Harnack, Filehne). The symptoms observed after these injections have been loss of appetite, trembling, weakness with loss of co-ordination of muscular movements progressing to more or less complete paralysis, slowing of the heart action and respiration, with death due to cardiac or respiratory failure. Vomiting may occur, and in continued cases diarrhœa and other symptoms of intestinal disturbance are usually present. Later symptoms of special interest are extravasations of blood in various places, due to destruction of blood corpuscles; jaundice, due to fatty degeneration in the liver; hæmaturia, due to congestion and later fatty changes in the cortex of the kidneys. The unabsorbed copper is chiefly converted into the sulphide and is found in the fæces. That which is absorbed is eliminated in part in the urine, but chiefly through the bile. Ellenberger and Hofmeister found from six to ten times as much copper in the bile as in the urine. They detected it in the urine within thirty-six hours after the first dose, but were unable to find it after nine days, while it was detected in the bile as late as forty-one days.

Acute Poisoning.—The ingestion by man of a large dose of a salt of copper is usually promptly followed by the symptoms of an irritant poison. The symptoms may begin within a few minutes, ten to twenty, or they may be delayed, from two to three hours. They begin with nausea followed by prompt vomiting of green or bluish material, and by a metallic taste, thirst, burning in the stomach, abdominal tenderness increased on pressure. There is usually purging, the passages being abundant and frequently bloody. Owing to the prompt emetic action the poison may be very completely removed and the case tend rapidly to recovery; indeed, this is the usual result.

In some cases death has followed a single large dose. The symptoms in these cases have been similar to those described, but more severe, and accompanied by intense headache, cramps in the limbs, great prostration, cold extremities, small rapid pulse, and other symptoms which accompany the collapse caused by extensive gastro-intestinal inflammation. Death may result in from four to twelve hours, but generally only after a longer period; two, four, or eight days, or even longer. After the first few hours there are added to the symptoms due to the local action of the poison, those caused by the action of that which is absorbed, on the kidneys, liver, and other organs. Thus the urine is more or less suppressed, is albuminous, and contains casts and blood. Jaundice may be present, but is usually a late symptom. If a case of this sort progresses to recovery the progress is slow. Chronic gastro-enteritis is a likely sequel.

Fatal Amount.—Metallic copper has been frequently ingested in the form of coins, etc., with no evil effect, but there are well-authenticated cases in which copper in the metallic form has produced the symptoms of copper poisoning. Experiment has also shown the toxic character of the metal. When fed to dogs in their food, copper dust produces vomiting in even small doses, but there is little evidence of systemic action even after long periods of feeding small doses (Filehne).

The lethal quantity of a copper salt for man is stated very differently by the authorities: Husemann, 25–30 gm.; Lewin, 15–20 gm. of the acetate, 10 gm. of the sulphate; Kobert, 10 gm.; Tardieu, 2–3 gm.; Seidel, 1 gm. These figures obviously refer to different modes of action, for a consideration of the reported cases makes it probable that only a large dose, 10–20 gm., of such a salt as the sulphate, would produce death by its direct local action.

That relatively small doses may prove fatal when absorbed is evident from the results of animal experiments. Rabbits are killed in twenty-four to thirty hours by the subcutaneous injection of doses of copper sodium tartrate, equivalent to 0.015 gm. of CuO per kilogram (Filehne). That the minimum fatal dose for man if administered in this way would likewise be small cannot be doubted, and therefore the minimum dose by the stomach would be small if administered under favorable conditions for absorption, though doubtless modified by the protective action of the liver. That the conditions for absorption from the stomach are unfavorable is shown by the usual type of the cases which occur, and also by the results of the administration of copper compounds for therapeutic purposes. Thus Husemann instances a case in which 17 gm. of sulphate were taken in six days with no toxic effect. The conditions effecting absorption must therefore control the amount which would be lethal in any given case.

Post-Mortem Appearances.—The marks of inflammation throughout the alimentary tract are the most common observation. These may consist of injections, ecchymoses, ulceration, or even gangrene and perforation.

