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A TREATISE ON

MATERIA MEDICA,

(Including Therapeutics and Toxicology.)

BY

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THE ACIDS.

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PHYSIOLOGICAL ACTION.

A few of the mineral acids, sulphuric, hydrochloric, nitric, and phosphoric acids, as well as a few of the inorganic (fatty) acids, of which acetic acid is considered the most important, form, both on account of their intimate relationship to the alkalies and albuminoid bodies, as well as from the similarity of their physiological action, a natural group of drugs which altogether have not a very extensive application. The general effect of the acids in destroying bacteria and preventing putrefaction is, when compared with other antiseptic agents, by no means so weak as the assertion of Bucholtz would lead us to suppose. Recent investigations by Sieber have shown that their antiseptic power is even stronger than that of phenol. The mineral acids and acetic acid will prevent putrefaction even in 0.5-per-cent solution; butyric and lactic acids, however, are much weaker; while even a 4-per-cent solution of boric acid $B(OH)_3$ could not prevent putrefaction of the pancreas.

Effect of small, greatly diluted doses.—The sour taste of acids is due to a specific effect upon the nerves of taste, since all acids produce the same kind of sensation; the puckering of the mucous membrane of the mouth and larynx, which always occurs after the taking of acids, is probably due to the withdrawal of water from the tissues; sulphuric and phosphoric acids have the strongest affinity for water.

Even at the commencement of the digestive canal, small quantities of acid find in the saliva and mucus of the mouth, and later on in the intestinal juices, bile, and pacreatic juice, so much alkali that they can combine with it to form salts, and are thus neutralized. The stronger acids can even decompose the salts of the weaker acids, contained in the gastric juice and food materials in the stomach, and take the place of these weaker acids; thus, for example, sulphuric acids will form sulphates out of the

chlorides, sulphates, and lactates, while the latter acids are set free.

Some of the organic acids, such as tartaric and malic acids, are changed in their chemical structure by the pepsin of the gastric juice, and converted into succinic acid (Meissner and R. Koch).

The acids take an important part in the process of stomach digestion. Free hydrochloric acid is one of the constituents of the gastric juice; pure gastric juice, therefore, has an acid reaction, and contains in man 0.25 per cent, in dogs 0.3 per cent of free hydrochloric acid. This acid, as we shall show later on, dissolves salts insoluble in water, and assists in the conversion of albuminoid bodies into peptones; indeed, these could be dissolved by the aid of the acids alone, while pepsin, without the acid, can exert no specific effect whatever.

Hydrochloric acid has the most powerful action upon the digestion of food. Next in order is lactic acid, which is normally set free in the stomach from the lactates occurring in meat, sugar, and starch diet; these lactates being decomposed by the free hydrochloric acid and lactic acid set free. Phosphoric and tartaric acids are still weaker digestive agents, while sulphuric, nitric, acetic, and oxalic acids are almost entirely ineffective (Meissner). Schiff, however, found that solutions containing 4 per cent of nitric acid, just as those containing 4 per cent of hydrochloric acid, could change fibrine into peptone in about forty minutes. The digestive power of the gastric juice is, up to a certain limit, increased by increasing the percentage of acids which it contains; this limit varies for different substances: for albuminoids it is, on an average, 0.1 per cent. If the acid be present in greater proportion, the digestive power of the juice is diminished until it becomes entirely inactive. When acids, therefore, are used for too long a time the appetite and digestion are finally injured, and a series of pathological conditions result.

It is readily supposable that the long-continued administration of diluted mineral acids to the living organism leads to the decomposition of the alkaline combinations with the weaker acids, *e.g.*, carbonic acid, or with the albuminoids; the stronger acids uniting with these alkalies, and being excreted with the urine as mineral salts; so that not only the blood, but the whole body, would become poorer in alkalies and salts. Salkowski found in the herbivora (rabbits) that

even acids formed in the body (*e.g.*, from an increased supply of tannin, $C_2H_2NSO_3$, giving rise to the formation of sulphuric acid) were excreted as neutral salts, and only to a very slight extent as free acids; while the acids introduced from without were also for the most part excreted as neutral salts. Salkowski and Lasar proved directly that the alkalescence of the blood is diminished by the internal administration of dilute mineral acids, so that the body furnishes the bases for neutralizing the acids thus absorbed. The difference thus produced in the alkalesence of the blood is, indeed, very slight; but we must remember that not only the blood, but the whole body, has given up its alkali for this purpose, so that the loss is greater than appears at first sight. On the other hand, it must not be forgotten that the organism holds the free alkali with great tenacity; there must, therefore, be some mechanism by which the balance between the acids and bases can be preserved; for the acids administered to his (Salkowski's) dogs and cats would have sufficed to turn the whole animals acid, if all the acid administered had been absorbed and excreted in the shape of some salt. But in both classes of animals (herbivora and carnivora) the blood remains alkaline in spite of the greatest possible administration of acids, and not until after death from acid poisoning (as, for example, from concentrated sulphuric acid) does the blood take on an acid reaction.

Wöhler showed that a series of the vegetable acids, when administered internally, became bound to an alkali, and thus appear in the urine; these acids, therefore, like the mineral acids, withdraw the alkalies from the blood, while, if they are introduced as salts of the vegetable acids, they are converted in the blood into carbonates, and as such are excreted. Wöhler thinks it probable, from the observations of Benzelius and Magendie, that the acids are excreted in the urine in a free state or as acid salts, only when given in larger quantities than are necessary to neutralize the bases contained in the blood or other portions of the body.

The greater difficulty in withdrawing alkalies from the carnivora, as compared with the herbivora, is due to the following cause, already spoken of in discussing the method of excretion of sal-ammoniac: it was shown, namely, that there was a great difference whether sal-ammoniac was given to herbivora or carnivora. In the body of the rabbit, for instance, the nitrogen of the sal-ammoniac or other am-

monium salts which are introduced is converted, for the most part, into urea. It is for this reason that feeding rabbits with sal-ammoniac increases the amount of urea in the urine, and not because the sal-ammoniac has any influence in increasing the decomposition of the albuminoids. In dogs, however, at most a small fraction of the sal-ammoniac taken into the body passes over into urea. The cause of this remarkable difference is as follows: Meat, the chief article of food of the carnivora, is to be considered in consequence of its deficiency in the salts of the organic acids, and on account of the acids which are formed from it in the body, as an acid food. The constant introduction of this acid food into the body, together with the fact that it is impossible for acids to pass through the body in an uncombined state, would soon deprive the bodies of these animals of all their fixed alkalies, were there not some arrangement by which the agency of the fixed alkalies would be unnecessary in the binding of these free acids. This arrangement is as follows: After the administration of acid food to the dog an increased formation of ammonia takes place (or perhaps the quantity converted into urea is diminished), so that the free acids combine with the ammonia, instead of the basic alkalies, withdrawing it from the body, and preventing its conversion into urea. In dogs, hydrochloric acid also requires ammonia for its excretion. If, then, for example, hydrochloric acid is given, it increases and binds the ammonia of the body; if sal-ammoniac is given, its hydrochloric acid utilizes the ammonia combined with it, and is excreted by its aid; as a result of this, however, the ammonia of the sal-ammoniac has not the opporutnity of being converted into urea. That the formation of ammonia in the bodies of the carnivora is in intimate relationship with the amount of acid introduced, is shown by the fact that when large quantities of alkali, such as sodium carbonate, are administered the excretion of ammonia is considerably diminished. In the herbivora the last experiment is performed physiologically. Their diet must be considered an alkaline one. An alkaline diet is accompanied by the excretion of a very slight amount of ammonia, for it is a characteristic property of vegetable materials that they do not possess enough ammonia to serve for neutralization; for this reason the amount of ammonia excreted in the urine in these animals can neither be increased by acids nor diminished by the administration of alkalies.

The acids, such as hydrochloric acid, administered to rabbits make use of the fixed alkaloids, so that in these animals a fatal alkaline effect may be produced by means of hydrochloric acid. Furthermore, the hydrochloric acid which is in combination with the ammonia of the sal-ammoniac does not make use of the ammonia for its excretion, but of the fixed alkalies, while the ammonia not needed for neutralization is converted into urea (Knieriem-Gaethgens, Salkowsi, Schmiedeberg-Walter, and Hallervorden).

The injurious effects of small quantities of acid upon the body and the individual organs have been to some extent much exaggerated and inaccurately described. Under any circumstances these acids must be used for a very long time before any ill effects appear. These are said to be (for instance after the excessive and long-continued use of food prepared with vinegar) a wasting of the body, anæmia, and paleness of the skin; they are said to depend upon the diminished alkalescence of the blood and the destruction of the red blood-globules. In discussing the alkalies, we spoke of the probable importance of the alkalies to the normal processes of life, and cannot, therefore, deny that the above symptoms may be due to the diminished alkalinity of the blood and body; but we must insist that there is no positive proof that wasting and anæmia are due to this cause. As to the destruction of the red blood-corpuscles, it is positive that this has been observed in acute sulphuric-acid poisoning; it can also be seen by mixing blood directly with acids; but, from such coarse experiments we cannot draw any conclusions upon the effect of dietetic doses. As far as acetic acid is concerned, a direct proof that this has any destructive effect upon the blood-globules has not been shown. We therefore, for the present, think it best if we account for the thinness and anæmia simply by disturbances of digestion and nutrition; these are the only necessary results of too long and excessive use of the acids. Whether tuberculosis, as has been affirmed, occurs more often in the vinegar aniline than in other forms of anæmia, is also questionable.

As to the effect of medicinal doses of dilute acids upon the circulation and temperature, we have only the old experiments of Bobrik and Hertwig, to which, however, we must oppose many contradictions based upon our own experiments (Rossbach and Hofbauer).

Bobrik asserts that when acetic, citric, or tartaric acid

are painted upon the skin of cold-blooded animals, introduced into the stomach, or injected into the blood they produce stoppage of the heart in diastole and long-continued slowing of the heart's action. Since a similar slowing of the heart occurs after decapitation, or section and paralysis of the vagus nerves, he concludes that this is not the reflex result of irritation of the inhibitory apparatus, but of a direct action of the acids which have gained entrance into the blood upon the heart. A similar slowing, as well as a considerable flattening of the pulse curves, were noted in warm-blooded animals and men, to the latter of whom he had given 80 grms. internally or vinegar foot-baths. After the administration of a large quantity of acetic or citric acid into the stomach of a rabbit, the temperature had fallen from 2–3½° C.

It is a remarkable fact that the mineral acids had entirely opposite effect upon the heart's action. It is true that sulphuric acid causes stoppage of the heart's action and slowing of the pulse in the frog, but not as the result of a direct action, but of a reflex action through the spinal cord and vagus nerves. Hydrochloric, nitric, and phosphoric acid, on the other hand, whether internally administered or externally applied, produced an increased frequency and force of the heart's action; since this effect did not follow after destruction of the brain and spinal cord, it could only be due to a central nervous irritation. Experiments made upon himself and also upon warm-blooded animals, with the same acids, at first showed an increase in the number and force of the heart's pulsation, followed, however, by a slowing of the heart's beats. According to Hertwig, after the internal administration of small diluted doses of mineral acids to warm-blooded animals, the pulse became smaller, harder, and somewhat slower, while the heart-beat was less perceptible; after a similar administration of vegetable acids the pulse became softer, weaker, and slower. The results of the direct injection of acids into the blood of course need not be considered here.

Even a superficial consideration will show the improbability of these assertions. If a drop of acetic acid be painted upon the foot of a frog, it can at most reach the heart as an acetate; but a much larger quantity of the latter salt than could be formed from this drop injected under the skin, whether it be a salt of sodium or potassium, has no effect. Then, again, acetic acid causes severe pain just as well as sul-

phuric acid: why, then, should the slowing of the pulse be a reflex effect in the case of the latter and a direct action in the case of the former, etc.? Our own experiments upon a large number of animals have shown how untenable the above results are. We found that the inorganic acids (sulphuric, nitric, and hydrochloric) have a similar effect upon the hearts of cold-blooded animals as that of acetic acid. All of these acids, however, produce a stoppage of the heart and a slowing of the heart-beat (when applied upon or under the skin) only when the vagi are still acting; in "winter frogs" with inactive vagi, and in atropinized frogs, a slowing of the pulse cannot be produced under any circumstances, either through inorganic or organic acids. If the sciatic nerve of a frog, in which the vagi are acting, be cut on one side, we can produce stoppage of the heart in diastole, and slowing of its action by painting the skin on the side in which the sciatic nerve is uninjured, while such a result cannot be produced on the side where the nerve was cut. If the vagi are paralyzed we cannot produce slowing of the pulse even by dropping acetic acid upon the heart. In those animals in which painting of an acid upon the skin causes slowing of the heart's action, a similar result is produced by burning the skin with a hot needle. So that the slowing of the heart produced as above in some frogs is only reflex. We also administered internally to three young men between the ages of 23 to 25 years, upon an empty stomach (four hours after eating), 150 grms. each of strong vinegar diluted with 90 grms. of water, and saw no sign of any increase in the rapidity or force of the heart's action. To a small healthy dog weighing 4 kilograms 35 grms. of strong vinegar diluted with water were administered in one day, and 60 grms. of undiluted vinegar injected into the stomach on the second day, without any change in the pulse or temperature being noted, even after many hours; as little effect was produced by 15 grms. of hydrochloric acid in equally strong dilution.

We therefore insist that although dilute acids in medicinal doses have a cooling taste, yet in healthy people they do not reduce the pulse or temperature even to the slightest extent. Nor did we find, as a result of experiments upon men and carnivora, that considerable doses given by us produced any signs of weakness. The general condition of the animal remained entirely normal. The effect of acids upon the organism in fevers we did not determine. Kobert

reports, recently, that several hours after, the administration of phosphoric acid to healthy and fevered individuals resulted in a slowing of the pulse and a slight diminution in temperature, if the drug were used energetically enough.

If in the herbivora (rabbits) the quantity of diluted hydrochloric acid administered is in excess of a certain limit (08 grm. to 1 kilo. of bodily weight), great difficulty and even paralysis of respiration set in, and as a result, also, paralysis of the heart. That this affection of the respiratory centre is due to the withdrawal of alkali from the blood by the acid, is shown by the fact that the injection of sodium carbonate into the blood saves the life of the animal (Walter).

As we have already stated, the acids appear in the urine, for the most part, in combination with an alkali; but still the normally alkaline urine of the herbivora is rendered acid, while the acid reaction of the urine of the carnivora is increased, by the administration of acids to animals.

A number of facts make it more and more probable that a splitting up of the salts of the blood takes place in the kidneys, so that acids pass over into the urine and here are partly combined with bases. If calcium phosphate or oxalate existed in the blood they could not be excreted, on account of their insolubility. We must, therefore, suppose that the phosphoric and oxalic acids on the one hand, and the calcium on the other, are excreted by different parts of the urinary tubules, and that the calcium phosphate and oxalate found in the urine are not formed into these salts until they have reached the urine.

It has not yet been shown that acids exert any effect upon the amount of urine excreted.

That there is an intimate relationship between the acidity of the urine and the acids of the stomach was shown by the observations of Quincke, who found in a woman suffering from dilatation of the stomach, that, after washing out the strongly acid contents of the stomach, the urine was alkaline in spite of the administration of meat diet: this was evidently due to the fact that in the animal organism there is a certain average degree of alkalescence (of the blood and other fluids of the tissues), which is regulated as far as possible at the same point by means of the excretions. Now, however small a quantity of sodium carbonate would suffice to alter the normally acid urine to an alkaline

fluid, the same effect can be accomplished by withdrawing very little of the acid from the stomach.

EFFECT OF LARGE AND CONCENTRATED DOSES OF ACIDS.

The terrible effects produced by large quantities of concentrated acids are due to several causes: First, to their great affinity for water which they withdraw from the tissues; the tissues therefore undergo a shrinking process, even under acids of moderate concentration. Again, owing to the power which many mineral acids (sulphuric, nitric, and hydrochloric) possess of coagulating albuminoid bodies, or even decomposing their tissues, together with the fats; also, because they have the power of dissolving and decomposing the horny tissues. Officinal phosphoric acid, together with a number of organic acids (acetic, tartaric, oxalic acids, etc.), are distinguished by the fact that they do not precipitate albuminates even when added in large quantities, although they may enter into combinations with them; precipitation does occur, however, after these solutions of albumen have been neutralized—for instance, by some alkaline carbonate. Even urea only swells up under the influence of acetic acid, and is only dissolved by boiling with the acid. A further cause of the strong action of acids lies finally in the strong affinity which these have for their bases, the combinations of which with the weaker acids they can even decompose. For these reasons the molecular structure of all the tissues of the body with which concentrated acids come in contact is destroyed. This action is termed an escharotic action.

Immediately upon the application of such an acid to the skin, or to any of the mucus membranes of the mouth, larynx, œsophagus, and stomach (when used internally), a fearful cauterization and destruction, accompanied by terrible pain, takes place. In consequence of the latter there is a high degree of general collapse, with great weakness of the heart, difficulty in respiration, vomiting, often of bloody materials—the common results of any cauterization of the stomach.

Death is caused either by suffocation, œdema of the larynx, or from perforation of the œsophagus (into the thoracic cavity) or of the stomach into the peritoneal cavity; the result being a peritonitis. If the caustic action has not penetrated very deeply, long-continued sickness, due to stricture of the œsophagus, pylorus, etc., will result.

If blood and mineral acids be mixed together the blood is coagulated. With phosphorus and the organic acids, however, it remains fluid, in consequence of the different reactions of its albuminoid bodies; the blood always becomes dark, however, and the blood-corpuscles and hæmoglobin are entirely destroyed. L. Mayer, Pflueger, Zuntz, and Strassburg have shown that by the addition of tartaric and phosphoric acid to the blood, the blood-corpuscles as usual are decomposed, while a body is formed which undergoes in its nascent state a higher oxidation, and thus binds the oxygen so fast that it is no longer given off when the blood is heated in a vacuum. Muscular tissue brought in contact with various acids has its myosin immediately coagulated, and the muscle becomes stiffened.

In consequence of the absorption into the blood in cases of acute poisoning, fatty degeneration of the liver, kidneys, and muscles have been noticed (Löwer); also inflammation of the kidneys, with fatty degeneration of the epithelium and fresh granular deposits in the interstices, especially along the vessels (Leyden and Munk); and finally there were found a large percentage of albumin, hæmatin, and indican in the urine. But even in the most severe cases of poisoning the blood has not been found acid during life, although it sometimes has this reaction after death. The above results (fatty degeneration of the organs and albuminous urine) some have attempted to explain by the destruction of blood-corpuscles. The weakness of the heart and muscles, etc., may be due to the direct action of the acids, on account of the administration of such a great excess of acids, while reflex causes may also have some share in the production of this result. There is no doubt that the temperature is really very much diminished under the above circumstances; this is due to many causes, such as weakness of the heart, abnormally low blood-pressure, a withdrawal of the alkalies from the blood and tissues, destruction of many red blood-corpuscles, etc.

Therapeutic Application.

The acids resemble each other in their therapeutic applications, just as they do in their physiological and chemical action.

We shall here point out these general therapeutic indications, particularizing which acids are to be preferred under certain circumstances. The special use to which any acid

may be put, however, will be indicated under the individual preparations.

In the first place, however, we will lay down the following general indications, which are based upon our own experience and that of others:

According to our opinion, the internal administration of acids is positively beneficial only in the following conditions and to meet the following indications: 1. To allay thirst both in feverless and in febrile conditions. 2. In certain dyspeptic conditions (here hydrochloric acid is used almost exclusively). 3. As antidotes to poisoning by the alkalies. In all other conditions in which acids have been used their utility is either problematical or entirely illusory.

For alleviating thirst, not all of the acids without distinction can be chosen; for some, such as the sulphuric and nitric acids, possess this property only to a slight extent. The most useful are phosphoric, acetic, citric, and various other vegetable acids; the latter are by far the best. Citric acid has the advantage of having a very agreeable taste: this, as well as acetic acid, can be used in cases in which the carbonic acid drinks cannot be given—as for instance where there is a tendency to hæmoptysis; in diarrhœas, also, where sweetened fluids cannot be given, acid drinks are permissible. Citric acid can be given in the form of lemonade. In dyspepsia, accompanied by an excessive secretion of acids, all acid drinks are contraindicated.

The utility of the acids in certain forms of dyspepsia, medicinally administered, not in the form of drinks, is beyond question. Lactic and hydrochloric acids are here to be considered. But since in practice (and very properly so) hydrochloric acid is the one chiefly used in this condition, we refer, for the discussion of this application of the acids, to hydrochloric acid. We should remark, however, that acetic acid is also used for digestive purposes—almost exclusively, however, in the preparation of materials of general diet: in this case it is used to render certain materials more easily digestible in part, and partly as a condiment.

As antidotes to alkaline poisons, we would of course not take an acid that was itself injurious, such as sulphuric, nitric, or hydrochloric, but one like citric or acetic acid in the shape of the ordinary vinegar. These should be administered in such cases for so long a time, until the vomited materials begin to give a slightly acid or at least neutral reaction.

A further indication for the use of the acids in practice is their application in *acute febrile processes.* It has not been shown, however, that they exert any influence upon the temperature and frequency of the pulse in acute febrile diseases, in which both of these are high. In typhoid conditions hydrochloric acid is also supposed to have an "antiseptic influence upon the diseased blood;" this, however, is a mere hypothesis. They are really only of use in these febrile processes for allaying thirst, and for the favorable effect that they may have upon febrile dyspepsia. In subacute inflammatory conditions, also, with moderate or little fever, and where the course of the disease is a more protracted one, we have never noticed any antipyretic action.

The acids are very much used in palpitation of the heart, but, as far as our experience goes, with very doubtful benefit. Under any circumstances they are best avoided in the palpitation of chlorotic and anæmic patients, while in the temporary palpitation which follows any psychical excitement they are entirely superfluous. The utility in the palpitation accompanying disease of the valves is very slight, in our opinion almost *nil*, and under no circumstances to be compared to the effect of simple physical and mental rest; that acids should ever take the place of digitalis, is entirely out of the question. They are most recommended when the palpitations (and arterial fluxions) occur in plethoric individuals, to be used in combination with cathartics; rest, etc., should also be enforced. The latter remedies are, however, probably of greater importance than the acids. If any acid were to be used in palpitations, the best would be sulphuric acid.

As styptics, the internal administration of acids in considerable hemorrhages is entirely without effect; slight hemorrhages will stop without the acid. In these cases, as a rule, sulphuric and acetic acid are used.

In debilitating perspiration, which the acids are also said to alleviate, their utility is very slight, if indeed it exists at all. The sweats of phthisis, for instance, are so little affected by their use that they can be well spared.

The external application of the acids, for caustic purposes for instance, will be discussed under individual preparations.

MINERAL ACIDS.

I. Sulphuric Acid—Acidum Sulphuricum.

We must distinguish: 1. Sulphuric-acid hydrate, SO_4H_2; this gives us the officinal acidum sulphuricum rectificatum, which contains 98 per cent of the hydrate, while the acidum sulphuricum crudum contains 92 per cent of the hydrate. It is a colorless, oleaginous fluid, which crystallizes at 0° C., but not at ordinary temperatures. At 30° C. it gives off fumes. This fluid has a great affinity for water, and when mixed with water it becomes heated.

2. The pyro or fuming sulphuric acid, $S_2O_7H_2$, formed by combining similar molecules of anhydrous sulphuric acid (SO_3) and sulphuric-acid hydrate; it corresponds to the officinal acidum sulphuricum fumans or Nordhausen oil of vitriol, a slightly yellowish-brown fluid, which fumes even at ordinary temperatures.

Physiological Action.—Sulphuric acid is a constant ingredient of human and animal urine; it is here derived partly from the sulphates taken with the food, and for the most part from the albuminoid bodies of the food and tissues which contain sulphur (which becomes oxidized into sulphuric acid); it is to be looked upon as one of the final products of decomposition of the nitrogenous tissues, so that the amount of sulphuric acid in the urine varies with the quantity of urea present. According to Kunkel, 60–70 per cent of the sulphur in the albuminoid materials which are absorbed pass off in the urine as sulphur and sulphates, while only the remaining 30 per cent are converted into other combinations, such as hyposulphurous acid, cystin, rhodan combination, taurine and tauro-carbamine acid, sulphamido-sarcosin and ethene-sulphuric acid, derived from the derivatives of the benzole group (Schmiedeberg, Salkowski, Schultzen, and Baumann); 3 per cent of the sulphur found in the bile is also in the form of a sulphate.

Small diluted quantities of sulphuric acid in 0.66-per-cent solution prevent the development of bacteria, while 0.62-per-cent solutions destroy the bacteria (Buchholtz), and are therefore antiseptic in their action. Diluted sulphuric acid has a cooling taste, and is converted in the stomach either into an alkaline salt or into an albuminate, and partly absorbed. We cannot ascribe to the acid any particularly favorable influence upon the appetite and digestion. It is entirely ineffective upon the heart and temperature. In the urine it appears under the form of a sulphate.

When given for too long a time, diminished appetite and digestive disturbances result; there is also diarrhœa in consequence of the alkaline sulphates formed in the stomach, which do not undergo absorption, but produce their characteristic effects in the intestine.

We doubt the assertion that such small quantities cause the blood in the living body to take on a darker color. Large and concentrated quantities have a violent caustic effect; on account of their great affinity for water they destroy albuminous, fatty, and the horny tissues.§ Upon the skin lighter concentrations produce a burning sensation, and in the beginning a contraction of the vessels with paleness of the surface, later on inflammation; upon the mucous membranes similar concentrations

produce a puckering effect, and a grayish-white discoloration, due to the coagulation of the albumen in the cells. In the more serious cases, where stronger solutions have been locally applied to the skin, the epidermis is destroyed, dissolved, and converted into a hard pigment-like mass of a characteristic brown color; the mucous membranes are similarly changed into a soft, grayish, punctated pulp. With the most concentrated solutions all the tissues are really burned up, the tissues becoming black as coal, and crisp, so that they can be pulverized between the fingers. Here, in fact, the carbon of the molecule remains behind while the other atoms are set free, as takes place in actual burning.

The symptomatology and the remote effects to which concentrated acids (which are not used therapeutically) give rise have been described in the introduction.

Therapeutic Application.—In addition to what was said when discussing the acids in general, we would mention concerning sulphuric acid in particular, that Gendrin and others have recommended it in the treatment of lead colic, and also in the form of a drink as a preventive against chronic lead-poisoning.

Tanquerel, however, and other valued observers have not been able to confirm this use of the drug. It has also proved ineffective as a cure for intemperance (taken in increasing proportions mixed with the brandy): here, indeed, there is even danger of the large quantities of acid proving injurious to the stomach.

Externally, dilute solutions are not used at all. Concentrated solutions are only used occasionally as a caustic in angiomata and hyperplasia of the skin, but for these purposes nitric acid is preferred. Sulphuric acid, on the other hand, can be used as an energetic disinfectant if its destructive caustic effect is not a contraindication.

Dosage and Preparations.—According to the German Pharmacopœia, four degrees of concentration are official: 1. Acidum sulphuricum crudum, oleum vitrioli—raw or English sulphuric acid,—oil of vitriol, sp. gr. 1.830–1.833, strength 91.8–93.1 per cent. 2. Acidum sulphuricum rectificatum s. purum, oleum vitrioli rectificatum s. purum—sulphuric acid, sp. gr. 1.840 and strength 98.5 per cent. 3. Acidum sulphuricum dilutum, spiritus vitrioli of a sp. gr. of 1113–1117, 1 part of acid sulphur to 5 parts of distilled water. 4. Acidum sulphuricum fumans—fuming sulphuric acid, Nordhausen oil of vitriol of sp. gr. 1860–1900. For internal use, only the acid. sulph. dilut. is ordered, 5.15 drops strongly diluted with water or in a mucilaginous vehicle (0.25–1.0 pro dosi, 5.0 pro die); as a component of acid drinks the organic acids are preferred. 5. Mistura sulphurica acida, elixir acidum Halleri—Haller's acid mixture, 1 part of a. s. depur. to 3 parts of spir. vini rectificat; by mixing the two ether is formed. This preparation is valuable not because of its stimulating effect, but because it does not so readily produce digestive disturbances. To be given like sulphuric acid in from 5 to 20 drop doses (0.1–0.5 pro dosi, 2.5 pro die). 6. Tinctura aromatica acida, elixir vitrioli Minsichti, aromatic acid tincture, prepared like the ordinary aromatic tincture, with the addition of 2 parts of sulphuric acid to the 50 parts of spir. vini rectifi., used, like the above preparations, where there are digestive disturbances.

7. Mistura vulneraria acida, aqua vulneraria thedeni, 1 part of acid. sulp. dil., 3 parts of spirit. dilutus, and 3 parts of mel., 6 parts of acetum crudum. Highly impracticable preparation; externally used as a dressing in contusions; seldom pure, but generally mixed with water.

II. Nitric Acid—Acidum Nitricum.

Nitric acid, $NO_2H=NO_2+OH$, which is obtained by distillation from equal parts of potassium nitrate with sulphuric acid, is a colorless fuming fluid having a sharp odor, and possessing a great affinity for water. It is prescribed by the Pharmacopœia in three distinct preparations. The strongest or fuming nitric acid is a solution of hyponitric acid (NO_2) in nitric acid. Like sulphuric acid, it dissolves most of the metals, and is a powerful oxidizing agent.

Physiological Action.—In small dilute doses it has the same effect upon the organism as sulphuric acid; but it alleviates thirst to a less extent, and disturbs the digestion more than the latter. It is also more diuretic.

In large concentrated doses it also coagulates the albuminoids; dissolves them, when in excess, to a yellow fluid, gas being given off. This fluid leaves behind, when evaporated, the so-called xanthoprotein acid, a yellow powder, which is insoluble in water and alcohol. This can also be formed by treating various other nitrogenous substances with nitric acid. It is for this reason that the skin when painted with nitric acid takes on a characteristically yellow color. The caustic effect of this acid upon the skin is greater than that of sulphuric acid, otherwise its effects are exactly similar to those of the latter. When inhaled it produces severe inflammations of the mucous membranes of the larynx and the bronchi, with severe cough and dyspnœa, together with inflammation and œdema of the lungs.

Therapeutic Application.—Nitric acid is not often used to fulfil the indications laid down for the acids in general, because for these purposes other acids are more useful. It has, however, been very much used in combination with hydrochloric acid, forming the so-called aqua regia in certain diseases of the liver. The method by which it exerts a favorable effect upon these diseases of the liver is unexplained, and the experience of various observers does not confirm its utility in these affections (for example, Bamberger). Others, however, speak favorably of it (Henoch and Frerichs). Aqua regia given internally or applied externally in the form of foot-baths or fomentations over the liver has been reported as having a curative effect in icterus of the form occurring in chronic hepatitis (cirrhosis of the liver), as well as in long-continuing cases of chronic catarrhal jaundice, after many other remedies have failed. Further experience is necessary to teach us under what circumstances we may expect good results from aqua regia in icterus. At the present time the opinions of various observers are contradictory, and we ourselves can only record negative observations. Frerichs thinks that the favorable results of its internal administration may be partly explained by the effect of the acid upon the swollen gastro-duodenal mucous membrane, and also upon the reflex influence of acids upon the biliary secretion.

Externally, it is used for baths, as already stated; concentrated nitric acid is also used as a caustic in condylomata, excrescences upon the skin, and rarely for lupoid and phagedænic ulcerations. In diluted condition it is used as a wash for chilblains and putrid wounds.

Dosage and Preparation.—The officinal degrees of concentration are: 1. Acidum nitricum, purified nitric acid, with a sp. gr. of 1185 and 30 per cent acid (anhydrous). 2. Acid. nitric dilutum, acid. nit., and aqua cestit.,

equal parts, sp. gr. of 1086–1089. 3. Acidum nitricum crudum, spiritus nitri, aquafortis, crude nitric acid, sp. gr. 1323–1331, 50–52 per cent. 4. Acidum nitricum fumans—fuming nitric acid, of a reddish-yellow color, giving off red fumes in the air, sp. gr. 1520–1525. Internally 5–20 drops pro dosi (0.25–1.0; 5.0 pro die), in solution or in a mucilaginous mixture. Externally it is used as a caustic applied with a stick or brush; 2-per-cent solutions are used as washes; for a general bath 50–150 grms; for a foot-bath, 40.0–50.0 grms. to a proper amount of water.

5. Acidum chloro-nitrosum s. nitro hydrochatum, aquaregia, King's bath, 1 part of nitric acid to 3 of hydrochloric acid. Given in jaundice like pure nitric acid.

6. Unguentum oxygenatum, oxygenated ointment, 50 parts of adeps suillus to 3 parts of acidum nitricum, entirely superfluous.

III. Hydrochloric Acid—acidum hydrochloratum.

HCl. (muriatic acid), obtained by adding sulphuric acid to sodium chloride, is a colorless, fuming gas having a sharp odor. Water at 0° C. takes up 500 times, at 15° C. 450 times, its volume of hydrochloric-acid gas, and forms therewith a colorless and very acid fluid, which is called hydrochloric acid. The officinal crude hydrochloric acid contains 30–33 per cent of the gas. The officinal pure hydrochloric acid contains 25 per cent; the latter gives off no vapor in the air.

Physiological Action.—In the introduction we gave the proportion of hydrochloric acid generally contained in the pure gastric juice. This acid is not formed in the stomach by a decomposition of the materials of the food (alkaline chlorides), but is produced even in the empty stomach by mechanical irritation of the mucous membrane, so that it must have been formed in the peptic glands by the decomposition of the sodium chloride of the blood; while the acid thus formed reaches the stomach in a free condition, the sodium set free returns into the blood, soon to be again partly excreted with the alkaline secretion of the small intestines and partly with the urine; the latter fluid, in consequence, in men and carnivora becomes less acid and sometimes even alkaline (Meissner, Quincke, and Maly).

This free acid of the gastric juice, which can only indifferently be replaced by other acids, best of all perhaps by lactic acid, is of great importance to the digestive process. It completes the solution of a large number of food materials, such as bone cartilage and tendons, by dissolving the lime phosphates and carbonates, and depriving the alkali (lime salts) of the power of gelatinizing these tissues. Even in 0.1-per-cent solution it converts the albuminates of the food, some more and some less rapidly into a modification which is soluble in acids, into parapeptone or syntonin, acid albumen, and is even capable of converting a part of the albuminates into peptone without the aid of pepsin; under the simultaneous influence of the pepsin, however, this action is very much accelerated, but this power of the pepsin is dependent upon the presence of the acid, and ceases as soon as all of the free acid is used up. With the same quantity of pepsin we can digest increased quantities of albumen by the addition of more acid. This process is explained by the formation of the hypothetical pepsin-hydrochloric acid, which, during the digestive act, gives up the hydrochloric acid to the albuminoid bodies, and produces

a decomposition of a hydrolytic nature in the molecules of the latter. Since the peptone thus produced from the albuminoid bodies can no longer be coagulated in any way, either by boiling mineral acid or metallic salts, which at the same time it diffuses much more readily through the walls of the stomach, we can easily understand how important is the action of the gastric juice to digestion. The amount of acid in the gastric juice must not rise above 0.1 per cent, for too large a quantity of acid disturbs the digestive power of the secretion, just as much as an excess of alkali does by neutralizing the acid.

In the normal condition an increased amount of alkali in the food increases the amount of acid secreted by the peptic glands, so that a kind of compensation takes place. When, however, in disease or after sodium-chloride starvation the production of acid of the gastric juice is diminished, or when, by the introduction of too much alkali the free acid has been neutralized, the digestive process can be aided by the artificial administration of hydrochloric acid.

Since hydrochloric acid in 0.066-per-cent solution retards the development of bacteria, and in 1.32-per-cent solution prevents it entirely (Buchholtz), it may be considered as an antiseptic and anti-fermentative agent. It, like other acids, however, is only one of the weaker antiseptics.

Further effects upon the organism are not observed with small medicinal doses of hydrochloric acid. The acid does not reach the blood as such, but in the form of some indifferent salt—as for example sodium chloride, which in these quantities can certainly produce no effects. The old statements of Boerhaave, Van Swieten, etc., that hydrochloric acid has a stimulating effect upon the brain evidently belong to the world of fable. That sodium chloride produces no effect upon the heart and temperature, even in quantities much larger than could possibly be produced from medicinal doses of hydrochloric acid, we demonstrated when discussing sodium chloride; for this reason the assertions of Bobrik, that the acid is primarily a heart irritant, are unfounded.

In large, concentrated doses hydrochloric acid has a much less intense effect than sulphuric and nitric acid.

Upon the skin it produces a severe inflammation, with burning and prickling; the skin becomes red, and pustules and indurations are formed. But only after frequent application is there any great loss of substance.

Upon the mucous membrane its action is more intense, so that in the mouth a whitish-gray eschar, in the stomach a yellowish one, is formed. There are also severe gastro-enteritic symptoms, which, even after the administration of 5.0 grms., are severe enough to produce death; but even after 15.0–60.0 grms. recovery has taken place (Allen).

Inhalation of hydrochloric-acid fumes produces tracheo-bronchitis, with severe cough. It cannot be denied that poisonous doses also produce serious general disturbances; but these are secondary, and dependent upon the gastro-enteritis.

Therapeutic Application.—Hydrochloric acid is the most frequently used of all the acids in diseases of the digestive tract; its physiological action sufficiently well explains the favorable results derived from its use. That hydrochloric acid is a good remedy in certain forms of dyspepsia (even with an abnormal production of acid) was known to the older observers (*e.g.*, Haberden). The peculiar circumstances under which it should be used were especially determined by the English pathologists (Prout, Begbie, Budd, etc.).

In the first place, it is useful where difficult digestion depends upon a diminished secretion of gastric juice, as happens in well-nourished individuals who lead an inactive life and take a good deal of nitrogenous diet. Leube recommends hydrochloric acid, especially in the dyspeptic conditions of anæmic subjects, in accordance with the findings of Manassëius, who showed that the gastric juice of anæmic subjects contained too little of it. Also in some cases of pyrosis due to too great a formation of acetic and lactic acid, in consequence of abnormal processes of fermentation going on in the stomach; here one trial of the acid will serve to show its utility or non-utility. In simple chronic gastric catarrh hydrochloric acid may also be used, together with the proper dietetic regulations. It should not be used, on the other hand, in the indigestion which is a symptom of an organic disease of the stomach or of an acute inflammatory condition. Even if the acid is indicated, it should not be used for too long a time, for it may otherwise have an injurious influence upon the digestive power of the gastric juice. It should be given from a quarter to three quarters of an hour before meals.

In diarrhœa also hydrochloric acid is more used than other mineral acids—not that it has better effect, but because it is better borne by the stomach. It is most valuable in that form of diarrhœa which is due to abnormal fermentative processes going on in the digestive canal; so also in children in summer diarrhœa, or in the gastro-intestinal catarrh due to fermentation of the milk in the stomach and intestine. As to the value of the acid in these conditions, opinions differ; according to our experience, calomel is better than HCl.

Hydrochloric acid was formerly much given in typhus, but we have already given our opinion of this application. Nor has it been shown to be of any real value in morbus maculosus Werlhofii in scurvy. Traube recommends hydrochloric acid in typhoid pneumonia, and here its use is proper, because of its effect upon stomach digestion. Energetic antiphlogistic remedies are here injurious; which remedies, like digitalis and veratrum, are contraindicated on account of the accompanying gastric catarrh.

According to the investigations of Manasseius it is probable, or at least possible, that hydrochloric acid is of value in febrile conditions accompanied by dyspepsia; and in this way, perhaps, may be explained its favorable effect in febrile diseases. Manasseius concludes that in the gastric juice of fever patients there is sufficient pepsin, while the acid is wanting. To produce a digestive secretion, acids must therefore be added.

The external application is entirely unimportant. Dosage and preparations (officinal) are—

1. Acidum hydrochloricum crudum s. muriaticum crudum, spiritis salis—crude sulphuric acid, 1160–1170 sp. gr., 30–33 per cent of anhydrous acid.

2. Acidum hydrochloricum s. muriaticum, spiritis salis acidus—purified hydrochloric acid, 1124 sp. gr., with 25 per cent of acid. Internally, 5–15 drops (0.25–1.0 pro dosi, 5.0 pro die) given in mush, sugar-water, or a mucilaginous vehicle; in children, 0.5–1.0 to 100.0 in mucilage.

3. Acidum hydrochloricum dilutum, acid. hydrochlor. and aq. dest., in equal parts; dosage, double that of the foregoing preparation.

IV. Phosphoric Acid—Acidum Phosphoricum.

Chemistry distinguishes four different forms of phosphoric acid:

1. The ordinary orthophosphoric acid, PO_4H_3: hard, transparent crystals, tribasic, easily soluble in water, having a strong acid taste, and forming insoluble salts with bases.

2. Pyrophosphoric acid, $P_2O_7H_4$: a colorless, opaque, crystalline mass, easily soluble in water, which is slowly changed into the foregoing preparation, in watery solution; tetrabasic and forming salts insoluble in water.

3. Metaphosphoric acid, PO_3H: a vitreous, transparent mass (acid phosphoricum glaciale), readily soluble in water, and then being converted into the first modification; monobasic.

4. Phosphoric acid anhydride, P_2O_5: a white, amorphous, voluminous mass, which is converted in cold water into metaphosphoric acid.

The phosphoric acid of the German Pharmacopœia is a 20-per-cent solution of ordinary phosphoric acid in water, PO_4H_3O; it is a clear, colorless, and odorless fluid, of a spec. grav. of 1.12.

Physiological Action.—The importance of phosphoric acid as a constant component of the body has been spoken of under the head of the alkaline phosphates. Under ordinary circumstances of nutrition and tissue changes, the amount of this acid, like that of sulphuric acid, present in the urine varies directly with the amount of urea excreted. On the other hand, any variation from the normal, either in the nutritive changes or in the tissue metamorphosis, is shown by variation in the relationship existing between the phosphoric acid and nitrogen; under the influence of nerve excitants (medium doses of alcohol, valerian oil, etc.) a diminution in the relative amount of the phosphoric acid excreted sets in, because in the decomposition of most albumen more nitrogen is given off than P_2O_5. On the other hand, in conditions of nervous depression (produced by chloroform, large quantities of alcohol etc.) there is an increase in the relative amount of P_2O_5, since there is more phosphoric acid in lecithin than nitrogen (Strübing, Eulenberg). As Edlefson has shown, however, an alteration in the relative proportion of phosphoric acid to the nitrogen in the urine, which sets in under the influence of drugs, cannot always be considered as due to an increase or diminution in the *formation* of one or the other of these substances, since, as far as the urea is concerned, it may be due only to an increase or diminution in the amount *excreted*. This is especially true of the effect of excitants, which at the same time cause diuresis. If, as in most of the experiments of Struebing, there is a diminution in the amount of phosphoric acid, together with an increase in the amount of urine, the objection might be made that the diminution in the amount of phosphoric acid excreted is due to the increased excretion of urea (in the larger quantity of urine).