The mucous membrane may have a greenish color due to the presence of some copper compound, which is easily distinguished from bile stains by the blue reaction with ammonia. Contrary to the usual condition, all signs of inflammatory changes may be absent. In late deaths the tissues may be bile-stained and the liver and kidneys swollen and fatty. The heart muscle has also been found fatty. These degeneration changes show clearly that in man copper may be absorbed from the alimentary tract in not inconsiderable amounts. Absorbed copper is found chiefly in the liver, but also in the kidneys and other organs, in the muscles and in the blood, where it is said it exists in the corpuscle in combination with hæmoglobin (Filehne). It may be easily isolated by the Fresenius method commonly used in toxicological examinations of tissues.

TREATMENT.—As antidotes milk and egg albumin may be used because of the difficultly soluble compounds which copper forms with proteids. Magnesia is a suitable addition as an antacid. Reduced iron has been recommended with the view of precipitating metallic copper. Potassium ferrocyanide produces an insoluble copper ferrocyanide and is the best chemical antidote, but is not without danger in large doses because of its tendency to form prussic acid. The stomach should be thoroughly washed out even if there has been free vomiting. The subsequent treatment should be directed with reference to the local lesions, the collapse or prostration, and to the condition of the kidneys.

Chronic Poisoning.—Contrary to the earlier teachings, recent observations tend to the view that there is no chronic copper poisoning comparable with that by lead. According to this view the long-continued ingestion of minute doses of copper by the stomach, and the exposure to absorption in handling and working the metal, are not capable of producing the systemic poisoning. This view is based on the negative results obtained in feeding-experiments with man and the lower animals, and in the therapeutic use of copper salts. There can be no doubt that the danger of poisoning with copper has been exaggerated, and that it is much less poisonous than lead. In view, however, of the well-known effect of the injection of copper salts subcutaneously it would appear that the question of a chronic systemic intoxication is largely a question of absorption, and that it would be unsafe to conclude that absorption may not occur from small doses to a sufficient extent to be toxic. Cases of poisoning have been described among workers in copper and brass that appear to admit of no other explanation, but those that can be classed as chronic are certainly rare.

The Use of Copper Utensils in Cooking Food.—Cooking-vessels of copper and copper alloys, especially of brass, have been used very extensively. Repeated experiments have shown that foods may be impregnated with copper on long standing in such vessels, and this is especially so of foods containing vegetable or fatty acids. Thus Mair found 0.024 gm. per cubic liter in rice soup which had stood twenty-four hours in a brass vessel. A liter of vinegar containing an acidity of three and a half per cent., on being boiled in a brass vessel and then allowed to stand has taken up 0.183 gm. of copper in twenty-four hours and 0.365 gm. in two days. Direct experiments tend to the conclusion that food cooked in the usual way in bright copper or brass vessels, but not allowed to stand in them, does not absorb a sufficient amount of copper to produce symptoms of poisoning. It seems impossible that enough could be present in food which would be eaten at one time to produce serious acute poisoning as has been frequently supposed, especially as the presence of as much as half a gram of dissolved copper in a kilogram of liquid food would produce a marked metallic taste.

The Use of Copper in Preserved Foods.—Copper salts are used in the preparation of canned vegetables such as peas and beans, and of pickles, in order to impart a desired green color. This is accomplished by heating in a very dilute solution of copper sulphate. The vegetables thus become impregnated with copper, which probably exists in combination with the proteids in part, and partly with the chlorophyll. The presence of 0.020–0.030 gm. of copper per kilogram is all that is needed to accomplish the desired result, but ten times these amounts have been found in canned peas. The copper fails to give its ordinary reactions in the compounds in which it exists in these preparations, and it is extracted only in part by acid of the strength of the gastric juice. According to Tschirch and Brandl the metal in these forms is but slightly toxic. From experiments with copper proteid Filehne concluded that an amount equivalent to 0.500 gm. of copper per day would produce no notable result in an adult. Copper sulphate has been used in bread-making to improve the appearance of the product made from inferior grades of flour. Only small quantities can be used, because the yeast is very sensitive to the toxic action of copper salts; 4–16 mgm. per kilogram have been found.

The Occurrence of Copper in Plants and Animals.—Plants exhibit great variation in their susceptibility to the toxic action of copper salts; some, like the fungi, are very readily destroyed by it, so that copper salts are widely used as fungicides in agriculture. The higher plants, however, are less easily affected by it as applied externally or as existing in the soil in which they grow. Indeed, some kinds may absorb notable quantities from the soil, and it therefore happens that many articles of vegetable food contain copper. Thus Lehmann found vegetables as sold in the Würzburg market to contain the following amounts of copper per kilogram of dry substance: lettuce, 0.003–0.010 gm.; gurkins, 0.030 gm.; beans, 0.018–0.020. In vegetables grown in a soil very rich in copper he found larger quantities; *i.e.*, 0.080–0.560 gm. copper per kilogram of dried substance. Animals feeding on vegetables containing copper naturally absorb some of the metal and it is found in variable small amounts in the tissues. Thus there have been found in fresh yolks of eggs 0.0005–0.002 gm. of copper; in muscle of the ox and sheep about 0.001 gm.; in kidneys 0.002–0.008 gm., and in liver 0.009–0.030 gm., per kilogram. Carnivorous animals contain less. In man it is very commonly found in the liver to the extent of a few milligrams. So constantly is copper found in man that it has been spoken of as normal copper by some writers. It performs no known function, and is to be regarded not as normal but as accidental, though nearly constantly present. The amount present depends on the character of food, and possibly on the occupation of the person.

Herbert E. Smith.

COPULATION, or sexual contact, is essential to the process of reproduction in all the more highly organized species of the animal kingdom. An analogous step in the process has in fact been traced upward from a comparatively early phase of plant life, for sexual reproduction is the rule among all but the lowest orders of plants. Actual contact is, however, exceptional. In most of the flowering plants fertilization depends upon an indirect transfer of pollen through the medium of air or water or by the agency of insects. Yet, on the other hand, in some of the lowest forms of cryptogams, flowerless plants, more or less intimate contact or union of two individuals is necessary, and in some of the higher species of thallogens the union closely resembles that of the animal kingdom.

In the lower forms of animal life much difference is observed both in the manner and in the duration of the connection, and in not a few instances peculiar changes occur in some of the organs or parts of one or both sexes for the purpose of copulation. Earthworms, for example, become firmly united, two segments of each having previously undergone necessary changes. In some orders of the crustacea the male organ resembles a rudimentary foot which is thrust into the vulva. The true character of this appendage is demonstrated by the presence in it of a vas deferens. A similar transformation of a member is seen among the cephalopods; for in some species of the cuttlefish the male and female become

firmly attached to each other, mouth to mouth, with the suckers of the arms in apposition. While thus embracing, one of the arms is detached by the male and it is deposited within the mantle of the female. The arm thus detached has been previously "hectocotylized," that is, a sac filled with spermatophores has been formed upon it. These are discharged within the mantle and are carried to the ova through a tube which perforates the terminal filament.

Among insects the alteration of limbs and abdominal segments is sometimes quite remarkable. Reproduction is invariably a result of sexual union except in a few instances of hermaphroditism. Among the hymenoptera (bees, ants, flies, etc.) the connection lasts from a few seconds to several hours. The male bee is sometimes so injured by prolonged contact that his death immediately follows the separation. The fantastic position of the dragon-fly during copulation is due to the peculiar position of the organs in the two sexes. That of the male is situated in a slit on the under surface of the second abdominal segment, that of the female on the under surface of the eighth segment. In spiders we find conditions which more resemble those seen in some of the cephalopods than in the insects, for the spermatic fluid is deposited in a receptacle in the chela, or claw, and is then thrust into the cloaca. The first appearance of a true penis is found among the amphibia.

Among the vertebrates also there is a gradual transition from a very simple to a more complicated method of copulation as we ascend from the lower to the higher orders. In the former the organs are rudimentary, recalling the altered segments of the earthworm. Some species of fish do not copulate; fertilization of the eggs occurs after they are in the spawn. In some there is a momentary contact, while others are said to remain united until they are accidentally separated. In some elasmobranchs peculiar "claspers" at the posterior extremity of the male, supposed to be rudiments of a third pair of limbs and intended primarily for maintaining contact, seem to be partially introduced. Among birds there seems to be no deviation from the copulative method of fertilization, but the process varies from a momentary contact in the smaller species to one as complicated as that of the higher quadrupeds in some of the larger, notably in the ostrich.