The effect of small diluted doses is the same as that of the other mineral acids; phosphoric acid, however, is weaker, and does not so readily affect the digestion. From its more agreeable taste it is preferred to the other acids. We have already stated that Kobert believes he has seen, several hours after the administration of diluted phosphoric acid, a slight slowing of the pulse and lowering of the temperature.

In large concentrated quantities dissolved metaphosphoric acid has a coagulating effect upon albumen; ordinary officinal phosphoric acid has

this effect only when the solution has been neutralized. Its caustic effect is much slighter than that of sulphuric, nitric, or hydrochloric acid. Hypodermic injection of poisonous doses (up to 2.0 grms.) in cold-blooded animals immediately causes muscular paresis and anæsthesia at the point of injection, soon followed by a comatose condition with loss of reflexes, and gradual stoppage of the heart's action (Munk and Leyden); pyrophosphoric acid is the most poisonous in this respect (Gamgee).

Warm-blooded animals die when concentrated solutions have been introduced into the stomach, with symptoms of the most violent gastro-enteritis. After death there is fatty degeneration of the liver, kidneys, and muscles as after sulphuric acid. It is not surprising that after the subcutaneous or venous injection of concentrated acid death sets in from coagulation of the blood, ecchymoses in the lungs, and paralysis of the heart.

The causes of death from large but diluted doses we have already discussed.

Therapeutic Application.—In addition to the indications already laid down in the introduction, phosphoric acid has, on theoretical grounds, been recommended for various other conditions: in the first place, in caries, rickets, and osteomalacia, where a deficiency of phosphoric acid was supposed to be the cause of the disease; also in lithiasis, with the formation of phosphoric-acid concretions, the idea being to dissolve these by forming a biphosphate. But experience has not shown that the remedy is of any use in these conditions, and the use of the remedy for these purposes has been discontinued. The external application of the acid in concentrated or dilute condition is also abandoned.

Dosage.—1. Acidum phosphoricum, from 10–20 drops (0.35–1.0) pro dosi (5.0 pro die) in mixtures (5.0 : 150.0; for children, 1.0–2.0 : 100.0); also in pill form (prepared from 1 part of a vegetable powder and 1 part of extract).

2. Acidum phosphoricum siccum—dry anhydrous phosphoric acid, is an unnecessary preparation, with the advantage, however, of being more adaptable for pill form (from 0.05–0.5 pro dosi, 2.0 pro die); several times daily.

V. Chromic-acid Anhydride—Acidum Chromicum, CrO_3.

The powerful caustic but not very painful action of this acid upon the skin and mucous membranes is due partly to its powerful oxidizing effect (its oxygen being readily given off), and partly, as in the other acids, to its great affinity for water. Its antiseptic power is not more powerful than that of the other acids, but it renders the tissues hard and yellowish brown.

Internally, even in 0.3 grm. doses, it produces a fatal effect, with symptoms of gastro-enteritis. Even its external application in man is followed by symptoms of general poisoning: metallic taste, peculiar odor, vomiting, diarrhœa, and profound collapse (Mosetig-Bruck).

Gergens saw a gastro-intestinal affection and albuminuria set in, in dogs, after the subcutaneous injection of a few drops of chromic acid; in rabbits even after the subcutaneous injection of neutral chromatic.

The potassium bichromate, $Cr_2O_7K_2$, both externally and internlly, has a similar caustic effect to that of chromic acid. The emetic, neutral potassium chromate, $Cr_2O_4K_2$, is also a poison, being in a high degree an irritant and escharotic upon all the mucous membranes, and paralyzing

the nerve-centres, especially the vaso-motor and motor (Priestley, Gamgee) centres.

Chromic acid is not applied in internal therapeutics. Externally, however, it is very much used as a caustic; it has been especially recommended for small and large condylomata (Schuh, Marshal); also in phagedænic ulcers, and by Lewin earnestly recommended for diphtheritic deposits and ulcers. In the last-named process it is said to be of more use than other caustics, since it not only destroys these deposits but acts as an antiseptic. Experience has not shown, however, that chromic acid affects the diphtheritic process more than other remedies.

For cauterizing condylomata, 10–20-per-cent solution may be used. In diphtheria a 5–10-per-cent solution, according to the thickness of the deposit.

Internally, potassium chromate is an entirely superfluous remedy. In the few conditions in which favorable results are obtained from its use (as an expectorant in bronchitis), it has no advantage over other valuable remedies. Even its application in syphilis, for which it has been recommended, is without any noteworthy utility, so that for internal application the remedy is best avoided entirely, since it readily produces gastritis, anorexia, and digestive disturbances.

Externally, potassium chromate is used as an astringent and drying agent under the same conditions as chromic acid.

We should add that the preparation is very much used for hardening and preserving anatomical preparations.

VI. Boric Acid—Acidum Boricum, $B(OH)_3$

is a weak acid, and is used as an antiseptic agent. It prevents the development of bacteria in a solution of 1 : 133. Small doses produce vomiting; large ones, gastro-enteritis.

Therapeutic Application.—In the last few years boric acid has been variously used in Lister's method of dressing, because, while it is an excellent antiseptic, it does not irritate the wound. The following preparations are in general use :

a. Boric Acid Water.—Concentrated solution of boric acid (3½ per cent), in which the boric-acid lint is soaked, and with which wounds treated by this lint are washed.

b. Boric Acid Lint.—Lint, strongly impregnated with boric acid, of a rose color, is used to put over the protective, damp or dry, instead of the carbolized jute, the antiseptic gauze, etc.

c. Boric Acid Ointment consists of 1 part of powdered boric acid and white wax, and 2 parts each of oil of almonds and paraffin. This ointment can be placed directly upon a wound in which the ordinary carbolized dressing cannot be applied, as in resections of the upper jaw.

VII. Hydrofluoric Acid—Acidum Fluoricum, FlH—

is extremely poisonous, even when inhaled, and is rarely used as a caustic.

VIII. Sulphurous acid—Acidum Sulphurosum and its Salts—Anhydride, SO_2,

is a colorless gas, having a sharp odor. When inhaled, it produces severe irritation of the laryngeal mucous membrane, and a reflex spasm

of the glottis. It is therefore non-inhalable, and causes death in a short time in all classes of animals.

Upon the blood it has a powerful reducing action, depriving it of its oxygen, coagulating it, and turning it brown. When inhaled, diluted with air, for a long time it tends to cause catarrhal inflammation.

The constant tendency of sulphurous acid to take up oxygen and water, and be converted into sulphuric acid, is the key to its action, for upon this depends its reducing power upon many of the metallic oxides and the blood, its bleaching action upon the vegetable colors, and its power of preventing decomposition and fermentation. It is for the latter reason that sulphuric acid preserves fruits, wine, etc. The germinating power of the lowest organism is destroyed by a solution of 1 : 666. Its action in this respect is twice as intense as that of salicylic acid, five times as strong as sulphuric acid, and sixteen times as strong as carbolic acid.

Sulphurous acid is not directly used for therapeutic purposes.

The sulphites of the alkalies and alkaline earths—potassium and sodium sulphides—are well borne by the organism in quite large doses. In the stomach these salts are partly decomposed, and part of the sulphurous acid set free, which exerts its anti-fermentative action. These salts, like the sulphates, have a cathartic effect. When absorbed into the blood they are converted into sulphates, and appear as such in the urine. The assertion that these salts have a destructive action upon septic materials present in the blood or organs is unproved, and highly improbable.

The same may be said of the sub-sulphites—the potassium and sodium hyposulphites.

The sulphites and hyposulphites, especially the sodium combinations, have been very much used in latter years by German and Italian physicians. Polli, reasoning from the assumption that in a certain class of diseases (typhus, malaria, acute exanthemata, pyæmia, etc.) an abnormal fermentative process goes on in the blood, believes that, in these conditions, anti-fermentative substances should be administered to the organism.

Such substances are sulphurous and hyposulphurous acids, which can be harmlessly introduced in the form of these salts.

Even the theoretical considerations upon which this method of treatment is based are disputable, the chief objection against it, however, is that it has not been practically confirmed. In Germany it has been but little applied.

Sodium sulphurosum—from 0.5–20 pro dosi (8.0 pro die) in solution

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ORGANIC (FATTY) ACIDS.

Among the many organic acids, there is a certain number which resemble the mineral acids in their physiological action, while others differ from the latter entirely. We shall here consider only the former, which chemically are derived by oxidation from the alcohols of the methane series, and are normal components of the animal body. Of the large number of these only few are therapeutically used, on account of the great similarity in their action, and their few indications. They differ from the mineral acids only in their weaker local action, and, on

account of their weaker chemical relationship, cause only inflammation, and not destruction of tissue; so that ordinary phosphoric acid may be considered as the mean between the two series. As for the rest of their action, they have some antiseptic power, and neutralize alkalies, while in medicinal doses they have as little influence over the circulation and temperature as the mineral acids.

I. Formic Acid—Acidum Formicum.

Formic acid, CH_2O_2, is the lowest member of the monobasic single atomic acids (fatty acids), having the formula $C_nH_{2n}O_2$, to which belong also acetic, propionic, butyric and valerianic acid, together with many others of a less physiological importance, but differs from these chemically in several respects. It is a frequent oxidation product of many other organic bodies of a higher molecular weight, especially of many of the acids of the lactic-acid series, such as malic, tartaric, and citric acid, and sugar, etc.

It is a colorless, sharp, and acid-tasting fluid, soluble, like all of its salts, in water, and decomposed, by heating with sulphuric acid, into carbonic oxide and water.

Physiological Importance and Action.—Formic acid is found as a free acid in a number of animals as a component of peculiar organs, as, for example, in ants, in the stinging apparatus of wasps, and also as formates in many of the organs (such as the brain, muscle, spleen, and pancreas), and in the blood of the higher animals. Everywhere they are the final products of the decomposition of nitrogenous and free components of the body (albumen and fat), from which they can be derived, even outside of the body, by ozone and other methods of oxidation. It leaves the body partly unchanged with the sweat, and partly burnt up to carbonic acid. The effect of small doses, taken internally, has not yet been studied. Applied externally, in concentrated form, it produces severe inflammation of the skin, with exudations and burning pain. Internally, in rabbits, it causes a violent gastro-enteritis, with inflammation of the kidneys, and the results of these affections (Mitscherlich). By the production of an inflammation of the kidneys, it differs physiologically from the other acids, as far as this is concerned.

Therapeutic Application.—Formic acid is no longer used internally. Externally, it is used as a cutaneous irritant, under the same circumstances as spirits of mustard. As a rule, the pure formic acid is not used, but some preparation containing formic acid.

a. Formicæ rufæ—wood ants: applied either by allowing the vapor of hot water poured over the ants to come in contact with the diseased parts, or by adding the crushed ants, placed in a bag, to a bath.

b. Tinctura formicarum: 2 parts of crushed ants to 3 of spir. vini rectificatissimus, poured over them; of a reddish-brown color; externally applied, pure, or with equal parts of water.

c. Spiritus formicarum: alcohol in which ants have been steeped; colorless.

II. Acetic Acid—Acidum Aceticum.

Acetic acid, $C_2H_4O_2$, the second member of the series of monobasic, single atomic, fatty acids, formed by the destruction of organic bodies, distillation of sugar, starch, etc., and oxidation of alcohol, is a color-

less, volatile fluid, having an acid odor and taste, the vapor of which is inflammable, and which is miscible with alcohol and water in all proportions. Acetic acid, free from water, has a sp. gr. of 1.056 at 15° C. By the addition of water the sp. gr. is at first increased, so that an 80-per-cent acid has a specific gravity of 1.0754; then it is again diminished, until the 50-per-cent acid has again the same sp. gr. as acid free from water.

Physiological Action.—Under a diet rich in sugar, acetic acid is found in the stomach, also in many of the organs of the body, in the blood of those addicted to chronic alcoholism, or leucæmia, in the sweat and urine, generally in combination with bases, and, like formic acid, is generally a product of retrograde metamorphosis.

When absorbed from baths, through the skin, or internally, through any of the mucous membranes, it is taken up into the circulation in combination with bases, and burned up into carbonic acid, to be again excreted as a carbonate. Acetic acid appears unchanged in the urine only when it is given in such large quantities that the free alkali or weak alkaline salts of the blood does not suffice to bind it. In that case the urine of the herbivora becomes acid, and that of the carnivora more acid than normal.

Effect of small, diluted doses.—Since these have been thoroughly discussed in the introduction, we shall say but little here.

The drinking of diluted acetic acid produces an acid taste in the mouth and alleviates thirst. It improves digestion slightly. The heart and temperature of healthy patients are uninfluenced, and the urine is unaltered.

Embrocation with this acid locally upon the skin causes evaporation of the fluids and a local feeling of cold, with local paleness. Perspiration is said to be hereby diminished.

Indulged in too long and too frequently, anorexia and dyspepsia result, together with diarrhœa, anæmia, and wasting. Tuberculosis as a result is questionable.

Effect of large concentrated doses.—Concentrated acetic acid soon passes through the unbroken skin, without dissolving the epidermis, and produces a severe congestion at the point of application, so that the skin beeomes red and painful. In consequence of the exudation poured out into the tissue of the cutis, we have a swelling at the locality, and paleness of the part, due to compression of the vessels. In addition to this, we have an effusion of serum under the epidermis; so that there are either blisters formed or there is a slight loss of substance of the upper layers of the corium, and separation of the epidermis, which, however, is rapidly regenerated.

The visible mucous membranes first become white, then brown in color, with severe burning pains. When it reaches the stomach, acetic acid produces gastro-enteritic symptoms, with severe burning pains, thirst, vomiting, meteorism, and death, with symptoms of collapse.

According to Mitscherlich's experiments on rabbits, the mucous membrane is found very much thickened in rapidly fatal cases. The blood-corpuscles in the vessels of the tunica propria were dissolved, as could be seen from the brown discoloration of the latter, while the acid had diffused through all the tissues into the abdominal cavity. In cases which died more slowly, the dissolution of the blood-corpuscles was still more marked, so that hemorrhage into the stomach took place. The mucous membrane, even into the duodenum, was very much hypertrophied,

white, opaque, and partly softened. It is not surprising that such violent effects as these are accompanied by a diminution in the heart's action, and a fall in temperature to 30° (Bobrik).

The application of Villati's solution (a ridiculous compound of 30 parts of liq. plumbi subacetici, 15 parts each of cuprum sulphuricum and zincum sulphuricum, and 200 parts of white wine vinegar) for injecting into carious bones and chronic fistulous abscesses, has several times been the cause of sudden death, due to the entrance of acetic acid into the circulation. These cases Heine has investigated. In a girl, shortly after the injection, the face became pale, and almost of a lead color, the whole body trembled, and all of the blood seemed to have left the veins. There was an intense feeling of cold, the extremities were cool, the pulse small and rapid, and the wound took on a dark-brown appearance. The temperature, which before the injection in the morning was 38°, increased toward noon to 38.6°. Then there was a gradual diminution, until, just before eight o'clock in the evening, it sank to 34.2. The pulse was thread-like and scarcely perceptible, beating 140 to the minute. There was some diarrhœa, and constant drowsiness, with which the patient died at midnight. Similar symptoms occurred in a ten-year-old boy, and also in animals. In the latter Heine observed quickened, spasmodic respiration, and tetanoid convulsions, which were rhythmically repeated, and always reproduced by irritation of the skin.

In the blood-corpuscles of the amphibia, the addition of dilute acetic acid produces a slightly granular precipitate, which redissolves in concentrated acetic acid. This precipitate is not produced if the animal has been starved, nor does it occur in the blood-corpuscles of birds and the mammalia. When mixed with or directly injected into the blood of the living animal, the blood corpuscles are dissolved and the blood loses its color. The blood-corpuscles not dissolved shrink, and take on a granulated, pale appearance, frequently becoming surrounded by little gas bubbles. The lack of color is due to decomposition of the hæmoglobin and the solution of the hæmatin in the serum. The gas bubbles are probably oxygen (Heine).

Heine accounts for the symptoms thus resulting from the direct injection of hæmatin into blood, partly by the destruction of the blood-corpuscles as carriers of oxygen, partly by the coagulation of the dead blood-corpuscles, which, undergoing further chemical changes, may produce septic materials, and partly by the deposit of emboli in the capillaries of the lungs, from the clots formed in the vessel into which the injection has been made.

Acetic acid has an effect similar to that of the other acids upon low organisms and septic processes.

Therapeutic Application.—All that can be said of the internal administration of acetic acid has already been said when discussing the acids in general. We should only add, that acetic acid is less frequently prescribed than the other acids simply for the reason that it is a domestic remedy.

Externally, however, acetic acid is very much used, not so much because it has an advantage over other acids in its effect, as because it is a cheap and everywhere obtainable remedy. In the first place, it is used as a mild styptic for capillary hemorrhages; thus in epistaxis, hemorrhage from the extraction of teeth, etc. The effect may be due to the local lowering of the temperature which it produces. It is also used as a wash for excessive perspiration; also as a dressing for slight contusions

of the joints and skin. It is added to clysters, with the intention of producing more energetic peristalsis; also used as an injection in the treatment of thread-worms; but vinegar is of less value in these cases than simple cold water. Acetic acid, as well as the vapor of vinegar, is used as a restorative in cases of fainting. This acid is useless as a disinfectant. Recently acetic acid has been used as an injection in malignant growths, which are thus caused to disappear. Apart from the fact that this method is sufficiently dangerous on its own account, we must not forget that it may give rise to the same dangers as liquor Villati.

Dosage and Preparations.—According to the German Pharmacopœia, three different degrees of concentration of acetic acid are officinal:

1. Acidum aceticum concentratum, alcohol aceti, acetum glaciale—acetic acid, alcohol vinegar; contains 83–85 per cent acetic acid, free from water, having a specific gravity 1058–1069.

2. Acidum aceticum dilutum, acetum concentratum—diluted acetic acid, concentrated vinegar, contains 30 per cent of acetic acid, free from water, and has a specific gravity of 1040.

3. Acetum, acetum crudum s. vini—vinegar, contains 6 per cent of acetic acid, free from water. This preparation is slightly yellowish, while the two former are colorless.

4. Acetum purum s. destillatum—pure vinegar, colorless, and also contains 6 per cent. Internally, vinegar is used in doses of 2.0–10.0 grms., pure or diluted. As an acid drink (oxytrat) we take 50–100 grms. of vinegar to 1 kilogram of water, with the addition of sugar. Acidum aceticum concentratum, from 0.25–1.0 (5.0 per day). Acidum aceticum dilutum, a double dose. Externally, both concentrated preparations are used as smelling drops, and for cauterizing. For other purposes vinegar is used, either pure or mixed in various proportions with water. For washing purposes, with water in equal parts; for clysters, 1–3 tablespoonsful. Apart from this, acetic acid is very much used pharmaceutically for preparing the acetum (tincturæ acidæ) of narcotic substances, extracts of various drugs, such as squill, digitalis, etc.

5. Acetum aromaticum—aromatic vinegar; contains in 1000 parts of distilled water, 200 parts of dilute acetic acid: 100 of the tinct. cinnamomi, 50 of tinct. aromatici, 5 of ol. caryophyllorum, 2 of ol. thymi, 1 each of ol. rosarum, ol. juniperi, ol. citri. Used externally for swelling and vaporizing purposes.

6. Acid. aceticum aromaticum—acetic acid, with many ethereal oils (violets, lavender, citron, bergamot, thyme, and cinnamon). Only applied externally.

III. Valerianic Acid—Acidum Valerianicum, $C_5H_{10}O_2$.

belongs to the monobasic and monoatomic fatty acids, together with formic and acetic acid; it occurs in a large number of officinal plants, such as valerian root; also in cod-liver oil. According to Reissner's investigations, has exactly the physiological effects of the other fatty acids, especially that of formic acid (if it really does give rise to kidney complications after the administration of large doses). Therapeutically, valerianic acid is not used as such; compare valerian root.

The following three fruit acids, and fruits, containing them, have an effect similar to that of acetic acid:

IV. Malic Acid (Oxysuccinic Acid), Acid. Malicum, $C_4H_6O_5$

belongs to the bibasic triatomic acids, having the formula $C_nH_{2n}O_5$;

is converted by heating into hydriodic acid, and in the animal organism into succinic acid; occurs free in unripe fruits, as, for example, unripe apples and grapes, and in combination with alkalies in the ripe fruits; in the cherry, for example, as a potash salt. Its crystals have a very acid taste, and deliquesce in the open air.

V. Tartaric Acid—Acid Tartaricum, $C_4H_6O_6$;

a bibasican tetratomic acid, having the formula $C_nH_{2n-2}O_6$; seen in various modifications, and is especially contained in large quantities in fresh grape-juice, from which it is crystallized by fermentation, as the acid tartrate of potash. The ordinary or dextro-tartaric acid is officinal; its solution turns the polarized ray to the right. The crystals are powerfully acid, odorless, and readily soluble.

An important therapeutic distinction between citric and tartaric acid is that it is not as well borne by the stomach; even older practitioners have asserted that its long-continued use is followed by serious digestive disturbances. For this reason, and also because tartaric acid is not as common a substance, it is very much less used than citric acid. Pharmaceutically, it is used for the preparation of "saturations" and effervescing mixtures, and also in preparing "wheys."

Internally, from 0.3–1.0 pro dosi (10.0 pro die) in powder, mixtures, pastilles, and "lemonades" (0.5–1.0 per cent solution, with the addition of sugar).

IV. Citric Acid—Acidum Citricum, $C_6H_8O_7$;

a tribasic tetratomic acid, of the formula $C_nH_{2n-4}O_7$; found partly in a free state in lemons and almost all the other acid and acid-sweet fruits (strawberries, whortleberries, gooseberries, crab-apples, etc.), and in beets. It has an agreeable acid taste, is colorless, and the crystals are readily dissolved.

Citric acid, in the shape of lemon-juice, is used, in addition to the ordinary uses of the acid, in scurvy, both as a preventive as well as a cure. In America and England the utility of lemon-juice for this purpose is so well recognized that every ship sailing on a long journey is always provided with lemons. Experience has shown that pure citric acid is not as effective as lemon-juice, nor are other pure acids of any use. This would agree with the theoretical views which are held concerning scurvy, namely, that not the vegetable acids are important in the treatment of this condition, but the citric acid and carbonic acid which is obtained from the salts of the vegetable acids found in fresh fruit, etc.

Much has been said concerning the value of citric acid in rheumatic affections. In the subacute cases of articular rheumatism, as well as in muscular rheumatism, it has been given as a diaphoretic; but it is doubtful whether this effect is not due to the hot menstruum as much as to the acid. In acute articular rheumatism citric acid has been given in large doses, mostly in the form of lemon-juice—120–150 grms. per day, but now salicylic acid is preferred.

There are other conditions in which citric acid is used, and in which it is of less value than in rheumatism: thus in catarrhal jaundice, in which it is useful on account of a certain influence which it has upon the complicating gastric catarrh; also as a diuretic in hydrops (lemon cure). Recently Révillout, Trousseau, and Claassen have lauded citric acid very

much in diphtheria; but large doses are said to be necessary in order to produce a favorable effect (four lemons every hour), and thus for days. It has not been shown, however, that this method is any more effective than a large number of others. Like vinegar, lemon juice is a convenient antidote against poisoning with the caustic alkalies.

Externally, citric acid is used for the same purposes as acetic acid, with the exception of disinfection, and as an addition to clysters.

Dosage and Preparations.—1. Acidum citricum, from 0.1–0.5 per dose (15.0 per day), in pastilles; as a lemonade (5.0 : 1000.0 with sugar). Fresh lemon-juice—succus citri recens expressus—is given in sugar water, in teaspoonful or tablespoonful doses. The acid, like the juice, is often used in "saturations" which taste more agreeably than vinegar "saturations" (1 part of potassium carbon. sol. to 6 parts of juice and 3 parts of acid). Externally used, pure (lemon-juice, or citric-acid crystals) or mixed with water.

2. Syrupus succicitri—lemon-juice syrup; 5 parts of succus citri recens expressus to 9 parts of sugar; yellowish in color; used as a corrective; clear.

3. Pulvis ad limonadum—lemonade powder; 10.0 of acid. citrici., 1 drop ol. citri, and 120.0 of sugar, on the point of a knife.

Many kinds of fruit, domestic and foreign, owe their taste chiefly to the presence of the three acids which we have just considered, namely, malic, tartaric, and citric. They are present in these fruits partly in their free state, and partly bound to bases; they contain also a quantity of sugar. Their nutritive value is very slight, on account of the small amount of albumen and vegetable gelatin which they contain. On the other hand, the sweetesh acid taste of ripe fruits, together with the agreeable ethereal oils which they contain, render the fruits one of the most agreeable articles of diet to the human race.

Their physiological effect is a mean between that of the organic acids, salts of the vegetable acids, and carbo-hydrates. The first, together with the large amount of water which fruits contain, increase the alkalescence of the urine (these acids being converted into alkaline carbonates). The taking of large amounts of raw fruits causes abdominal pain, especially if the rest of the diet be unsuitable. This pain may be due to the cold temperature of the fruits. Fruits have no effect upon the circulation and temperature. On the other hand, together with water, they alleviate thirst, and are more refreshing than when taken alone.

Since the proportion of acids, sugar, etc., in fruits varies according to the climate, season, and locality, the following calculations should be taken as only relatively true:

In 100 Parts.	Free Acid.	Acids in Combination, Vegetable Jelly, Fat.	Sugar.	Albumen.	Ash.	Water.
Grapes	0.75	0.36	14.31	0.74	0.61	80.2
Apples	0.69	5.51	7.96	0.39	0.36	82.1
Pears	0.03	3.23	8.78	0.23	0.35	83.2
Cherries { Acid, unripe	1.75	....	1.12	0.21	0.62	88.2
Cherries { Sweet, ripe	2.01	....	18.12	0.57	0.65	74.2
Prunes	0.97	4.19	6.78	0.87	0.76	80.1
Currants	2.14	0.16	6.37	0.54	0.75	84.5
Huckleberries	1.34	0.55	5.78	0.79	1.40	77.5
Strawberries	1.36	0.10	5.09	0.51	0.75	87.4
Raspberries	1.48	1.41	4.00	0.58	0.54	86.1

Therapeutical Application of Different Kinds of Fruit.—Grapes only are of value therapeutically; all other fruits have merely a dietetic importance, but used in the form of various preparations as correctives for different medicines.

The grape-cure has only a limited application in a few conditions, and even in these there is no idea of their exerting any specific influence. Fresh grape-juice, taken in large quantities, exerts an effect upon the intestinal canal, producing diarrhœa, and thus withdrawing nutritious substances from the body.

The percentage of albuminates and sugar is too small to enable grapes to have any nutritious effect. The grape-cure, methodically carried out, is therefore used when we wish to diminish the nutrition of the body. It is of most value in corpulence, accompanied by plethora; also in well-nourished individuals suffering from chronic constipation, while they (grapes) should be avoided in the same condition of pale and weak individuals.

We should remember that the immoderate use of grapes may give rise to a dyspeptic condition. Indeed, there are no cases in which the grape cure cannot very well be replaced by a spring-water cure; and we must not forget that the grape-cure can only be applied during the months of September and October. In cystitis the grape-cure is decidedly inferior to other methods of treatment. In phthisical conditions, or where there is a tendency to phthisis, it might do harm, by the diminution in the diet which it causes. If any favorable result does take place, it would probably be owing to the exercise which accompanied the cure as such. But ordinarily the utility of this procedure is so slight, and so easily accomplished by better means, that we almost regret the grapes thus wasted, which might be better used in preparing some refreshing wine.

The grape-cure can be carried out wherever grapes grow in sufficient quantities; but since it can only be practised in September and October we should prefer those places the climate of which is still favorable for open-air life at this time of the year. For this reason Dürkheim, Gleisweiler, Edenkoben, Kreuznach, St. Goar, Ruedesheim, Meran, Gries, Montreux, Vevay, Krems, Pressburg, etc., are the best.

Officinal Preparations from Fruits.—Syrupus rubi idaei—raspberry-juice or syrup; of a beautiful red color and pleasant taste. Used for mixing with water in the preparation of a pleasant drink, and also as an addition to acid mixtures. By the addition of salts and alkaline substances raspberry-juice loses its color.

Acetum rubi idaei—raspberry water; contains only the ethereal oil, and only used to improve the odor of articles to which it is added.

Aqua rubi idaea concentrata, contains slightly more of the spirit.

Syrupus cerasi—cherry-juice; of red color, and has the odor of and contains a minimum amount of hydrocyanic acid, the pits, together with the meat, being used in preparing the syrup. It is used partly as a corrective for mixtures, or mixed with water as a cooling drink.

VII. Lactic Acid—Acidum Lacticum—Lactic or Oxypropionic Acid, $C_3H_6O_3$;

belongs to the monobasic diatomic acids, having the formula $C_nH_{2n}O_3$, and, like all these acids, is intimately related to the fatty acids.

We can distinguish: 1. Fermentation-lactic acid, which is prescribed by the Pharmacopœia, and is formed during the fermentation of milk, grape, and cane-sugar, and starches, gums, and all sweet fluids, which have the property of turning sour; thus in sour milk. When heated with sulphuric acid it is decomposed into aldehyde and formic acid. Chromic acid oxidizes it to acetic and formic acids, while hydriodic acid reduces it to propionic acid. It is a colorless, odorless, exceedingly acid and non-volatile fluid, which can decompose the salts of other volatile acids and several of the mineral acids. 2. *Paralactic acid*, which is obtained from juice of meats, and only differs from lactic acid in that it turns the polarized ray to the right; when treated with sulphuric and chromic acid it yields the same products as the former.

Physiological Importance and Action.—Lactic acid is formed in the stomach and intestinal canal, under similar conditions as outside of the body, from starchy and saccharine materials. It has the same influence upon digestion as hydrochloric acid, and is the next best acid to use for digestive purposes. Concerning this point we may refer to what was said under hydrochloric acid. Some modification of lactic acid is found as a product of retrograde tissue changes, combined with alkalies or iron, in almost all of the organs, such as the brain, liver, spleen, pancreas, etc.; paralactic acid in all of the muscles during their activity, and at the period of rigor mortis, which it helps to produce by coagulating the myosin. The neutral reaction of muscle during rest, and its acidity during motion, are probably accounted for by the fact that the alkaline blood passing through the muscle is sufficient to neutralize the small amount of acid formed during rest, but not the larger quantities formed while the muscle is in motion. In the blood lactic acid is said to be formed only as a result of pathological conditions, such as leucæmia, septic fevers, etc.

The lactic acid taken into the body as well as that formed in the process of digestion is taken up by the blood in combination with alkalies, where it is soon burned up to an alkaline carbonate, and excreted with the urine as such, thus rendering the urine of the carnivora alkaline in reaction. If it leaves the body unaltered with the urine, as happens when the animal takes little exercise, or when the diet is very starchy, or in phosphorus poisoning, acute atrophy of the liver, leucæmia, etc., it is a sign that the oxidation process going on in the body is diminished.

In small diluted doses introduced into the stomach lactic acid has at most the effect of aiding digestion. If given in large quantities for a long time it would probably withdraw alkalies from the body, disturb digestion, cause eructation of gas, vomiting, and diarrhœa (owing to the unabsorbed lactates in the intestine), like all the other acids. The fact that rickets arises in children, in whom lactic acid is formed in too large quantities, has led to the opinion that there is an etiological connection between lactic acid and rickets. It is supposed that the lactic acid being in excess is only partially converted into carbonates in the blood, and the remainder has a dissolving action upon the lime-phosphate of the bones. Indeed, Heitzman pretends to have produced, by experimental injections of or feeding with lactic acid, osteomalacia in herbivora, and rickets followed by osteomalacia in carnivora. Heiss contradicts these observations, basing his contradiction on the observation of a dog carried on for 308 days, to which he gave the enormous quantity of 2286 grms. of lactic acid with the diet. After the animal had been killed he found no abnormalities either in the bones or in any part of the body. The quan-

tity of lime and magnesia contained in the blood, muscles, and bones was normal, so that in this case we can positively say that the lactic acid has not withdrawn any lime from the body. Indeed, were as much lactic acid to collect in the blood as is necessary to dissolve the bones, then death of the whole animal would certainly set in. So also the idea that acute rheumatism or endocarditis are the results of excessive production of lactic acid in the body is highly improbable.

In large concentrated doses, lactic acid, like all acids, produces gastro-enteritis and death.

The lactic acid is in these cases excreted, unchanged, with the urine; the urine becomes diabetic.

When injected directly into the blood, symptoms similar to those described under acetic acid must occur. The heart and muscular paralysis occurring in the course of these experiments is caused by lactic as well as by other acids.

Therapeutic Application.—Lactic acid has been most frequently recommended as a remedy for digestive disturbances. Rational as this appears, experience has shown that practically almost all the other acids are preferred to lactic acid for this purpose. We cannot therefore, from want of experience, lay down any rules in which forms of dyspepsia lactic acid is particularly indicated; *à priori* we might suppose that they were the same as those laid down for hydrochloric acid. Since lactic acid has considerable power of dissolving the earthy salts, it has been recommended in the "phosphoric-acid diathesis;" but our experience concerning its practical value for this purpose is very limited. Concerning the hypnotic action of lactic acid compare what is said on sodium lacticum (page 69).

Externally, lactic acid has been used for cleansing the teeth when they are covered with lime concretions. Recently it has been very warmly recommended in croup (Bricheteau and Adrian, Weber and others) because of its power of dissolving croup membrane; for this purpose it is given in inhalations (10–20 drops to 15.0 water). Experience with this method of treatment does not permit us to expect more from it than from other methods of treating croup and diphtheria (Wagner and others).

Dosage.—Acidum lacticum, from 0.25–1.0 pro dosi—5.0 pro die internally, shortly before meals in pastilles or in watery solution.

VIII. Oxalic Acid—Acidum Oxalicum, $C_2H_2O_4$;

belongs to the bibasic diatomic acids, having the formula $C_nH_{2n-2}O_4$. Oxalic acid is a peculiarly poisonous acid, not entirely homologous with any of the other acids of the series, and the strongest of all the organic acids; succinic acid, which belongs to the same series as oxalic, is entirely analogous to the group of acids discussed in this chapter. Oxalic acid occurs in nature very widely distributed—as an acid salt of potassium, as a calcium salt in many plants, such as rhubarb; also dissolved in the urine, and in gravel stones of the urine. It reaches the animal organism partly with the food (vegetable), while it is partly formed like other acids as a product of retrograde metmorphosis. Its occurrence in the urine in increased quantity is partly due to a diminution in the oxidation processes going on in the body. It presents in the shape of colorless prisms, less soluble in water than in

alcohol; these decompose when rapidly heated into carbonic acid, carbonic oxide, and formic acid. In contradistinction from most other organic acids, its salts, with the exception of the alkaline salts, are soluble with great difficulty in water.

When introduced in a free state, it appears partly in the urine as a salt; partly, it, as well as its salts, is burned up into carbonates and excreted as such.

According to Herrman, our experience concerning the toxic power of oxalic acid and its salts is ambiguous. In large concentrated doses, oxalic acid exerts a caustic action, producing gastro-enteritis like sulphuric acid, but causing death more rapidly; it differs markedly, however, from the other acids in that, in very small doses, even of the neutral sodium salts, it has a paralyzing effect upon the central nervous system, (drowsiness, loss of reflexes, etc.) and the ganglia of the heart, although the sodium salts of the other acids (see the alkaline salts of the vegetable acids) are not poisonous. Frogs are killed by doses of 0.04 to 0.08 grm. of sodium oxalate.

The assertions of Onsum, that oxalic acid precipitates the potassium salts of the blood, and that the precipitate of insoluble calcium oxalate kills by the deposits of emboli in the capillaries of the lungs cannot be true; for the additional supply of calcium to the blood renders even fatal doses of oxalic acid harmless. Under the influence of oxalic acid the urine becomes saccharine. Between the capsule and cortical portion of the kidney a white zone formed by the deposit of oxalates is generally found.

Therapeutically, oxalic acid is not used.

9. Succinic Acid—Acidum Succinicum, $C_4H_6O_4$,

belongs to tho same acid group as oxalic acid; we are familiar with two modifications, and it is found in amber, peat, plants and in animals (organs, urine) as a normal component after eating articles of diet containing malic acid, or formed in the body as a product of retrograde metamorphosis, as for example from the oxidation of benzoic acid (G. Meissner). It is also produced by the fermentation of sugar and the malate of calcium. According to the experiments of Hallwachs, Hermann, and others, it acts exactly like the other acids, and when given in the shape of a salt, is converted into a carbonate in the blood (and not into a hippurate, as Kühne thought).

Succinic acid is not used therapetuically; for although it was formerly thought to be indicated in certain conditions, its utility is so slight that we shall not enumerate the indications formerly given for its use.

Treatment of Poisoning with Acids.—Unless antidotes are immediately administered, the caustic effect of the concentrated acids can no longer be prevented, and treatment must be directed to the results of this caustic action. We should therefore always give the best antidote that happens to be at hand, without waiting to obtain the real chemical antidote from the drug-store. All of the non-caustic alkalies are direct antidotes of the acids; such are soap, chalk, ashes, etc. If these are not obtainable, we should use milk, albumen, or even water (to dilute the acid). We may send to the apothecary for magnesia usta. The rule is to give the alkali until the vomited matters have an alkaline, or at least neutral reaction. The further treatment should be the counteraction of the severe pain, collapse, and the stomato-œsaphago-gastro-enteritis.

CARBONIC ACID—ACIDUM CARBONICUM.

Carbonic acid, Co_3H_2, cannot be isolated as such, because it immediately decomposes into its anhydride and water.

Carbonic-acid anhydride is a constant component of atmospheric air, which contains 0.04 vol. proc. of it. It is colorless, soluble in water, a condensible, non-inflammable gas, in which all burning bodies are immediately quenched, and has a sharp acid odor and taste.

PHYSIOLOGICAL IMPORTANCE AND ACTION.

Carbonic acid, in its relation to the animal body, occupies such a peculiar position that we shall give it especial consideration. It has the effect of a weak acid, as well as those of a stimulating and later paralyzing agent, like alcohol.

Carbonic acid is a constant component of the animal organism; is derived to a slight extent from the air, also from articles of diet (carbonates and alkaline salts of the vegetable acids), but for the most part from the tissues and blood, as one of the most important products of oxidation and tissue metamorphosis.

It is taken into the blood by the capillaries from the tissues in which it is formed. In arterial blood there are, on an average 30 per cent, in venous blood 35 per cent, by volume of carbonic acid.

In the blood carbonic acid is to be found partly in the blood-corpuscles as hæmoglobin alkali (Pflüger, Zuntz), partly in the serum as sodium carbonate, and again in combination with globulin and and alkali (Setschenow). In the serum Co_2 is more firmly bound than in the red blood-corpuscles; the latter withdraw the carbonic acid from the serum, this action being greater the more oxyhæmoglobin they contain. According to Bert, carbonic acid does not exist in a free state, either in arterial or venous blood, or in the tissues, but generally in combination with an alkali. In carbonic-acid poisoning the dangerous symptoms generally set in when the alkalies of the blood are entirely saturated, and death takes place at the moment when the limit of saturation of the tissues has been reached.

It escapes from the blood in the process of respiration through the lungs. In addition to this, also through the skin and mucous membranes.

The process by which carbonic acid is given up by the tissues to the blood, and by the blood to the atmosphere, is termed by Donders a process of "dissociation;" this he

defines to be, in a broad sense, the decomposition of the molecules of a body into two or more molecules of a less complicated structure. If, however, the original conditions of tension and temperature return, the separate molecules can unite again into the original molecule. It is an important consideration in this process that it always occurs under the influence of a certain temperature without the intervention of another body. The above-mentioned salts, and perhaps a few of the albuminoid bodies of the blood, are the agents of "dissociation" for carbonic acid, which give it (Co_2) up to the air, because in these the carbonic acid exists at a lower tension than in the air (Pflüger, Wolfberg), and take it up from the tissues, because there the tension of the carbonic acid is greater than in them.

Although carbonic acid is purely an excrementitious material, and life can only be maintained as long as it is gotten rid of by the body, it would be erroneous to deny it any further function in the organism. Even apart from the hypothesis of Pflüger, that animal warmth, and indeed life, are dependent upon the formation of carbonic acid internally, it appears that certain animal functions which are necessary to life, such as respiration more especially, find their chief stimulus in the normal changing quantities of carbonic acid present in the body. It is believed that the toxic symptoms which occur from the inhalation of large quantities of Co_2, disturbances in the respiratory, vagus, and vaso-motor centres, are only an exaggeration of the processes taking place physiologically and normally in the body.

Inspiration of Carbonic Acid.—Formerly no poisonous action, as such, was ascribed to carbonic acid, because of its intimate relationship to the processes of life, but the toxic symptoms which occurred after inhaling of carbonic acid, were ascribed to the want of oxygen. This explanation, however, is not tenable.

The effect of inhalation of carbonic acid (according to the experiments of Friedländer and Herter on rabbits) naturally vary according to the quantity and percentage of atmospheric air inhaled with it. 1. When the mixture contains about 20 per cent of carbonic acid, the phenomena are those of stimulation, more rapid respiration, and increased blood-pressure. Even after one hour's inhalation no symptoms of poisoning occur. 2. When the mixture contains 30 per cent of Co_2, these symptoms of irritation

are followed very rapidly by slowing and weakening of the respiration, sinking of the blood-pressure, weakening, and finally suspension of the voluntary and reflex movement; lowering of temperature, and finally, after hours of inhalation, death. 3. With very large quantities of Co_2, the stimulating effect lasts but a few minutes, followed very rapidly by symptoms of paralysis of the voluntary and reflex movements. Death results in about half an hour, from increased paralysis of respiration and heart's action. The irritability of the motor nerves and muscles is not diminished; Co_2 only acts upon the nerve-centres.

A closer consideration of these phenomena teaches that carbonic acid exerts an injurious effect upon tissue metamorphosis, because even if oxygen be present it prevents its absorption, partly by weakening the respiration, and partly by diminishing the power of the tissues to use up the oxygen, which power, indeed, is entirely suspended before death.

The dyspnœa observed with Co_2 poisoning is the result of the severe irritation of the respiratory centre, which also affects the motor centres of the spinal cord. The slowing of the pulse is the result of an irritation of the inhibitory centre of the brain, and is absent only when the vagi are cut. The increased blood-pressure is due to a contraction of the peripheral arterioles, and is the result of an irritation of the vaso-motor centres. Traube and Hering have found that these three functions increase and diminish simultaneously, even in ordinary life (normally). It is probable, although not positively determined, that carbonic-acid gas tends to increase the peristaltic movements of the intestine (Nasse). The peripheral nerves, as has been already shown, do not seem to be influenced.

Friedländer and Herter have performed a series of experiments, with a view of determining what portion of the disturbances produced by the inhalation of carbonic-acid gas is due to that gas, and what portion is due to the lack of oxygen. 1. The dyspnœa, increase of blood-pressure, and diminution of oxygen are the results of carbonic-acid poisoning as well as of the lack of oxygen. 2. The diminished excretion of Co_2 is peculiarly the results of the Co_2 poisoning. 3. The irritation symptoms (neurotic) occurring just before death are due to the lack of oxygen. It therefore necessarily follows that the symptoms, both of acute suffocation (as from strangling or hanging) as well as

chronic suffocation, are due more to the lack of oxygen, and only to a slight extent the consequence of the carbonic acid.

In *drinking water rich in carbonic acid* the effect upon the mucous membranes is like that of a weak acid, there being a sharp acid taste—a feeling of warmth in the stomach; while thirst is better allayed, so that less water need be drunk.

The assertion that the saliva and gastric secretion are increased, and appetite improved, need further confirmation: if these results do follow, it is only to a very slight extent. So also the increase of intestinal peristalsis does not follow when carbonic acid is directly introduced into the intestine. Its influence upon abnormal fermentative processes going on in the stomach is very slight, and in no way to be compared to that of alcohol or many derivatives of the benzol series. But yet the lower forms of organisms die in carbonic acid quite rapidly, even if oxygen in quantities sufficient to support life be present (Rossbach). The chief effect seems to be that carbonic-acid gas, developed in the stomach, when eructated, carries with it other decomposition and intestinal gases. The excretion of urine is increased, so that more fluid passes out with the urine than was introduced with the carbonic-acid water. Quincke says this is probably owing to the fact that under the influence of Co_2 the stomach and intestinal canal absorb fluids more rapidly than normally.

This method of administering carbonic acid can never result in general poisoning, for any excess that may reach the blood can be gotten rid of with the normal respiratory movements. Our own experience does not confirm the idea that a few bottles of soda-water produce a feeling of lightness, and a condition somewhat resembling mild intoxication, the only result of the large quantity of cold water thus taken is pressure in the stomach and difficult digestion.

Effects upon the Skin.—The effect of a stream of carbonic acid upon a circumscribed portion of the skin is a temporary feeling of cold, with a resulting hyperæmia and feeling of warmth; finally, it is said, that portion of the skin becomes entirely insensible. The same symptoms, together with hyperidrosis, occur when the whole body is immersed in an atmosphere of carbonic-acid gas, provided, however, that pure air only is supplied to the respiratory organs. In

carbonic-acid-water baths we have the combined effect of the water at an elevated temperature and the carbonic acid. Paalzow-Pflüger, however, on the strength of experiments performed upon himself and on rabbits, denies that even the slightest cutaneous irritation or redness ever occurs; nor can we thus effect any increase in tissue metamorphosis; the opposing statements of physicians at the bathing waters are probably due to the fact that the effects of alkaline salts contained in these waters were supposed to result from the carbonic acid.

Carbonic acid, like all gases, is absorbed into the blood by the skin, and if the absorption be not too great, or continued for too long a time, the lung can get rid of the excess. If too long continued, however, the animals die from carbonic-acid poisoning, even if pure air be supplied to them for breathing purposes (Röhrig).

Effect upon Wounds, and Tissues separated from the Body.—Upon wounds carbonic acid produces a burning sensation, increased redness, and resulting anæsthesia. Blood shaken up with carbonic acid rapidly becomes venous; gradual decomposition of the hæmoglobin gives rise to a brown discoloration, and streaks of acid hæmatin.

Muscles placed in carbonic acid rapidly become stiffened. This effect of carbonic acid on the blood and muscles never occurs in animals poisoned with carbonic acid: the death of the animal occurs long before the quantity of carbonic acid necessary to produce these alterations has entered the body.

The ciliary movements become paralyzed under carbonic acid.

THERAPEUTIC APPLICATION.

Internally carbonic acid is very much used—mostly in the form of carbonic acid-water, which contains the gas in so-called solution. Carbonic-acid gas is also evolved when sodium bicarbonate is administered, but here its action is secondary to that of the salt. Carbonic acid is contraindicated, in any considerable amount, in those cases in which there is any active congestive condition either of the brain or lungs, and where the heart is readily thrown into a condition of irritation.

Water impregnated with carbonic acid is very much used as a cooling drink and for alleviating thirst. In the last few years this application has been very much extended, so

that drinks of this kind, in summer, have become almost indispensable. They are also very much used as drinks for fever patients, subject, however, to the above contraindications. This gas, in the form of an effervescing mixture, has become a popular remedy for conditions of excitement, combined with palpitations. Imagination, however, has much more to do with this effect than carbonic acid.

Furthermore, carbonic acid is used against various affections and symptoms on the part of the stomach. First against the nausea, which is the result of too much indigestible food in the stomach, or of excesses in drinking. In these cases relief results partly from the eructation, with which the fermentation gases in the stomach are also gotten rid of, and partly, it is said, because Co_2 accelerates the passage of the stomach contents into the intestine. It is also useful in severe vomiting, which occurs either as an accompaniment of organic disease of the stomach or gastric mucous membrane, or merely as functional troubles, as for instance in pregnancy or as a result of hyperemesis after strong emetics. Its utility in these cases may perhaps be explained by a diminution in the abnormal irritability of the vagus nerves. To how great an extent carbonic acid is directly curative in *chronic gastric catarrh* we are unable to say, since it is always taken in the form of a drinking water, which contains the salts of the alkalies and alkaline earths (Ems, Vichy), and we cannot estimate what part the free gas takes in the effect. But experience has shown that those springs which contain free carbonic acid are in fact more useful than others in these cases. The mineral waters also, in the prescribing of which we expect a result chiefly from the minerals which they contain,—as for example iron,—fulfil their purpose better, especially in patients with a delicate stomach, if they contain in addition free carbonic acid.

Carbonic acid plays an important part in the treatment of various affections of the respiratory apparatus. In tuberculosis and in phthisical conditions especially, inhalations of carbonic acid were even formerly recommended, and, as it is reported, with good results. We can, however, sum up the results of more recent experience in saying that these inhalations should be carefully avoided in tuberculosis; they are injurious, and do not benefit even symptomatically. The former custom of advising patients with phthisis to breathe the air of stables, etc., has been given

up, but the carbonic-acid waters are still very much used in the treatment of phthisis. These should be avoided, however, if there be a tendency to hæmoptysis, congestion of the lungs, or directly febrile and inflammatory conditions; even the use of Seltzer water is to be avoided in cases in which hæmoptysis is present (because of the influence of carbonic acid upon the action of the heart). Those carbonic-acid waters also having a higher temperature, like that of Ems, should be avoided in tuberculosis. So that the only water to be used is the Seltzer water, which is generally given together with milk. That is to say, carbonic acid is of no recognized importance in the treatment of phthisis.

Such is not the case, however, in simple chronic laryngitis and bronchial catarrh; for here indeed the use of Co_2 waters is beneficial. We should give either the Ems or Seltzer water, either alone or together with milk and whey.

In what way the carbonic acid exerts a favorable effect upon the catarrh is not determined; perhaps the Co_2 is entirely inactive, and the whole of the effect is due to the amount of alkali, water, etc., thus administered. As to the utility of inhalations of the gas, experience is still contradictory, so that no decided opinion can yet be expressed. This only is positive, that carbonic acid when directly applied produces irritation, and that therefore it must be avoided in inflammatory processes; furthermore, the contraindications laid down above hold good for the inhalation of the gas even more than for its administration by the stomach, because it is much more readily absorbed through the lungs. These inhalations have been frequently recommended in chronic angina and follicular pharyngitis, so that, if other means fail, they can be tried at least in these conditions.

The recommendation of carbonic acid as a diuretic in dropsy and in cystitis is inexplicable, and it is doubtful if its utility is not due rather to the alkaline salts introduced with it (the waters of Ems and Vichy being generally used for these purposes).

Carbonic-acid is also very much used externally in the form of baths and douches, spring waters rich in carbonic-acid being generally used for these purposes. But these again contain other substances in addition to the carbonic-acid (Rehme, Nauheim, Ems, and Kissingen). They have also been very much used in chronic rheumatism of the muscles

as well as the joints. Here, again, we would simply repeat the contraindications to the use of Co_2 waters above stated, remarking that if these contraindications are not present we may use indifferently in these affections (indifferent thermals, sulphur thermals, sodium-chloride thermals, etc.). The same remarks will hold good concerning the use of these baths in paralysis. They have shown themselves of especial service in the so-called rheumatic or peripheral paralyses, several cases of which they are said to have cured. In *old functional or "rheumatic" neuralgias*, carbonic-acid baths have proved themselves very valuable; in such neuralgias as sciatica, for instance, and the neuralgias as well as cutaneous anæsthesia of hysterical patients.

Finally, these baths are of great utility in chronic eczema and psoriasis. All these applications are purely empirical, inasmuch as we are unable to explain the method of the action of these baths.

Carbonic acid is very much used as a gas douche, or dissolved in water as a local douche in the diseases of the genital organs of women, but their utility in these affections is very much overestimated. Experience has shown that it is of greater benefit in the ulcerating processes of these organs, since healing is thus hastened, or when this is impossible, the putrid odor is diminished. These douches are spoken of very highly in amenorrhœa, suppressio mensium, and sterility, without any distinction as to the cause of these affections in individual cases. The carbonic-acid douche is entirely useless, however, in those cases in which deep disease of the uterus or misplacements are the cause of the above symptoms; on the other hand, it is often of great benefit in cases in which no objective pathological condition exists in the genital organs, and the symptoms appear to be due to "atony of the uterus;" or in chronic metritis, when there are no acute inflammatory conditions present. So also in "neuralgia of the uterus" some good results have been obtained, and sometimes also in leucorrhœa.

The carbonic-acid douche is also useful in chronic coryza and otorrhœa if there be no osseous disease behind these conditions. Old ulcers also which have withstood all treatment have seemed to heal under the influence of carbonic acid—especially ulcerations in which the granulations are indolent and torpid; it is questionable, however, whether this remedy is to be preferred to others. Carbonic acid is injurious to ulcers in which there is a tendency to hemor-

rhage, which are very painful, and which readily undergo inflammation. As a deodorizer in putrid wound-surfaces it is in no way superior to other substances which are more readily applied.

Preparations.—When carbonic acid is to be used internally, we generally give carbonic-acid waters, all of which, however, also contain other ingredients. Selters and Schwalheim exert the purest CO_2 effect; so also efferverscent mixtures and powders. Carbonic acid is also contained in soda-water and other effervescent drinks (champagne, Berlin white beer, etc.) As a pleasant drink, soda-water and Selters are generally ordered.

Effervescent Powder. Pulvis aërophorus (compare page 27).—When water is added, sodium tartrate is formed and carbonic acid set free. When it is thus dissolved in water before it is taken a large part of the carbonic acid escapes before it reaches the stomach.

It is therefore best to take the powder dry and drink water afterwards. Effervescent powder is the preparation which is generally given when we wish to allay the nervous excitement and palpitation. It is given in teaspoonful doses. Pulvis aërophorus anglicus—English effervescent powder. Pulvis aërophorus laxans.

Another form in which carbonic acid is applied is in the form of saturations; and here the question is only as to the effect of a salt of a vegetable acid (compare page 27.)

The Potio Riveri, formerly much used, which consisted in taking a potassium-carbonate solution in tablespoonful doses, and adding from ½–1 teaspoonful of lemon-juice, is to be avoided. For, although it is true that the carbonic acid is set free in the stomach by this procedure, yet it is set free in such large quantities that it produces a disagreeable flatulence. A preparation consisting of 4 parts of citric acid, 190 parts of distilled water, and 9 parts of sodium carbonate, which has again become officinal, has not this disadvantage, but, on the other hand, it is likewise only a "saturation."

THE ALCOHOLS.

ALCOHOL—ETHER—CHLOROFORM—CHLORAL HYDRATE—AMYL-NITRITE.

A VERY large portion of the methane or marsh-gas series, to which the alcohols and their derivatives belong, resemble each other in that they all have an intoxicating and anæsthetic effect upon the organism; so that they are allied not only chemically, but physiologically.

We would be unable to judge from the physical and chemical properties of any of these substances that they must necessarily exert an intoxicating and anæsthetic effect upon the animal body. The older theories of Nunneley, Aran, and Ozonam, which maintained that such a connection exists between the chemical, physical, and physiological properties of different substances, have been shown to be faulty; the fact, however, that the methane derivatives as a class, together with their chloride combinations, have so many anæsthetics in their number, would seem to show that there is such a connection—which, however, has not yet been established.

It is furthermore very probable that all these substances resemble each other in their action upon the organic substrata of the animal body; so that the similarity of the symptoms depends upon a similarity in the chemical relations. But this action is not well understood; although many facts make it probable that the protagon or lecithine, the albuminoid bodies and fats of the nerve-substance, are the substances primarily affected by the intoxicating agents. The difference between the various agents is less due to any variation in their physiological action than to a higher or a lower boiling-point, greater or less volatility, as well as the manner of their introduction into the body. The more volatile, which enter the body by inhalation, have a much more temporary effect than those which are less or not at all volatile, and which are introduced hypodermically or by the stomach.

The practical utility of these substances depends very much upon their physical properties. The bodies which at ordinary temperatures are in a gaseous condition are very

inconvenient for application, because a gasometer would be necessary for this purpose, and because their effect is very evanescent; if we were to employ them as anæsthetics, only operations lasting a very short time could be performed. In this last respect those *fluid* bodies of this group which have a low boiling-point and which rapidly evaporate, resemble those which are gases, although the effect is longer in duration; while, on the other hand, those bodies having a very high boiling point take a very long time to produce anæsthesia. Chloroform holds its popularity because its boiling-point is just at a mean between the two (62° C.), while the density of its vapor is neither too high nor too low (4.199). Ether, which has been recommended and preferred by many for the same purpose, has too low a boiling-point (35° C.), while the density of its vapor is 2.565.

GENERAL CONSIDERATIONS CONCERNING THE MEMBERS OF THIS SERIES:

Before taking up specially those of the members of this group which are most used therapeutically, we consider it best to make a few remarks concerning those of the *methane derivatives which up to the present time have been found physiologically active.* A large number of these bodies belonging to this group have not been used at all.

I. The *ethane or hydrocarbons of the marsh-gas series*, $C_n H_{2n+2}$, produce unconsciousness and anæsthesia when inhaled, but not when injected hypodermically, even in fatal doses.

Methane—Methyl hydride CH_4; Ethane—Ethyl hydride, C_2H_6; Propane—Propyl hydride (?), C_3H_8; Butane—Butyl hydride C_4H_{10}, when inhaled with sufficient oxygen, are active (Hermann). These gases produce anæsthesia very rapidly when oxygen is excluded (Richardson).

Pentane—Amyl hydride, C_5H_{12}. According to Richardson, when inhaled with sufficient oxygen it has an anæsthetic effect in a few minutes. He considers it when mixed with ether the best agent for the production of anæsthesia for small operations.

Octane—Capryl hydride C_8H_{18}. First having an exciting action for a long time and producing vomiting; finally acting as an anæsthetic like chloroform.

Petroleum Ether and Petroleum.—A mixture of several of the above ethanes (butane, pentane, hexane) is obtained by the distillation of the American petroleum, and is known as petroleum ether. Like its components, it has an anæsthetic action, and is often used as an external application in painful conditions (rheumatism, etc.). It is, however, entirely superfluous. American petroleum of course contains many more such ethanes (off. name, Oleum Petræ italicum). The percentage of these ethers contained in petroleum being a variable one, its physiological action must necessarily be variable and uncertain.

According to Lassar, petroleum is not at all injurious to animals which live for days in an atmosphere impregnated with it. Nor is it injurious when given in moderate quantities internally (rabbits,—15 ccm.). On the other hand, rabbits which have been painted with it a few times, or even only wet with it, although at first they show no alteration in the

urine, yet later on there is a resinous body formed, which, since it yields a precipitate with nitric acid, might readily be taken for albumen were it not that it redissolves again in alcohol and ether; later still peptone appears, or at least a body reacting like peptone; and finally albumen. The kidneys remain unchanged, the epithelium intact, while the vascular system of the kidneys remains without a trace of inflammation, either during the balsamuria or the peptonuria. On the other hand, during the albuminuria inflammatory anatomical changes occur, similar to those characteristic of animals poisoned by chromic acid. The proof that the resinous bodies formed in the organism by the oxidation of the petroleum, destroy the integrity of the renal epithelium, can only be shown by analogy (copaiba balsam, for example). Simple anatomical investigation, however, will show that petroleum and substances similar to petroleum—that is to say, in physical properties—are absorbed by the unbroken skin, and taken up into the circulation. (Compare what is said under the Fats.)

Inhaled in large quantities, petroleum produces a choking sensation, and, when taken internally, local symptoms of irritation and collapse. No intoxicating or anæsthetic effect is observed.

Therapeutically, it is useless for internal application; so also it is superfluous for external use where it has been applied in various affections, like oil of turpentine. We have better remedies than petroleum for the treatment of scabies, for it is not as positively injurious as the balsams (balsam of Peru, styrax, etc.) to the parasite, and therefore not as effective.

II. *The monatomic substitution products of ethane, and the derivatives of the univalent alcohol radicals* (alkyle), C_nH_{2n+1}, give us an uncommonly large number of intoxicating and anæsthetic agents.

1. The following members of the homologous series of the alcohols have hitherto been investigated:

*Methyl alcohol, CH_4O (wood spirits);
Ethyl alcohol, C_2H_6O (spirits of wine);
*Propyl alcohol, C_3H_8O;
*Butyl alcohol, $C_4H_{10}O$;
*Amyl alcohol, $C_5H_{12}O$ (fusel oil).

The action of all these is exactly similar to that of the best known of the group—common alcohol or spirits of wine, but in an increasing series; so that methyl alcohol is the weakest and amyl alcohol the strongest—30 times as strong as methyl alcohol and 15 times as strong as ethyl alcohol (Cross). The anæsthetic effect of the higher members of the series also lasts for a much longer time than that of the lower members (Richardson), so that the evil effects experienced from drinking liquors containing much fusel oil is due to the relatively stronger action of the latter rather than to any difference in physiological effect. Therapeutically, ethyl alcohol only is used. We shall discuss this thoroughly on page 345.

2. The following halogen compounds of the univalent alcohol radicals have been investigated; these are mostly colorless fluids, having an agreeable, sweetish odor.

*Methyl chloride, methane monochloride, CH_3Cl, is a gas, which, when inhaled or given internally in the shape of a saturated solution, produces an anæsthesia which is quite durable (Richardson).

*Ethyl chloride, ethane monochloride, C_2H_5Cl, has an effect similar to that of ethyl ether, which is presently to be considered (Richardson);

a fluid containing ethyl chloride and many other similar preparations has hitherto been used for smelling. This fluid is the spiritus ætheris chlorati (spir. salis dulcis).

*Amyl chloride, $C_5H_{11}Cl$, a fluid anæsthetic.

*Ethyl iodide and bromide, the latter (C_2H_5Br), according to Rabuteau, produce anæsthesia more rapidly. Not so positively determined, however, is the anæsthetic action of:

**Methyl* and *amyl* iodide and bromide.

3. Of the *ethers*—that is, the compounds of double alcohol radicals with one atom of oxygen—we are familiar with the following:

*Methyl ether, $C_2H_6O = CH_3.O.CH_3$ (metameric with ethyl alcohol), is a gas which Richardson considers the best anæsthetic; the inconveniences attending its application, however, prevent its becoming generally useful.

Ethyl ether, $C_4H_{10}O = C_2H_5.O.C_2H_5$, is the most important anæsthetic agent next to chloroform, and will be discussed after this drug.

*Amyl ether—also an anæsthetic. The other ethers have not been investigated, nor have their products of substitution by a chlorine atom.

4. *The compound ethers*, also, which are formed by mixing the alcohols with strong acids in such a manner that the alcohols are converted into the corresponding salt of the alcohol radical and the acid (water being separated from the alcohols), are also, as far as known, anæsthetic and intoxicating agents.

*Ethyl nitrate. The nitrate of ethyl, $C_4H_5.O.NO_2$, has a pleasant odor; is slow in producing anæsthesia, and destroys life rapidly (Chambers).

*Ethyl nitrite, $C_2H_5.O.NO$, boils at 16° C., is readily explosive, and when inhaled in small quantities causes headache and asphyxia; in larger quantities (10 drops in animals) severe convulsions with paralysis and death result (Richardson and Flourens). It does not seem to produce a useful anæsthesia; it is therefore useless, for we have for the production of its other effects the *spiritus ætheris nitrosi* of the Pharmacopœia, which, in addition to ethyl nitrite, contains ethyl alcohol, aldehyde, acetic ether, and acetic acid.

Amyl nitrite, $C_5H_{11}.O.NO$. This drug, which is to be discussed later, has remarkable effects upon the vascular system.

Methyl acetate, ethyl acetate, and amyl acetate are said to have effects similar to those of ethylic ether, although there is a lack of accurate physiological modifications concerning these preparations. The therapeutic application of acetic ether, ether aceticus (ethyl acetate) is therefore only a volatile smelling agent.

5. *The trisulphocarbonates*, the sulphur combinations of the alcohol radicals in the organism, are decomposed into carbon sulphide and hydrogen, the physiological effects of these latter substances thus appearing (Lewin). Xanthic acid is decomposed in the body into carbon bisulphide and alcohol, and, like the former, produces anæsthesia. The xanthates of the alkalies are excellent preservative and disinfectant agents, and in every way can replace the carbon bisulphide which is unfitted for medicinal application (Lewin).

Carbon bisulphide, carboneum sulphuratum, CS_2, whether used for a long or a short time, has an effect like that of chloroform, but is not used therapeutically because of its disagreeable taste.

6. *The alkyl-amines*—that is to say, ammoniacs in which one or more of hydrogen are replaced by an equal number of alcohol radicals, as for

example, trimethyl-amine, etc., are chemically and physiologically similar to the ammoniacs, and were discussed under this head.

7. *The alkyl-nitres*, nitro-ethane, $C_nH_{2n+1}NO_2$, that is to say, the nitrous ethers, isomeric with the nitril compounds of the alcohol radicals, have, according to Filehne and Schadow, the following action:

*Nitro-methane, $CH_3.NO_2$, and nitro-ethane, $CH_3.CH_2.NO_2$, produce, in cold-blooded animals, analgesia of central origin, motion and "muscular sense" being retained; in large doses they cause complete paralysis of the central nervous system, from which recovery, however, may take place.

*Nitro-pentane, $C_5H_{11}NO_2$, produces in cold-blooded animals at first a characteristic restlessness and finally light anæsthesia; this is followed by an attack of delirium, and later of convulsions originating in the medulla oblongata; finally, there is exhaustion, from which recovery is still possible. If the poisoning, however, be continued, generally paralysis of the nerve centres of the brain and spinal cord, followed by a paralysis of the intramuscular nerve-fibres like that resulting from curare. In warm-blooded animals (rabbits) there are epileptiform convulsions, intestinal cramps, with increased excretion of urine and fæces, salivation, and enlargement of the pupils. The blood-pressure undergoes periodical variations of a peculiar character, depending upon the interference of two exciting actions, the first of which has a tendency to elevate the blood-pressure, while the later one depresses the blood-pressure.

*8. In reference to the arsenic combinations of the alcohol radicals, see page 208.

*Mercurial compounds of the alcohol radicals. Such are the mercury dimethyl, $CH_3.CH_3.Hg$, and diethyl, $C_2H_5.C_2H_5Hg$. We have reports of chronic poisoning of two chemists with this substance; symptoms were those of nervous disturbances (blindness, deafness, and general loss of sensibility), leading gradually to well-defined symptoms of mercurial poisoning.

III. *Of the diatomic substitution products of ethane and derivatives of the bivalent alcohol radicals (alkene)*, C_nH_{2n}. These have not been thoroughly investigated physiologically. Most of these, however, have an anæsthetic action principally.

*1. Of the aldehydes (alcohol dehydrogenatum) only ethyl aldehyde (aldehyde), C_2H_4O, the first oxidation product of ethyl alcohol and ether, is known as a cerebral irritant and anæsthetic, which readily causes asphyxia and death (Boutigny, Poggiah, Lallemand, and others).

2. Of the haloygen compounds of the adelhyde radicals the following two are known, and partly used therapeutically:

*Methane dichloride (dichloromethane—methalene chloride), CH_2Cl_2, is a good anæsthetic; it is a fluid similar to chloroform, and having no advantage over the latter as Richardson believes (Nussbaum, Jüngken).

*Ethidene chloride (ethylidenum bichloratum), $C_2H_4C_2$, or $CH_3—CHCl_2$. This gas, according to Steffan, has an effect similar to that of nitrous oxide, producing rapid and agreeable anæsthesia; recovery takes place in a few seconds, leaving no disagreeable sequelæ; this gas would, therefore, seem to be a good anæsthetic for minor operations, and for use in children. It has a pleasant odor, like that of chloroform.

3. Of the ketones, we are familiar only with *acetone (dimethylketone), C_3H_6O, an anæsthetic and intoxicating agent, which has a stronger action than alcohol and much weaker than ether or chloroform (Kuss-

maul). Peters has found acetone in the blood and urine of diabetic patients.

4. Of the glycol derivatives, we are only familiar with *amyl, C_5H_{10}, a fluid having a disagreeable odor similar to chloroform, and exerting, even when inhaled, a dangerous action (Spiegelberg).

Ethene chloride (Dutch liquid, known since 1795), Ethylenum chloratum, $C_2H_4Cl_2$, or CH_2Cl-CH_2Cl, isomeric with ethidene chloride, a fluid which has the odor and action of chloroform; recommended by Nunneley as a general anæsthetic; used at the present time either pure or with ointments as embrocations in rheumatic and other painful affections.

IV. *The triatomic substitution products of ethane and derivatives of the trivalent radicals*, C_nH_{2n-1}.

1. Among the formyl compounds we have the best of all anæsthetics, namely:

Formyl trichloride, or *chloroform*, $CHCl_3$, to be discussed thoroughly later on. Also

*Formyl tribromide, or *bromoform*, $CHBr_3$, which has a higher boiling point (150°) than, but similar effects and perhaps of equal value with chloroform.

Formyl triodide, iodoform, CHI_3. While the two foregoing are fluids, this is a shining, yellowish, soft powder, having a saffron odor, and crystallized in scales. Not easily soluble in water, acids, and alkalies, but readily in ethers, fats, and ethereal oils. It contains more than $\frac{9}{10}$ of its weight (90.07 parts by weight) of iodine; it has, however, a mild, non-caustic taste.

Whether iodoform dissolved in the fats of the organism reaches the circulation as such (Binz), or is changed into iodine albumen (Högyes), is still a disputed point. It is certain, however, that it is not again excreted as iodoform, but probably as sodium iodide; which proves that the iodine of the iodoform is set free in the organism. Locally, it is entirely non-irritant to the skin and mucous membranes. Even large quantities can be absorbed from the stomach, intestine, and peritoneal cavity without causing any congestion or hyperæmia, which is certainly a great advantage for this strong iodine preparation. Inhalations of iodoform have no anæsthetic action (Binz); given internally or subcutaneously (0.3–1.4 to 1 kilo. of bodily weight), it produces in dogs and cats marked symptoms of narcotism (drowsiness and diminished reflex irritability). In rabbits narcotism is not produced even by fatal doses. To men we (Rossbach) have given 1.5–2.0 of iodoform daily without any visible effect. If the qualitative action upon men and dogs were relatively the same, the narcotic dose for a man weighing 60 kilos. would be 60.0–80.0 (Högyes). Death from fatal doses (4.0–5.0 in medium-sized dogs) occurs with general wasting, and paralysis of the heart and respiration, unaccompanied by convulsions. In cats which were thus killed fatty degeneration of the liver, heart, and kidney were found (Binz). Oberlander observed the following toxic symptoms in one case after administering 0.8 grm. of iodoform daily for seven days (altogether 5.0 grms.), and in another case, after giving 42.0 grms. of iodoform in eighty days: Dizziness, vomiting, and drowsiness, lasting several days, interrupted by temporary conditions of irritation, delirium, severe headaches, anxiety, and twitching of the facial muscles.

The action of iodoform can be looked upon as a protracted iodine action. It is absorbed and excreted more slowly than potassium iodide;

it is possible, however, that the carburetted hydrogen contained in the molecule imparts some of its influence to the general effect.

We expect to see the therapeutic uses of iodoform, internally, clearly demonstrated during the next few years, for it is now being tried in a large variety of conditions. As yet we are unable to state with any positiveness the conditions in which it should be used. The statement of Moleschott, that it hastens absorption of serous exudations, and that it can even cure acute hydrocephalus, needs confirmation. So also the results said to have been obtained from its use in neuralgias of various nerve-tracts (with the exception, perhaps, of syphilitic neuralgias), articular neuralgias, cardialgia, etc., do not appear to us to be any more reliable. We ourselves have never seen it exert any influence upon the heart's action in valvular lesions, in which it has been recommended. Iodoform seems to be most effective in venereal ulcers, although even here it is no longer indiscriminately used in soft and hard chancres, and the most various tertiary affections; so Sigmund recommends it only in putrid necrotic processes, ozœna, etc. Internally administered, it does not seem in any way preferable to potassium iodide. In other forms of ulcers and in skin diseases it is not more effective than other remedies. It has not yet been proved that it is more effective in glandular enlargements than the tincture of iodine. Rossbach has not seen a noteworthy diminution of such a swelling under iodoform in even a single case. Internally, 0.05–0.3 several times daily (=2.0) in powder, pill, and alcoholic or ethereal solutions. Externally it may be used as iodoform collodion (1 to 15) or in the form of ointment (1 to 10–15). Also the

*Carbon tetrachloride or tetrachloromethane, CCl_4, a colorless oil, having the odor of ether and acting like chloroform. It produces paralysis of the heart very readily.

2. The allyl compounds, to which group belong the active ingredients of oil of mustard, seem to differ from the other compounds of this group in many ways, especially in the severe local irritation which these bodies produce.

3. Of the glycerine compounds we are familiar with the haloid derivatives of glycerine.

*The di- and trichlorohydrine, $C_3H_5.Cl_2.OH$ and $CH_2Cl.CHCl.CH_2Cl$, occupying, according to Hermann Rowensky, a position between chloroform and chloral, as far as their hypnotic power is concerned. They can never come practically into use because of their inflammatory action upon the gastric mucous membrane, and also because of their volatility.

Of the ether-like derivatives of glycerine, we ourselves have investigated *epichlorhydrine, C_3H_5OCl. When inhaled, this causes severe irritation of the respiratory passages, so that in rabbits death results from the stopping up of the nasal passages; injected subcutaneously, it causes anæsthesia, paralysis, and finally death.

V. *Derivatives of the quinquivalent and over, hydrocarbons.* Of these the chloral hydrate, $CCl_3.CH(OH)_2$, which we will consider later on, is of especial importance. Allied to this is the poisonous

*Bromalhydrate, $CBr_3.CH(OH)_2$, which at first produces symptoms of irritation in animals, such as hyperæmia and hypersecretion of the respiratory mucous membrane; later on, anæsthesia with drowsiness; in dangerous cases, dyspnœa and cyanosis (Steinauer).

*Butyl chloral, or, as it was formerly called, croton chloral; this was recommended by Liebreich in the belief that it is decomposed in the blood into bichloride of allylene and formic acid, and as dichloride of

allylene has an effect similar to ethedene chloride (anæsthetic); this, however, is denied by Mering. When the latter injected the trichlorcrotonate of sodium, which in diluted alkaline solutions is decomposed into bichloride of allylene, into rabbits, no effect was seen; even the vapor of the bichloride of allylene when inspired by animals produces no anæsthesia. The effect, therefore, cannot be due to decomposition of this substance. The assertion of Liebreich that butyl chloride in the beginning produces anæsthesia of the head, and does not affect the rest of the system until later on, contradicts Mering: it produces both in healthy and sick people a similar narcotism, and anæsthesia, although slighter in degree to that produced by chloral; nor can any specific action upon trigeminal neuralgia be shown, and against these morphia is much more effective. Some other observers assert that there is such an effect produced in neuralgias, especially of the head. We ourselves (Nothnagel) have had no results from its use in certain old cases. The drug has been used as a local application in carious teeth. From 0.1–0.3 pro dosi, in powder, pill, or mixture.

* Trichloro-ethyl dichloride, C_2HCl_5 (the principal component of Aran's ether anæstheticus), is said to produce a good local anæsthesia; the results of extended trials are still wanting.

*Perchloro-ethane (carboneum sesquichloratum), C_2Cl_6, is said, like camphor, the odor of which it also has, to produce an excitant action.

Alcohol—Spirits of Wine.

Alcohol—spiritus vini—is the next to the lowest member of the single acid alcohols, and is known as ethyl alcohol, C_2H_6O (compare page 340).

It is produced from every saccharine vegetable juice, under the influence of the yeast plant by fermentation, which goes on until the sugar has entirely disappeared and alcohol has been produced in its place. One molecule of grape sugar is converted into two molecules of alcohol, and two of carbonic acid.

$$C_6H_{12}O_6 = 2C_2H_6O + 2CO_2.$$
(Sugar) (Alcohol) (Carbonic acid)

In addition there are formed small quantities of succinic acid, glycerine, and members of the alcohol series which are rich in oxygen, (fusel alcohol and fusel oil).

By repeated distillation, these substances, together with water, are gotten rid of. After a second distillation there is still left 10 to 15 per cent of water, which cannot be driven off by further distillation, but only by means of substances which absorb water, as for example anhydrous baryta.

Absolute and pure alcohol, free from water, is a colorless, agreeably smelling fluid, which boils at 78.5, takes fire readily, and burns with a blue flame. It has a strong affinity for water, and absorbs it greedily from the air; when mixed with water the temperature is increased and the volume diminished.

Absolute alcohol at 20° C. has a specific weight of 0.7895; on the addition of water this is increased, but not in proportion to the quantity of water.

Alcohol is a good solvent for fats, fatty acids, resins, alkaloids, and iodine.

A more accurate description of the various alcohol preparations will be given in conclusion.

Physiological Action.

The general distribution and frequent dietetic and medicinal application of this remedy, as well as its presence in ordinary wines, etc., justifies its extended consideration.

Alcohol, being a volatile body, is absorbed by the unbroken skin; more readily, however, by subcutaneous cellular-tissue ulcers, and mucous membranes of the respiratory as well as the digestive canal.

The transformations of oxygen in the organism are, we regret to say, not as well known as we would desire. Small quantities are oxidized in the stomach to acetic acid (Lallemand); the larger part of it, however, reaches the blood and organs unchanged. The unanimous observation of all experimenters shows that a part of the alcohol is excreted with the expired air from the lungs, with the urine from the kidneys, and also through the skin. According to Subbotin-Voit, in the first five hours 2 per cent of the alcohol absorbed leaves the body by the kidneys, 5 per cent by the lungs and skin, 7 per cent by the lungs and kidneys; so that we can estimate that almost none is excreted by the skin, while the lungs excrete the most; in the course of twenty-four hours 16 per cent of the alcohol absorbed is said to leave the body in this way. According to Binz-Heubach these figures are too high, especially those having reference to the excretion by the lungs: he thinks that in the first five hours scarcely a recognizable portion of the alcohol is thus excreted; the assertion that the alcohol can even be smelled in the expired air he considers untrue. We do indeed recognize an odor if a person has taken brandy, Rhine wine, rum, beer, etc.; but this is due to the stronger ethers and fusel oil which are mingled with these drinks. No odor is experienced if pure diluted alcohol has been taken, and the mouth and pharynx well cleaned afterwards. However this may be, this much is certain, that only a small fraction of the alcohol absorbed leaves the body unchanged. Notwithstanding this, according to Schulinus-Buchheim, even two to three and a quarter hours after the absorption of alcohol at least one fourth and probably a much larger portion of the alcohol absorbed has disappeared again from the body. Liebig, therefore, seems warranted in his belief that the larger part of the alcohol absorbed into the body

is oxidized, and only a smaller portion is excreted unchanged by the lungs and kidneys. It is true that hitherto none of the products of oxidation of alcohol, such as aldehyde, acetic acid, and oxalic acid, have been found in the body—which is rather suspicious, since aldehyde has a characteristic odor; however, we can believe that the acetic acid formed from the slow oxidation of alcohol in the system enters into a combination with some base, and that this acetate is oxidized into carbonates and water, and under this form leaves the system with the urine (Subbotin). But since Liebig's theory requires the further confirmation which can only be given by finding the oxidation products of alcohol, many investigators will not accept it, and believe rather, also without foundation, that the alcohol leaves the system unchanged (Hermann).

Before we consider the manner in which the absorbed alcohol is distributed among the individual organs of the body, we must refer to the observations of Rajewski, Hoppe-Seyler, according to which the normal organs (brain, liver, and muscles) of animals which have had no alcohol given to them in any form will either yield alcohol after distillation in a perfectly air-tight apparatus, or are even found to already contain alcohol. According to Schulinus, many organs have so great an affinity for alcohol, that in the first few hours after its administration they withdraw it entirely from the blood. Not until all the organs have been saturated and the administration of alcohol is still continued do we find the amount of alcohol contained in the blood increased; this is in the later stages of alcoholic poisoning. The brain has the greatest affinity for alcohol from the very outset: at first, therefore, it receives the largest share of alcohol; as soon as it becomes saturated, the other organs (lungs, kidneys, muscles) absorb it. The muscles also seem to reach the point of saturation very rapidly, and later on suffer no more changes. The percentage of alcohol in the lungs, according to Schulinus, does not stand in direct relation to the temperature of the inspired air. He therefore does not consider himself authorized to conclude from his experiments that the percentage of alcohol in the lungs is relatively affected by a low temperature of the inspired air. The liver absorbs less alcohol relatively, than the other organs. The maximum amount of alcohol which can be absorbed by equal portions of different organs varies in each organ; so that the various organs dif-

fer in their affinity and saturating power for alcohol: this difference, however, is not so great by far as Lallemand, Perrin, and Duroy believe.

The fact that alcohol is better borne in localities possessing a higher temperature and lower atmospheric pressure, as in the mountains, than in cold and low places, has led some observers to the conclusion that under the latter circumstances alcohol is not excreted more rapidly. More accurative comparative observations have not yet been made.

The influence of alcohol upon the substrata of the animal organism has only been superficially investigated. For the present, the following properties are considered as most probably belonging to alcohol: 1. Its ready volatility, even at a low temperature. 2. The great affinity for water, which it withdraws even from the tissues. 3. Its property of precipitating all albuminoid bodies, peptones, mucous and gelatinous matters, from their solution. 4. That it dissolves the fats. 5. Its antifermentative and antidigestive action. All of these effects diminish in intensity in direct proportion to the degree of dilution of the alcohol with water. And when we consider the enormous dilution which the alcohol undergoes, even when taken in large quantities, when it comes in contact with the large mass of fluid in the organism (according to Binz, 50.0 grms. of alcohol in a man weighing 75 kilos., equals a dilution of 1 to 1000), we cannot explain, even with a knowledge of the effects it produces when applied in some strength, how it is that it produces such serious functional disturbances in the system. Its antifermentative and antiseptic power are, compared with other agents, so slight, that they cannot yield any explanation for its action in the animal body. Even men strongly addicted to alcohol, after death decompose as rapidly as other men: indeed, only in great concentration (as compared with other antiseptic agents) can alcohol prevent the decomposition of flesh.

The color of the blood is unchanged, even after the absorption of considerable quantities from the stomach; but if death sets in from paralysis of respiration, then the blood becomes a dark-brown, from the excess of CO_2: this is always seen after death from suffocation. Some writers found an increase in the fat, and some in the sugar of the blood.

The red blood-globules increase in size under the influ-

ence of alcohol, even in animals suffering from fever, although ordinarily they are smaller in febrile conditions (Manassëin). This enlargement is said to be due to an increase in the amount of oxygen which they contain. This is all that is known concerning the alteration of the blood in the living alcoholized organism.

Schmiedeberg-Bonwetsch found that by the direct admixture of alcohol with the blood outside of the body the reduction of oxyhæmoglobin by reducing agents is retarded, and they explain this by the supposition that alcohol causes a firmer union of the oxygen with the hæmoglobin. But this has not yet been proved for the living organism. So that this observation, as well as that of the coagulation of the blood, the solution of the red blood-globules, and the crystallization of the coloring matter of the blood by the addition of concentrated alcohol, have only a theoretic interest. None of the above facts seem to be in favor of the old idea, that much oxygen is withdrawn from the blood by the burning up of the alcohol in the blood.

There is a great difference between acute and chronic alcohol action; nor can we as yet say what part of the effect depends upon the alcohol and what portion upon the oxidation products of the alcohol.

Acute Alcohol Poisoning.

The more diluted the alcohol, the weaker are the local effects which it produces; the degree of dilution, however, does not affect the general physiological effects.

Local Action.—An actual effect upon the skin is only observed with alcohol which does not contain more than 50 to 70 per cent of water. Absolute alcohol, however, has the most intense effect.

When the conditions are such that the alcohol can evaporate rapidly, there is a great lowering of the temperature at the point of application, a feeling of cold, contraction of the vessels of the skin, and paleness of the skin. If evaporation be prevented by covering the point of application with a cloth, we have, on the contrary, a feeling of heat, burning, redness, and inflammation of the skin, resulting in a peeling off of the epidermis.

Although, when the skin comes in contact with very cold water there is a disagreeable, painful sensation produced,

this does not follow if the skin comes in contact with alcohol cooled to 5° (Horwath). Indeed, already existing painful sensations can thus be suspended, so that cold alcohol may be used as a local anæsthetic.

Washing the skin with dilute alcohol is said to prevent sweating; whether this is the result of contraction of the vessels or other causes is not known.

Alcohol has a similar (but weaker) effect upon ulcers and wounds to that of carbolic and salicylic acid; that is to say, it prevents purulent decomposition, diminishes the formation of pus, and hastens the healing process. Concentrated solutions of alcohol cause severe inflammation and burning of the base of the wound; this is followed, however, by an improvement in the appearance of the wound and a hastening of the healing process.