Considered merely in its relation to procreation, copulation, in the human being, consists essentially in nothing more than the deposit of seminal fluid within the vagina, even in the vestibulum, for it is well known that conception may occur without actual penetration. This would limit the act in the male to the period of life between puberty and an indefinite time of old age, and in the female to the period of ovulation. A man may procreate so long as his seminal fluid contains living spermatozoa, although he may be able to perform the sexual act but imperfectly; but in the female the possibility of impregnation ceases with the completion of the menopause. But no such limit can be drawn. The ability of the male to copulate, as the term is ordinarily understood, depending almost wholly upon erection of the penis, begins in early childhood and lasts until the development of senility. There is practically no age limit to its possibility in the female after childhood. The part taken by the male and the female will be more conveniently considered separately.

The Male.—To place a physiological limit upon the frequency of copulation in the male is hardly possible, for in the human being there is no such natural limitation as we see in most of the lower animals, and under the many exciting influences of civilization, sexual desire is exceedingly variable. Neither is desire a proper criterion of the normal requirements, for in some men it is aroused not merely by the accumulation of seminal fluid after prolonged continence, which seems to be the normal stimulus, but by the perception of an attractive female through any of the senses or even by the imagination alone. Although we admit that the testicular secretion is constant and that absolute continence is not strictly physiological, still the normal limit of indulgence may undoubtedly be exceeded. A man may indulge so frequently that, although he experiences the usual excitement and an apparently normal orgasm, the ejaculated fluid becomes devoid of fecundating property. Such frequency is clearly abnormal. It is generally followed by undue depression if not by more lasting evil effects. On the other hand, it must be admitted that the evil effects of continence are seldom of consequence in the absence of unnatural excitement and uninfluenced by previous immoral practices. The emergency rarely arises in which the physician can recommend illicit intercourse without compromising himself professionally as well as morally. Within the bounds of legitimacy there can be no question that the practice should not exceed the gratification of natural desire, a desire which varies, however, with the physical vigor and health of the individual, his mode of life and climatic influences, and usually diminishes to some extent with advancing age.

The anatomy of the male organs is appropriately considered in another volume of this work, and it will be necessary therefore to describe only briefly the mechanism of erection. It has been shown that the erection and rigidity of the penis depend upon a temporary increase in the size of the arterioles which supply blood to the erectile tissue of the spongy and cavernous portions, more than upon constriction of the veins which carry away the blood; but such constriction probably increases the turgescence, especially for a short time during the period of greatest excitement. The nervous control of these vessels comes from the sacral plexus and is practically the same as that of the integument and muscles of this entire region.

The sensation experienced in coitus depends for the most part upon the sensitiveness of the glans, the acuteness of which increases with the rigidity; it is aided by nervous excitement and by friction within the vagina until the orgasm occurs. As this stage is reached a different sensation is developed, probably by increased peristaltic action of the vesiculæ seminales and by the rhythmical contraction of the bulbo-cavernous muscle, which culminates in the forcible discharge of semen. Following this the venereal excitement quickly gives place to a variable degree of lassitude and the sensitiveness of the organ to a feeling resembling fatigue.

The Female.—The part of the female is passive, at least to a much greater degree than is that of the male. To some women there is no feeling of pleasure, much less an orgasm comparable to that of the consort. Others undoubtedly experience sensations fully equal to those of the male. Conception is probably more likely to occur when full venereal excitement is experienced, yet it is by no means conditioned upon such enjoyment, for it may result from connection in a state of unconsciousness. The mechanism of the act closely resembles that of the male. The parts are supplied by a corresponding set of nerves and the circulatory changes are the same in nature. There is a certain degree of erection of the clitoris which causes it to become more acutely sensitive, and of the erectile bulbs at the sides of the vulva. The erectile tissue of the vagina also participates and there may be an ejaculation from the glands of Bartholin opening at the sides of the labia minora. To what extent the higher organs are involved is not definitely known. The uterus sinks lower in the vagina and the cervix is said to become softer. A certain amount of erection takes place in the uterus, by contraction of its muscular fibres and those of the round ligaments, and the cavity is thus reduced in size, causing the expulsion of a few drops of mucus from the os. The subsequent relaxation is supposed to favor the entrance of seminal fluid if it does not in reality draw it in as by aspiration. No one has yet confirmed the descriptions by Litzmann, in 1846, and by Beck, in 1872, of a gasping, opening and closing of the os as a part of the orgasm. For the consideration of the method by which the spermatozoa are carried through the upper passages the reader is referred to the article on *Impregnation*.

The normal frequency of copulation in the female is