Upon the mucous membranes, alcohol even in 25-per-cent solutions causes a disagreeable burning; in 50-per-cent solutions, inflammation; in 80-per-cent solutions, cauterization and shrinkage, owing to coagulation of albumen and the withdrawal of water.

The following local disturbances are produced in those who are unaccustomed to its use:

Small quantities (1–2.0 grms.) of a 20–70-per-cent. alcohol produce, on swallowing, a feeling of warmth, and burning in the mouth, œsophagus, and stomach, due partly to a direct alteration of the substance of the superficial nerves of sensation, and partly to a reflex hyperæmia. If the vapor of the alcohol which is given off in the mouth be inhaled, there is immediately caused a reflex contraction of the glottis, which gives rise to a feeling of pressure on the chest. The production of saliva, like that of the gastric juice, is very much increased. Of all the irritants which have been tried on dogs with gastric fistula, alcohol seems to exert the most powerful effect upon the stomach; if but a few drops be placed on the tongue, or even one drop directly upon the gastric mucous membrane, the gastric juice immediately begins to flow in a thin stream out of the fistula: this occurs even in starving dogs, in which the gastric juice was not previously flowing. Bernard's statement, that diluted alcohol does not increase the secretion of the gastric juice, is certainly not true as far as dogs and probably men are concerned. In consequence of this the digestion is quickened and appetite improved; fats being dissolved in the alcohol are thus, especially, more readily digested. In-

testinal peristalsis as well as that of the stomach seems to be strengthened.

Too large quantities have a bad effect upon digestion: first, because of the coagulation of the albuminates and peptones; and further, the diminution of the blood supply in the gastric mucous membrane, and therefore the diminished secretion, owing to contraction of the blood-vessels of the stomach (Bernard). Long-continued use of large quantities by chronic topers causes chronic gastric catarrh, diminished appetite and digestion, and often vomiting.

The drinking of concentrated alcohol is followed by a painful burning sensation in the digestive canal. Gastro-enteritis results, followed by irritation of the mucous membrane, vomiting, and diarrhœa, together with the passage of bloody masses; in consequence of this local affection, even death sets in, brought about by an arrest of the heart's action from reflex inhibitory influence transmitted through the vagus.

The gastric mucous membrane of animals and children who died from a dose of 20–30.0 grms. of absolute alcohol was in a condition of cell-shrinkage and hemorrhagic softening; the blood had coagulated even in the blood-vessels of the mucous membrane.

The general physiological effects occur both in men and the different warm-blooded animals, always varying, however, with the individual, age, manner of life, and habits. There is also a difference in the effect produced by the various forms in which the alcohol is taken, as for instance beer, wine, brandy, etc. Here we shall consider the effect of pure alcohol sufficiently diluted with water, so that the general picture may not be marked by the occurrence of symptoms due to the local action. Since alcoholic drinks are articles of daily consumption among all civilized nations, the more evident symptoms resulting from the use of alcohol are so well known, even to the laity, that we shall only briefly touch upon them here. To the important results, however, of more scientific investigation we shall give a more extensive consideration.

Taken in moderate quantities, alcohol produces, in addition to the stimulation of digestion, a general exhilarating effect in most people; it gives a feeling of mental and corporeal strength, together with greater capability of endurance. This effect disappears after a time, without being followed, however, by any reaction in the opposite direc-

tion. After larger intoxicating quantities the face and conjunctivæ become red. The eyes become more glistening, and take on a lively expression. The integument, especially, of the head, is warmer, and the pulse beats faster and stronger. There is mental excitement; the thoughts flow faster and are expressed more fluently. At the same time there is an increased motor activity: gesticulations are indulged in; singing, dancing, and other noisy demonstrations occur. While this motor excitement increases, strength of will and resistance to the passions are diminished; the individual is carried away by fancy, and the more superficial passions, such as anger; while the deeper passions, such as love and hate, remain in the background: so that the most worthy characters are for the time being degraded. Even at this stage complete restoration can soon set in (in twelve hours), leaving marks, however, of the psychical strain.

If the administration of alcohol be continued, the symptoms of stimulation gradually pass over into those of weakness; speech becomes stuttering and thick. The motions of the body become swaying and uncertain. Sensation is dulled. Nausea and vomiting set in; there is drowsiness, and finally sleep, which resembles the normal, but is less deep and less quiet. After waking, the head feels heavy and painful, and for days there is bodily and mental weariness; there is also a severe gastive catarrh, with nausea and vomiting left as sequelæ.

In severe alcoholic poisoning the primary stage of stimulation may even attain to the point of a lively delirium, madness, and entire loss of judgment (temporary insanity); finally, consciousness is rapidly lost, coma sets in, and the patient is as insensible as one who has been chloroformed. The face is either of a bluish-red, dusky hue, and the eyes staring, or there is extreme pallor, while the eyes are closed. The breathing is stertorous, the heart sounds weak, and the pulse small and slow. The muscles are relaxed; the skin is cool, and often covered with a cold sweat. The urine and fæces are passed involuntarily, and death may set in from stoppage of respiration.

Individual variations from the picture just given occur chiefly during the first stage of intoxication. There are many men, for example, who from the very beginning are neither mentally nor bodily excited, but are sad and quiet, passing gradually into the second or paretic stage.

Influence of acute alcoholic poisoning upon the individual organs and functions.—We begin with the *nervous system*, the alteration in the functions of which is most readily observed. It has been shown to be highly probable, from the investigations of Schulinus, that alcohol produces a chemical alteration in the contents of the nerve cell-itself; whether this alteration is in the fat, the lecithine, the albuminoid bodies or the water of the nerve-cell, is entirely unknown. It is not very probable that the symptoms of the slighter cases of poisoning are due to a change in the quantity of blood contained in the brain or spinal cord, for the reason that such a change is scarcely observed in these cases. In the severer and extreme cases of alcoholic poisoning it is not to be denied that the enormous increase of blood in the vessels in the former cases (severer), and the great degree of anæmia in the latter (extreme) cases, do probably exert some influence on the general effect, although even in these cases the symptoms are chiefly due to changes in the brain substance itself. That this must be so, is evident from the fact that the sequelæ of acute poisoning last for some time, and the psychical disturbances of chronic drunkards last for years, after they have been deprived of all alcohol. First, the ganglia of the gray substance of the cerebrum are affected; from this results the rapid occurrence of mental irritability; later on those of the cerebellum, and hence the incöordination of movement; later still those of the medulla, and hence the respiratory disturbances; finally the spinal cord, from which results an interruption in the transmission of sensation and motor impressions.

The peripheral, sensible, and motor nerves are probably affected only in the extreme degrees of intoxication, although we have no proofs of this fact. The sensitive apparatus is always much sooner paralyzed than the motor.

The voluntary muscles are probably influenced in some way, since Schulinus has shown that they rapidly absorb the maximum quantity of alcohol; but we do not know in what way. The spreading of the toes, as happens in frogs after chloroform narcosis, is not seen with alcohol. Myosin solutions become turbid only after a very long time, under the influence of alcohol vapor (H. Ranke). The increase of strength in the first stage and the decrease in the second stage are due for the most part to the influence upon the nervous system.

The respiration in animals (dogs), in the beginning, is

little or not at all hastened, in men it is slightly quickened; later on, however, both in men and animals it becomes slower almost by half, intermittent, and stertorous, chiefly owing to a direct influence of the respiratory centre in the medulla, and partly also on account of the alterations in the circulation. A severe irritation of the peripheral terminations of the vagus in the lungs, might in extreme cases of alcoholic poisoning have some influence in causing this slowness of respiration; but even here it is questionable, because in these cases the reflex irritability of the spinal cord has been so weakened that even a powerful irritant could no longer affect it.

The organs of circulation are comparatively little influenced by alcohol, and when the other important organs are paralyzed and dead from enormous doses, the heart, although weakened, can still continue to beat. Opinions concerning this point are slightly contradictory, because individual variations have been falsely considered as due to the alcohol. Moderate quantities seem to have no influence upon the heart's action in men, dogs, and cats. During the stages of excitement, the rapidity and force of the heart's action in some men is often increased—perhaps as a result of the more rapid movements of the body, and perhaps as a result of some influence over the musculo-motor nerves of the heart. That there is increased blood pressure and quickened circution, we can see better from the red color of the face, the bright gleam of the eye, and the increased warmth of the skin, than from experiments upon animals, in whom the violence necessary to bring them under the influence of the alcohol also causes an increased blood pressure. In cold-blooded animals, even after small doses, there is diminution of the heart's action.

After the largest intoxicating doses, it is true that the heart's power is diminished by $\frac{1}{10}$ and the blood-pressure by $\frac{1}{6}$ lower than the normal—partly as a reflex result of the severe irritation of the gastric nerves (vagus), partly from a direct affection of the nervous apparatus of the heart and the vagus centre in the brain; for in animals under the influence of alcohol the heart's action and blood-pressure are both again increased as soon as the pneumogastric in the neck has been cut. The hyperæmia (of the stomach, for example) may be due to dilatation of the blood-vessels from paralysis of the vaso-motor nerves. When the force of the

heart has been finally weakened to an extreme, all of the peripheral vessels are seen greatly dilated.

The temperature was formerly believed to be increased under the influence of alcohol; subjectively, this would seem to be so. But a large number of recent investigations have shown what Nasse showed in 1845, that small quantities do not influence the temperature to any considerable extent: in some there is an increase of $\frac{1}{10}$ of a degree, in others a diminution to a similar extent; such variations as these are only normal. Large doses, on the other hand, certainly diminish the temperature both in the normal and in the febrile organism, the amount of reduction depending upon the size of the dose. To reduce febrile temperature (septic, etc.), long-continued administration of not too small doses is necessary; in extreme cases of alcoholic poisoning the temperature may fall from 20–5° C. This reduction of temperature depends partly upon the greater radiation of animal heat, owing to the dilated blood-vessels of the skin; partly upon the increased perspiration; partly to the paresis of the muscles, the movements of which, in the normal state, are the chief source of animal heat; partly also to diminished oxidation of the tissues, as was shown by the facts ascertained by Binz-Bouvier, who found that in animals dying from alcohol poisoning the post-mortem temporary rise of temperature did not take place: here the first-mentioned causes were no longer active.

Concerning the influence of alcohol upon tissue changes we know the following: Small quantities which have no influence upon the more evident functions diminish the excretion of carbonic acid and the absorption of oxygen in dogs, without, however, altering the relative proportions of these gases; it is uncertain whether this effect is the result of more superficial respiration, or an interference with the decomposition going on in the cells. Larger quantities, which have an exciting effect upon the animal, in the beginning increase the excretion of carbonic acid as well as the absorption of oxygen, while later on these two functions are diminished: in this case the increase is the result of the increased motor activity, the more rapid respiration and the quickened heart's action, and not an effect of the alcohol. What the conditions are in animals in a state of stupor has not yet been investigated; we shall not be far wrong, however, if we assume that in the condition of stupor there is a considerable diminution in the amount of carbonic acid

excreted and oxygen absorbed. What is true of animals is probably also true of men (v. Boeck and Bauer). Fokker, Obernier, Rabuteau, Zülzer, and Strübing found a diminution in the amount of urea excreted—that is, of the albumen used up in the human body—both after small and intoxicating doses. Parkes and Wollwicz failed to obtain these results, probably because they experimented upon animals who were accustomed to alcohol. Fokker assumes that this diminution in the amount of albumen used up is due to the same conditions as those resulting from the large administration of fats, sugar, and other carbo-hydrates. It follows, then, that under the long-continued use of moderate quantities of alcohol, combined with the ordinary diet, the body becomes richer in albuminates. During the stage of excitation the excretion of phosphoric acid is diminished even more than that of nitrogen, but during the stage of depression this again rises. We shall show under the head of chloroform that the decomposition of nerve-substance is less during the stage of excitement, greater during that of narcotism, than the decomposition of muscular tissue during the same stages. The excretion of uric acid and of salts are also diminished under the influence of alcohol. The quantity of the urine is increased, although the amount of water taken remains the same.

Chronic Alcohol Poisoning.

Up to a certain limit the animal body accustoms itself to increasing doses of alcohol without causing any great disturbances. Beyond this limit, which varies in different individuals, there appears a series of serious symptoms which are grouped together under the terms chronic alcoholism and alcoholic insanity (delirium tremens).

At first diminished appetite and impaired nutrition and digestion set in; eructation and vomiting of watery and sometimes acid (from decomposition of the food) at other times alkaline, masses. There is constipation, alternating with diarrhœa. On account of the diminished nutrition, there is a high degree of anæmia, paleness of the skin, with deposit of large quantities of fat, both under the skin and in the cavities of the body, and on the heart. The eyes take on a peculiar glassy look; the features have a relaxed appearance; the speech is slow and hesitating; the hands tremble; in some, various eruptions on the skin and red-

ness of the nose occur. The bodily and mental strength are diminished. The disposition of the patient is altered; he becomes mournful; there is loss of the sense of duty; and the patient becomes vulgar, both in speech and action. By repeated indulgence in the alcohol, the physique can still be temporarily stimulated to a certain degree of activity; entire withdrawal of the alcohol causes complete breaking-up of the system, and the appearance of a number of severe symptoms, among others delirium tremens; this latter condition may also break out during a period of uninterrupted intoxication.

Delirium tremens is generally preceded by a melancholic or maniacal prodromal stage, and begins with the well-known hallucinations of sight, feeling, and hearing: the patient sees small animals and horrid forms; he hears various voices, and feels as though spiders' webs were all over him; later on, mental conditions, which resemble similar states produced from other causes; insane ideas of conspiracy, suicidal and destructive tendency, together with anæsthesia and apoplectiform or epileptiform convulsions. These affections are not due to the alcohol alone, but to the general bad hygienic conditions under which the patient lives, the mal-nutrition, the tobacco, as well as the pricking of the conscience during the healthy moments. So that we are unable to picture very clearly the symptoms of pure chronic alcoholic poisoning.

There is paralytic insanity, and death, with symptoms of a general breaking-up of the system. Postmortem we generally find signs of the chronic gastric catarrh, fatty degeneration of the liver, kidneys, heart, muscles and brain, pacchymeningitis, adherent pia mater, and a dry, anæmic brain.

The Value of Alcohol as a Nutritive Substance and Appetizer.

This matter has been discussed by Voit as follows: We can distinguish two kinds of nutritive substances. 1st, those which are necessary for the production of the substances of the body, such as albumen, fats, water, and salts; and, 2dly, those which prevent the rapid destruction of the bodies of the first class, and thus retain them for a longer time for the uses of the body—as for instance starch flour, which prevents or diminishes the loss of the fat of

the body. Nutritive materials cannot be defined as those which by their decomposition give strength to the body, for according to this definition water and salts would not be nutritive materials. Alcohol, then, must be considered as a nutritive material of the second order, since under its influence fewer substances are decomposed in the body. Its action in this respect is similar to, although quantitatively less than that of starch flour; for it prevents the decomposition of the fat of the body, and when taken in excess causes the fat to be collected in the organs, and thus produces fatty degeneration of these. If, as we may now believe, a portion of the alcohol is decomposed in the body into lower combinations, it must thus give rise to some vital force, which can be utilized in the body as heat, or perhaps even for the production of energy. Of a different nature, however, is the question of the importance of alcohol as an article of diet when compared with the other nutritive materials, such as albumen, fat, flour, etc.; or whether we can use it only in order to save a little adipose tissue or vital energy. We must here remember that we could not use alcohol, like the other nutritious materials, in sufficient quantity, because of its ill effects upon the nervous system. In the quantities in which it can be taken without harm its importance as an article of diet for healthy people is very slight. Subbotin very properly protests against the idea that the stoutness of habitual alcohol drinkers is a sign of a well-nourished state; on the contrary, the deposit of fat in these people is a result of disordered nutrition, comparable to the fatty degeneration of internal organs produced by arsenic, phosphorus, antimony, etc. The fatty degeneration occurs at the expense of important components of the tissues, such as the albuminoid bodies. In the healthy condition, therefore, we do not use alcohol on account of its nutritive value, but because of its action as a stimulant and its agreeable taste.

In sick people the case is entirely different; and we think Binz is perfectly right in saying that alcohol is an important nutritive material when other articles of food cannot be borne. In these cases it has the advantage of being very readily absorbed, when diluted with water, even when the digestive organs are weakened; nor does it require as much work on the part of the body for its assimilation as is required for the decomposition of fats, for instance. This fact is confirmed experimentally, when we see in pa-

tients suffering from a serious disease, and who reject all other food, that wine enables them to withstand the weakening influence of their malady and leads them to recovery.

We cannot ascribe the favorable effect of alcohol in these cases to any stimulating action of the alcohol upon the heart and nervous system; for such continued stimulation would finally result in a more rapid exhaustion if the alcohol had no further action. This favorable effect depends not only upon the vital energy which the alcohol yields by its combustion, but also upon the fact, as already stated, that the alcohol prevents to some extent the using up of the fats and albuminoids, and thus economizes the vital forces in these weakening maladies.

The great value of alcohol as a stimulant and appetizer is much underrated. Indeed, it is not so long ago when appetizers were considered not necessaries, but luxuries, and even injurious ones. Voit's writings have shown the falsity of this idea. Voit has shown that purely nutritive materials are tasteless and unfit for food, and only rendered proper articles of diet by the appetizers, spices, etc. These appetizers and condiments not only give an agreeable taste to the food, but directly aid digestion and nutrition, by increasing the digestive secretions, and strengthening the gastro-intestinal movements, and have besides this a remarkable influence upon the nervous system and general feeling of health. In the lower spheres of human animal life, therefore, the appetizers and condiments exert an influence somewhat similar to the ambition for love, fame, power, and wealth in the higher spheres of the psychical life. Without really increasing the energy of the body, all these things regulate the conservation and use of this energy, and can even incite to the greatest efforts.

Voit's comparison of these appetizers to a whip appears to us somewhat inapt, since the whip, while it spurs on, also produces pain, while the appetizers give pleasure at the same time that they produce increased activity (digestive): this difference the driver does not feel, but the horse appreciates it.

When we have the choice, we should certainly not use alcohol, but alcoholic drinks as appetizers and as nutritive drinks; and generally we should prefer wine, the king of all drinks, because of its divine taste and odor.

Temperance societies are certainly wrong in their vain fight against all alcoholic liquors. If the members of these

associations were compelled to give up the appetizers they are fond of, such as coffee, tea, chocolate, spices, etc., or at least not to use them until they had supplied their poorer brethren with the necessaries of life, albumen, fats, salts, and water, they would soon recognize the folly of their demands.

Moderation, however, is necessary in everything—not only in the use of alcohol.

The therapeutic and dietetic application of alcohol will be discussed under the individual alcoholic preparations.

Treatment of Alcohol Poisoning.—The slighter degrees of poisoning, the symptoms of ordinary intoxication, disappear in the course of a few hours, after sleep, without any treatment. The sequelæ in the form of headache, etc., are best treated by fresh air. The dyspepsia and other symptoms of the acute gastric catarrh disappear most rapidly under complete abstinence from food and drink. Nausea is controlled by ice and Selters water. We do not recommend the much-lauded administration of a few drops of liquor ammonii caustici during this period.

If the intoxication be very great, so that dangerous symptoms set in, then the alcohol still remaining in the stomach must be removed by the stomach-pump or by emetics. Ipecac, tartar emetic, copper and zinc sulphate, are generally ineffective in these cases; and for this reason the older physicians recommend in these cases the use of mustard if the patient can swallow, and we consider apomorphine injections even better.

Since there is no antidote to the alcohol which has already been absorbed, further treatment must be symptomatic. Ice or cold compresses are placed upon the head; where there is danger of paralysis of the respiratory centre we must seek to maintain respiration artificially—by Hall's method, cold douching, etc. Bloodletting in these cases is now no longer practised, although it appears doubtful whether we are warranted in its entire abandonment as a plan of treatment. The condition of the pulse and strength of the heart's action should give us the indications as to whether local or general bloodletting is advisable.

We would add that older physicians prescribe the liquor ammonii caustici in this stage of alcoholic poisoning.

ALCOHOLIC DRINKS.

WINE.

Wine, a liquor prepared from grapes, is the noblest of all alcoholic liquors, and should, therefore, be preferred. On account of the expense, however, some drink beer, brandy, etc., instead.

Chemically as well as dietetically considered, ethyl alcohol is the most important component of wine. Its percentage in different wines varies with the locality and season in which the grapes have grown. The better German wines from the Rhine, Main, and the Moselle on

an average contain 10 per cent, by volume, of alcohol. The heavier southern wines, such as Malaga, Madeira, Port-wine, etc., contain about 20 per cent. Schibert found the percentage of alcohol contained in Würzburger, of different seasons, vary from 7 to 13 per cent. The quantity of alcohol also depends, on the one hand, upon the quantity of sugar in the grape, on the other, upon the degree of fermentation in the must. Old wines are, therefore, richer in alcohol than new wines.

Another component of wines is grape sugar. Wine obtained from grapes poor in sugar may be entirely without sugar, since all the sugar may be converted into alcohol by fermentation. In the German wines the percentage of sugar varies from 0 to 8 per cent. The Rhine wines contain the greatest amount of sugar. If there be much sugar in the grapes, as in the southern grapes, then considerable alcohol is formed in the wine (20 per cent). This quantity of alcohol has the effect of preventing fermentation, so that fermentation ceases as soon as about 15 per cent of alcohol has been formed; some of the sugar then is not fermented, and such a wine remains sweet. Wines which contain considerable sugar may have their sweetness masked by a large percentage of acid.

The most important of the acids in wine is tartaric acid, of which there is from 0.1 to 0.7 per cent in wine (Mulder). In addition we find tartrates (of calcium, potassa, and the double tartrate of alumina and potassa). The more alcohol in the wine the less of these salts it can hold in solution, and they are therefore deposited at the sides of the barrels. Even for the reason that wines rich in alcohol contain so little of these salts, they would be sweeter than those poor in alcohol. If unripe grapes are also placed in the wine-press, there will be some malic acid in the wine. In red wine there is a considerable amount of tannic acid, due to the grape-skins pressed with the grapes. In the course of time the oxidation of the alcohol in the wine-barrel gives rise to the formation of a little aldehyde and acetic acid (up to 0.1 per cent), and, if malic acid was present, it may give rise to the formation of succinic acid. Large quantities of carbonic acid are found in new wines, the fermentation of which has been purposely interrupted.

The delicate and individual flavor of the various wines is due to small quantities of various ethers—according to Liebig and Mulder, acetic-acid and butyric-acid ether—which are formed from the tartrate of ethyl oxide. A certain amount of free tartaric acid is therefore necessary for their formation, and since the formation of these ethers binds the tartaric acid, the wine becomes sweeter as it gains in flavor.

The œnanthylic ether, contained in wine in small quantities (0.002 per cent), can only be recognized by its odor, when the ethers have evaporated from wine which is kept in an open receptacle.

Besides these, there are coloring matters, upon which the red and golden color of the wine depend, and which are derived from the grape-skins. There are also perhaps small quantities of albumen and fats.

Physiological Action.—The chief effects of wine are certainly due to the alcohol which it contains. Those are the strongest which contain the most alcohol. The strongly acid wines readily produce digestive disturbances, diarrhœa, and are more diuretic than the other varieties. The effervescent wines have also some of the effects of carbonic acid, while the red wines, from the tannic acid which they contain, have a slightly constipating effect. Albertoni and Lussana have found that the ethers are of no importance as far as the coarser physiological effects of wine are concerned. Even 1.0 grm. of œnanthylic ether produced no further

effect in men than an oleaginous taste and slight improvement in digestion. The same is true of the mammalia and birds. Butyric-acid ether has a caustic action upon mucous membranes, but otherwise, even in 3.0–5.0-grm. doses, is entirely without any effect. So is also acetic ether. When we consider the very small amount of these substances contained in wine, we can only conclude that, at most, they have the effect of gratifying the sense of smell, taste, and sight (coloring matters). To these things, however, wine owes its ancient popularity among all nations and of all times. We doubt whether water mingled with these ethers and coloring matters would be as popular as the alcoholic wine.

Artificial wines which contain, in addition to the alcohol, fusel oil have a very injurious influence—similar to that of brandy containing fusel oil.

Dietetic and Therapeutic Application.—Wine can only be commonly an article of general diet among the wealthy on account of its price. Daily experience therefore teaches that, like other alcoholic drinks, it is not a necessity. But, on the other hand, we know that a moderate indulgence in this drink can be borne indefinitely, without producing any injurious effects upon any organ of the body. In aged persons the daily administration of from one to three wineglassfuls may even be a necessity. It improves their digestion, and acts as a mild nervous stimulant.

In the neighborhood where wines are produced they are more commonly used, although the variety is necessarily limited to that common to the particular locality. Otherwise the following facts should guide our choice of any particular variety: For daily and frequent use a light wine—that is, one poor in alcohol—should be chosen, so as to avoid chronic alcoholic poisoning. Even wine-drinkers may become sick with delirium tremens. Again, gout is more frequently developed in countries in which a strong wine is ordinarily (because native) used, such as Tokay, sherry, etc. Then, again, a light red wine seems to have a better effect upon digestion than light white wines, which as a rule are slightly more acid than the former.

The continued use of white Moselle, Pfaelzer, Upper Rhine, and Rheingau wines produce dyspepsia much more readily than light French wines, such as Bordeaux, for instance. The latter indeed is perhaps the best for dietetic use, although we do not prefer it to the king of wines, the Rheingau wine. The use of the more acid—that is to say, the lighter white wines—and the stronger wines should be avoided by those who have a tendency to the passage of gravel in the urine; so also where there is a tendency to diarrhœa. On the other hand, red wine which is rich in tannic acid should not be used by those in whom there is a tendency to constipation.

Medicinally, wines are used under the following circumstances: First, as an important agent for maintaining the strength of patients, or of strengthening weakened individuals. Thus it is used in the treatment of chlorosis, anæmia, and conditions of weakness the result of profuse hemorrhages, long-continued suppuration, and exhausting conditions; also in convalescence from severe acute diseases. The benefits derived from the use of wine and a proper diet in these cases is so well recognized that it is sufficient simply to mention it here. In these cases it is best to use a strong wine, such as the Hungarian wines, or some good red wine, Burgundy or Bordeaux. The latter are especially indicated when diarrhœa is present.

Wine is useful in the treatment of rickets and scrofula—especially the

Hungarian wines, from the lime phosphate contained in them; the importance of this ingredient of the wine, however, is questionable.

Wine is also used as a stimulant where a weakening of the heart's action either exists or threatens. The causes which may produce such a condition, which generally consists of a sudden or subacute diminution in the energy of the heart's action, are manifold. This condition is further characterized by contracted arteries, small pulse wave, weak apex beat, and, as a rule, dull heart sounds. There is faintness, paleness of the face, and cool extremities. This condition is often seen in the course of acute febrile conditions, especially the acute infectious diseases, in the vomiting of children, in cholera, after great loss of blood, sometimes in fatty heart, individual poisoning, and in some other conditions, a more complete enumeration of which may be omitted. The best wines to use for this purpose are those containing carbonic acid; such are champagnes, and their rapid effect is due, according to Quincke, to the fact that the carbonic acid hastens the absorption of alcohol. In some cases we might give warmed red wine or Hungarian wine.

During the last twenty years wine has been very much used in the treatment of acute febrile diseases, and more especially by the English physicians. The latter think they have observed under its use not only no increase of the febrile process, in such conditions as pyæmia, typhoid fever, acute exanthemata, or pneumonia, etc., but even a diminution, together with a favorable influence upon the course of the disease. We shall discuss this question only from a practical standpoint, without especially considering theoretical facts.

The physiological investigations on men and animals, spoken of above, as well as a series of experiments performed by some of the already mentioned observers upon the artificial production of fever in animals, seem to prove that alcohol has the power of reducing the temperature of the fevered organism. This antipyretic effect can only be utilized for therapeutic purposes by administering large doses, while other antipyretics can produce the same effect more certainly. Besides this, some observers have noticed that alcohol sometimes causes a rise of temperature in fever patients. Furthermore, even if it were positively demonstrated that alcohol is an antipyretic, we must not forget that it also exerts other effects which might entirely nullify the benefits to be derived from the reduction of temperature. Thus it has not been shown that medicinal doses, in reducing the temperature, also reduce the frequency of the heart's action. So also its well-known exciting effect upon the brain, frequently caused by large quantities, is not an unimportant consideration in typhus, as well as the acute febrile exanthemata, the more so since experiments seem to have shown that alcohol produces dilatation of the cerebral vessels. Otherwise, as Binz has shown, alcohol would be very useful in protracted febrile conditions, where the nutrition is impaired, because of its power of diminishing rapid tissue waste (see page 358). This, perhaps, is the chief indication for its use in febrile diseases.

The special conditions in which the older observers have considered the use of wine to be indicated are the following:

Alcohol (wine) is indicated in the febrile process of anæmic individuals who become sick with moderately elevated temperature, pale skin, and a pulse of low tension. Such treatment is also apt to be indicated in affections of long duration (typhoid and pyæmia); in affections of short duration, as for instance in pneumonia, they

are seldom needed. Stimulants are also indicated when there is a sudden lowering of the heart's action, with the symptoms above enumerated. Also in conditions of collapse, as for instance in typhoid, owing to profuse intestinal discharges. Graves and Stokes consider alcohol indicated when there is great weakening of the heart's action, so that the first sound becomes indistinct or entirely vanishes.

We think wine is indicated in all protracted febrile diseases in which the nutrition is very much impaired. We should therefore use it in typhoid. In this disease we prescribe it, according to the individuality of the patient, one quarter to one half litre of strong wine per day. Generally we give Hungarian, Marsala, Spanish, or, in severe diarrhœa, a good red wine. Wine should be given in the very beginning of these cases, without any regard to the fever. It is only when any of the contraindications, which will be given later on, are present that the cases should be more accurately individualized. The same holds good in pyæmic fever, as well as in the fever of phthisical patients, when they are reduced in health and nutrition is very much impaired. Not only do such patients bear wine well, but they generally improve under its use.

On the other hand, we do not think that wine should be used in acute febrile diseases of short duration—such as pneumonia, erysipelas—unless it is especially indicated from some other cause. Experience has not shown that wine is actually injurious in these conditions; but since, in diseases of short duration, its action in preventing tissue waste is not an important consideration, and since we have more reliable antipyretics, while, on the one hand, wine has a tendency to quicken the heart's action and increase the headache, it appears to us to be better not to give wine in these cases, unless there exist, as we have already stated, special indications for its use.

Externally, wine has been used for the same purposes as brandy; this is especially true of the red, which are rich in tannic acid. In gonorrhœa red wines are often used as menstrua for injecting mixtures containing such articles as tannin.

Pharmaceutically, wine is used in the preparation of various tinctures, and also as an addition to syrups, etc.

In various physiological and pathological conditions, wine as well as brandy and even beer are contraindicated. There are, first, childhood or youth; secondly, a condition of "nervous irritability," such as is often seen in females; again, the so-called apoplectic habit, with a tendency to congestion of the brain, or with hæmoptysis or disease of the heart.

We can specify no exact dose for the administration of wine; the dose varies according to the quality. We will only emphasize the fact that in young children it is necessary to be very careful—10 to 15 drops per dose.

It well known that alcoholic drinks are prepared by fermenting the juices of other fruits than grapes; these are also sometimes called wines. But since these have no medicinal value, we shall pass them over, mentioning only apple wine (cider) which contains some alcohol, with malic acid, acetic acid, and salts. It has a slightly diuretic and cathartic action.

Beer.

Beer is supposed to be brewed from barley, malt, and hops; but we regret to say that other injurious ingredients are now sometimes added

to it. Here, however, we shall only consider the beer properly brewed as above stated.

The following are the ingredients found in various quantities in the different beers:

Under the influence of the diastase formed from the germinating barley the starch is changed to grape sugar and dextrine. Of the former there are in the various kinds of beer from 0.3 to 1.3 per cent; of the latter 5 to 10 times as much.

Under the influence of the yeast, the sugar is converted into alcohol and carbonic acid. The percentage of alcohol in the lighter kinds of German beer is on an average 3; in the heavier 6 to 7 per cent by volume; in the stronger English beers this percentage rises to 8 or 10 or according to Smith, even to 20 per cent by volume.

The largest part of the carbonic acid which is formed, can only remain dissolved in the beer under considerable pressure; even then it has four times the volume of the beer. As soon as the pressure is removed or diminished the gas escapes very rapidly, thus causing the foaming with which we are familiar. In beer that does not foam there are only very small quantities of carbonic acid—from 0.1 to 0.2 per cent.

The percentage of albuminoid substances is very slight; in German beer there is about 0.5 per cent.

Of the fatty acids (lactic and acetic acids) from 0.001 to 0.5 per cent have been found on analysis. Tannic acid is present, especially in young beer, in uncertain quantity.

Hops give to the beer an oil of hops, a resin of hops, and lupuline, which has a bitter taste. The addition of hops prevents the development of fusel oil from the malt; for these reasons fusel oil is only found in beer which contains no hops.

The salts in the beer originate partly from the water and partly from the plants used in making it. Analysis of beer shows the presence principally of potassium and phosphoric acid; also sodium, calcium, magnesium, sulphuric acid, and chlorine. The whole quantity of salts varies from 0.15 to 0.42 per cent.

The quantity of water varies from 80 to 90 per cent.

Physiological Action.—Beer is a nutritive material, as can be seen from its composition; its value as a nutritive agent is less due to the quantity of the nutritive materials, than to the fact that it is readily absorbed and assimilated. Its value lies in its agreeable taste, the power which it has of relieving thirst, owing to the carbonic acid which it contains, and its favorable influence upon stomach digestion. Its effect upon the brain is not as agreeable as that of wine, owing probably to the oil of hops which it contains, and which has an effect similar to oil of turpentine, producing in men headache and general depression.* Moderate indulgence in beer allows the effects of this oil of hops to be more prominent; these are unwillingness to make any physical or mental effort, and psychical depression. When taken in large quantities the intoxicating effects of the alcohol set in. Equal quantities of alcohol mixed with water do not cause intoxication as soon as the beer (Hilger). The stage of excitement caused by the beer-intoxication passes over much more rapidly and is more brutal in character than that of wine, while it leads to paralysis of the tongue, dulness, and somnolence, much more rapidly.

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* Compare Hops.

But it is because of this depressing effect of beer that it is indicated in cases in which there is nervous irritability, if an alcoholic stimulant be necessary.

Beers which are adulterated with tobacco, cayenne pepper, sulphuric acid, salts of iron, etc., naturally exert the effects of these substances, in addition to that of pure beer.

Dietetic and Therapeutic Application.—Beer is very much used dietically, but very rarely as a therapeutic agent. On account of its cheapness, it is much more popular than wine; on account of the small amount of alcohol which it contains, much larger quantities can be taken. We must remember, however, that beers rich in alcohol, especially the English beers, frequently give rise to chronic alcoholism, delirium tremens, and gout; but experience has shown, that those who drink habitually only the light beers, such as Berlin white beer, often suffer from delirium tremens, because of a habit which they have of taking drinks of whiskey, between the periods of their indulgence in almost fabulous quantities of beer.

We can lay down no general rules as to the quantity and quality of beer which it is best to use; our personal experience would lead us to prefer for dietetic purposes the lighter varieties of Bavarian beer.

There is no doubt that well-brewed and unadulterated beer has the power of improving the appetite when taken in small quantities, while to a slight extent it is also a nutritive agent. It should therefore be recommended for individuals who are anæmic and thin, and whose appetite is poor. In convalescence from acute diseases beer is also useful, especially when the heavy wines cannot be prescribed on account of their cerebral effects. Indeed, beer is to be preferred when alcohol is ordered for so-called nervous people, in whom wine has so exciting an effect. Wittich has prescribed from 1 to 2 litres of 4-per-cent beer to produce sleep, and often with good effect, in insane patients (not, however, in acute mania). We ourselves have given it for a similar purpose with excellent result in nervous patients suffering from sleeplessness.

Recently beer has been very much recommended in a great many conditions, as a sort of panacea. It certainly has some nutritive value, especially if it contain a large proportion of sugar and albumenoids, but more cannot be expected from its use.

We would add, that persons disposed to corpulence should indulge in beer very rarely.

Brandies, etc.

These liquors are nothing more than strong solutions of alcohol in water, with which are mingled various ethereal oils, from the various fruits used in the preparation of these brandies. Thus we can distinguish potato, corn, prune, and cherry brandies; cognac made from the skins of the grapes, rum from sugar, arrack from rice, gin from juniper berries, caraway brandy, bitter brandies, owing to the addition of gentian, and absinthe, made by the addition of oil of wormwood. At the present time, when it is understood how potato brandy can be purified of its ill-smelling fusel oil, almost all of the above brandies are prepared from this, the various flavors being given by the ethereal oils. Brandies to which much sugar has been added are called liqueurs.

The amount of alcohol in the different brandies varies from 20 to 50 per cent.

Physiological Action.—It is like that of dilute alcohol, and differs only

from it when the brandy is adulterated with many injurious substances. Thus the fusel oils, which are higher members of the homologous series to which ethyl, amyl, and propyl alcohol belong, although they have an action similar to that of ethyl alcohol, yet they are the most frequent cause of the evil effects which the cheaper brandies, which are rich in fusel oil, have upon the lower classes.

So also the oil of wormwood * present in the absinthe is the cause of the tetanoid and epileptiform convulsions, which are not ordinarily found in chronic alcoholism. Adulteration with nitrobenzole † may give rise to even fatal diseases.

Dietetic and Therapeutic Application.—We cannot here enter upon any long discussion concerning the dietetic value of the brandies. Their injurious effect when taken in too large quantities is so generally known, that it is useless to discuss it. We cannot deny, however, that under proper circumstances, and when taken in proper (small) quantities, brandy is a useful agent. A small quantity given after a rich meal with fatty food, has an excellent effect upon digestion. The custom of passing around liqueurs after meals is therefore a good one.

Nor can we deny that the addition of a small quantity of brandy to the water which is drunk to cool off the heated body renders the water less injurious than when it is taken pure under the same circumstances. Furthermore, it is certain that a dose of brandy enables a workman employed in damp and cold weather, and who has been very much wearied by considerable physical exertions, to undergo a larger amount of labor. Furthermore, brandy, with poor people, takes the place of the expensive spices with which the well-to-do person renders his food more agreeable, and also more digestible.

It is true that even in these cases, as the temperance societies urge, brandy is not an absolute necessity. A sufficient supply of food, or, what is not so good, the use of coffee, etc., will replace it. We do not urge, however, that even a moderate indulgence in brandy is an absolute necessity, for it is undoubtedly true that with those who have not the proper amount of control over their appetites even this moderate dietetic use of brandy may end in the habit of intemperance. But what we affirm in spite of all this is, that, when properly used, these liquors are beneficial.

Medicinally, brandy is used as a stimulant only in cases of sudden sinking of the heart's action, when it is important to stimulate it promptly. But for this purpose wine should be preferred, and the indications for its use have been thoroughly discussed. In other conditions also, in which alcohol is given medicinally, wine should likewise be preferred: thus in febrile diseases, which we have indicated above; here also the contraindications to the use of alcohol were given. When alcohol is to be used as a disinfectant, spirits and the brandies are to be preferred; thus Leyden uses brandy with success in gangrene of the lung.

Externally, dilute alcohol and brandy are very much used; first of all in hyperidrosis, both local and general. We have seen the night-sweats of phthisis almost entirely disappear for a time by washing with brandy or spirits, and the same procedure is very useful in the disagreeable local perspiration of the feet or hands. Even when taken internally

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* Compare Oil of Wormwood. † Compare Nitrobenzole.

(cognac and milk), before bed-time, it seems to have the effect of diminishing these sweats. Frictions with brandy (to which are added various substances) are very much prized by the laity as counter-irritants to deep inflammatory affections, such as contusions, chronic rheumatism, etc. Of course this procedure is decidedly inferior to other similar remedies, and it is a remedy very much abused by the laity, who often use it in acute inflammatory affections, while properly it should only be used in chronic diseases. As an injection to produce adhesive inflammation, tincture of iodine is preferable to alcohol. C. Schwalbe, however, recently recommends injections of 15 to 80 per cent ethyl alcohol, to cause healing of various diseases of the vessels, such as venous angiomata, varices, hemorrhoidal knots, and varicoceles. The injection should be carefully made, in the neighborhood of the diseased vascular area.

Alcohol is much used in the pharmaceutical preparation of a large number of drugs, such as tinctures, alcoholic extracts, etc.

Alcohol mixes with water in various proportions, the different concentrations giving us various preparations.

1. Spiritus vini absolutus s. alcoholisatus—alcohol free from water; properties, page 346.

2. Spiritus vini rectificatissimus, alcohol vini,—highly rectified alcohol,—has a specific gravity of 0.830 to 0.834, and contains from 90 to 91 per cent of alcohol.

3. Spir. vini rectificatus, spiritus dilutus—rectified alcohol; specific gravity 0.892 to 0.893; has 68 to 69 per cent of alcohol. Both of the latter preparations are not used internally, but only in the preparation of drugs; the first is not at all used.

*Spir. vini—raw spirits—ordinarily contains 50 per cent of alcohol, and is prepared from various substances. The ordinary kinds are: Spiritus solani tuberosi—potato alcohol—has the disagreeable odor of fusel oil; spiritus frumenti; whiskey; spiritus vini gallici—brandy obtained from fermented grapes—and has an agreeable odor. Spirits rich in alcohol are arrack, rum, and cognac. Ordinary diluted spirits are sometimes termed aqua vitæ. Liquors are simply ordinary diluted spirits flavored and sugared. The taste, odor, and action of ordinary brandy and spirits can be modified by bitter and aromatic-bitter substances.

Kumys.

The milk of some species of mares has as much as 9 per cent of sugar, while that of women contains at most 6 per cent. Cow's milk contains at most 4 per cent of milk-sugar. On fermentation, such milk turns into a strong alcoholic drink, of white color and agreeable acid taste (owing to the CO_2), which has long been used for similar purposes by the Bashkirs and Kirgis. Fresh kumys contains, in addition to the milk components (such as fats, lactic acid, milk-sugar, and salts), 1 to 2 per cent of alcohol and 0.8 per cent of carbonic acid.

Physiological Action.—When kumys is taken fresh, at the ordinary temperature of fermentation or by the addition of warm water (as Postinkoff and Messing think it ought to be taken), it causes a feeling of warmth in the stomach and over the whole body. It is only when it is taken cold that, according to Stahlberg, it produces a cold feeling in the stomach.

At the beginning of a systematic kumys cure the stomach always gets out of order. When one has become accustomed to it, however, and the

patient can take from 5 to 6 bottles (3000 to 4000 grms.) daily, the following effects are obtained from its use:

The appetite for other food is diminished; the excretions are increased, and have a peculiar odor; the specific gravity of the urine is also augmented; perspiration, especially in warm weather, becomes very profuse. The mucus membranes are irritated and secrete an increased amount of mucus: this irritation may even go on to the production of a conjunctivitis. The sputa of those suffering from phthisis become more copious, but looser, and have the odor of kumys.

The rapidity of the heart's action is at first slightly increased, and then rapidly diminished. The psychical effects are the same as those produced by alcohol: there is a slight degree of intoxication (6 bottles of kumys have about as much alcohol as two bottles of champagne), a feeling of well-being, and increased physical and mental capability, followed by weariness and drowsiness, which are apt to continue throughout the cure.

After several weeks the face takes on a rosy red color, the eyes glisten, and the respiration is less frequent but deeper, while the capacity of the lung in phthisical patients is increased. The patient becomes fatter and the weight is increased.

Menstrual loss is at first diminished in quantity, but soon becomes normal again. The effect upon the movements of the bowels is uncertain, but it is probable that they are more frequent and the amount of fæces increased. All these physiological effects can be accounted for by the components of kumys.

Therapeutic Application.—Kumys is very much lauded, especially by the Russian physicians, as a cure for phthisis. It is of course not a specific against this process, but is without direct influence upon the local action going on in the lungs, although Postinkoff and some others affirm that under its influence infiltration is diminished and cavities contracted. The statement needs further confirmation.

The importance of kumys in the treatment of phthisis lies especially in the fact that it is a superior nutritive agent.

Stahlberg and Brzcinski advise that the cure should not be begun when the phthisical process is accompanied by a continual fever. Where there is a tendency to hæmoptysis great care should be taken in using kumys.

The kumys cure has not shown itself so important in the cure of phthisis as it was expected ten years ago.

Kumys is also said to be an excellent nutritive agent in other cachectic and anæmic conditions. Thus, in ordinary, or in anæmia from loss of blood; so also in diseases accompanied by extensive suppuration, in continued diarrhœa or in bronchorrhœa, in anæmia after long acute disease.

Contraindications generally given are organic disease of the heart and vessels, general plethora and apoplectic habit, organic disease of the nervous centres, liver, and kidneys.

The opinion that the good effect of kumys is only obtained by a sojourn in the Steppes is erroneous, for good results have been obtained in Moscow, Warsaw, Wiesbaden, etc.; while, on the other hand, experience has shown us that the climate of the Steppes is without effect in the cure of consumption, when for any reason (individual idiosyncrasy, etc.) the daily quantity of kumys is diminished to 2 or 3 glasses.

Chloroform.

Chloroform or formyl trichloride, $CHCl_3$, is produced by the direct action of chlorine upon methane and methyl chloride; also by the distillation of methyl and ethyl alcohol, and of acetone, etc., with chloride of lime, or by warming chloral in a potash solution.

It is a colorless, clear, highly refractive fluid, not miscible with water, and boiling at 61° C.

The commercial chloroform is frequently rendered impure by admixture with alcohol, aldehyde, ethylene and ethylidene dichloride, and cannot therefore be used therapeutically.

The following are the reactions of pure chloroform:

It does not change vegetable colors. A mixture of chromic and sulphuric acid is not turned green; while the chloroform should not turn brown under the action of sulphuric acid or potash lye.

Even pure chloroform is rapidly decomposed under the action of sunlight, chlorine gas and hydrochloric acid being given off. To prevent this it should always be kept in the dark, and mixed with 1 per cent of absolute alcohol. This latter admixture renders its decomposition difficult, even in diffuse sunlight.

A piece of potassium iodide and starch is a good test for free chlorine in the chloroform; if the gas be present, it will turn the part blue. To purify any suspicious (undergoing decomposition) sample of chloroform, mix with 4 volumes of water and pour off the supernatant liquid.

Physiological Action.

The action of alcohol and chloroform are qualitatively very similar; that of the latter is more rapid, more intense, and does not last as long as that of the first, on account of the greater volatility, more rapid absorption and excretion of the chloroform.

Before chloroform was known, the insensibility of alcoholic intoxication was used for the performance of painful surgical operations.

The Absorption of Chloroform into the Organism.—Since the absorption of chloroform into the blood and organs is more dependent upon its physical properties (volatility) rather than its affinity for the tissues of the body, the rapidity with which it produces narcosis and the length of its duration vary with the temperature and atmospheric pressure. At higher temperature and a greater pressure it is more rapidly absorbed. At higher temperature also the narcosis passes off more quickly.

Like all volatile bodies, chloroform is absorbed by the unbroken skin; it can even produce general narcosis after one and a half hours' application to the integument, in spite of all means taken to prevent its absorption through the

mucous membranes or the lungs (Roehrig). According to Parisot, substances which are not absorbed by the skin when in watery solution are absorbed when dissolved in chloroform. Thus atropine, when applied to the skin of the forehead in the shape of a chloroform solution, in the space of 5 minutes produces a maximum dilatation of the pupil, being absorbed because the chloroform has dissolved the fat of the skin; this is confirmed by the fact that even a watery solution of atropine will be absorbed by the skin, if it has first been deprived of its fat. Roehrig, however, thinks that the atropine is vaporized with the chloroform, and thus exerts its effect.

Of course chloroform is more readily absorbed through the mucous membranes and in the form of a vapor by the lungs.

Under what form chloroform remains in the blood of living beings, we do not know; after death from chloroform, only small amounts have been found in the blood, but its decomposition products (such as hydrochloric acid and formic acid; Buchheim) have not been shown to be present in chloroform. It is therefore an open question whether, in the living organism, chloroform undergoes any alteration or not, the more so since the circumstances under which it is excreted have not yet been thoroughly studied. Lallemand has found that it is excreted unchanged, in from 30 to 50 minutes, by the skin and respiratory organs. In the urine it has also been found (Hegar).

The prime effect of the chloroform is chiefly upon the substance of the nerve-cell. But what portion of nerve-substance is thus altered, and what chemical alterations of the nerve-cells and fibres are the basis of these functional disturbances, we can only surmise. The hypothesis of Lacassagne, that chloroform only suspends the vibration of the nerve-molecules, is no explanation. L. Hermann believes that chloroform, like many other anæsthetics, has the effect of swelling up and dissolving the protagon of the living nerves; and furthermore, he believes that the efficacy of the various anæsthetics depends upon their greater or less solvent action of this substance. Kussmaul has also shown that chloroform renders albumen more filterable and less coagulable, while H. Ranke has demonstrated that bubbling chloroform through a clear solution of nerve-substance in a short time causes a cloudiness; besides this, we know that the myosin sometimes coagu-

lates in chloroformed animals. Neither hyperæmia (Carter) nor anæmia (Cl. Bernard) of the nerve-centres will account for the nervous phenomena to which chloroform gives rise. The alterations in the blood itself, as we shall show later on, are certainly not the cause of the functional disturbances.

Acute Chloroform Action.

Locally, the evaporation of chloroform upon the skin produces a feeling of cold. If the evaporation be prevented we have a burning sensation, inflammation and reddening of the skin, and an eruption, with the formation of blisters. After a time a local anæsthesia sets in, due partly to the cold or, if evaporation was prevented, to the paresis of the sensory nerves of the skin from the effects of the chloroform absorbed through the skin.

Upon all of the mucous membranes, the conjunctiva, mouth, pharynx and stomach, chloroform produces a sensation of warmth and burning; in the nose it produces the effect of a sweetish odor; it also causes difficult respiration, and, by reflex action, increases the secretion of saliva and tears. Later on there is deafness and diminished sensibility at all localities with which it comes in contact. Taken in larger quantities it causes symptoms of gastro-enteritis, abdominal pain, vomiting and diarrhœa, which persist long after the disappearance of all the general symptoms to which the chloroform may have given rise.

The purely general effect is best studied by inhalations of chloroform vapor mixed with a sufficient amount of oxygen; for, when given by the stomach, the local effects mask the general symptoms; when administered without a sufficient amount of oxygen, death results from suffocation. Recovery from the effects of the drug takes place much more slowly when it is given hypodermically, or by the stomach, than after inhalation, because in the former case additional quantities of chloroform are being constantly absorbed.

Different animals bear chloroform with about the same general effects, but the narcosis resulting from the inhalation of chloroform is neither as deep nor does it last as long in cats, rabbits, and dogs as in men. In birds the anæsthesia is of shorter duration. Cats and rats die very

quickly from chloroform, from paralysis of respiration. In frogs a few drops cause paresis and loss of sensibility and the reflexes in a short time, without causing any preliminary excitement; other cold-blooded animals, such as snakes and lizards, can stand much more.

We shall now describe the general symptoms resulting from the inhalation of chloroform. The "intoxication" here produced, like that of alcohol, can be divided into two stages—that of excitement or irritation, and that of paresis. The relative duration and intensity of each of these stages varies in the different individuals: in children complete unconsciousness and insensibility set in after a few respirations. In irritable people, however, or those addicted to drink, the stage of general irritability is very much increased in length, and may even take the form of a violent mania; in some unconsciousness and insensibility (anæsthesis) only set in after fatal doses.

The first of the general effects observed is a feeling of warmth which spreads over the whole body; also a disappearance of all disagreeable sensations, such as tickling, pressure of the clothes, etc., thus giving rise to a feeling of extreme well-being. This is followed by formication and prickling in the extremities; the fingers and toes are numb, and the acuteness of sensation is dulled. Then clearness of thought disappears, the speech becomes confused and incomprehensible. Everything appears as though covered by a veil; sight is not clear, and the hearing diminished; sounds become dull, and as though coming from a great distance. Hallucinations and illusions occur, ideas flow faster, and a delirium characteristic of the individual sets in; some sing and rejoice, others cry and complain. While this stage of alcoholic intoxication is accompanied by clearness of thought, speech, and wish, this is not the case with chloroform: the chloroform excitement resembles in the very beginning that of alcohol and wine after large quantities have been taken.

Besides the above symptoms, we see the face become red, the skin warm and moist, the pulse and respiration more rapid, while the pupils are contracted. If the patient be chloroformed immediately after a meal, vomiting frequently sets in.

Soon complete insensibility results. The stage of excitement is followed by rest of mind and body. The muscles are relaxed; if an arm or leg be raised, it drops as though

it were dead. There is no resistance to any movement. The masseters are last of all the voluntary muscles to be relaxed, and even after all the other muscles are paralyzed there is still a convulsive contraction of the masseters; sensibility disappears last of all in the region of the forehead and temples, so that no reflex movements can set in. The only reflex result of the irritation of the skin or auditory nerve is a slight dilatation of the contracted pupils. The eyelids are closed, and sensibility is lost. Still a dream-like state seems to continue, so that the anæsthetized patient murmurs disconnected sentences, as though in a dream. Now the most painful operations may be undertaken without the pain being felt; some say they felt touch but not pain during the operation, while others cry out and struggle slightly, and yet have no recollection of pain after the operation is over.

The pulse is calm, slow, and sometimes weakened; there is a slowing of respiration, and snoring in consequence of paresis of the soft palate.

If no more chloroform be inhaled, the anæsthetized patient awakes after 5 to 30 minutes, sometimes only after 10 to 20 hours; the less the respiration is affected the more rapid the awakening. He opens his eyes, but is still confused and his recollection clouded; the heart's action becomes stronger, and finally motility returns; some vomit again, or shiver and fall into collapse. There may be no further sequelæ, or vomiting and severe headache may persist for twenty-four hours; sometimes there is jaundice, and bile is found in the urine; at other times there is temporary albuminuria.

When the inhalation of chloroform is continued, the paralysis of all parts becomes more and more complete, until finally no reflex dilatation of the pupil and no closure of the eyelids occurs when the conjunctivæ are touched; continuance of the respiration and the beat of the heart show that life still exists; these functions also constantly become weaker and slower. The pulse is thread-like, irregular and intermittent; respiratory movements slow; there are signs of carbonic-acid poisoning; cyanosis and protrusion of the eyeballs; dilatation of the pupil, and finally the patient dies from paralysis of the heart and respiration.

The amount of chloroform necessary to produce these symptoms varies in different individuals from 1.0 to 30.0 grms.

Effect upon the Individual Organs and Functions.

There is no doubt that chloroform as well as alcohol produces direct alterations in the nerve-substance, and that most or all of the nervous disturbances are due to these, and not secondary to changes in the blood (anæmia, hyperæmia, stasis in the cerebral capillaries, etc.). Flourens, Longet, and Coze have shown that in etherized and chloroformed animals the different portions of the central nervous system lose their irritability to the electric current and other irritants in the same order that they lose their functions. Bernstein and Lewisson chloroformed bloodless frogs, or those in whose veins only a 0.7 per cent solution of sodium chloride circulated, and saw all of the ordinary effects of chloroform result, although they set in rather more slowly. According to L. Hermann, animals which have only a colorless circulating fluid can be brought under the effects of chloroform.

The nerve-cells, and of these those sensible nerve-cells lying in the gray substance of the cerebral hemispheres, are most rapidly brought under the influence of chloroform. The motor nerve-cells withstand its effects for a longer time, as is seen from the ordinary phenomena of chloroforming, and also from direct experiment.

Hitzig's motor manifestations, following upon irritation of the motor centres of the brain, will take place for a long time after the animal has been brought under the influence of ether or chloroform.

In the stage of complete insensibility we have still left a reflex irritability of the voluntary muscles, as well as the involuntary muscles of the vessels and pupils; after these are paralyzed we have still the movements of respiration and the heart. It is due to the difficulty with which the ganglia of the medulla oblongata and heart are paralyzed that we are able to use chloroform in practice. Doses which paralyze the motor ganglia also are dangerously near lethal doses. The centres for reflex movement in the spinal cord are sooner affected, however, than the respiration and circulation.

Even after all of the ganglia in the brain and spinal cord are paralyzed, the nerve-fibres both of the peripheral, sensory, and motor nerves are still irritable; only when the

drug is applied locally does a diminution of paralysis of motion in the periphery, or sensation locally, take place, while central irritability remains intact.

Even after the paralysis of the motor nerve-ends has set in (from the largest doses of chloroform) the muscles may still retain their irritability. When bare nerves are directly exposed to the vapor of chloroform their irritability is at first increased, to be later on diminished; if the action of the chloroform be suspended for a time, the nerve may entirely recover, otherwise it will die (Bernstein, H. Ranke).

The pupils both in men and animals are dilated during the excitable stage; at first they react sluggishly to light, later on not at all (Budin and Coyne). They contract considerably during the stage of anæsthesia, but will still dilate in response to sensitive irritation—pricking of the skin, shouting, etc. (Westphal). During the greatest anæsthesia there is continuous dilatation of the pupils. How to explain these things is not very clear. A central irritation of the oculomotorius is thought to be cause of the contraction; paralysis of the nerve is considered the cause of the dilatation. The reflex temporary dilatation of the first stage is probably in the region of the sympathetic.

The rapid cessation of sensibility is due, according to what has been said, not to paralysis of the central, but of the peripheral apparatus. The excitable stage, the singing and raving, is due partly to paralysis of the power of the will, —situated in the cerebrum,—so that voluntary motion is no longer controlled by the will. In addition to this we have the fact that the reflex apparatus of the spinal cord remains intact, and the peripheral sensitive nerves are still irritable, although sensations of pain are no longer carried to the centre of intelligence, but to the reflex centres (in the spinal cord) of the voluntary muscles of the extremities and larynx, and the unstriped muscles of the vessels and the pupils. The primary excitable stage is therefore due to paralysis of the central inhibitory apparatus, and increased or undiminished irritability of the peripheral sensory nerves and reflex apparatus of the spinal nerves.

The remarkable fact that some patients when under the influence of chloroform do feel the operation, not as a painful sensation but simply as touch, is explained by the theory that painful sensations are transmitted through the gray matter of the spinal cord and touch through the posterior white columns; the former are supposed to be already

paralyzed by the chloroform, the latter not. We know that when this gray substance of the cord is cut through there is not anæsthesia, though there is complete analgesia. This hypothesis, however, would necessitate the assumption that the gray matter of the spinal cord is more rapidly paralyzed by chloroform than that of the brain. We would therefore consider it more probable that the irritability of the gray matter of the brain is the first to be diminished, though not paralyzed, by the chloroform, and, as a result of this diminution, painful sensations are not received as pain, but simply as touch.

Voluntary Muscles of the Body.—In frogs, which are subjected to the influence of chloroform vapor under a bell jar the voluntary movements are the first to cease. Direct as well as indirect irritation of the nerves causes a contraction of the muscles. Then the intra-muscular nerve-ends become paralyzed, and the muscle responds only to direct irritation. Finally, the muscle itself becomes non-irritable, without, however, having its electro-motor power diminished; the latter is only destroyed when the muscle becomes stiff (H. Ranke).

Rigor mortis sets in much sooner than after death from other causes. As early as half an hour after the beginning of the above experiment the toes of the paralyzed animal are stretched out; if the frog be now exposed to the air the rest of the muscular system will become stiff in from 10 to 15 minutes; the heart muscle still continues to beat. The stiffened muscular fibres as well as the lymph which surrounds them have an acid reaction, while the blood still remains alkaline. The stiffness develops even in muscles the blood-vessels of which have been tied off and whose nerves have been cut out.

In warm-blooded animals as well as in men this rigidity sets in more rapidly; this is especially well seen in birds which have been chloroformed only very slowly (H. Ranke, Senator).

The cause of the rigidity is the effect of the vapor of chloroform upon the muscular tissue; clear myosin solutions are rapidly precipitated by chloroform (H. Ranke).

If the chloroform be injected into the vessels, the muscles, including the heart muscle, become rigid immediately (Kussmaul).

Ether and the amyls have a similar although weaker ef-

fect (H. Ranke); so also butyl ether, and probably many other substances of this class.

As to the effect upon the involuntary muscles, we know little. The uterus can contract even in the deepest chloroform narcosis, so that a paralysis of the uterine muscular tissue can only be imagined after the largest doses; the muscular coats of the vessels are also only with great difficulty influenced by chloroform.

After the injection of chloroform under the skin or into the stomach (less often after inhalation), the heart and voluntary muscles undergo fatty degeneration (Nothnagel).

Respiration.—In the very beginning of chloroform inhalation the local irritation of the branches of the trigeminus which supply the nasal mucous membrane causes, as a reflex result, either a slowing or even a temporary stoppage of the respiratory movements, a cessation of expiratory movements, and convulsive closure of the glottis. These symptoms are entirely wanting if diluted chloroform be inhaled, or if the animal experimented upon be tracheotomized (London Committee). In the latter, on the contrary, the respiration is rendered very superficial because of the irritation of the vagus. By means of this reflex action the organism is prevented from absorbing too much of the chloroform. In animals in whom the vagi have been cut the respiration ceases entirely after two minutes of tracheal inhalation (in consequence of a severe irritation of the respiratory centre) (Knoll). In deep chloroform narcosis, without exception, the respiration becomes slower and softer, and it may cease entirely, death setting in.

The pure chloroform effect is often clouded by carbonic-acid poisoning, which sets in either in consequence of insufficient respiratory movements, and the dyspnœa due to the insufficient amount of air inhaled.

Circulation and Blood.—Of all the nervous apparatus, in most men and animals, that of the circulation has the greatest power of endurance, so that the heart can act for a long time after the paralysis of the brain and medulla. Still there are exceptions; and the London Committee observed that when concentrated chloroform vapor was inhaled through a tracheal fistula the heart was the first to be paralyzed.

Generally, both in men and animals, the rapidity of the pulse as well as the blood-pressure are at first increased, but diminished later on, when there is a slowing, weakening, and irregularity of the heart's action (from $\frac{1}{3}$ to $\frac{1}{2}$ of the

normal) and dilatation of the peripheral vessels (Scheinesson, Vierordt, Lenz); all this owing to primary irritation followed by secondary paralysis of the musculo-motor nerves of the heart and vessels. In some men and in rabbits (Dogiel) immediately after the first inspiration of concentrated chloroform vapor there is a temporary slowing of the pulse for the same reasons as those given above to account for the slowing of the respiration.

In deep chloroform narcosis, irritation of the sensory nerves in animals produces little or no reflex increase in the blood-pressure (Bowditch and Minot).

In the living circulating blood of animals under the influence of chloroform no alterations from the normal have been demonstrated, even when the chloroform vapors have been allowed to play directly around vessels lying free, such as those of the frog's mesentery (Schenk). If, however, blood be taken directly from the vein and mixed with chloroform it undergoes great alterations. The blood-corpuscles swell, become round, and dissolve finally, as Hermann thinks in consequence of the dissolution of the protagon, which forms the blood-corpuscle stroma; in some animals also (not in man) if the blood be in an oxidized condition the hæmoglobin is crystallized from it (Böttcher); furthermore, there is a brick-red deposit, which contains much chlorine. Notwithstanding this, but little chloroform can be gotten back again from the blood, while if the chloroform have been mixed with blood-serum alone almost the whole of it can be obtained back again from the solution. Although alcohol coagulates all of the albuminoid components of the blood, with the exception of globuline (the fibrinoplastic substance), chloroform acts only upon the blood-globules and the globuline, the latter of which it precipitates from the serum also. We must suppose that chloroform enters into a firm combination with the red blood-globules (Schmiedeberg). Blood mixed with chloroform is much more slowly reduced by reducing agents than normal blood (Bonwetsch). For the present, it does not seem probable that these theoretically important facts will hold good in reference to living blood; for if the blood-corpuscles were dissolved by chloroform in the living body, then we should expect to find the coloring matter of the blood in the urine—which is not the case. Besides this, the fact, demonstrated by Schmiedeberg, that chloroform does not combine with the blood-corpuscles, even outside of the

body, if the blood be oxidized, is against the idea that such a combination takes place in the living body.

The bodily temperature rises during the period of excitation in the axilla from 0.1° to 0.8° (Simonin), and sinks in the stage of anæsthesia from 0.5° to 3.0° C. (Dumeril and others), without, however, diminishing directly as the depth of the anæsthesia. According to Mendel this sinking is more rapid in the cranial cavity than in the rectum (?). In the ear of the rabbit, however, sometimes a slight rise of temperature was noted, coincident with a dilatation of the blood-vessels. The cause of this lowered temperature is partly the increased radiation of heat by the skin, together with a diminution in the production of heat, owing to diminished blood-pressure slowing the circulation, and muscular inactivity.

Tissue metamorphosis has always been supposed to be diminished by chloroform, without however any accurate experiments having been made upon the subject. This conclusion was arrived at from the lowered heart's action, and blood-pressure and muscular inactivity. According to Eulenberg-Struebing, chloroform in the system alters the relationship existing between the amount of nitrogen and phosphoric acid excreted, in such a manner that the relative amount of the phosphoric acid is very much increased; they believe this to be due to the action of chloroform upon lecithine (a combination of neurine with fatty acids and glycero-phosphoric acids); and thus the theory of Hermann would be confirmed, according to which chloroform has a chemical action upon the nerve-substance, and in this way produces anæsthesia. They also seem to agree with the opinion of Zuelzer in conditions of depression of the nervous system—the wear and tear in the nerve-substance is greater than that in the muscular tissue.

We have already called attention to the fatty degeneration of the heart, liver, etc., which is apt to take place in intense chloroform-poisoning.

In the urine both of men and animals after the internal administration of chloroform, we often find the presence of biliary coloring matters (Nothnagel, Naunyn), but never the coloring matter of the blood; sometimes albumen, and a class of substances which reduce copper in Fehling's liquor, and which were supposed to be sugar, but according to a note in the *Lancet*, and according to the experiments of

Hegar, it is nothing more than the chloroform excreted with the urine, which also has the power of reducing Fehling's solution.

Death from Chloroform.—Many cases of so-called chloroform death are due to the use of impure chloroform, or the administration of chloroform with an insufficient amount of air, in consequence of unskilful manipulation, or insufficient ventilation of the air-cells where the respiration is superficial (death in these cases being due to suffocation and not to chloroform); some also are due to shock from operating during imperfect anæsthesia. There still remains a large number, however, which are due to the poisonous action of the excessive amount of chloroform which has been inhaled (such are cases of suicide), or to some individual peculiarity (weakness of respiratory or circulatory apparatus, fatty heart, disease of the valves, etc.). We can distinguish two ways in which death is produced by chloroform: either the heart is suddenly brought to a stand-still through paralysis of its musculo-motor apparatus, or the patient dies suddenly from collapse (syncopal). Several respiratory movements may be made after complete disappearance of the pulse. On the other hand, the respiration may cease suddenly in consequence of paralysis of the respiratory centre in the medulla, the heart still continuing to beat: the respiration cannot be again restored in these cases. We saw a case in which artificial respiration was continued for half an hour, as long as the heart continued to beat, without success. What share the gas bubbles (which gas is unknown) which have been found after death from chloroform in the vessels and heart take in the cause of death from chloroform, has not yet been shown (Langenbeck, Sonnenberg).

The fatal dose of chloroform is not readily determined. Death has followed after the inhalation of 2.0 grms., while other individuals can stand 30.0 to 60.0. Sometimes death sets in after the first few inhalations, while at other times not until chloroform narcosis has lasted for hours.

An autopsy reveals nothing abnormal further than the presence of a chloroform odor).

Chronic Chloroform Poisoning.—Chloroform is much more rarely used chronically than alcohol or other anæsthetic agents. In addition to disturbances of nutrition due to loss of appetite, there are also periodic psychical disturbances, so that there are intervals of freedom from psychical symp-

toms, alternating with madness or melancholic attacks (Büchner, Böhm).

Therapeutic Application.

For therapeutic purposes chloroform is either inhaled or rubbed upon the skin externally; recently it has been injected hypodermically.

These methods of application are quite sufficient, and experience hitherto has shown no conditions in which one of them did not answer the purpose.

In the first place, the remedy has been very little used in diseases belonging to the field of internal medicine. We shall not enumerate the conditions in which it has been tried and then again given up—such as pneumonia, cholera, intermittent fever, and many other conditions. Husemann praises it as a palliative remedy in vomiting (of pregnancy, phthisis, alcoholism). Chloroform is indicated, however, and does good (inhaled, or injected hypodermically) in those conditions in which, owing to its anæsthetic action, it is necessary to relieve temporary pain, or when it can be employed as an anæsthetic. In its application we must always remember that its power of relieving pain or spasm is not due to any effect upon the peripheral, but upon the central nervous apparatus.

Chloroform inhalations are very useful in some cases of spasmodic cough and spasmodic dyspepsia, which often cannot be relieved by any other remedy; thus, in the so-called spasmodic asthma, also in the asthmatic attacks, of emphysematous patients, or in pulmonary phthisis. In other spasmodic affections indications may become necessary to satisfy an indicatio vitalis: thus in chorea when the muscular movement is constant; also in epilepsy when the attacks are almost constant, and œdema of the lung is imminent. It has also been used in severe cases of tetanus, when life is endangered by a direct spasm of the inspiratory muscles. In neuralgic affections chloroform is less useful, and is secondary to morphia. Its application in delirium tremens is not altogether unthought of, but since we have chloroform it will be entirely superfluous; this is especially true of the psychopathies (mania, etc.).

The use of chloroform as an anæsthetic in surgical operations is very extensive. We cannot here mention the individual operations in which it may be inhaled, but only those

in which it should not be used. For there are very few operations in which it cannot be used. The object of anæsthesia is chiefly to avoid the pain of the operation. In addition to this we have the advantage gained by operating upon a patient who is quiet. Again in some cases the relaxation of the muscles which anæsthesia produces is an important consideration: thus in reposition of hernias and the reduction of dislocations and fractures. In children, narcosis may be necessary in order to be able to make a thorough examination. Finally, the psychical irritability produced by and the after effects of the severe pain from any operation may be avoided by anæsthesia. Thus Snow and Simpson have shown that under precisely similar conditions the mortality from operations in which chloroform has been used is smaller, than when chloroform was not used.

For all of these reasons chloroform has become a very popular anæsthetic, to be used in most surgical operations. There are few operations in which it is not used—such as the reduction of slight dislocations, extraction of teeth, and opening of abscesses: in these operations it is only used in very sensitive individuals.

Husemann very properly observes that the relatively large number of cases of death from chloroform which are seen in these important operations are possibly to be explained by the neglect to wait for complete narcosis before beginning these trifling operations, and thus shock is produced; besides this, we must remember that in these minor operations narcosis is produced and the operation conducted without the assistance of another physician. Chloroform should not be used, or, if used, only with the greatest precautions, in operating around the mouth and pharynx, for there is danger of the blood running down the trachea and not being coughed back during the anæsthesia. Anæsthesia should be avoided in performing tenotomy where the tendon is to be held tense; also in lithotripsy so that the patient may be able to testify as to his subjective sensations. On the other hand, chloroform should be given in operating upon vesico-vaginal fistulæ, notwithstanding the opposite views of some few individuals. We will give the general contraindications to the use of anæsthetics later on.

In ophthalmic surgery chloroform is very much used in cataract operations, etc. We do not think it necessary to state all of the individual operations on the eye in which

chloroform should be used; we shall leave that to special works on ophthalmology.

The employment of anæsthesia during labor has been very much discussed. Experience teaches us the following facts: Upon the child in utero, chloroform (used during labor) has no evil effect; at least no case is known in which the use of the anæsthetic was followed by any evil results upon the fœtus.

The effect upon the uterus is like that upon the rest of the muscular system—that is, a relaxing one; in the first 10 to 15 minutes pains entirely cease, but return again. It also seems that after the use of chloroform post-partum hemorrhage and retained placenta from deficient uterine contraction are apt to occur more frequently than without anæsthesia. For these reasons chloroform is not much used in perfecting normal labors. It is only used in women who are hypersensitive to pain, or in cases in which the pains are strong and frequent, and where there is danger of rupture of rigid soft tissues in consequence; in these cases the diminution in the number and force of the pains which chloroform produces gives time for the soft tissues to dilate, and thus prevents laceration. Anæsthesia should also be employed in cases of "stricture of the uterus," spasmodic or hour-glass contraction of the uterus, after other remedies have been ineffective. In the "eclampsia parturientium" excellent results have been obtained, the attacks being entirely prevented by the narcosis, while the labor is completed. The greater and more painful obstetric operations (with the exception of the lighter forceps operation) are generally performed with the patient under the influence of chloroform (such operations are cases of turning, embryotomy, etc.). Where the placenta must be separated by the hand from the uterine wall, inhalations of chloroform have been found very advantageous, provided that there is no hemorrhage. In severe after-pains, after all other remedies have failed, chloroform may be tried.

There is a number of conditions in which chloroform should be used with great care or even entirely avoided. The first is true of young children, especially infants at the breast and very old people. It is true that chloroform narcosis often passes off in these cases without harm; on the other hand, we must remember that children are often anæsthetized after a few respirations, and that in old people paralysis of the central nervous apparatus sets in very readily. Chlo-

roform is best altogether avoided in cases of extreme corpulence, or where there is a tendency to cerebral hyperæmia, or syncopal attacks; also in epileptics. The same is true of very anæmic and very reduced individuals. Diseases of the heart, aneurisms, and affections in which a considerable portion of the lung is crippled, are positive contraindications to the use of chloroform. The same is true of chronic alcoholic intoxication.

The condition of anæsthesia always demands great attention on the part of the surgeon. The chloroform should be pure (compare the remarks on page 370). The clothes should be loosened so as to leave the breathing unobstructed. The best apparatus for the administration of the chloroform is simply a folded pocket handkerchief. The handkerchief should be so held over the mouth and nose as to secure the inspiration of a *sufficient amount of atmospheric air simultaneously with the chloroform.*

As to the dose necessary to produce narcosis, we can make no exact statement. It varies from 1 to 50 grms., according to individual cases. As a rule, however, 5 to 15 grms. will suffice. The technical points about the administration of chloroform are best learned practically by observing its administration once or twice. Pulse and respiration should be observed continuously; the least irregularity in either (apart from the primary acceleration) requires the immediate suspension of the chloroform, and the application of the necessary methods of relief. The other dangerous symptoms (paleness of the face and signs of asphyxia) have been already spoken of. When these really exist the chief indication is to administer fresh oxygen. To accomplish this we should seek to stimulate the respiration in some reflex manner, as by irritating the nasal mucous membrane and douching the skin with an energetic stream of cold water, or, if necessary, Marshall Hall's method of artificial respiration may be carried out. In some cases of commencing asphyxia the dangerous symptoms may be quietly relieved by pulling forward the tongue, which has sunk back, and thus caused the asphyxia. If all this is unsuccessful, the faradic current may be passed through the phrenic nerves in accordance with Ziemssen's method. Tracheotomy and transfusion have been tried, but the application of both of these is founded upon false assumptions.

When operations are to last from one to two hours, anæs-

thesia has frequently been maintained for so long a time by the use of chloroform; the anæsthetic is suspended when the patient is deeply under its influence and again resumed when he is coming out of the coma. It is nevertheless positive that in cases of this kind the use of the chloroform for so long a time may cause death by bulbar paralysis. Nussbaum has recommended that in such cases, as well as in those operations where a repeated application of the anæsthetic is very difficult (as, for instance, in exsection of superior maxilla), the use of morphine to continue the anæsthesia—a subcutaneous injection (0.01 to 0.05)—should be resorted to. This method of procedure seems in fact to be useful. Other observers have also noticed that the ordinary chloroform anæsthesia is very much deepened if a morphia injection be made a short time previously to the administration of chloroform.

The question as to whether chloroform or ether is to be preferred in the production of anæsthesia will be considered later on.

Finally, chloroform is also very much used externally. For the production of local anæsthesia, by the freezing effect, a spray of the anæsthetic ether is preferable. Chloroform ointments are very much used as pain-relieving agents in neuralgias, especially of superficial nerves, in muscular rheumatism, and in hyperæsthesia of the cutaneous nerves. Chloroform applied to the pulp of carious teeth relieves the pain.

Chloroform has been injected into hydrocele sacs, for the purpose of setting up an adhesive inflammation (V. Langenbeck). In some cases it has been effective, but it is inferior to iodine used for the same purpose.

Dosage.—Chloroformium. For inhalation to produce anæsthesia we require on an average from 5 to 15 grm. Internally it may be given in from 3 to 15 or 20 drops pro dosi, pure or in mixture. For relieving pain, externally applied, we use either a liniment or ointment (1 part to 5 to 10 parts). When dropped upon the surface of the body, in a pure state, its effect is due to the cold produced by its evaporation. For injecting under the skin we use from 1 to 2 of the Pravaz syringes full.

ETHER—ETHYL ETHER.

Ethyl ether—diethyl oxide (known as sulphuric ether, or simply ether), $C_4H_{10}O = C_2H_5 \cdot O \cdot C_2H_5$, is made by distillation of a mixture of sulphuric acid and ethyl alcohol. In a pure state it is a clear, limpid fluid, having a penetrating odor; it boils at 35°, and evaporates very rapidly at ordinary temperatures.

Physiological Action.

Since the physiological action of ether is very similar to that of chloroform, we shall here only refer to the few points of difference between the two agents.

Since ether, on account of its lower boiling-point, evaporates much more rapidly than chloroform, it produces a more intense sensation of cold, and is even capable of freezing portions of the living body; local ether anæsthesia is therefore deeper than that produced by chloroform.

If considerable quantities of ether are taken into the stomach, the normal temperature of which is higher than the boiling-point of ether, the vaporization is so rapid and enormous, that the stomach swells up, interfering with the respiratory movements of the diaphragm, and thus even death from suffocation may follow.

The general phenomena which characterize the ether narcosis are the same as those of chloroform, both in the stage of excitement and anæsthesia; the first stage, however, is said to be longer, the second shorter, than that of chloroform. The increase in the quantity of all the secretions which Claude Bernard says results from small quantities of ether, also follows from chloroform. The effects upon the blood and muscles, as well as the circumstances of its excretion from the body, are the same as those of chloroform; muscular rigidity sets in more slowly after the use of ether (H. Ranke). The dissolving action upon the protagon of the blood-corpuscles and the nerve-substance follows the use of ether as well as chloroform (Hermann).

Therapeutic Application.

As an anæsthetic, ether was formerly more frequently used than chloroform (Morton and Jackson), but has been entirely replaced by the latter. More recently, however, it has again been questioned as to which agent is preferable. The following is a brief statement of the views as they now exist:

Chloroform has the following advantages: In the first place, its odor is more agreeable to the patient; it is less irritating to the respiratory mucous membrane; anæsthesia sets in more rapidly, and, what is more important, lasts longer and is deeper. These advantages are counterbalanced by the fact that ether is much less dangerous, and

produces asphyxia with much greater difficulty, for the reason that its action is not so intense and rapid. The possibilities of a fatal termination are much less: were the latter point positively proved, ether would undoubtedly deserve to be preferred to chloroform, in spite of the advantages of the latter; but this point has not been proved. We cannot judge from the larger number of deaths produced by chloroform, for the latter is much more frequently used than ether; besides this, cases of death have been reported, even after the use of ether, although some deny this. But even a theoretical consideration shows how probable it is that a substance which has such an energetic action upon the functions of the brain and nerves should, under certain conditions, have a paralyzing effect upon the centres in the medulla; so that for the present we should recommend * the use of chloroform, on account of its many positive advantages over ether.

Internally, ether has been given in a large variety of conditions. In the first place, as one of the most powerful stimulants in unconsciousness, or in collapse setting in suddenly from any cause (thus in cholera, typhus, etc.). It excites the functions of the brain more strongly, and is therefore very useful in the form of a subcutaneous injection. But if we wish to stimulate the heart's action, then alcohol is better indicated. Ether is given in the various neuralgias, and affections which occur as symptoms of hysteria. Experience has shown that, like many other remedies, its favorable action is only temporary and symptomatic. It cannot be positively determined in which cases ether is of special utility, nor is it certain that it is to be preferred to other remedies. A purely empirical application of ether is in cardialgia, with vomiting (especially if this occurs in hysterical patients, and without the presence of any anatomical lesion). Its utility in meteorism is problematical. It may perhaps be of some use in hysterical patients. Of the many conditions in which the remedy can also be given, we would add cholelithiasis, because in this disease we have seen some results from its use, without being able to explain the ground of its action. It is not very trustworthy in this condition.

Externally, ether is used in two different indications.

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* Translators remind the reader that this is a foreign view of the matter.

First, as an irritant, for the purpose of exciting respiration by reflex irritation: thus in unconsciousness and asphyxia. It is thus used by inhalation, as an addition to clysters, and by causing it to be evaporated from the skin. In the latter case it acts by producing a local feeling of cold, and is better replaced by a stream of cold water. Recently, ether has been more generally used for the production of a local anæsthesia (Richardson). The cold produced by evaporation of the ether from the skin is very much increased if it be applied as a fine spray to any particular spot, either by means of the ordinary pulverizing apparatus, or any form of special apparatus used for this purpose (Richardson and Junker). The physiological effect of this freezing action is enormous. A portion of the skin can be rendered anæsthetic in the space of a few seconds, and if the vaporization lasts for a longer time, even deeply situated tissues, such as the surface of the brain, can be frozen in small animals through the skull. Anæsthesia thus produced has been very much used in the last few years to produce insensibility to the pain experienced from slight operations, especially operations on the teeth, cutting the prepuce in phymosis, epilation, etc. Even in the larger operations this procedure has been tried with success; thus in ovariotomy, where it has the advantage of not causing vomiting. According to our present experience, the cold does not generally seem to exert any bad influence upon the later progress of the wounds, although in some few instances inflammation has set in. Besides chemically pure ether, which causes local anæsthesia most quickly and energetically, many other drugs have been used for this purpose, which, however, are all inferior to ether, and therefore superfluous. Such are mixtures of ether and alcohol or chloroform, chloroform alone, chloride of methyl, etc.

Ether may also be used to relieve pain in superficial tissues—here it is sprinkled on externally; it is also especially used in hysterical hyperalgesia of the skin, especially in cephalæa. In this case ether also acts because of the cold resulting from its evaporation.

Dosage and Preparation.—Ether internally from 5 to 20 drops (0.3–1.0 pro dosi, 5.0 pro die) in some sugar water, in a tea, or upon sugar. For subcutaneous injection, 1 to 2 Pravaz syringeful.

2. Spiritus ethereus, spiritus sulphurico-ethereus, liquor anodynus mineralis Hoffmanni, spirits of ether, Hoffmann's drops—a mixture

of 3 parts of spiritus vini rectificatissimus with 1 part of ether; clear, colorless. Frequently used as a domestic remedy for syncope. In the various convulsive affections (especially of hysterical patients) in the same manner as ether. From 10 to 25 drops (0.5–2.0 pro dosi, 5.0 pro die) alone or as an addition to mixtures. 3. Collodium, liquor sulphurico-ethereus constringens—one part of gun-cotton (collodium cotton) dissolved in 18 parts of ether and 3 parts of spiritus vini rectificatis. Collodium is a thick opaque fluid. When this is applied to the skin, the ether evaporates, cold being produced, while a firm, horny-like membrane is left behind, which at first is closely applied to the skin, but later on contracts, becomes broken, and peels off. At the moment when the collodium hardens, it produces a considerable pressure upon the skin, which causes the vessels to contract and makes the skin pale.

This preparation is often used alone as a dressing, or for the purpose of producing fixation of other dressings (such as cotton, charpie, sticking-plaster, etc.). Because of its contractile power, it is often applied in the inflammatory conditions of the skin (erysipelas, light burns, frost-bites, mastitis, etc.); in these conditions it causes a contraction of the inflamed blood-vessels. The pain resulting from its application (due to the contraction) and the rapidity with which it breaks off are objections to its use. The latter objection is overcome in the newly officinal *collodium elasticum s. flexile*, 1 part of ol. ricini to 50 parts of collodium. Collodium is also used as a menstruum for applying various active substances to the skin. The most common of these preparations is the collodium cantharidatum (s. cantharides).

Chloral Hydrate.

Chloral (ethyl aldehyde trichloride), $C_2HCl_3O=CCl_3CHO$, is produced by the action of chlorine upon aldehyde, alcohol, and sugar, and is a colorless fluid of a penetrating odor. Even in weak alkaline fluids it is decomposed into chloroform and formic acid, the latter combining with the alkali.

Chloral hydrate $CCl_3CH(OH)_2$, is formed by mixing chloral with water, crystals of a rhombohedral form being formed; these crystals have a sharp, aromatic, bitter taste; boiling point at 98°, readily soluble in ether, alcohol, and water, forming a solution of a neutral reaction.

For medicinal use chloral hydrate is the most practical, because its crystals retain their properties for a long time, are not so readily changed as those of chloral, and more readily admit of convenient dosage. But since the formation of chloral is accompanied by the production of a number of additional chlorine products, which have an injurious action, we must be careful to see that the preparation of chloral which is used be a pure one.

Physiological Action.

The introduction of chloral by Liebreich may be said to have really enriched the materia medica, since it serves to fulfil a number of therapeutic indications which cannot be satisfied by chloroform or morphine.

Its Absorption and Progress through the Organism.—Chloral

hydrate is a far less volatile body than chloroform, and much more soluble in water. It is therefore absorbed with more or less readiness from the stomach; from any of the other mucous membranes, or when given subcutaneously.

Under what form it exists in the blood is still doubtful. Liebreich knew that chloral is decomposed in alkaline fluid into chloroform and formic acid; 147.5 parts by weight of chloral, with 40 parts by weight of sodium hydrate, are decomposed into 119.5 parts of chloroform and 68 parts of sodium formate. The quantity of alkali necessary to decompose 1.0 grm of chloral (free from water) is 0.271 sodium hydrate; this produces 0.810 of chloroform and 0.312 of formic acid. Chloral therefore requires about ¼ of its weight in alkali to be entirely decomposed. Liebreich thought that a similar decomposition took place in the alkaline blood of the body. It is true that according to his own calculations the percentage of alkali contained in the blood is insufficient to convert the chloral into chloroform; but the alkali of the blood is being constantly renewed, and therefore the decomposition of the chloral in the blood does not advance so rapidly as to be explosive; but as small quantities of alkali appear, so small quantities of chloral are decomposed, until the whole of the chloral has been decomposed. Every moment minimum quantities of chloroform are being formed, which are immediately absorbed by the cerebral ganglia, and later on by the ganglia of the spinal cord and heart; physiologically the effects of chloral are so similar to those of chloroform that it would seem to confirm the above theory.

Experience, however, as well as weighty theoretical considerations, are opposed to this theory. For we know that even the most powerful acids are unable to suspend the alkaline reaction of the blood; thus surely chloral does not possess this power. And if it really used up all of the free alkali of the blood the life of the individual could not continue. Furthermore, there are a large number of derivatives of the methane series which exert an effect similar to that of chloroform, and yet are not converted into the latter in the blood; while, conversely, Hermann and Thomaszewicz have shown acetic acid trichloride, which, like chloral, is decomposed in alkaline fluids into chloroform, exerts none of the chloroform effects.

It has not been possible to find the slightest trace of chloroform reaction in expired air or blood of animals

who were under the influence of chloral (Hammarsten, Rajewsky, Hermann, v. Mering, and Musculus). When chloral is mixed directly with the blood chloroform is always found, even after the mixture has been warmed to 40° C. Positive proof of the decomposition of chloral in the blood cannot be given, but in this connection Liebreich's claim is a valid one, namely, that this decomposition takes place in such small quantities at a time, and these small amounts of chloroform are immediately further decomposed.

According to Mehring and Musculus only small quantities of the chloral which have been absorbed can again be found as such in the blood; the substance has been converted into urochloral acid $C_7H_{13}Cl_3O_6$; after a dose of 5.00 grms. of chloral, there are found to 1000 ccm. of urine 10.0 grms. of the acid.

Lewisson's observation, that salt frogs in whose veins only solutions of sodium chloride circulate are affected by chloral, cannot be taken as helping to prove the falsity of the decomposition theory; first, because Lewisson's frogs may not have been entirely deprived of blood, and, secondly, because even the alkaline lymph might have the power of splitting up the chloral.

As will be seen, then, the weight of evidence tends in the direction of proving that the action of chloral hydrate, as well as that of many other methane chlorides, is specifically to these bodies themselves, and is not the result of the decomposition of the chloral. The fact that chloral exerts a local action upon the skin, mucous membranes, etc., where there can be no question of its being split up, is in favor of the view that its effect upon the system is due to itself. Its great antiseptic power is owing to this local action.

Acute Chloral Action.

Locally, upon the skin, very concentrated chloral-hydrate solutions produce pain, inflammation, and may even cauterize and form blisters. So also when injected under the skin, when the solution is stronger than 15 per cent. Ulcers, when painted with it, become covered with a white eschar (Liouville and Porta).

Upon the mucous membranes of the mouth it produces a sharp, bitter taste; in men and animals it causes vomiting, when the solution is too strong; therapeutically, therefore,

it must be given greatly diluted. The respiratory mucous membrane is also irritated by the inhalation of concentrated chloral-hydrate vapors.

The general effect of this drug has been studied by a great number of investigators (Liebreich, Hammersten, Porta, Rajewsky, Rupstein, Oppenheimer, and others) on men and animals, administered both hypodermically and by the stomach, the effect being the same from both methods of administration.

As is usual, there are individual variations in the effects produced by chloral hydrate. Animals (warm and cold blooded) are affected in a manner similar to the effect upon man, but in the former (dogs and rabbits) a primary irritable stage is more frequent than in the last. Rabbits and cats are particularly sensitive to the action of chloral, and readily fall into a condition of sleep and anæsthesia.

Children, anæmic and weak individuals, are less easily affected by chloral than other people; so also are those suffering from delirium tremens and nervous diseases. In all of these cases larger doses than ordinary are necessary to produce a narcotic effect. Nervous people are rather excited than calmed by a small dose; some individuals remain unaffected even after enormous doses.

Experience teaches us that the narcotic and fatal doses are as follows:

Animals.		Narcotic Dose. Grms.	Fatal Dose. Grms.
Frogs		0.05	0.1
Hens and doves		0.2	0.5
Rabbits		1.0–2.0	2.0–3.0
Cats		1.0–3.0	.....
Dogs		5.0–10.0	10.0–16.0
Human beings	Children	0.1–1.0	2.0–3.0
	Adults	2.0–3.0	5.0–10.0
	Drunkards	5.0–8.0	10.0

There is a report of a case of a woman who took 30.0 grms. of chloral hydrate, and was saved by energetic treatment (Ludlow and Eshelmann). The following is the chloral-hydrate effect in healthy and diseased individuals:

After doses of from 2 to 3.0 grms. there occurs in 5 to 15 minutes an overpowering weariness and drowsiness, followed by a natural sleep, lasting about five hours. During this sleep the respiration is regular, quiet, and slow; the heart's action somewhat slower; the patient can readily be

aroused from this sleep by calling him, or by tactile or painful irritation; he awakes with his mental powers in a normal state. During this sleep the pupils are contracted, as is the case in chloroform narcosis; reflex irritability is unaffected. Upon awaking the pupils immediately dilate, and there is no nausea nor vomiting, such as result from the use of chloroform or morphia. There are exceptional cases, however. After doses from 3.0 to 5.0 grms. the deep sleep lasts much longer (up to ten hours). The body is entirely anæsthetic, and reflex irritability paralyzed; even irritation of the cornea is followed by no contraction of the eyelids.

After the use of larger doses, or even after the above doses in susceptible persons, the most important organic functions may be seriously disturbed; life is endangered, the respiration or circulation being extraordinarily weakened, and finally entirely paralyzed. In consequence of the weakened respiration carbonic-acid dyspnœa sets in, death resulting ordinarily from complete paralysis of respiration. In rarer cases there is sudden paralysis of the heart (Jolly); the latter cases are generally complicated, however, by acute œdema of the lung.

Influence upon the Individual Organs and Functions.

Nervous System.—The gray substance of the cerebral hemispheres is first affected (with smaller doses only the apparatus of consciousness), but not to a degree of complete paralysis. Larger doses, however, cause complete unconsciousness and anæsthesia in men and animals. Now the spinal cord also is affected, the central respiratory apparatus and heart ganglia being the last to yield to the influence of the drug.

Frogs have their reflex irritability at first excited by small doses, but later on, as well as after large doses, there is loss of reflex power; the paresis of reflex irritability is so intense that even strychnia convulsions can be suspended by this drug (Liebreich, Rajewsky). On the other hand, however, the paralysis of reflex action, caused by chloral, cannot be suspended by the use of strychnia. What has just been said is also true of all warm-blooded animals. In a few animals tactile irritation has caused reflex movements, when consciousness was entirely suspended; and even severe painful irritation, such as burning, cutting, etc., caused no reflex manifestation (Hammersten).

The peripheral, sensitive, and motor nerves do not seem to be affected (Rajewsky); the skin affections of chronic chloral-hydrate poisoning would seem to indicate that the vaso-motor nerves are affected.

As to the effect produced upon the voluntary muscles, we know nothing accurate; even in intense poisoning they retain their direct and indirect irritability. Muscular rigidity occurs only when the chloral-hydrate solution is directly injected into the arteries (Zuber).

In men and animals the respiration becomes slower during the stage of narcotism, although in some cases it was previously somewhat hastened. After dangerous doses it becomes somewhat irregular and very shallow. The final stoppage of respiration, after chloral-hydrate poisoning is generally due to paralysis of the respiratory centre. It does not seem to be due to the pulmonary vagus (Rajewsky).

Circulation and Blood.—The results of individual observations vary very much as to the effect of chloral upon the heart's action. Most observers say that during the stage of narcotism the heart's beats become slower, both in otherwise normal animals, as well as in those in whom the vagi have been cut across, or the inhibitory apparatus of the heart has been paralyzed by atropine. This slowing, then, depends not upon an excitation of the vagus in the brain or at the heart, but upon a diminished irritability of the motor ganglia of the heart. Blood-pressure is also very much diminished, even while the heart is still pulsating quite strongly, until it is reduced to near zero. The vaso-motor centre reacts less readily to peripheral sensitive irritations, until finally there is no increase in blood-pressure produced by such irritations (Cyon); this is due to paralysis of the vaso-motor centres and the peripheral vasor nerves, and partly to the sudden deepening of the respiration produced by the sensitive irritation (Heidenhain). We have already stated that fatal stoppage of the heart's action in diastole may follow as a result of very large doses.

The blood of living animals, under the influence of chloral, is not altered, even after the largest possible doses introduced by the stomach (Porta, Djurberg); while, after the direct injection into a vein, the blood-corpuscles alter their form, and hæmoglobin passes out from them, so that the latter is found free in the serum and urine (Ritter and Feltz). After the direct mixture of blood, freshly drawn, with chloral hydrate, Djurberg said the blood-corpuscles

become swollen and paler, but never dissolve (opposed to Porta).

The body temperature is lowered in healthy animals and men from 0.5° 1.0° C. by doses large enough to produce sleep; by dangerous doses it may fall 5.0° C. or more. In animals affected by fever the temperature is also said to be lowered. This diminished temperature may be due to the increased radiation of heat from the body (the ears of rabbits, on account of the dilatation of their blood-vessels, were warmer than the rest of the body); it is also partly due to the diminished formation of heat (in consequence of diminished blood-pressure and lessened muscular activity); for this sinking of the temperature took place even in animals who were kept very warm, being wrapped in cotton batting (Hammersten).

Digestive disturbances rarely occur, even under the use of large doses, if these are taken well diluted. Nausea and vomiting are often noticed when the solutions are too concentrated. Some people, however, have an idiosyncrasy even against greatly diluted solutions. A slowing of the intestinal movements has not been observed; in rabbits diarrhœa has even been seen under the use of this drug. The jaundice sometimes seen does not seem to depend upon the use of the chloral hydrate.

Urine.—The urochloral acid which has been seen in the urine after the use of chloral hydrate has the power of reducing Fehling's liquor, so that it was formerly believed that sugar was present in the urine in these cases (Hoffmann). Mering and Musculus, applying the fermentation test, however, did not confirm this. The quantity of the urine is said to be increased, and some observers have even found hyperæmia of the kidneys.

Chronic Chloral Poisoning.

The use of chloral may become a vicious habit. In such cases, as well as in neurotic patients who have taken chloral for a long time therapeutically, a form of poisoning sets in which is somewhat different from chronic alcohol and chloroform poisoning.

In the first place, although the patients acquire a tolerance for chloral hydrate, so that the dose must be gradually increased, yet this tolerance is not as great as that entertained for alcohol. In some people symptoms of poi-

soning set in even after the chloral has been used for only a short time, while others can take with impunity medium doses of chloral for 100 or more days (Macleod).

In addition to digestive disturbances, cutaneous eruptions are very frequently seen. These are sometimes of an erythematous nature; at other times there are papules, petechiæ, purpura hemorrhagica, œdema of the skin, etc. The erythema and urticaria occur very suddenly, frequently directly after the taking of the drug, or when, in addition, a hot drink, such as alcohol, tea, or coffee, has been taken, and disappears after a few hours (Schüle). There is often seen a tendency to superficial gangrene of the diseased portions of the skin; also bed-sores in various parts of the body. Furthermore, there is often seen an inflammation of the conjunctiva and red spots upon the retina (Balfour and Schüle).

Some people are seized with great dyspnœa and fright, and may even die of suffocation; but these symptoms also often only set in after drinking alcoholic liquors.

Finally, the immoderate use of chloral hydrate, as well as of alcohol and chloroform, is followed by psychical disturbances, with symptoms of general depression, dulling of the senses and mental capabilities, peripheral muscular paresis, and marasmus, which may lead to death (Kirkpatrick and Anstie).

The difference between the physiological action of chloroform and chloral hydrate is, according to the above, decided, although not very great. Chloral hydrate, in comparatively small doses, causes sleep lasting for hours, without any suspension of sensibility and reflex irritability, a primary period of excitement being very rare; while chloroform in similar doses causes a preliminary stage of great excitement, followed only by sleep of very short duration. It requires very large doses indeed for chloral hydrate to produce anæsthesia and suspension of reflex irritability; its effect, however, is always more enduring than that of chloroform. The cause of this difference is probably that chloral hydrate, being a very soluble substance, is rapidly absorbed into the blood, and is thus enabled to act upon the nervous centres in large quantities, and hence the rapid induction of sleep and the absence of the stage of excitement. On the other hand, it is excreted much more slowly from the body, and therefore has a more enduring action than that of the volatile chloroform.

Therapeutic Application.

Chloral is decidedly a hypnotic; it is the best sleep-producing agent we possess. This is the principal therapeutic application of the drug; for other purposes it is best replaced by other agents. As a hypnotic, chloral is superior to opium and its alkaloids, as far as the energy of its application is concerned; still it cannot replace opium, for morphine satisfies many indications which chloral can never satisfy.

The advantages of chloral as a hypnotic are as follows: Sleep follows more promptly than after morphine; the effect is more certain and more powerful. Chloral often produces sleep when morphine has entirely failed.

Disagreeable after-effects, feeling of fulness of the head, nausea, vomiting, etc., upon awakening are rarer. Furthermore, the remedy can be used for a long time (although not an unlimited time) without its power diminishing; and it is an important fact that, even when used for a long time, it does not cause diminished appetite, indigestion, or constipation. Further advantages of chloral are that, first, it can be given to children without any injurious effect—a fact which is the more important in that we have no other trustworthy hypnotic for children, opium being contraindicated in these patients and potassium bromide being untrustworthy; and secondly, chloral may be given in febrile conditions, while morphia is contraindicated in these states (compare below). In opposition to this, we must call attention to the fact that there are many communications, especially on the part of the alienists, which seem to show that the long-continued use of chloral is not without injurious consequences. In order to avoid repetition, we would refer in this connection to what was said in the physiological portion of the discussion. These disadvantages are not serious enough, however, to influence the utility of the drug, if it be used with some care.

On the other hand, morphine has this advantage over chloral, that it acts not only as a hypnotic, but also, even in small doses, diminishes pain. Under the head of morphine, we shall show that it not only produces sleep by its direct effect upon the brain, but also by causing an alleviation of pain and dyspnœa. We have, indeed, some com-

munications, according to which chloral is said to be capable of exerting a "soothing" effect only, without at the same time producing sleep, as, for instance, in the conditions of dyspnœa resulting from heart-disease where compensation is insufficient (Levenstein). But there are other observations in which no effect was produced upon the cough and dyspnœa (in pulmonary affections), although sleep resulted from the action of chloral (Jacobi, Willième, and others). It has not been shown that peripheral neuralgic pains are removed by subcutaneous injections of chloral without sleep being produced, although painful conditions are sometimes alleviated for a time after awakening from chloral sleep. More frequently, however, we see the pains return immediately after awakening. Many observers confirm the statement that little benefit is to be derived from the use of chloral in external—that is, peripheral—pains, especially when these are neuralgic in character. So that, from present knowledge, we should say that chloral only causes an alleviation of pain when it produces sleep, and then not by influencing the peripheral sensitive nerves, but by diminishing abnormal irritability or pathological irritation.

All cases of *sleeplessness* are special indications for the use of chloral, irrespective of the cause of the sleepless condition (the few contraindications we shall speak of below). It is impossible, however, to mention the individual diseases in which sleeplessness is a prominent symptom, and in which chloral should be used. But we would call especial attention to the use of this remedy in delirium tremens potatorum; there is no other drug which can compare with chloral in its power over this disease. The delirium is diminished, sleep produced, and the duration of the malady shortened. To produce these effects large doses are necessary (up to 8.0), but even in these patients we must be careful, for, in addition to the observations of others, we ourselves know of a patient, a young man suffering from delirium tremens, who died after two doses of 2.5 grms. each; the results of the post-mortem examination were negative.

Immediately after the introduction of chloral, much was expected from its use in the treatment of psychical diseases. The opium preparations were temporarily discarded. But during the last few years there has been a reaction; the use of chloral has been limited, while the hopes which were formerly entertained of cures to be derived from its long-

continued use have been disappointed. Indeed, its injurious effects (when used for a long time), which are especially marked in these patients, have very much limited its application, for morphine used for a long time is less injurious than chloral. Still chloral should be used in these cases as a temporary hypnotic and quieting agent. It is most frequently given in maniacal conditions, and, as far as its hypnotic power is concerned, it does not make any difference whether it is used in acute mania or in maniacal attacks in the course of other psycopathies. Experience teaches that in these cases large doses are necessary, and it is stated that small doses even increase the severity of the attack. Upon acute peripheral mania chloral seems to have a particularly favorable action, but even in this disease there are cases in which the remedy is useless. In melancholia the utility of the drug is more doubtful.

In the delirium of fever and febrile conditions J. Russel accomplished by the use of chloral not only sleep, but in many cases an improvement in the psychical condition of patients after awakening from sleep; he observed, however, a disagreeable effect upon the action of the heart. The pulse became smaller, was more easily compressed, and even became arhythmical. Further observations, however, are few, and we must suspend our judgment of the utility of chloral in fever, until we have a broader experience upon which to base it. Liebreich found that even small doses (1.5) were sufficient to produce sleep in typhoid fever; this we can confirm from our own experience, for we have seen even doses of 1.0 of chloral having a strong hypnotic action in cases of typhoid with delirium, even after morphine has remained ineffective.

In gouty subjects, as far as is now known, chloral generally has a weak action, or, in some cases, no effect at all, unless alkalies have been previously administered (according to Liebreich, the necessary quantity of alkali for the decomposition of chloroform is wanting in these cases).

Of the convulsive affections we would first of all mention tetanus, in which the use of the drug has been abundantly observed. Although some patients died in spite of the use of chloral, yet other serious cases recovered under this remedy alone. In all cases it had at least a palliative effect. Our own experience leads us to the conclusion that chloral is one of the best remedies to be used in tetanus; from 1 to 2 grms. should be given every two hours in order to produce

the physiological effect. In lyssa humana it has a palliative effect. In chorea also it has a favorable effect, and cases have been reported in which chloral has accomplished a great deal after other remedies have failed; in other cases, however, it was useless. In epilepsy it is not particularly successful; but in eclampsia parturientium it has been used with good results.

Here Liebreich is disposed to assign a double effect to the drug: first, that exerted upon the muscles (antispasmodic action); and, secondly, he believes that the hydrochloric acid which originates from the further decomposition of the chloroform has some influence upon the cause of the eclamptic attacks,(which, according to Frerichs's theory, depend upon the ammonium carbonate). This latter view, however, needs further authorization.

In tussis convulsiva chloral is symptomatically indicated, but Hartwig recommends it on the strength of an extensive experience, in whooping-cough, to be given every two hours; so that a child under three months shall receive 0.3 grm. per day, below six months 0.04, nine months 0.5, and older children daily doses of 0.6 grm. for every year of their age. In asthma nervosum it is of utility in some cases, generally under the same conditions as those given for morphine. In irritable coughing, however, morphia is to be preferred.

In the treatment of neuralgias, chloral is decidedly inferior to morphine. As to its utility in obstetrical practice, in surgery (as an injection into vascular tumors, aneurisms, etc.), and in various other conditions, judgment must be suspended, since observation and experience concerning these uses are limited and contradictory.

Ulcerative and especially inflammatory processes upon the mucous membranes of the digestive tract, especially of the stomach, are contraindications to the use of chloral. It is true that recently Hertzka has recommended the use of chloral in ulcus ventriculi, but the published histories of his cases do not impress us favorably with this use of the drug. It also seems to be contraindicated in hysteria, in which it often excites rather than allays excitement. In gout also it is contraindicated. It should be used with care in cases of heart-disease, especially of the heart muscles (fatty degeneration), as well as in conditions which readily lead to such a degeneration (typhus, etc.); large doses, at least, are to be avoided. The cases reported by Wernich, of icterus catarrhalis and other varieties of icterus, suggest

caution in the use of chloral in these maladies. Its use in the insane must sometimes be suspended when physiologically injurious effects have been attained.

Dosage.—Chloral hydrate can be given internally, per rectum, and hypodermically. When given internally, 1.0 to 2.0, with mucilag. salep, gummi arabicum, and as a corrective syrup. cort. aurantii, syrup. rubi idæi, etc., to be taken at one dose. In drunkards and in conditions of excitement larger quantities (3.0 to 8.0). Per rectum the same dose as per orem is indicated. The subcutaneous administration is less useful, and only to be chosen in cases of necessity, for in the first place several syringefuls must be injected, and secondly abscesses have been seen to result. From the recent recommendation of some French physician to inject the remedy directly into the veins, there are scarcely any future expectations, since death has been reported to have resulted from its use in several cases. The external application of chloral as an irritant and antiseptic has no advantage over better agents.

The treatment of acute chloral poisoning ts the same as that of acute chloroform poisoning.

Amyl Nitrite.

Amyl nitrite, $C_5H_{11}.O.NO$—which must not be confounded with amyl ether nitrate, which has entirely different properties—is an oily fluid, at first colorless and later on of a greenish-yellow color, very volatile, and possessing a not disagreeable fruity odor and taste. Its boiling-point is 96°. When used therapeutically we should be careful that it is uncontaminated with hydrocyanic acid.

Physiological Action.

By the investigations of Guthrie, Gamgee, Lauder Brunton, Wood, Eulenburg and Guttman, Pick, Schramm, Filehue, Mayer, Friedrich, and others, it has been shown that amyl nitrite has a powerful effect upon the vascular system, especially when inhaled, and less or not at all when injected under the skin.

Brain, Spinal Cord, and Consciousness.—A few moments after the inhalation of small doses, the head becomes heavy, without loss of consciousness—the sensation is very much like that experienced from a temporary intoxication. The gait is unsteady and staggering. The pupil is dilated, and if a point upon the light wall be fixed with the eye, it, together with a circle around it, appears yellow in color; the yellow district is on a violet-blue ground, and is outlined by a wavy line. A high degree of anxiety and unrest result from the increased rapidity and force of the heart's action. All of these effects gradually disappear, leaving no evil sequelæ. If the inhalation of the amyl nitrite be continued

for a longer time, dizziness and stupor of eight minutes' duration are observed, followed by a headache lasting two hours; when one is subjected to an atmosphere containing the vapor of amyl nitrite, as happens while preparing the drug, there is a feeling of fulness in the head, nausea, weakness, and coolness of the extremities, with warmth of the trunk, profuse sweating, and restless sleep.

Severe poisoning and convulsions have not yet been observed to follow the use of amyl nitrite; this may be due to the short time during which the drug has been used. In animals, great restlessness, trembling, and tonic convulsions, often as severe as those caused by strychnia, result, if the inhalation be continued even a few seconds after the decline of blood-pressure has taken place. These convulsions do not, however, depend upon irritation of the spinal cord, but are cerebral in their origin; nor is the spinal cord connected with the circulatory disturbances. After small doses the convulsions are only very short in duration, but their duration and severity increase with the dose. Very large doses exhaust the irritability of the nervous centres, until finally even the convulsions of suffocation are absent.

Some say that consciousness and sensibility are preserved to the end; others state that in thirty minutes there is gradual loss of sensibility.

The peripheral nerves and muscles remain unchanged, even after very large doses; but they are paralyzed by direct contact of the poison.

Influence upon the Circulatory Organs.—Half a minute after the inhalation of five drops of amyl nitrite there appears a deep blushing of the face, which spreads rapidly to the neck. Numerous red spots, of irregular form, appear upon the breast, which gradually become larger, until a diffuse redness covers the breast. On the right, this redness spreads to the region of the liver, on the left to the epigastrium, then it runs down both sides of the abdomen, leaving the region of the navel free. In the loins the redness is still evident, although entirely absent upon the lower extremities. In some individuals this redness is more sharply defined, and limited to the face, neck, and upper portions of the chest. But not only are the vessels of the skin dilated, but even those of internal organs, as, for instance, those of the pia mater, which are enlarged to double and treble their diameter. The vessels of the lung and retina are, however, said to be unaffected.

In consequence of this vascular dilatation, the effect of amyl nitrite is seen in increased pulsation of the carotids, as well as the flushed and heated face.

The blood-pressure is, of course, diminished in consequence of the dilatation of so many peripheral arteries, and the longer the inhalation is continued, the deeper does the blood-pressure sink. The average is about 50 mm. of mercury.

The frequency of the heart's action is increased by the inhalation of even very small quantities of amyl nitrite; often to double the normal rapidity, both in men and in warm-blooded animals—not in cold-blooded animals.

The force of the heart's action does not seem to be influenced by ordinary doses of amyl nitrite, even if the blood-pressure be greatly diminished. Only by the inhalation of large quantities of amyl nitrite, or by the direct injection of the same into the circulation, does the heart become weakened, and finally paralyzed.

Influence upon the Respiration.—In men an alteration in the frequency of the respiratory movements has not been observed, although there is a feeling as though the respiration was accomplished much more easily; the vital capacity of the lung remains unchanged.

In animals, the respiratory movements are often much retarded and deepened by amyl nitrite. Finally, after very large quantities, they become slower and softer, but remain rhythmical.

As far as circulation and respiration are concerned, we can distinguish two stages in the amyl-nitrite action: a first, which is produced by small quantities, and in which the blood-pressure is very much diminished, while the heart-beats and respiratory movements become slower; a second, in which the blood-pressure as well as the heart's action is reduced, but the heart's action remains regular.

When the inhalation takes place through the nose (instead of through the mouth exclusively, or, in tracheotomized animals, through the trachea) we have produced, in the first moments of the inhalation, a temporary elevation of blood-pressure, owing to irritation of the terminal branches of the trigeminus distributed to the nose.

Blood.—After a short inhalation of the vapor, the absorption of oxygen into the blood sinks by one third (in the dog); if the duration of the inhalation be longer, by one fourth. The diminution in the amount of carbonic acid

formed is greater than the diminution in the oxygen absorbed. In the red blood-globules methæmoglobin is formed, which, however, is rapidly reduced to hæmoglobin in the liver. This explains why it is that the action of amyl nitrite, although so marked, is so temporary.

The temperature of the skin, especially of the face and the upper portion of the body, rises, while the general internal temperature falls.

Excretions.—The urine is excreted in large quantities, and, if sufficient amyl have been taken, contains sugar (up to 2 per cent). Especially large quantities are present immediately after its application, but when the maximum has been attained the quantity rapidly falls. In the blood no sugar has been found. It is possible that this excretion of sugar is due to dilatation of the blood-vessels of the liver.

There is a difference of opinion as to the causes of the effects produced by amyl nitrite. We shall here only state the recent views held by Filehue as to the theory of the amyl-nitrite action:

1. The vaso-motor nerve-centre is paralyzed; hence the blushing and the diminished blood-pressure. In consequence of the latter, the tonus of the vagus centre is diminished, and hence the increase in the frequency of the pulse. If this effect be long-continued, the central nervous system and the heart become paralyzed.

2. In consequence of the alteration of the coloring matter of the blood into methæmoglobin, a portion of the former becomes useless as a carrier of gases (oxygen and carbonic acid). As a result, we have a condition of the blood resembling that of dyspnœa; this, together with the circulatory disturbances, is the cause of the quick and deep respirations and asphyxial convulsions.

Therapeutic Application.—A drug which manifests so decided a group of physiological effects would be used *a priori* to fulfill many indications. Thus, amyl nitrite has been tried and recommended in many conditions in which a spasm of the cerebral arterioles seemed to be the pathological condition. Thus, it has been used symptomatically to shorten attacks of migraine, or hemicrania sympathica tonica. In the variety of sick headache, with flushing of the face, it is ineffective—thus establishing what would be expected *a priori*. Many observers have furthermore stated that it has the power of suppressing real epileptic and puerperal epileptiform (eclamptic) convulsions, provided the aura be long enough to admit of its application. Others

have not confirmed this observation. A priori, both observers might be right, for an epileptic attack may be produced in various ways. According to our opinion, amyl-nitrite inhalations should only be used where the patients turn pale at the beginning of the attack, and where there are signs of cerebral vascular spasm. If the color of the face be at first cyanotic, the amyl should not be given. As to its action in cases in which the color is unchanged, careful observation is necessary. A curative effect upon epilepsy, or even a diminution in the frequency of the attacks, is not to be expected. On the contrary, some observers have noticed increased frequency of the aura and intensity of the attacks after long-continued use. Amyl nitrite can only cut short a *commencing* paroxysm in *favorable* cases.

In the attacks of angina pectoris amyl nitrite has been very much recommended. In the reports of some cases, it is stated that under the inhalation of this drug the deadly feelings of anxiety and pain rapidly disappear (Brunton, Smith, and others). A similarly good effect is reported to be obtained in the pseudo-stenocardiac attacks which occasionally occur in valvular diseases. We should here, however, recommend especial care, on account of the diminution in the blood-pressure which this drug produces. As to its utility in asthmatic attacks, there are no decided reports. The same is true of many other recommendations for its use.

Very recently inhalations of amyl nitrite have been tried in amblyopia, in cases in which strychnia injections are commonly used. The cases were chiefly those of amblyopia and amaurosis after acute hemorrhages, or cases in which no abnormal ophthalmoscopic appearances could be seen, with exception, perhaps, of a little anæmia of the fundis oculi. After the repeated inhalation of 3 to 6 drops, improvement, and sometimes a cure, was produced, even after strychnia had been of no utility.

Dosage.—Amyl nitrite—only by inhalation—1 to 5 drops pure, poured upon a handkerchief or paper and inhaled.

AROMATIC COMPOUNDS.

All the so-called aromatic compounds are derived from benzol (C_6H_6), the common nucleus of all these bodies, and are formed by the substitution for its hydrogen atoms of other elements or compound radicals; they are therefore called benzol derivatives.

These chemically allied bodies have considerable in common in their physiological action and therapeutical indications.

A portion of these, to be treated of last,—the volatile aromatic oils (terpenes and camphors),—have been in medical use from time immemorial, and because contained in a large variety of vegetable and animal products have tended to overburden the list of remedies. We have endeavored to put an end to this.

Another portion, under the form of distillates, in the distillation-products of wood, has, as " tar," etc., been used in the remotest times, without our having any knowledge of the constitution of these complex substances.

The first step in the analysis of these bodies was made by Reichenbach, by the derivation of creasote from wood and coal tar; in 1834 Runge produced carbolic acid and recognized its antiseptic properties.

PHYSIOLOGICAL REMARKS.

A considerable number of aromatic compounds have a preventive action upon fermentative aud putrefactive processes. When organic substances are mixed with them they neither ferment nor decompose, and any previous fermentation and putrefaction is arrested upon their addition.

Since ancient days meat has been preserved by smoking, and bodies were preserved for ages by being embalmed with aromatic spices. Reichenbach, who had appreciated this antifermentative and antiputrefactive action of creasote, derived its name from this (from *χρέας* meat, and *σάζω* preserve: meat-preserving), and traced it to a combination of creasote with the albuminoids. He recommended creasote Lemaire recommended phenol to preserve meat and bodies from decomposition, and to destroy foci of infection.

We next proceed to the consideration of the obscure and much-contested field of the nature of the miasmatic, contagious, septic, and similar diseases. A brief sketch of our knowledge upon this subject must precede a discussion of the physiological action and the practical and therapeutical indications of remedies used in these affections.

Pasteur's conception, which makes fermentative and putrefactive processes dependent upon low organisms, organized ferments (bacteria, fungi, vibrios, schistomycetes), has received strong objections from Liebig and Hoppe-Seyler; namely, that the action of a ferment upon other substances, accompanied by chemical changes, must depend

upon its chemical structure and not upon its form; that no insight is as yet obtained into the nature of these processes, when organisms are considered as their cause, for each organism is made up of different parts, exercising different functions, so that the final question still remains as to which of these functions give rise to the fermentative and putrefactive process.

Pasteur's teachings give us as little insight into the minute changes, as the statement that man digests albumen will explain the nature of albumen digestion.

Owing to the lack of a clear knowledge as to the exact relation of low organisms to fermentative and putrefactive processes, we are as yet unable to state with certainty whether in this connection the aromatic compounds act by destroying the organisms or by changing the fermentative substances themselves. Hoppe-Seyler reports observations in which both with and without death of the low organisms putrefactive processes continued.

Since Henle's theoretical deduction, made about thirty years ago, that the contagious and miasmatic diseases depended upon the entrance and development in the body of low organisms, we have succeeded in recognizing in the body, in some diseases organisms which bear the greatest possible resemblance to those accompanying putrefactive processes.

Some assert even that these organisms, not only in some, but in all diseases are the sole cause.

Even accepting this fact, we are, just as before, still in the dark with reference to the nature of the process. The question again arises, If these organisms act as a simple body, are their secretions or excretions the active agents, or are they only the carriers of this unknown contagion?

It is generally accepted that a healthy body does not permit an invasion of these low organisms: only such whose epidermis, normal digestion, and normal blood have been interfered with. The diseases are not the expression, therefore, of the presence of low organisms and their active metamorphoses, but rather the result of the action and enormous development of foreign organisms in a body in a previous pathological condition. We cannot say when the time for the answer to all these questions will arrive. Physicians, who are always compelled to act even before the nature of their enemy has been learned, have accepted the germ theory, and have acted upon it.

As it is of more moment to the practitioner to have a cer-

tain remedy against a disease than to know the manner of its action, the question arises, Has the above theory yielded him such remedies, and does the success speak well for them?

We must next emphasize that therapeusis has made rapid strides in advance in having with great acuteness identified the exciting agents of putrefaction in dead tissues with those of disease, and the putrefactive process with the disease process, and in having employed against these diseases remedies long known as destroyers of putrefaction.

This bold and entirely theoretical method of treatment has yielded the following results:

The same agents which prevent and retard fermentation and decomposition will, in Lister's method, preserve wounds from putrid decomposition, thus guarding the body against septic absorption.

Even when a wound has already been infected, a plentiful application of a 5-per-cent phenol solution will yield excellent results (König).

If the whole body have been infected from a putrid wound,—that is to say, if septicæmia, pyæmia, and erysipelas have set in,—then the administration of these remedies will exert an antipyretic effect, but not a curative action upon the disease process; this is due to the fact that these agents become converted in the body into other materials which have no antiseptic or antifermentative power. Thus the simple phenols (phenol, kresol, thymol) and homologous agents are converted into ethereal sulphates of the same bodies (Baumann and Herter). Of all miasmatic and contagious diseases, malaria only has hitherto been cured by the internal administration of these remedies. Other diseases of this class were entirely unaffected by these drugs, unless we consider acute articular rheumatism as a parasitic disease.

The cure of malaria by quinine, salicylic acid, salicin, arsenic, etc., cannot be taken as positive proof that the disease is parasitic in its nature, although this is probable.

In conclusion, we can only say, that there is a large field before us. None of the above questions can at the present time be answered with any certainty, either from the results of purely scientific research or from practical experience.

It would be of greatest possible practical importance to know which bodies exert the strongest antifermentative or antiseptic power. Hitherto no uniformity of results has been attained, since the character of the putrefying or

fermenting fluid, its age, etc., all have some influence in the effect produced by agents which are to prevent these processes. According to Binz, the most powerful antiputrefactive agent is mercuric chloride; then follow, in diminishing series, phenol, quinine, arsenious acid, green vitriol, and sodium chloride. Plugge gives us the following diminishing series: phenol, quinine, sulphuric acid, chlorine, chloride of lime, and green vitriol. Illisch found that the most powerful disinfectants upon cholera-stools were nitric acid and phenol; then, weaker, sulphuric acid, hydrochloric acid, oil of turpentine, crude wood, vinegar, blue, white, and green vitriol, alum, tannin, neutral ferric-chloride solutions, and sodium chloride. According to Fleck, urine decomposition is best prevented by aluminium sulphate; then come tannin, benzoic acid, salicylic acid, and, weakest of all, phenol. In order to reach more uniform conclusions, Billroth examined the effect of these different substances upon similar organisms (micrococci and microbacteria: Billroth) in exactly similar solutions—10.0 grms. of candy sugar, 1.0 grm. ammonia tartrate, and 0.5 grm. of potassium phosphate in 100.0 grms. of water. He attained the results expressed in the following table:

Substances preventing the Development of Bacteria.	Dilution.	Substances preventing the Formation of Bacteria.	Dilution.
Mercuric chloride	1 : 20000	Chlorine	1 : 25000
Thymol	1 : 2000	Iodine	1 : 5000
Sodium benzoate	1 : 2000	Bromine	1 : 3333
Creasote	1 : 1000	Sulphurous acid	1 : 666
Oil of thyme		Salicylic acid	1 : 312
Carvol		Benzoic acid	1 : 250
Benzoic acid		Methyl-salicylic acid	1 : 200
Methyl-salicylic acid		Thymol	
Salicylic acid	1 : 666	Carvol	
Eucalyptol		Sulphuric acid	1 : 161
Ol. carui	1 : 500	Creasote	1 : 100
Sodium salicylate	1 : 250	Phenol	1 : 25
Phenol	1 : 200	Alcohol	1 : 4.5
Quinine			
Sulphuric acid	1 : 151		
Boric acid	1 : 133		
Copper vitriol			
Hydrochloric acid	1 : 75		
Zinc vitriol	1 : 50		
Alcohol			

Although these results are manifold and partly incorrect, yet we can from them discern the truth that the aromatic compounds exert, by far, the most powerful antiseptic and antifermentative action, and are most deadly to the lower organisms, mercuric chloride and chlorine being their only superiors.

PHENOL—CARBOL—CARBOLIC ACID.

Phenol or carbol, $C_6H_5.OH$ (known also as phenic acid, phenyl alcohol, hydroxybenzol, and among physicians carbolic acid), does not possess the properties of an acid. It does not decompose carbonates, while its salts with the metals are decomposed by carbonic acid; nor does it redden blue litmus paper. It is distinguished from the alcohols in that the hydrogen atom of its hydroxyl is more readily displaced by strong basic metals. Most of the above terms, therefore, are to be put aside, and the term phenol is to be preferred.

Phenol is the principal constituent of the acid portion of coal-tar oil, from which it is manufactured.

Pure anhydrous phenol crystallizes in large colorless prisms, which melt at 40°, dissolve in fifteen parts of water, and all proportions of alcohol and ether.

The two phenols prescribed by the German Pharmacopœia are not chemically pure substances. They are: (1) Acidum carbolicum crystallisatum, a slightly reddish mass, consisting of long, sharp crystals, neutral in reaction, and having a characteristic odor and sharp taste; they melt at a temperature of 25° to 30°, boil at 180° C, and dissolve in 50 parts of cold water, and miscible with every proportion of alcohol, ether, chloroform, bisulphide of carbon, and glycerine. This preparation only can be used therapeutically. (2) Acidum carbolicum crudum, a reddish brown, more or less transparent solution, of a peculiar odor, slightly soluble in water, more soluble in alcohol, and mostly soluble in hot caustic-soda solution. It contains at least 50 per cent of pure carbolic acid, and should only be used for ordinary disinfecting purposes.

Since it would be difficult to dispense the crystallized carbolic acid, druggists generally keep it in solution, consisting of equal parts of crystallized carbolic acid and dilute alcohol.

PHYSIOLOGICAL ACTION.

Since phenol is chiefly used externally to prevent or retard decomposition, fermentation, and putrid poisoning, while its internal application becomes more and more restricted, we shall first give the first-mentioned series of effects.

The Effect of Phenol upon Ferments, Infecting Agents, and the Process of Fermentation and Decomposition.—The chemical ferments, like pepsin, ptyalin, emlusin, and myrosin, only lose their physiological effects upon albumen, starch, amygdalin, and sinigrin after prolonged contact with con-

centrated phenol solutions or sometimes phenol in substance (Lemaire, Buchheim, W. Bucholtz, and Plugge). Similarly phenol weakens the catalytic power of many ferments over hydrogen peroxide (Schaer) but little. Organized ferments, on the other hand, are destroyed by much weaker solutions. We have shown in the introduction, however, that phenol takes a very low place among the agents which destroy ferments. According to Lemaire, substances undergoing decomposition under the influence of bacteria and vibriones are preserved by 0.1 per cent of phenol solutions. L. Bucholtz asserts that in artificially maintained bacteria solution the development of the bacteria is prevented by the addition of 0.2 to 0.5 per-cent solutions of phenol, while it takes 40-per-cent solutions to prevent their formation. In this respect he agrees with the assertions of Sanderson, Hoppe-Seyler, and Paschutin.

The average infusoria are destroyed by a 1-per-cent solution of phenol. Plugge indeed thinks that this results from 0.1-per-cent solutions.

The growth of the mould fungus is stopped by 1-per-cent solutions (Plugge), and the yeast plant loses its fermenting power when subjected for twenty-five hours to the influence of a 0.2-per-cent solution (W. Bucholtz).

Infecting Virus.—Since all the bodies of this class are not yet positively known, it follows that our knowledge of the influence of phenol upon them is still uncertain. We know only that the addition of a 1-per-cent solution of phenol to vaccine virus does not in any way interfere with the activity of this virus, while a 2-per-cent solution renders it inoperative (Rothe and Michelson). Furthermore, that healthy as well as decomposing pus obtained from acute abscesses is rendered entirely aseptic by the addition of a 5-per-cent solution of phenol. The minimum strength necessary to produce this result is unknown, although it is certain that a 1-per-cent solution will not accomplish it. Already decomposed pus seems to be unaffected even by 5-per-cent solutions, and requires stronger ones to render it aseptic; a 0.5-per-cent solution will prevent the septic decomposition of healthy pus (Rosenbach).

Fermentation.—Alcoholic fermentation of a sugar solution is said to be suspended, according to Plugge, by a 4-per-cent solution of phenol, according to Bucholtz by a 0.476-per-cent solution; lactic fermentation by a 0.377-per-cent. solution; butyric-acid fermentation by a 0.33-per-cent solu-

tion (Paschutin); urinous fermentation by 1-per-cent solutions (Hoppe-Seyler).

Putrefaction of albumen or meat is stopped by a 2-per-cent solution (Hoppe-Seyler), and entirely prevented in fresh meat, bread, blood, and urine by a 0.1 to 0.5-per-cent solution (Lemaire and Plugge).

As to the cause of this antifermentative and antiputrefactive action, this is as much in the dark as the physiology of these processes themselves. The supporters of the theory that all fermentation and putrefaction is the result of the devolopment of minuter organisms, believe that the prevention and interruption of these processes is due to the destruction of these organisms. Then one would inquire why these agents should be so destructive to these organisms.

Hoppe-Seyler, however, who denies these theories of Pasteur, and believes that putrefaction is the result of the action of a ferment which has perhaps been formed by these minute organisms, but is entirely independent of them in its action, claims that a 0.5-per-cent phenol solution is sufficient for the destruction of these organisms, while the decomposition of albumen continues, somewhat more slowly, it is true, even under 1-per-cent solutions; 2-per-cent solutions, however, prevent it. The final destruction of the activity of the ferment is due to a purely mechanical cause: the phenol causes a coagulation of the albuminoid substances in the fermenting or putrefying solutions, which, when precipitated, carry the ferment along with them.

It cannot be denied that the whole subject still rests upon a hypothetical basis, although it is very reasonable to suppose that the direct influence of the phenols upon albuminoid bodies is an important factor in their antiseptic action. Lime and albuminoid bodies are thrown down from their solutions by the addition of a 5-per-cent phenol solution (according to Hoppe-Seyler and Zapalsky only by a saturated phenol solution); the phenol is supposed to act by withdrawing the water from these, and not (at least at ordinary temperatures) by combining chemically with the albumen. In proof of this, we find that the phenol can be evaporated from the precipitate. According to Tauber, carbolic acid when added to fresh albumen, meat, or urine will give evidences of its presence to chemical reaction for weeks after it has thus been added, while if similar putrefying materials are treated by the carbolic acid the latter

will yield evidences of its presence for only a very short time (Bill); this would seem to indicate that there is a direct union between the phenol and the decomposition products.

Even Plugge recognized that the decomposition odors were destroyed, simultaneously with the cessation of the decomposition process, under the influence of phenol. Many other odorous materials are not influenced by phenol.

EFFECT OF PHENOL UPON THE ORGANISM OF THE HIGHER ANIMALS AND OF MAN.

Phenol is readily absorbed into the body, even by the unbroken skin. In some cases, indeed, the painting of the skin in men with phenol solution has been followed by fatal results, under symptoms similar to those resulting from the internal administration of the acid (Husemann and Hoppe-Seyler). This poisonous action through the skin can be readily experimentally demonstrated upon every animal. Care, therefore, should be taken even in the external use of the drug.

With equal readiness carbolic acid is absorbed by wounds, subcutaneous connective tissue, and all of the mucous membranes of the digestive and respiratory tract.

Action and Excretion of Phenol.—When phenol has been absorbed into the circulation, it does not, as was formerly supposed (Städeler, Lieben, Landolt) pass unchanged through the body to be finally excreted with the urine, but it disappears, to a great extent (almost one half), without leaving any trace of its decomposition products (Tauber, Shaeffer). Most probably it is oxidized into oxalic and carbonic acids, and excreted as such. The other half undergoes various combinations, which Hoppe-Seyler and Buliginsky term phenol-forming substances, and one of which has been termed by Baumann an acid, the ethereal sulphuric acid of phenol (phenol sulphuric acid, $C_6.H_5.O.SO_2.OH$).

In the blood of the living dog half an hour after the administration of phenol we find considerable quantities of phenol and small quantities of phenol-forming substances. Two or three hours later, however, there are many more phenol-forming substances and but little phenol. This is especially the case in the liver, brain, and kidneys. In the urine we find, accordingly, the greater part of the phenol

which has been administered, in the form of the above-mentioned phenol-producing substances, with but slight traces of phenol. By treating the urine with hydrochloric and sulphuric acids the phenol-forming substances can be reconverted into phenol in a free state. If small quantities of phenol are administered, it appears in the urine as the phenol sulphate of an alkali; when very large quantities of phenol are administered, it appears in the urine only to a slight extent as phenol sulphate, but for the most part as the yet unknown phenol-forming substances. This is probably due to the fact that the phenol does not find sufficient alkaline sulphates in the organism with which to combine. If, with the phenol, sodium sulphate, for example, be administered, there is a combination of the two into the sodium-phenol sulphate. For small quantities of phenol the body has sufficient alkaline sulphates, with which the former may combine to form the above salt; and since this salt is not injurious to the organism, it follows that the body possesses its own antidote for small quantities of phenol, while for larger quantities the best antidote to give is sodium sulphate or any alkaline sulphate (Baumann).

Here we would call attention to the fact that, normally, phenols (phenol, cresol, etc.) are formed in the intestinal canal from decomposing albuminoid bodies; that is to say, from decomposing bodies antiseptic substances are formed. It is for this reason that the ethereal sulphate of phenol and cresol are found in the intestinal canal, being here formed from the phenols thus arising in the intestine (Baumann and Brieger).

The excretion with the urine goes on very rapidly. Retention of the phenol in the body does not take place, so that we need not fear a cumulative action (Salkowski). Under the influence of phenol the urine very often takes on a very dark color, varying from a light olive green to a dark brown and grayish black: it is darkest when the phenol is applied externally to the skin or wounds. This color is due, according to Baumann and Preuse, to the fact that a considerable quantity of the phenol administered or absorbed has become oxidized to hydroquinone ($C_6H_6O_2$) and that it appears as hydroquinone sulphate in the urine. As a consequence of the oxidation of the hydroquinone we have these unknown brown-colored bodies. The percentage of the phenol does not vary directly with the darkness

of the color. It is not, therefore, necessary, as is now the custom, to suspend the administration of phenol as soon as the urine begins to show a dark color, but we should rather be guided by the other symptoms of poisoning, such as digestive disturbances, and, above all, the quantity of sulphuric acid in the urine (sulphats). As soon as the latter begin to fail and diminish, we may say that toxæmia has begun to set in (Baumann).

Kohn frequently noticed that large doses are followed by albuminuria; small doses very rarely (Salkowski).

Hoppe-Seyler has found the phenol (introduced by inunction) in the saliva as well as in the urine. Lémaire thinks it highly improbable, however, that phenol is excreted with the expired air.

Local Action.—Strong solutions (above 5 per cent) cause a severe burning sensation upon the skin and produce an eschar which is at first white, soon after red, and which in a few days may lead to a superficial separation of the burnt integuments. The burning lasts but a few minutes, and is followed by almost complete anæsthesia of the affected portions of the skin, so that the skin can even be cut through without the knife being felt; even a paronychia can thus be opened without any pain being felt (Smith). This anæsthesia is greatest when the skin has been previously painted with vinegar, while glycerine solutions of phenol have no anæsthetic power whatever. Very concentrated solutions burn the skin and render the affected tissues transparent.

Upon the mucous membranes such solutions of phenol cause severe burning pain and produce a white eschar; all the places to which the phenol solution has been applied become anæsthetic. When inhaled, phenol gives rise to coughing; when taken into the stomach, it causes nausea, eructations and vomiting, and, in strong concentration, inflammation of the gastro-intestinal mucous membranes, with severe colicky pains, vomiting, and purging. Death, which frequently follows very rapidly, is supposed to be due to a reflex paralysis of the heart.

All of these local effects only occur in man after the administration of doses over 0.5 grm., and even then they may be very slight as far as the gastro-intestinal mucous membrane is concerned, provided the stomach be full at the time of the administration.

General Effects.—Here we do not include those general

effects which are the result of the caustic action of the drug, but only consider those general effects which are the result of the absorption of largely diluted phenol into the blood. Husemann, Salkowski, Hoppe-Seyler, and others studied the effects in this manner.

Different men and animals differ in the power of withstanding the poisonous effects of this drug. We cannot help observing a certain amount of similarity between the physiological effects of this drug and those of alcohol.

Frogs die after taking 0.2–0.3 grm.; rabbits, from 0.3–0.5 grm.; cats, from 0.5 grm.; dogs, from 2.5 grm. (Ummethun.)

In adults, 0.5 grm. are not followed by any injurious effects; yet 1.0–2.0 grm. is not a safe dose, whether given by the stomach or hypodermically. Men who have been accustomed to alcohol can take more, and women and children less: doses of 0.1–0.2 grm. may have injurious effects upon the latter (Oberst). The general symptoms are also less marked when the drug is given upon a full stomach than upon an empty one. The fatal dose for adults is from 10.0–20.0 grms.

Cold-blooded animals begin to collapse in from three to five minutes after the subcutaneous or internal administration of the drug; the voluntary power is diminished, while the reflex irritability of the cord is much increased; convulsive movements of the feet occur, and these gradually increase to almost tetanoid tonic spasms. Later on the convulsions cease, and death from paralysis of the spinal cord sets in twenty-four hours later. Toward the end the heart beats very feebly, and the muscles and nerves retain but little irritability after death. The blood after death is thin bluish red, the urine clear and without albumen.

In the mammalia, and birds also, the chief toxic symptoms consist of clonic convulsions, with resulting paralysis and collapse. Soon, also, dyspnœa sets in; during the convulsive stage the blood-pressure is at first increased, then returns to the normal, not sinking until life is almost extinct; the small arterioles are dilated, so that the blood circulates more rapidly and the venous blood becomes of a brighter red. The veins become very much swollen. The salivary and lachrymal secretions are increased. Sensibility is retained for a long time. The muscles retain their irritability until after death.

The duration of the poisonous action is rather long; the

blood becomes gradually darker, the respiration shallow and irregular, muscular contractility weaker, the temperature is lowered, and death sets in generally as a direct result of the paralysis of respiration and the spinal cord. Sometimes death takes place suddenly as the result of a convulsive seizure.

An autopsy shows not only the caustic effects of the drug, but also hyperæmia of the cranial organs, and the liver and spleen; the blood is dark and clots with difficulty; the pneumonias observed in some cases are more than accidental complications, and are perhaps dependent upon the entrance of some of the carbolic acid into the lung.

In men non-fatal doses of 0.5–2.0 grm. are followed by dizziness, slight dulness, ringing in the ears, formication, some deafness, great weakness, and also hyperidrosis, diminished frequency of the pulse, and lowered temperature (about $\frac{1}{10}$ of a degree—Danion's experiments upon himself).

In addition, we have the already mentioned nausea and vomiting.

Large doses (5.0–20.0 grm.) cause death very rapidly; rapid loss of consciousness supervening, then weakness of the heart and insufficient respiration. Volkmann ascribed the sudden death of a boy after resection of the hip to collapse from the phenol used, children being especially sensitive to phenol.

Hoppe-Seyler relates the history of two men who rubbed in a very concentrated solution of carbolic acid for the cure of the itch. Even during the application of the drug, first one, then the other, cried out that he felt dizzy, and cried out from pain over the surface to which the phenol had been applied. Both patients were found perfectly unconscious by those who had been attracted by their cries. One died in a short time; the other gradually recovered, and then stated that he had first felt a tightness in the head, and then dizziness, after which he lost consciousness.

It is a remarkable although at present an inexplicable fact, that while in all other animals large doses of phenol cause clonic and tonic spasms, in man, on the contrary, there is no spasm, but rather immediately a paralysis of the nervous centres. We have only one reported case of poisoning by carbolic acid—it is one reported by Winslow—in which a boy after swallowing 8.0 grm. of the ill-smelling Calvert's Phenol No. 4 uttered a loud cry, and fell down

in deep coma, with cyanosis and mydriasis; there were also *clonic convulsions, and later on tetanoid convulsions with spasm of the glottis;* he then recovered temporarily, only to die, twenty hours later, from a laryngitis caused by the drug.

Chronic poisoning from doses in themselves harmless is, as Salkowski has shown, impossible, for the reason that the drug is so rapidily excreted. Direct observations made by Kohn, Neumann, and Salkowski have also shown that, apart from the color imparted to the urine, there were no toxic symptoms even in a case in which 65.0 grm. of phenol were taken in the space of three months. When toxic symptoms suddenly occur under the use of antiseptic dressings, they are the result, not of the cumulative action of the drug, but of the accidental absorption of too large quantities of phenol from dressings either too closely applied or too thoroughly saturated (Salkowski). In adults we would then find nausea, vomiting, and headache; in children, first excitement, restlessness, and increased temperature, followed by a peculiar condition of collapse.

THERAPEUTIC APPLICATION.

The great importance of phenol in medicine during the last few years depends upon the introduction of the Lister method of treating wounds. Besides its use in surgery, we have its application as a disinfectant for the excretions; while internally it is of very little importance.

It is therefore proper to discuss the surgical application of the drug first; and since our personal experience is limited, we shall be compelled to confine ourselves here to facts gained from the literature of the subject. The Lister method is becoming more and more general every day, and the literature increases correspondingly, so that we have a large field to select from.

The controlling principle of Lister's method, introduced about ten years ago (Lister's first communication was published in March, 1867), namely, the method of autiseptic or aseptic dressing of wounds, is that the injurious influences of atmospheric air upon the wound-surface should be avoided, and open wounds thus be brought under the same favorable relations as characterize subcutaneous wounds (fractures, etc.), and to which we owe the absence of fever, pyæmia, erysipelas, etc. Whether these injurious

effects really depend upon micrococci, bacteria, etc., or are of another nature, cannot yet be decided. It is true that Lister was led to his discoveries by some such idea, but the presence of micrococci under the phenol dressing has been demonstrated. However, whatever may be the true state of affairs, the practical importance of Lister's dressing remains assured.

We must remark, however, that the success of Lister's dressing is not necessarily dependant upon phenol; this is readily conceivable, and Lister recognized the fact as early as 1868. Phenol owes its preference to the fact that it is a volatile substance. The occurrence of some disagreeable effect of serious toxic symptoms, and even death, under its use, has led to an attempt to substitute other antiseptic substances in its place; such are salicylic acid, benzoic acid, boracic acid, menthol, thymol, and zinc chloride. But since most of our experience with antiseptic dressings has been gained under the use of phenol, the following statements are made, principally in relation to this drug. We shall follow, in our description, the teachings of Volkmann, who, under the persevering and faithful application of Lister's method, has achieved the most brilliant results; we shall follow also Steiner, Nussbaum, and others.

In the treatment of fresh wounds, that is to say those of surgical operations, from their very inception, with the antiseptic method the advantages attained are as follows:

The discharges are entirely odorless: not only is the ordinary disagreeble odor of the pus absent, but even when extensive gangrene has occurred there is an absence of all odor. The blood that may be present in the wound, under the antiseptic dressing is not decomposed.

The inflammatory reaction of the tissues surrounding the wound is very slight, and often entirely absent; even the largest surgical wounds, such as amputations, show no redness, swelling, or inflammatory œdema of the margins even on the fourth to the eighth day.

As would be expected, then, even in cases where there is no union by first intention, the secretions from the wound remain very slight; and for this reason the dressing may often be left on for two or three days or longer. Later on the secretion which may be present is serous and very thin, having few pus-corpuscles present in it.

Primary union is more frequently attained, and often in cases in which formerly it was obtained with difficulty; not

only the skin is superficially united, but even the deeper tissues. To what extent and how often this is desirable, we neither think it necessary nor are we able to discuss in this place. It is rather a subject for especial surgical experience to decide.

Evidently, partly as the necessary result of what has already been said, there follow three important effects: first, the patients experience less pain, there being often a partial or complete analgesia; secondly, patients treated by Lister's method have less fever, and sometimes none at all; the greatest and most serious operations are often followed by very little or no fever; finally, the time of healing is very much shortened.

The most important effect of Lister's method of treatment consists in that many of the most serious and incurable complications and consequences of wounds do not appear at all, or only to a very limited extent. Such are acute phlegmonous and purulent infiltrations, necrotic or diphtheritic inflammations, and septicæmic or pyæmic processes. Erysipelas, however, is somewhat less frequently prevented by this dressing. Since, then, these complications are the most frequent cause of death after operations, it follows that Lister's method of treating wounds greatly diminishes the mortality.

These results are, then, so beneficial that Lister's method of treating wounds must be counted among the greatest therapeutic benefits to humanity. Almost all surgeons who have followed it carefully in all its details praise it. It is true, however, that a few cases have been reported in which not only severe symptoms of poisoning (vomiting, collapse), but even death, have resulted from its use; these accidents happened especially in anæmic and cachectic, very young or very old individuals. It is for this reason that search has been made for other harmless substances, in order to exclude phenol from the Lister method. But to give up this method even if a satisfactory substitute for phenol should not be found would, in our opinion, be as foolish as if anæsthesia were to be abandoned because of an occasional death from chloroform.

All are agreed that the minutest particulars of this method (Lister's) must be observed to insure success, and to keep the atmospheric air, with the substances which it contains, away from the wound, from the very beginning, and throughout the course of its healing. The hands, sponges,

instruments, etc., must be disinfected, the operation must be performed under the carbolic-acid spray, and the wound must be protected by a thoroughly antiseptic dressing. Failure is generally due to a neglect of some of the regulations. We cannot here give a detailed account of all the regulations which Lister provides, the least of which is necessary to the production of a beneficial result: this is the province of surgical monographs, such as have been published by Volkmann, Thiersch, Steiner, Nussbaum, and others. The more experience that a surgeon gains in the practical application of Lister's method, the better the results he attains in its practice. We consider it necessary, however, to recount and describe the preparations and materials prescribed by Lister in the carrying out of his antiseptic method, and this we shall do under the head of preparations.

Old wounds, where open suppuration is already going on, can, of course, not receive the same benefits from a Lister dressing as wounds which have been maintained in a strictly antiseptic condition from the very beginning; still even here good results have been observed.

As we might expect, phenol has been used in the last few years in many other ways for external application. Such are its use in the putrid secretions of mucous membranes, especially that of the bronchi: in these cases it is frequently of great benefit. Leyden advises the use of phenol inhalations, in addition to the internal use of phenol, in gangrene of the lung: here it is better than the inhalations of turpentine that are ordinarily used. We ourselves have found that in some cases phenol was better borne than the inhalations of turpentine.

In diphtheria, also, phenol has been much used as a gargle, inhalation, and local application.

A few observers report favorable results; but, taking the large mass of experience in the use of this drug into consideration, we cannot say that the mortality of this terrible disease has been in any way diminished under its use. The lighter cases are, it is true, cured by the use of this as by other agents; the serious cases, however, are as unaffected here as by others. For the sake of completeness we mention the use of the drug in whooping-cough: the patient is to inhale weak solutions frequently, while strong solutions are sprinkled about the room.

In gynecological practice phenol is used according to

the principles advocated by Lister; in obstetrical practice it is used for disinfecting the hands and instruments. As to its use after labor, opinions differ; some prescribe carbolized injections and washings as a routine practice in every case, while others content themselves with washing the genitals after labor, and then not again using carbolic washes, unless puerperal fever, putrid or diphtheritic affections of the genitalia should set in. A few observers have seen cases in which carbolized injections into the uterus were followed by symptoms of poisoning (Schuelking, Kuestner, and others). Caution is therefore necessary.

As a parasiticide (scabies) or germicide (pityriasis versicolor) phenol is inferior to other efficacious and at the same time less injurious substances. In scabies, as we have already said, its application has been followed by toxic symptoms, with sometimes a fatal result. As a direct caustic it is also of little importance. It is used in dentistry, however, as a local application to relieve the odontalgia of carious teeth, and also for the purpose of cleaning out carious cavities which are to be filled.

Internally phenol has been used in a large variety of conditions, but nowhere have beneficial and reliable results been attained. So that up to the present time we feel that we could dispense with phenol as an internal remedy. We shall not recount the large number of conditions in which it has been used, but shall content ourselves in giving the more important uses; they are as follows: In diabetes mellitus it is recommended by Ebstein and Mueller. Experience has shown that in some cases of this disease (we have no means of knowing which) phenol 0.3 pro die) rapidly diminishes the excretion of sugar; sometimes, indeed, the sugar disappears entirely from the urine. As soon as the remedy is suspended, however, the sugar reappears, although sometimes it remains away for weeks. In another series of cases the sugar remains uneffected.

Senator recommended subcutaneous injections of phenol in the region of affected joints in acute articular rheumatism, but sodium salicylate and benzoate are preferable remedies. On the other hand, the subcutaneous injection of 2-per-cent solutions in the neighborhood of erysipelatous regions of the skin (Hueter) seem to be of some value; the objection is that the process in an extensive erysipelas is somewhat disagreeable. So, also, subcutaneous injections

have lately been recommended in white swelling and subacute inflammations of glands.

Phenol is nowadays very much used as a disinfectant. Apart from its use in the Lister method, we use it in disinfecting hospital-wards and water-closets, and vessels in which the dejecta of typhus and cholera patients have been placed.

Its disagreeable odor is a prime objection to its use in the sick-room; furthermore, it has not yet been proved that the phenol vapor prevents the spread of infectious disease through the atmosphere of the sick-room; we should feel safer in having such patients isolated.

Dosage and Preparations.—1. Acidum carbolicum crystallisatum, for internal use best given in pill form. The officinal dose is at most 0.05 pro dosi! ad 0.15 pro die! It can, however, be given up to 0.3 and even 0.5 pro die without injury. For external use also, and as an inhalation only, this preparation should be used; the latter in the strength of ½–1-per-cent solution; Leyden has, however, gone as high as 4-per-cent solutions in gangrene of the lung. Aquæ menth. pip. may be used as a flavoring agent in these inhalations. The solutions for external use vary in strength from $\frac{1}{10}$ to 5 per cent, according to the effect desired. The latter is only to be given when we desire a caustic effect. All observers acknowledge, however, that solutions of such strength are dangerous.

2. Acidum carbolicum crudum, used only for disinfecting water-closets, etc. We should prepare either an at least 2-per-cent solution of phenol or a mixture of phenol with other deodorizing or disinfectant substances (such as charcoal-powder, green vitriol, etc.)

3. Liquor natri carbolici. 5 parts of pure carbolic acid, 1 part of caustic soda, and 4 parts of distilled water—a superfluous preparation.

4. The carbol or phenol sulphates; the potassium, sodium, ammonium, and magnesium sulpho-carbolicum sive sulpho-phenylicum, $C_6H_4So_3.OK$, etc., are said to have a similar though weaker antiseptic and anti-fermentative power to that of phenol (Baumann), while they have little or no toxic effect. Doses of 5.0 grm. produce only a little dizziness (Sansom). Since, however, as Baumann has shown, phenol loses its entire power when it is given internally and converted into these very salts, we must doubt very much the authenticity of the statements of some observers, who believe that these salts have given favorable results in typhoid, typhus, scarlet fever, diphtheria, phthisis, abscesses, etc. (The dose recommended by these is 1.0–5.0 grm. pro die.) The same is probably true of the zincum sulpho-carbolicum s. phenylicum (officinal). This preparation as a powder has but little of the carbolic-acid odor; in solution (1–100 Wood) it has no odor at all. Bardeleben, however, asserts that he has obtained excellent results from the substitution of this preparation for phenol in the Lister method of treating wounds; he moreover has no disturbances of the general health resulting from its use. His injection (1 per cent) of the same preparation in gonorrhœa is also said to be very useful.

The following is a list of the solutions, materials, and preparations which are used at the present time in Lister's dressings and operations.

a. Solutions of phenol in water. Strength as follows: 5-per-cent (1–20) solutions for washing the hands before and after the operation; for washing the site of operation; for cleaning an already existing wound (for this we may use a 2½-per-cent solution also); for disinfecting all instruments (knives, sponges, syringes, catheters, drainage tubes) that may be used during the operation. These should be placed in the solution during and before the operation; for moistening the protective ("calico") which is used in case the carbolic spray is interrupted; for filling the cup of the spray apparatus in case the latter be of the variety in which the phenol spray is diluted by steam.

2½-per-cent solutions (1–40), known as "carbolic-acid water," for producing the spray when the Richardson spray apparatus is used; for soaking the bandages; for moistening the protective and the antiseptic gauze; for preserving the sponges, drainage tubes, and jute.

1-per-cent solutions were at first used for washing wounds during the changing of the dressings, where for some reason the spray cannot be used.

b. Solutions of phenol in olive oil of various strengths. 10 per-cent carbolized oil, for soaking lint which is laid in deep wounds, or used as a drainage pledget.

5-per-cent solution of phenol in oil, for anointing the examining finger and hands; also for catheters, sounds, specula, etc.

c. Phenol—Vaseline. A 10-per-cent mixture of phenol and vaseline good for chapped hands; also to protect the hands from the spray.

d. Protective, either of green silk or of cotton. In its preparation oiled silk is painted on both sides with "copal-lac," then on one side with a mixture of 1 part of dextrine, 2 parts of starch, and 16 parts of a 5-per-cent solution of phenol. Before it is used the protective is again washed with a 2½-per-cent solution of phenol, in order to disinfect it, for the protective in itself has no disinfectant properties. Its purpose is rather to be applied directly to the wound, and thus to preserve the latter from the irritant effects of the phenol contained in the remainder of the dressing. The protective, although soft and non-irritant, is impermeable to the phenol on one side and the secretions of the wound on the other.

e. Antiseptic gauze is a coarse cotton cloth; it is treated with 1 part of crystallized phenol, 5 parts of ordinary resin, and 7 parts of paraffin. The resin prevents the volatilization of the carbolic acid, while the paraffin prevents the cloth from sticking to the skin. This antiseptic gauze is laid in many thicknesses over the silk: first 6 or 8 layers wrung out in "carbolic-acid water," then 6 to 8 layers in a dry state over these. This is the really antiseptic protecting agent in the Lister dressing, and in its application we must be careful that it overlaps the wound from 12 to 15 centimetres on all sides, according to the size of the wound. In this way the secretions are compelled to travel through quite a stretch of antiseptic material before coming in contact with the outer air.

Bruns has substituted for this a gauze which is soaked in a solution of phenol and resin in alcohol, castor oil being used instead of paraffin. Bruns has recently published the following prescription for the preparation of the antiseptic gauze: 600.0 phenol, 2 kilograms of colophonium, and 500.0 stearin (or 1 kilogram of glycerine) to be dissolved in 10 litres of alcohol. 2½ litres of this solution are required to impregnate 1 kilogram of gauze.

f. Phenol-jute is the well-known cotton tissue, which has been saturated with a 2½-per-cent solution of phenol. Some surgeons use it instead of the antiseptic gauze to place over the protective; it is kept constantly moist with this solution.

g. Mackintosh: stuff similar to that used for lining hats, composed of cotton material which is covered with rubber. Is laid between both of the most external layers of the antiseptic gauze, and used to prevent the percolation of the secretions through the dressing. Instead of mackintosh, surgeons sometimes use carbolized parchment paper, or darkened silk paper.

h. Catgut, threads made of the sheep's gut; used for ligaturing vessels, and for deep stitches in the Lister dressing. Catgut strings are prepared in the following manner: they are soaked for at least two months in an emulsion prepared as follows: 5 parts of oil, and 1 part of a solution of 100 parts of crystallized phenol to 10 parts of water. They are kept constantly in this emulsion, and before their use it is well to place them in phenol water for half an hour. Catgut has the great advantage of being non-irritant to a wound, and that the threads are absorbed. They can be used for ordinary sutures.

i. Phenol silk (Czerny), prepared by boiling silk in a 5-per-cent solution of carbolic acid. It should be constantly kept in this water.

Antiseptic silk; that is, silk which has been kept from a half to one hour in a hot mixture of 1 part of phenol to 10 parts of wax. It should be kept in a glass.

k. Rubber drainage tubes, used for draining away the secretions of the wound, and well known to be of the greatest importance in the Lister dressing. They, as well as the sponges, should be constantly kept in a 2½–5-per-cent solution of phenol.

These various preparations have been slightly altered by different surgeons, but all agree upon the great principle to be observed in antiseptic surgery. Among other things P. Bruns has recently recommended

l. "Phenol powder," consisting of 25 parts of phenol, 60 parts of colophonium, and 15 parts of stearin, all mixed together, and this mixture to be further diluted with an indifferent powder such as calcaria carbonica præcipitata, in the proportion of 1 to 7 or 8 parts by weight. This powder, which contains from 2½ to 3 per cent of phenol, is dusted directly over small wounds and ulcers and atonic granulating surfaces. It can thus be used on the battle-field even in serious wounds. Over this should be placed several layers of jute, and over the whole is placed wax or paraffin paper.

Treatment of Phenol Poisoning.—If possible, the stomach-pump should be used.

Among antidotes we have that praised by Husemann and Ummethun, namely, saccharated lime; and, furthermore, that recommended by Baumann, the sodium sulphate. The latter was found by Sonnenberg to be of practical utility, who recommended doses of 5.0 : 100 for adults and 4.0 : 100.0 for children. Milk and white of egg may be given on general principles.

None of these would be of any utility in poisoning from impure phenol preparations.

Appendix to Phenol.

The following substances are also used therapeutically, although not as commonly as those given above:

Benzol.—Benzol (coal-tar benzol or benzine), C_6H_6, is found in the tars which are produced in process of manufacturing illuminating gas from coal. It is here found mixed with many of its homologues and the solid aromatic hydrocarbons. Chemically pure benzol is a light, peculiar fluid, having the odor of chloroform and bitter almonds. It boils at 80.5° C, evaporates without residue, and burns with a light, spluttering flame; insoluble in water, but misicible with alcohol and ether in every proportion. It is a solvent for sulphur and phosphorus, but especially for iodine, fats, resin, india-rubber, and wax; it is therefore used to get rid of fat stains, etc.

It must not be confounded with the officinal petroleum benzine, which is only a mixture of hydrocarbons, having the formula $C_n H_{n+2}$. It is unknown in its physiological effects, and it is therefore only applicable for washing away ointments, etc., from the skin.

Physiological Action.—Benzol is strongly poisonous upon lower organisms, such as insects, trichina, etc.

Upon man, according to Mosler, its internal administration has no injurious result when given in doses of 2.0 grms. or 8.0 grms. daily. Pigs can even take 15.0 grms. without injury. Perrin, however, has seen larger doses followed by deep narcosis.

When inhaled it causes muscular trembling and convulsions, vertigo, and finally even narcosis.

Therapeutic Application.—At the present time we can form no positive judgment concerning the utility of benzol in disease, for the reason, according to Husemann, that sometimes coal-tar benzine (benzol), and sometimes officinal petroleum benzine, has been used.

Naunyn recommended benzol against the vomiting which results from fermentation going on in the stomach. Here it acts only symptomatically, but in these cases we find it best to wash out the stomach, so that benzol would be of little importance in most cases.

Mosler has recommended the use of benzol in trichinosis, but this application has not been confirmed in its beneficial results. Its external application in itch is superfluous.

Dosage.—Benzol, or carboni fossili, internally from 0.5 to 1.0 per dose (5.0 pro die), in mixture with succus liquiritiæ and mucilago gummi mimosæ.

Dihydroxy-benzenes, $C_6H_4(OH)_2$. Procatechin, hydroquinones and resorcin, in the order of their toxic and antifermentative strength, have the power of stopping alcoholic fermentation when present in the strength of 1 per cent. A 1-per-cent solution of the first and second of these substances completely prevents the decomposition of albumen, while ½-per-cent solutions of the first and third prevent butyric-acid fermentation.

Qualitatively, the effect upon cold- and warm-blooded animals is the same as that of phenol (Brieger).

Therapeutically these substances have the advantage over phenol, in that they are not caustic, so that they can be applied in cases where phenol cannot be used. Hydroquinone is especially to be recommended, in that it is much less poisonous than phenol, although powerfully antifermentative. Brieger has had excellent effects from the use of 1 to 2 per-cent solutions in gonorrhœa, and recommends its use in contagious ophthalmia, it having no caustic action upon the cornea.

Amido-benzole (phenylamine or aniline), $C_6H_5NH_2$, is used in preparing the beautiful aniline colors; is soluble in 31 parts of water, and all

strengths of alcohol and ether. It produces local inflammations, anæsthesia and difficult breathing, cyanosis, and death from paralysis of respiration. Most of the aniline and rosaniline colors, such as fuchsin, are not poisonous, provided they are not impure from admixture with arsenic, phenol, etc.

Nitro-benzol (nitro-benzine), $C_6H_5NO_2$, is an irritant and paralyzer upon the central nervous system. Under its influence the blood loses its power of absorbing oxygen; the blood-corpuscles are dissolved. It is not changed in the body into aniline or hydrocyanic acid (Lewin, Filehne). Before its poisonous effects were recognized, it was used for perfuming instead of bitter almonds and for flavoring liqueurs.

Trinitro-phenol (picric acid), $C_6H_3(NO_2)_3$, is made by treating phenol with nitric acid; has a bitter taste; is scarcely soluble in cold water, but better in hot water. It produces a yellowish discoloration of the skin and all the organs; also nausea, vomiting, diarrhœa, and a great alteration of the red blood-globules (Erb). Potash picro-nitrate has been recommended in intestinal worms and against trichina, without, however, any beneficial results.

Pyrogallol, $C_6H_3(OH)_3$, pyrogallic acid, although it has no acid reaction, appears in colorless shining crystals, which are very slightly soluble in water. Concerning its antifermentative and antiseptic action we have various observations. Kolbe denies that it has any power over alcoholic and similar fermentation. According to Bovet, 1–1½-per-cent solutions prevent the decomposition of animal tissues. Foul-smelling substances lose their foul odor in 2–2½-per-cent solutions. Bovet believes that the affinity for oxygen of the pyrogallic acid is the cause of its antifermentative and deodorizing properties.

Pyrogallic acid must be used in only very small doses on account of its power of destroying the blood-corpuscles and producing hæmoglobinuria. In larger doses it is an intense poison because of its power of changing the blood (makes it of a coffee-grounds color, exceedingly fluid, rapidly coagulable, while it diminishes the number of red blood globules, fibrin, and the hæmoglobin to $\frac{1}{10}$ of their normal quantity, and also gives rise to the formation of thrombi). It makes circulation of the blood an impossibility. The poisonous effect is produced both from the external and internal application. Death occurs in a few days with vomiting, anæsthesia, and loss of sensibility, great diminution of temperature, and the passage of dark (black and dark-brown) urine. 1.0 grm. doses can be borne without harm (Jüdell and Neisser). Upon the bones pyrogallol is said to have an effect similar to that of arsenic and phosphorus (Marx).

This drug should therefore never be used when any other drug can be employed. Hebra and Jarisch have proposed it in 5–10-per-cent ointments for the treatment of psoriasis and to destroy lupoid and carcinomatous formations. We prefer, however, chrysophanic acid in the treatment of psoriasis of extensive surfaces. In the psoriasis of the face and head, however, pyrogallic acid is to be preferred, because it does not alter the healthy skin; since but small quantities (5–20: 100 of vaseline or alcohol) are required in the treatment of lupus and epithelial cancer: the drug is safe in these latter conditions. In addition, pyrogallic acid is a good coloring agent for the hair, and is not injurious to the hair, while gallo-tannic acid makes the hair too dry and brittle.

Chrysarobin, $C_{26}H_{22}O_7$, is obtained in large quantities from Goa powder, araroba, which is found in the seams and cracks of the Brazilian tree angelim amargosa; from this substance it is extracted by means of

benzol, from which it crystallizes in small yellow scales (Liebermann). Most probably it is a product resulting from the reduction of chrysophanic acid. Both the chrysarobin and the chrysophanic-acid produced from rhubarb are non-injurious substances for the organism (Neisser), cause a more or less severe inflammation of the skin, and have been recently used in the treatment of psoriasis, eczema squamosum, pityriasis, and herpes tonsurans, and are used either in conjunction with a simple cerate or with collodion (1 : 7–10).

Thymol, $C_{10}H_{14}O = C_6H_3(OH).CH_3.C_3H_7$, can be obtained from the oil of thyme, as the monohydroxyl phenol of the methylisopropyl benzol or cymol, by shaking it with soda lye, and then decomposing the watery solution by hydrochloric acid. It appears in large crystals, leaving a mild and characteristic odor, and which are slightly soluble in cold water (1 : 1000), more easily in alcohol and ether.

Physiological Action.—According to Liebreich and Lewin, as well as Husemann, thymol is even more powerful as an antiseptic and antifermentative agent than phenol and salicylic acid. It has the further advantages of a very agreeable odor, besides being strongly deodorizing and less volatile than phenol. It also retards and prevents the growth of the mould germ, and suspends the action of putrid pus upon the animal organism. Solutions of $\frac{1}{10}$ per cent are sufficiently strong for all these purposes; so that its high price cannot be considered as a disadvantage, since less of it is required.

Husemann believes thymol much less poisonous than phenol to the animal organism. While rabbits die from 0.5 grm. of the latter, it takes 3.0–4.0 grms. subcutaneously administered, or 5.0–6.0 grms. by the stomach, of the former drug to produce a fatal result.

Locally, upon the mucous membrane, thymol acts as an irritant, but never as caustic. Local anæsthesia can also be produced by its use.

Rabbits.—The effects here upon the heart and respiration are similar to those produced by phenol.

The nervous effect also is in both cases a central one, and the peripheral terminations of the nerves are little affected; but thymol has a paralyzing effect from the very beginning upon all the motor centres, while phenol causes convulsions by primary irritation of these centres.

In addition to these effects, thymol even in doses of 2.0 grms. reduces the frequency of the respiratory movements, and a lowering of temperature to the extent of 1°. The heart's action, however, is diminished in rapidity.

In fatal doses, respiration, temperature, and circulation steadily diminish; animals become apathetic and powerless, breathing is stertorous, and finally coma sets in (Küssner). Post-mortem examination shows the lung congested and in a condition of hepatization; bronchial mucous membrane very much congested, and secreting a large quantity of mucus. The kidneys were to a great degree hyperæmic and in a stage of primary nephritis. The urine was always bloody and albuminous, and contained thymol in a partially unaltered condition. The liver undergoes fatty degeneration, as in poisoning from phosphorus. All the organs smelt of thymol. These differences in the effect of thymol and phenol upon the lung, kidneys, and liver are accounted for by Husemann on the theory of the varying diffusibility of both bodies. Thymol is oxidized with greater difficulty than phenol, because it contains more carbon, and therefore it is more irritant than the latter upon all the

organs; so that in its physiological action thymol resembles oil of turpentine much more than phenol.

Human Organism.—Here we only know that 1.0-grm. doses of thymol pro die are very well borne, only a slight epigastric burning sensation being produced (Küssner).

Therapeutic Application.—In the last few years thymol has been used in many ways, both internally and externally, as a substitute for phenol in the Lister method of treating wounds. Baelz, Coghen, and Küssner have used thymol in the treatment of general diseases (such as typhus, typhoid, pneumonia, pertussis, diabetes, etc.), and also in local diseases (such as catarrh of the bladder, diphtheritic angina, etc.). In most cases it proved itself useless; at most there was a slight improvement in cases of phthisis and in a few cases of gastro-intestinal catarrh.

Although phenol has many advantages over thymol in the Lister surgery, yet the disadvantage of its sometimes seeming poisonous effects on the system has led to the substitution of the latter for the former drug by some surgeons. Ranke claims that careful thymol dressings are certainly antiseptic, while they are perfectly harmless and cheap. Yet thymol has not replaced phenol in general use, for the reasons that 1-per-cent solution, which is the best that can be used, is not sufficiently antiseptic, in addition to the fact that the odor of the drug after a time becomes disagreeable, although sweetish, and attracts swarms of flies.

These were the views of Bardeleben, Küster, Schede, and others at the Surgeons' Congress in 1878. The effects upon the heart and respiration are similar to those produced by phenol.

Dosage.—Thymol from 0.05 to 0.1 per dose in watery alcoholic or alkaline solution, or in emulsion or as a powder in capsules. As antipyretic 1–2.0-grm. doses have been given. The slight addition of alcohol and glycerine increases the solubility (1.0 thymol, 10.0 alcohol, 20.0 glycerine, and 1000.0 of water). Ranke uses thymol only for all his antiseptic procedures, with the single exception that the catgut is steeped in phenol preparations.

Creosote, Creosotum—beechwood tar creosote of Reichenbach,—a colorless fluid, which gradually turns yellow, has a characteristically penetrating odor, is slightly soluble in water (1 : 80), less in alcohol, ether, etc. Is not, as was supposed by the discoverer, a chemically pure substance, but is only a mixture of guaiac oil, $C_7H_8O_2$, and creosote, $C_8H_{10}O_2$.

Physiological Action—Creosote acts in every respect like pure phenol; in its antiseptic power especially it is not inferior to phenol. According to Husemann and Ummethum, it has a similar effect to that of phenol, both locally and generally; the differences between the two substances being, 1st, that phenol causes severe convulsions, while creosote produces paralysis; 2d, phenol diminishes the coagulability of the blood, while creosote increases it.

The uncertainty of chemical composition of the various creosotes, and the impossibility of determining their exact action (some forms produce vomiting, for instance; others do not), render it desirable to discard the use of creosote, and to use instead phenol. We must, however, use rather smaller doses of phenol, internally, than we might give of creosote, to produce certain effects. The less poisonous action of creosote is more than overbalanced by the uncertainty of its strength and composition.

Therapeutic Application.—For the sake of completeness we shall give the conditions in which creosote has hitherto been used. It was given

in vomiting, under the same circumstances as we mentioned under benzol. Also in diarrhœas of various kinds, even in the summer diarrhœa of children, although we have never seen any benefit from its use. In broncho-blenorrhœa it is better replaced by other remedies. Curschmann, however, recommends it recently in putrid lung affections, because it excites less cough than phenol and oil of turpentine. Bouchard and Gimbert recently praise the long-continued use of creosote (up to 0.5 daily) in mixtures, for consumptives. Fraenzel also saw the secretion and fever favorably influenced by it in a series of cases. Further confirmation of these views is necessary.

In all cases, phenol is preferred for external use.

Dosage and Preparations.—1. Creosotum, internally, from ½ to 1 drop, ad 0.05 pro dosi! ad 0.2 pro die! several times a day, in emulsion, mucilaginous vehicles, and gelatinized pills.

2. *Creosotum Solutium,*—aqua creosoti s. binelli,—3 parts of creosote, 400 parts of water; dose ʒi to ʒiv.

Tar—Pix liquida—is obtained by the dry distillation of pine wood, coincidently with wood vinegar, and is a thick, oily, dark-brown fluid, which contains a variable mixture of creosote, phenol, toluol, xylol, acetic acid, and other substances.

Physiological Action.—In such a mixture of substances we cannot expect any uniformity of action; the principal effect, however, is due to the phenol and creosote. Upon the skin and mucous membranes the action is antiseptic; the skin becomes red and the epidermis is raised in blisters. In most cases, the drug, whether applied to the skin or given internally, causes vomiting and diarrhœa, together with inflammation of the kidneys. Too large doses have been followed by death, with symptoms similar to those resulting from phenol poisoning.

Therapeutic Application.—The internal administration of tar has been almost entirely suspended. But externally it is very much used, and in some diseases with excellent effect.

First in eczema: tar ointments should only be used in chronic eczema when no new vesicles or papules occur, accompanied by inflammatory symptoms; in other words, when the eczema is a dry one we should begin with the weaker tar ointments (1–4), and gradually increase the strength. It is entirely useless when the eczema has become chronic, and when the skin has undergone considerable anatomical changes, such as thickening and hypertrophy and callosities. In psoriasis which is not too chronic the tar ointment is often followed by good results; it is true that relapses occur, but the ointment is a great aid to the internal treatment of the disease. Good results, often cure, are seen in prurigo, especially when the latter is only a local affection; in prurigo senilis, or when the disease is symptomatic of a general condition, the remedy is not so successful. It is of very little utility in tinea, impetigo, rupia, and ichthyosis.

We should never forget that when tar is applied to a large extent of surface that its active components may be absorbed and produce toxic symptoms, such as vomiting, headache, and dizziness.

It does not appear that one variety of tar is in any way superior to another variety, as far as can be judged from the physiological action. On the other hand, the physical properties of some varieties, and superior facility in their application, may give them the advantage over others.

Tar has been recommended for inhalation in broncho-blenorrhœa, without, however, any advantages resulting from its use.

Dosage and Preparation.—1. Pix liquida: if used internally, the dose would be 0.3–1.0 in pill or capsules. Externally, the tar is either given in substance (a line in thickness), or used in the form of an ointment (1 to 4 parts—10 parts of ung. simp.), or as a plaster (with rosin and lard). 2. Aquæ picis s. picea: 1 part of tar to 10 parts of water, mixed; dose, internally, ℥ss.; externally used as a dressing, and astringent wash and injection. 3. Pix navalis s. solida: common ship tar; used for plasters.

Coal-tar,—pix lithantracis,—a product of the dry distillation of coal; therefore one of the products in the manufacture of illuminating gas. In its composition it resembles ordinary tar in its active components. Its effects, apart from the antiseptic action which is due to the phenol, are unknown, but probably similar to the foregoing preparation. Therapeutically it is superfluous.

Oil of Cade,—oleum juniperi empyreumaticum—is a tar produced by the dry distillation of the juniper species of trees, and only differs from the other wood tars in that it has a more pleasant odor.

We agree with Hebra in the opinion that in the diseases of the skin in which tar is useful the oil of cade should be preferred to other tars, especially in children, because it is more easily applied. It has a more pleasant odor, dries more readily, and adheres to the skin if the latter be immediately powdered with rice, flour, etc. Children cannot then so readily wipe it off, and the effect is a more prolonged one. It is used either pure or diluted (in ointments).

Wood Vinegar.—Pyroligneous acid, obtained from wood by dry distillation, together with tar. It is a yellowish, strongly acid liquid, having a creosote-like odor, and an exceedingly variable composition of formic and acetic acids, pyrogallol, methyl alcohol, creosote, and many other substances. It can be considered really a solution of creosote in acetic acid, inasmuch as it contains 5 to 10 per cent of acetic acid. It is, like creosote, an antiseptic and antifermentative agent, poisonous, in large doses, for animals, and applicable wherever a combination of vinegar and phenol would be applicable, but yet entirely superfluous therapeutically. Preparations: 1. Acetum pyrolignosum crudum. 2. A. p. rectificatum.

AROMATIC ACIDS.

The aromatic acids, formula $C_nH_{2n-8}O_2$, have also given a large number of antiseptic and antifermentative agents. Of these, those that have been found effective in this respect are benzoic, salicylic, cresotinic, chlorsalylic, chlordrakylic, paracressylic, and tannic acids. The non-effective members of the group are the meta- and para-oxybenzoic acids, which are isomeric with salicylic acid, phthalic and isophthalic acids, and gallic and pyrogallic acids (?);

furthermore, salicylic acid, methyl ether (?), salicylic acid aldehyde, and sodium salicylate (?).

The reason why the first group is effective and the latter not, is unknown. Kolbe says: "It is very remarkable, and at present inexplicable, that while salicylic acts as an antiseptic, and prevents alcoholic fermentation especially, para-oxybenzoic acid, which has the same composition, and which is as readily decomposed, under the influence of heat, into carbolic and carbonic acids, and which can also be formed from these acids under the same conditions as salicylic acid; and, finally, which can be formed from salicylic acid, by simple processes of decomposition—that this acid should not possess similar antiseptic properties to those of salicylic acid.

It is an important fact that while other substances having antiseptic and antifermentative properties, such as corrosive sublimate, and other metallic combinations, quinine, phenol, etc., are more or less poisonous to the higher animals, the aromatic acids which possess these properties are, as a rule, non-injurious to the higher animals and man, although fatal to the lower organisms.

Several of these bodies, such as salicylic acid and its sodium salt, as well as the sodium cresotinate, although harmless, have an antipyretic action; while antipyretics formerly known, such as digitalis, etc., produce additional injurious effects.

The hope which salicylic acid seemed to hold out in the beginning, "that putrid disease processes in man and the higher animals could be combated by its use, in a manner similar to that by which decomposition can be prevented outside of the body," has proved an illusive one.

As to their disposition in the organism, many aromatic acids have this in common, that shortly before their excretion in the urine, they are converted with glycocol into hippuric and its related acids. Some of the aromatic acids, such as the isomerics of salicylic acid (oxy- and para-oxybenzoic acids), are partly converted like, the phenols, into ethene-sulphonic acid, partly into combinations analogous to hippuric acid.

Para-oxybenzoic acid, to a very slight extent, is decomposed in the intestine with the formation of phenol (Baumann and Herter.)

Benzoic Acid—Acidum Benzoicum.

Benzoic acid, $C_6H_5.Co.OH$, occurs frequently, either free or in the form of combinations, frequently with cinnamic acid in many plants (in the resins of styrax benzoin, myrrh, and balsam of Peru; in many plants with ethereal oils, such as calamus, cloves, vanilla, anise, pimpinella, cinnamon, etc.); also in the urine of the herbivora, and in the præputial secretion of the beaver. It can be prepared artificially by the oxidation of oil of bitter almonds and many organic bodies, such as toluol, and all the fatty acids in which the phenyl root has not been substituted, by chromic and sulphuric acid. Synthetically it has been produced from bromo-benzene, benzol-sulphonic acid, and phenyl cyanides. It is produced in small quantities by the oxidation of albuminoids and benzol.

The benzoic acid of commerce is prepared chiefly from hippuric acid and benzoyl-glycocol, which when boiled with acids or alkalies, as well as when urine undergoes decomposition, is changed into glycocol and benzoic acid.

The officinal sublimed benzoic acid—acidum benzoicum (sublimatum), flores benzoes—must be prepared by sublimation from the resin of benzoin, and presents whitish crystals, which gradually turn yellow, have a benzoin odor, and are soluble in 500 parts of cold, 25 parts of boiling water, and in small quantities of alcohol ether and oil of turpentine. When heated it melts and evaporates.

PHYSIOLOGICAL ACTION.

Effect upon Fermentation and Decomposition.—As will be more thoroughly shown under salicylic acid, benzoic acid is an antifermentative and antiseptic agent, which in some fluids, such as in beer, solutions of putrid flesh, etc., is even more effective and kills bacteria, in less concentration than salicylic acid (Fleck, Salkowski, and Bucholtz); this is because, as Kolbe has shown, the benzoic acid does not so readily enter into combination with the salts found in these fluids as salicylic acid does. According to Bucholtz, 0.1-per-cent solutions of benzoic acid were sufficient to prevent the development of bacteria, and 0.02-per-cent solutions have a greatly retarding effect to this process. Bacteria are entirely destroyed by 0.3–0.4 per cent.

Effect upon the Organism of the higher Animals and Man.—Benzoic acid passes through the greater part of the organism unchanged, for which reason it is found in the blood as such. In the kidneys, however, it combines with 1 molecule of glycocol, and the giving off of one molecule of water, to form benzoyl-glycocol or hippuric acid,

$$\underset{\text{(Benzoic acid)}}{C_7H_6O_2} \quad \text{and} \quad \underset{\text{(Glycocol)}}{C_2H_5-No_2} - \underset{\text{(Water)}}{H_2O} = \underset{\text{(Hippuric acid)}}{C_9H_9NO_3}$$

and appears as such in the urine. In birds the benzoic acid

reappears in the urine as ornithuric acid (Jaffe). In the perspiration and saliva it never reappears as hippuric acid, but either as benzoic acid, or after active exercise as succinic acid (Nencki, however, denies that it ever appears as succinic acid, asserting that the acid was mistaken for phthalic acid by Meissner). Meissner, therefore, believes that the succinic acid is the result of increased tissue metamorphosis after exercise. When the kidneys were extirpated from animals, the administration of benzoic acid was followed by the appearance of hippuric acid in the blood, in addition to benzoic acid, so that we must believe that either the extirpation of the kidneys has led to the increase in the hippuric acid of the blood (the kidneys no longer getting rid of it), or that the abnormal condition has given rise to an abnormal formation of hippuric acid in the blood or other organs. The nitrogenous component (glycocol) which must combine with the benzoic acid to form hippuric acid, comes neither from the urea nor the uric acid, for there is no diminution of these products in the urine, notwithstanding that Garrod, Kletzinsky, and Ure have made contrary assertions. According to Weiske, benzoic acid is converted into hippuric acid only under the influence of a diet which naturally gives rise to the formation of hippuric acid; when beans, potatoes, etc., are used as food in herbivora, the benzoic acid is excreted in the urine unchanged. Thus the theory that benzoic acid has a favorable effect in uræmia, or in any abnormal formation of uric acid, gout (Frerichs, Golding Bird), etc., is disproved theoretically and practically. Bunge and Schmiedeberg have recently confirmed the statements of Meissner that the kidneys are the only place where hippuric acid is formed, and have added that the blood-corpuscles here play an important part.

The physiological effect of benzoic acid is, like that of salicylic acid, a trifling one, and, as far as is now known, very similar to that of the latter acid.

The odor is like that of vanilla, only stronger. The taste is at first aromatic, followed by burning and scratching in the mouth and throat. The vapors when inhaled are strongly irritant, and cause cough; when snuffed as a powder they cause sneezing.

Even large doses have not been followed, either in men or animals, by any noteworthy disturbances. Meissner only has seen nausea and vomiting follow the taking of 5.0 grms.

of sodium benzoate by himself. Schreiber also saw 15.0-grm. doses followed by the above-mentioned local effects, together with fulness of the head, increased rapidity of the heart's action, increase in the subjective sensation of warmth, hyperidrosis, and increased expectoration of mucus. More accurate observations are very desirable, especially as to how benzoic acid affects diseases and febrile conditions which are the result of septic infection.

According to Salkowski, benzoic acid also produces a considerable increase in decomposition of albumen in the dog, without in any way affecting the formation of hippuric acid.

Benzoate of Sodium—Sodium Benzoate.

PHYSIOLOGICAL ACTION.

Theoretically we would believe that benzoic acid would lose all its antiseptic and antifermentative power in neutral and alkaline solutions in combining with sodium. But Bucholtz asserts that the neutral sodium benzoate is even superior to benzoic acid in its antiseptic power; 0.05 to 0.06 per cent of the salt were sufficient to interfere with the development of bacteria in fluids upon which he experimented; we do not yet know, however, just how far the antiseptic power is shown by the above experiment. We also have little idea as to the physiological effect upon the higher animals and man; we only know that in the latter from 15.0–30.0 grms. of the salt can be taken in twenty-four hours without any noteworthy effects, and that in fevers it is antipyretic. It is very likely, however, that it resembles benzoic acid in its action, except that it does not produce the irritating local effects of the acid. We would indeed expect the general effects of both to be the same, if only for the reason that benzoic acid can only circulate in the blood as benzoate of sodium.

THERAPEUTIC APPLICATION.

Formerly only benzoic acid was given in quite a number of conditions; at the present time, however, it is only preferred as an expectorant, especially when we also desire a directly exciting effect. Especially desirable is this in the catarrh of old people and weak individuals, when these are either non-febrile or accompanied only by slight fever, and

when the bronchi are filled with a loose secretion; also in pneumonias of old men and very weak individuals, when the above-named conditions are present. Sometimes this indication for the use of benzoic acid is also present in typhus and typhoid fever, where the respiratory apparatus is much affected. We must acknowledge, however, that our experience has not shown a very decided effect in these cases from the use of the drug.

In all other conditions in which this remedy has been used, the beneficial effect is still more uncertain, and this is especially true of uræmia, in which Frerichs has recommended its use, in accordance with his well-known theory. We would advise no one to limit himself to the use of this drug in uræmia, but to use at the same time the other remedies that have been found effective in this condition.

The alleged diminution in the formation of uric acid which results from the use of benzoates, has led Ure and others to try it in the uric-acid diathesis, and where there is a tendency to the formation of uric-acid concretions. Since then, however, the inaccuracy of theory upon which the treatment is based has been shown, and practically the drug has been found useless.

Sodium benzoate has only recently been used as a result of the recommendations of Klebs, and the experiments of Brown and Schueller; so that there is no sufficient practical experience to lead to any conclusion as to its value. We can only give a list of the conditions in which it has been tried. It has been used in the various parasitic (acute infectious diseases), especially in accidental diseases of wounds, such as erysipelas; also in diphtheria, typhus, polyarthritis rheumatica, acute gastro-enteritis of children, etc. The result of our own experience, together with that of others, may be summed up as follows: Large doses (10 to 20 grms. pro die) have often been followed by a great diminution in the fever, but the effect is not in any way different from that resulting from sodium salicylate, and sometimes there have been in addition serious disturbances, such as fulness in the head, somnolence, sweating, and even collapse. Sometimes, indeed, even the diminution of temperature does not result from large doses.

Thus in typhus recurrens we have given as much as 60 grms. in 48 hours without the least effect upon the temperature. But here we should remark that in a relapse in typhus fevers even salicylic acid and quinine are often pow-

erless upon the temperature. We certainly have not seen any specific effect from the use of the drug in acute infectious diseases, nor has Fürbringer seen any marked result in the local and general use of the drug in pharyngeal diphtheria. Senator asserts that a specific curative power over polyarthritis rheumatica is possessed by this drug; but this effect is not as well marked as that possessed by salicylates. Benzoic acid has, however, produced a cure where salicylic acid was unsuccessful.

In such cases, or where salicylic acid cannot be taken for any reason, benzoic acid may be used.

General attention is at the present time directed to the treatment of tuberculosis by the benzoate of sodium. After Schüller, led by experimental investigations on animals infected with tuberculosis, had recommended that this remedy should also be tried in men, giving the proper dose as 1 grm pro mille of bodily weight, Rokitansky reported from his clinic that sodium benzoate appears to be a cure for tuberculosis and phthisis. Consumptives were not only improved but even entirely cured. He even asserted that cavities were made to disappear in a few weeks, and although this was very surprising, yet in the face of such assertions it was certainly right to try the remedy in phthisis, since this is otherwise an almost incurable disease. Other observers, however (Schnitzler, Guttman, Waldenburg, and others), have seen none of these wonderful results. We ourselves have allowed patients with febrile and non-febrile phthisis to inhale the drug in daily doses, $\frac{1}{4}$, $\frac{1}{8}$, $\frac{1}{2}$ to 1 pro mille, without having noticed any remarkably curative results. Some of the patients felt pretty well, but these were generally the milder cases, and such have periods of well-being even without this treatment. In some the inhalations had to be suspended because of their too strongly irritant effects upon the cough. In those who suffered from febrile phthisis there was no lasting interruption in the fever, although temporarily this was kept away, as happens sometimes under no treatment at all; there was certainly no curative power exercised over the disease. We will not, however, dispute the possibility that in certain incipient cases of tuberculosis sodium benzoate has a curative effect, but we think that this is a point to be determined by future experience. We would, however, decidedly dispute the idea that far-ad-

vanced cases with destruction of lung tissue can be favorably affected by this drug.

As to the treatment of diabetes mellitus and several other conditions with sodium benzoate we have at present insufficient material for us to express any decided views.

Dosage.—1. Acid. benzoicum sublimatum,—flores benzoes,—from 0.05 to 0.5 pro dosi. in powder or pill. 2. Sod. benzoicum, internally, from 0.5–1.0 to 4.0 pro dosi, according to the purpose (10.0 to 30.0 pro die) in solution or powder. For inhalation in phthisis from 50.0 to 60.0 daily.

Salicylic Acid—Acidum Salicylicum.

Salicylic acid or ortho-hydroxy-benzoic $C_6H_4(OH).CO.OH$, is one of the chief ingredients of the American oil of wintergreen (Gaultheria procumbens). Synthetically, it can be prepared from phenol under the simultaneous action of sodium and carbonic-acid anhydride. At high temperatures (220° C.) it is decomposed into phenol and carbonic acid. It can be sublimed unchanged if heated gradually and carefully.

PHYSIOLOGICAL ACTION.

Salicylic acid is of great value as an antiseptic and antifermentative agent, because it is odorless, has no disagreeable taste, is not poisonous to higher organisms, and is nonvolatile.

It is to be regretted, however, that it loses its power very rapidly in meat and other fluids containing a large proportion of phosphates and carbonates, unless present in great excess, or added to a very strong acid, because the salicylates which are formed, such as sodium salicylate, have no antifermentative or antiseptic power (Kolbe).

On the other hand, salicylic acid, as well as its sodium and probably its other salts all have great antipyretic power; and here the non-poisonous character of most of these salts is a great advantage.

The disadvantages of salicylic acid as compared with phenol, are its difficult solubility, its high price, its irritant effect upon the mucous membranes, especially when inhaled, and finally the fact that it is injurious to surgical instruments which are dipped in its solutions.

Chemical Remarks.—In order to understand the action of salicylic acid, it will be necessary to call attention to some of the chemical relations of this drug to other acids and salts, which have been shown by Kolbe and Fleischer.

Salicylic acid decomposes acetates and carbonates, form-

ing salicylates, although the salicylates are not decomposed by carbonic, acetic, oxalic, or tartaric acids.

Neutral ether does not withdraw the salicylic acid from a watery solution of sodium salicylate, but it does this if at the same time carbonic or acetic acid be present. Hydrochloric, lactic, and phosphoric acids precipitate salicylic acid from the sodium salicylate.

When salicylic acid is added to a solution of bisodium phosphate (Na_2HPO_4), a decomposition takes place by which the salicylic acid unites with one of the atoms of the sodium, thus giving rise to the presence of sodium salicylate with the acid sodium phosphate (NaH_2PO_4), a combination the more remarkable from the fact that phosphoric acid alone of all the acids has the power of driving out the salicylic from its combinations. According to Kolbe and Meyer, one molecule of bisodium phosphate binds two thirds of a molecule of salicylic acid and only half a molecule of benzoic acid.

Effects upon Fermentation and Decomposition.—According to Kolbe and others, salicylic acid hinders and prevents the action of emulsin upon amygdalin, the formation of the oil of mustard, the digestive power of pepsin, the fermentation of grape-sugar, the souring of beer, the after-fermentation of wine, the decomposition of urine, and the souring of milk. The growth of the mould-fungus is prevented in all of these fluids by 0.1-per-cent salicylic-acid solutions. Meat does not decompose in a 1-per cent solution for a week; in a concentrated solution, for four or five weeks.

The reason why many observers failed to see the antifermentative action of salicylic acid in some solutions and fluids (such as solutions of meat, beer, spices, etc.), or why others found the benzoic acid more powerful in this respect than salicylic acid (Fleck and Salkowski), is because these fluids were probably rich in alkaline phosphates and carbonates, thus giving rise to the formation, with the salicylic acid, of alkaline salicylates, which, as we have already shown, have no antifermentative or antipyretic action. In these cases, to obtain the effects of the salicylic acid the acid would have to be added in excess sufficient to combine with the bases present, and to leave an excess which would exert the characteristic effects of the salicylic acid; or, instead, other acids, such as hydrochloric acid, or acid salts, might be added, these preventing the binding of the salicylic acid (Meyer and Kolbe). That in the solutions

experimented with by Fleck the benzoic acid was more powerful than the salicylic acid would be accounted for by the fact that benzoic acid was not so readily bound by bases, so that some of it was left free to exert its effects.

Under any circumstances this much is certain, that both Fleck and Salkowski are right in supposing that in the fluids mentioned salicylic acid does not exert the antifermentative action, and for reasons such as have been stated only can this be satisfactorily accounted for.

Upon the ferments, even those that are organized (such as yeast and bacteria), salicylic acid exerts an injurious and even fatal influence upon their vital properties; indeed, it is certain that bacteria are affected by much smaller quantities than were necessary of phenol to accomplish the same purpose (Bucholtz).

Effects and Disposition of the Salicylic Acid in the Organism.—Salicylic acid cannot be absorbed through the skin when the epidermis is uninjured (Kolbe).

Upon the mucous membranes it acts as an inflammatory irritant; inhalation of very diluted solutions is followed by sneezing, roughness in the throat, and cough. Concentrated solutions are even strongly caustic, discoloring the mucous membrane temporarily (white eschar), so that it does not appear wise to apply the drug in powder to the mucous membranes (Kolbe). Wolfberg observed in fact a burning in the throat, difficulty in swallowing, together with a hemorrhagic pharyngitis, erosions and ulcers of the stomach and intestines. Dilute solutions, however, as well as sodium salycilate, never produce these ulcers (Riess).

Wounds treated with salicylic acid heal in a similar manner to those treated by phenol (Thiersch).

Feser and Friedberger believed that the salicylic acid entered into a combination with the albuminates in the blood; but it is more probable, as Salkowski supposed, and as Fleischer proved, that it decomposes the sodium phosphate and carbonate of the blood, combines with their bases, and circulates in the blood as sodium salicylate. So that the observation of Feser and Friedberger that the herbivora bear salicylic acid better than the carnivora can be explained partly by the fact that the herbivora excrete the acid more rapidly with the urine than the carnivora, and partly also by the fact that in the blood of the herbivora there are more alkaline carbonates, while in the carnivora the phosphates predominate; and since carbonic

acid is more readily borne than the acid sodium phosphate in the blood, hence the herbivora bear the salicylic acid better than the carnivora.

Free salicylic acid can only be present in a free state in the blood if it be given in such quantities that the alkalies of the blood are no longer capable of binding it. But such severe poisoning would hardly be possible, for life would be extinct long before sufficient acid had been taken into the blood to produce this result; for even after fatal poisoning by the strongest mineral acids, the blood was not found to have an acid reaction after death.

In regard to the hypothesis of Binz that the carbonic acid of the blood is capable of setting free the salicylic acid from its salts, we would say that in neutral sodium salicylate solutions the bubbling of carbonic acid does not cause any salicylic acid to be set free; this only occurs when at the same time the solution be shaken with neutral ether (as is stated above), and this is certainly not a condition present in the blood. We must not imagine that these salts are absolutely stable combinations, but rather consider their component atoms as in active motion. It is possible, indeed, that the excess of carbonic acid may constantly succeed in decomposing individual molecules of the salicylate, and combining with the base, but only, however, to be again decomposed by the salicylic acid thus set free, and immediately to be reconverted into salicylates. This momentary setting free of the salicylic-acid molecules cannot, indeed, be shown by chemical tests, but by shaking with ether we are enabled to separate these acid molecules from the attractions for their bases, so that the salicylic-acid molecules remain dissolved in the ether, while the alkaline carbonates remain in watery solution, and further mutual decompositions are thus prevented. Now the free salicylic acid in the ether can easily be demonstrated. It is highly probable that the salicylic acid behaves in a similar manner to the carbonic acid in the blood. Direct experiments in which the blood of animals treated with salicylic acid (Feser and Friedberger), and fresh arterial and venous blood which was mixed with alkaline salicylates outside of the body (H. Köhler), were shaken with ether, have never shown a trace of free salicylic acid, although in the blood of asphyxia such has been found (Köhler). This would prove that in the normal blood, at least, there is too little carbonic acid present for it to separate appre-

ciable quantities of salicylic acid from their salts, although in the blood of the asphyxial state this would not be true. Since, according to Ewald, the tension of the carbonic acid in inflamed tissues is much greater (three times as great) than normal (15–20 vol. proc.), it is possible that in the inflamed tissue of a sick person salicylic acid may be set free, just as in the blood of the asphyxial state, and thus exert its specific effect upon these tissues. Binz has referred to the injurious effect of sodium salicylate upon the lowest organisms and protoplasm (Bucholtz), which would also speak in favor of the setting free of salicylic acid in the tissue-cells. Bucholtz's assertion has not, however, been confirmed by any one else, and Kolbe denies that sodium salicylate has any antifermentative or antiseptic power. Kolbe, therefore, proposes the experiment that, just as in fermenting fluids, so also in the living organism, proper acids (hydrochloric, sulphuric acid, potassium sulphate) should be given before or together with the salicylic acid, with the idea that then it will perhaps pass through the body in a free state. We know in advance, however, that such an attempt would fail, so that our present knowledge concerning this subject may be thus briefly stated:

Salicylic acid is converted into sodium salicylate in the blood. If this salt has no effect upon the development of lower organisms, a fact not acknowledged by Bucholtz, then under ordinary circumstances the administration of salicylic acid will have no effect upon bacteria present in the organism, or upon the diseases to which they give rise. Feser and Friedberger, indeed, saw no beneficial result follow the administration of salicylic acid to sheep that had been infected with septic pus; Zimmermann met with the same failure in rabbits suffering from septic fever. However, it is still possible that in certain abnormal conditions, such as severe inflammations of some tissues, salicylic acid might be set free in the tissues themselves: the favorable effects in articular rheumatism might be taken as an example. Under any circumstances, direct proofs are still wanting.

The general effects of medium doses (4–8.0 grms.) strongly diluted do not appear to be very marked either in men or animals.

In healthy men, Buss saw doses of 4.00 grms. of the acid followed by a rush of blood to the head, increased warmth of the skin, sweating, diminished acuteness of sight and

hearing, and two hours after taking the drug a singing in the ears which lasted for six hours; nausea rarely occurred. The normal temperature was unchanged; so, also, the heart's frequency. In healthy people there was never any narcotic effect observed.

The administration of sodium salicylate to healthy peo, ple, according to Riess, who used solutions of salicylic acid-sodium phosphate, or carbonate in water, was followed only by fulness of the head, ringing of the ears, and amblyopia, as well as a diminution in the temperature by about 0.9°, but no more intense disturbances, although the amount of salicylic acid in the salt given was 2.5 grms. for children from 6 to 12 years, and for adults 5.0 grms.

The general effects of sodium salicylate and salicylic acid are entirely similar.

H. Köhler has shown that in healthy animals (rabbits and dogs) both preparations after their absorption into the blood produce slowing of the respiration (by diminishing the irritability of the respiratory branches of the vagus) of the pulse, sinking of the blood-pressure and temperature. He accounts for this similarity in effect by the fact that in the body both the acid and salt are under the same form.

Fürbringer, Feser, and others never found any variation in temperature even as a result of very large doses, while Köhler has seen a lowering of 3° C.

In men and animals suffering from febrile diseases (almost every form of fever, except that produced by the injection of putrid pus into the blood of animals—Feser, etc.), it is now positive that salicylic acid and sodium salicylate have a *marked antipyretic action.* The sodium salicylate is to be preferred to all other antipyretics.

The other effects of the acid and salt are similar to those in health, except that the hyperidrosis is more intense; collapse never occurs from its use in fever-patients.

Köhler accounts for the antipyretic action by the lowering of the blood-pressure and the frequency of the heart. Other observers saw a lowering of the temperature without any change occurring in the pulse; while others again saw the pulse fall only after the temperature had already gone down. It might be accounted for by the antiseptic power; it is positive, however, that it is not dependent upon the sweating, for the temperature fell in cases in which there was no sweating (Riess).

Both after the taking of sodium salicylate and salicylic

acid the decomposition of albumen is diminished (Jaffe, Wolfsohn), just as after benzoic acid (Salkowski). This effect cannot be due to the increased diuresis.

In very large doses both the acid and salt are poisonous, sometimes fatal, owing to the diminution in the frequency of the pulse, lowered blood-pressure, and paralysis of respiration, followed by convulsions (Feser, Friedberger and Köhler). Rabbits of 2 kilo. in weight die from the introduction of 1.0 grm. of sodium salicylate into the stomach. In dogs the fatal dose of salicylic acid is 1.0 grm. to 5 kilo. of bodily weight.

Excretion.—According to Buss, salicylic acid is present in the saliva, sweat, mucus, and urine: in the latter in the largest proportion. According to Feser and Friedberger, 63 per cent of the absorbed salicylic acid is found in the urine, always as a salt. According to Bertagnini, salicylic acid in the animal body enters into a partial combination with glycocol, forming salicyluric acid.

$$C_6H_4\begin{cases}OH\\CO.NH.CH_2.CO.OH.\end{cases}$$

Even three hours after the internal administration of 0.3 grm. of salicylic acid its excretion from the urine takes place, and is not finished after twenty hours (Kolbe); doses of 5.0 grms. begin to be excreted in from one to one and a half hours (Fleischer). In herbivora it is excreted more rapidly than in carnivora (Feser).

In herbivora the urine remains alkaline even after large doses of salicylic acid (Feser). In men with alkaline fermentation of the urine Fürbringer found under its use a diminution in the alkalinity of the urine.

Both after the use of the acid and its salt the urine turns brown under direct light, and green by transmitted light, but not as a consequence of an increase in the indican (Fleischer, Jaffe). A substance which Fleischer found, and which reduced a copper solution, was neither alkapton, nor pyrocatechin, nor quinone.

* Sodium Salicylate—Sodium Salicylicum.

PHYSIOLOGICAL ACTION.

The general effects of this readily soluble substance, which tastes like free salicylic acid, have already been discussed under salicylic acid, because the latter is converted in the body into this salt.

We would only repeat that, according to Kolbe, the salt possesses no antifermentative or antiseptic properties, while, according to Bucholtz, its presence in 0.4-per-cent solution prevents the development of bacteria; and furthermore, that it is an antipyretic of as much more as a corresponding amount of salicylic acid.

THERAPEUTIC APPLICATION.

Although only introduced into medicine a short time ago, sodium salicylate has become one of the indispensable drugs in daily practice. It has been used in a very large number of conditions, but of these we can only give three indications in which its value is undisputed: first, it is a good antiseptic; second, it is an excellent antipyretic; and third, it is an incomparable remedy for acute articular rheumatism. The last two purposes are almost as well answered by the acid as by the sodium salt.

For internal use the acid and sodium salt are of equal utility; some think even to-day that the acid is more powerful and effective than the salt; others think that the salt is to be preferred because it has no caustic effect. More extended experience seems to prove, and this is our view also, that for internal use the sodium salt should be preferred. The chief reason of this preference is that, as Wolffberg first pointed out, the pure acid is much more irritant and even caustic to the mucous membranes with which it comes in contact. Since the use of the salt is followed by the same effects as follow the use of the acid, we should certainly prefer it in all cases except where an antiseptic or antifermentative action is desired.

In acute articular rheumatism salicylic acid, first recommended by Buss, and also by Stricker, has come to be very much used in the last few years. The results have been so uniformly excellent, and all observers agree almost unanimously in its praise, that it is here proper to compare the results obtained. It is true that some few observers have reported failure in the use of the remedy in this disease, but their number is so few, as compared with that of the large majority who have seen positive and unmistakable beneficial results from its use, that we must suppose that the reason of the failure of the few is an improper mode of administering the remedy.

Salicylic acid and its sodium salt exert a specific action

upon acute rheumatism, in a manner similar to that of potassium iodide upon tertiary syphilis, or quinine upon malaria. All other remedies hitherto used are left far in the background.

The administration of the remedy is followed by a diminution or disappearance not only of the fever, but also of the pain and swelling; that is to say, of all the important symptoms of polyarthritis rheumatica.

There seems to be no doubt that it directly affects the disease itself, or its cause. The frequently astounding rapidity with which the patients recover, sometimes even after one, two, or three days, often in eight or ten days, and the reliability of the remedy, provided it be properly used, which no other method of treatment yields us, prove that sodium salicylate has a peculiar influence upon the disease-agens, whatever this may be. The cure is not due to the lowering of the temperature alone, since quinine and sodium benzoate would produce this without causing any cure of polyarthritis rheumatica.

It is the acute form of polyarthritis rheumatica which is the best affected by the remedy; the more recent the case, the better the effect. All cases are well fitted for the treatment in which the ordinary general symptoms are accompanied by diffuse local ones, or where the affection travels from one joint to another.

The question as to how far the serious complications of acute articular rheumatism, such as the endocarditis and inflammation of serous membranes, are affected by the salicylic-acid treatment, and as to whether they are prevented by this treatment, is yet in a doubtful stage. It appears probable, however, that even these complications are favorably affected, that is to say, they are kept from appearing by the removal of the disease. It is hardly of any importance to state that some cases do not yield to this drug, for this is true even of the treatment of malaria by quinine. Nor does the fact that relapses occur speak against the efficacy of the treatment, for these only mean that more of the drug must be used, until the last joint has been entirely cured. It is of the greatest importance that the proper method of administering the drug should be adopted. Stricker, who had immense opportunities for comparative observations at the military hospital in the Prussian army, recommends the following method of administration: The salicylic acid must be given hourly. In strong young men, in maximum

doses of 1.0 grm.; in older and weaker individuals, 0.5; in children from five to fifteen years, 0.25 grm. If the patient does not sleep, it should also be given at night. Improvement occurs after the administration of from 10 to 20 grms. The doses for the sodium salt are about the same. To this "cure" should be added the administration of 2 to 3 grms. daily for about eight days after recovery. Large doses (5.0 grms.) given twice a day are much less effective. This we have found also in our own experience.

The other forms of so-called rheumatism, muscular rheumatism, arthritis deformans, chronic and subacute rheumatism, are less or not at all effected by the use of the drug. On the other hand, several observers report good results obtained from the use of the drug in rheumatic neuralgia and one case of rheumatic tetanus is also reported as having been cured by this remedy. Further experience is necessary on these points. In chronic, so-called rheumatic, neuralgias we ourselves have never seen any good results. Leber has found salicylic acid very good in the iritis which is supposed to occur as a result of rheumatism.

In addition to this specific action of salicylic acid, the drug is also an excellent antipyretic; quinine only, and perhaps sodium benzoate, can compete with it in this respect (leaving out of consideration those antipyretics which are at the same time very poisonous in their action, such as veratrum). But here, also, a few observers have been unsuccessful, probably, however, because of the improper method of administering the drug (too small doses, etc.). An extraordinary number of observers confirm the antipyretic action of the drug, to which Buss was the first to call attention. We ourselves have succeeded in numberless cases of various fevers in reducing the temperature by the giving of sodium salicylate as positively as by quinine. We use the salt almost exclusively. Thus we have succeeded in pneumonias, pleurisies empyema, phthisis, typhoid, etc. In typhus recurrens, however, we have found, together with other observers, that this remedy is just as useless as quinine or sodium benzoate.

In the methodical treatment of febrile affections, especially typhoid fever, by sodium salicylate or salicylic acid, it is necessary to consider whether the use of these drugs does not carry with it disadvantages which are not present in the case of quinine. The irritant effect upon the mucous membranes of the digestive apparatus can no longer be

looked upon as a contraindication, since we know that the sodium preparation does not have this disadvantage. So, also, the slight toxic disturbances observed from the use of this drug cannot be looked upon as a contraindication, since the use of quinine is accompanied by similar disturbances. The sweat which occurs soon after taking the drug is inconvenient, it is true, but unimportant as an objection.

Experience shows that the reduction in temperature from salicylic acid sets in sooner and more quickly than from quinine. After two or three hours, as a rule, a considerable fall has taken place. This is a great advantage, although, on the other hand, the defervescence after quinine lasts longer than after salicylic acid. We also consider it an advantage for salicylic acid that its effect upon the temperature is less dependent upon the time of the occurrence of the natural remission in the fever; its effect is just as marked if it be given at the period of exacerbation.

We do not, therefore, find any objection to the use of this drug as an antipyretic. Were it true, however, that salicylic acid diminishes the strength of the heart, and causes collapse, it would be a decided objection to its use. There have been reports of collapse occurring in cases of pneumonia under its use; so, also, in typhoid patients. Of course the positive statements to this effect cannot be doubted, although we ourselves have reduced the temperature in typhoid patients to 35.8° by its means, without any apparent symptoms of collapse. And yet, on second thought, this collapse would speak in favor of the antipyretic power of the drug, for even when a spontaneous critical fall in temperature takes place sometimes a condition resembling collapse occurs; we must therefore adopt certain preventive measures in order to avoid this when using sodium salicylate as an antipyretic. The dose must be diminished when we expect a critical fall in temperature (as in pneumonia); this is especially true of weak individuals where the heart is weak in the very beginning: here the doses must be smaller than usual. With these precautions we have never observed any injurious effect upon the heart, and other authors also are entirely silent concerning any such effects.

So that we believe ourselves warranted in the conclusion that salicylic acid is an antipyretic which will compare very favorably with quinine. Nor do we know which of these is to be preferred, for the fact that they desert us in some cases holds good for both.

The best method of administration is that usually observed also in the use of quinine; that is to say, large doses are given at a time, generally best when naturally a decline in temperature is expected—that is, in the late evening hours. As antipyretics we may use 2.0 to 4.0 grms. of the acid—that is, 3.0 to 8.0 of the sodium salt—in two divided doses, at intervals of a quarter to a half hour.

As to the circumstances under which these internal antipyretics are desirable, compare with what is said under quinine.

In malaria intermittens the salicylic-acid preparations are decidedly inferior to quinine. As we have already mentioned, both drugs are antipyretics; but while one has a specific action in acute rheumatism, the other has a specific action over malaria; and in these cases they are not mutually convertible. As to the treatment of diphtheria by salicylic acid (both internally and by inhalations), we would only repeat what was said under phenol. Epstein has recommended the remedy in diabetes mellitus; but although other observers have confirmed the fact that temporarily an improvement in the symptoms does set in, no permanent cures have yet been seen.

The enumeration of all the other conditions in which salicylic acid has been recommended we shall postpone until experience has proved its utility.

On account of the inconveniences and sometimes dangers which accompany the use of phenol in the Lister method, it has been attempted (at first by Thiersch) to substitute salicylic acid for the phenol in the antiseptic treatment of wounds. It goes without saying that for this purpose only the acid can be used, for the salt has no antifermentative or antiseptic power. As compared with phenol, salicylic acid is less poisonous, even when absorbed in considerable quantities, and has not the disagreeable odor of the phenol. On the other hand, it is only slightly soluble, so that it can hardly be used for the spray, and furthermore it is a direct irritant to the respiratory mucous membranes.

So that our experience seems to show that salicylic acid cannot act as a substitute in the Lister method of treatment. Volkmann and several other eminent surgeons are of opinion that the protecting power of salicylic acid against sepsis is not so great as that of phenol, which means that it cannot replace phenol except in cases where for some reason phenol is inapplicable. As to the particulars concern-

ing the minutiæ to be observed in the salicylic-acid dressing, we must refer to special surgical works, since only the greatest care and attention will secure the desired result.

Salicylic acid, combined with talcum preparations, is an excellent local application in profuse sweating, and sometimes also in the sweating of phthisis. (Ac. salic. parts 3, amyl 10, talcum 80.) A cloth should be held over the mouth while the powder is dusted on, to prevent the cough due to its inhalation.

Dosage and Preparations.—Acidum Salicylicum.—As to the sizes of the dose for various purposes we have already spoken in the text; it varies from 0.5 to 5.0 grms. (in children from .02 to 0.2), best given as a powder in capsules, or as a spirituous solution with mucilaginous vehicles. In any case much water must be taken after it in order to free the mucous membranes from the local irritation. Externally the powder or solution can be used.

For antiseptic purposes the following preparations are used:

a. Salicyl Water.—1–300 for spray, and washing the wound cavities.

b. Salicyl Cotton.—Cotton, deprived of its fatty matter, and steeped in a solution of salicylic acid in alcohol and water, in such a way that one 3-per-cent and another 10-per-cent cotton are prepared. For various reasons this salicyl wadding has been laid aside by Thiersch for *salicyl* jute (4 per cent), prepared by soaking jute in a solution of salicylic acid in water and glycerine. The salicyl jute is applied dry in a layer three fingers thick over the wound, covered with a piece of Lister's antiseptic gauze, and fixed by bandages.

2. Sodium salicylicum, for internal use only, in doses of 1.0 to 6.0, as a powder in capsules, or in solution with succus liquiritiæ as the best corrective. In children from 0.5 to 3.0 grms.

Appendix to Salicylic Acid.

Salicin.—The salicin (C_{13}, H_{18}, O_7) presents in the bark and leaves of most willows and poplars; is obtained from the former by boiling, the tannic acid being precipitated from the hot solution by lead acetate; the lead is then deposited from the filtered solution by sulphuretted hydrogen, and the salicin is allowed to crystallize from the solution.

Physiological Action.—Salicin, even in dilution of 1–1500, has an exceedingly bitter taste. Its antiseptic power seems to be very slight, and there is need of a very strong concentration of the drug to produce any effect (1:50), such as the destruction of lower organisms (Binz.) It has no effect whatever upon fermentation. In the stomach it renders the digestion of albuminoids slower, and produces constipation.

Internally it can be given and borne in very large doses, both by animals and men, in daily doses of 30 grms. (Ranke). Only after very large doses have some observers noted ringing in the ears and fulness of the head. It is exceedingly doubtful whether it is true that the spleen is diminished in size.

The latest investigations of Marmé yield the following results: All warm- and also cold-blooded animals convert the salicin into salygenin in the digestive canal; also into salicylic acid, salicylous acid, and salicylu-

rous acid. This conversion takes place to a partial extent in the saliva, but especially in the small intestines under the influence of ferment and the lowest organisms, and is continued in the blood. Much larger quantities are converted into salicylous acid than into salicylic acid. The former in larger doses, both as an acid and salt, acts as a strongly local irritant, also as a heart-excitant, does not lower temperature, and produces death, with convulsions, by paralysis of the heart and respiration. So that salicin owes its antipyretic action to its conversion into salicylic acid; and since it forms this only in very small quantities, it is no substitute for the latter, and is decidedly superfluous as a drug.

Therapeutic Application.—Willow bark was given in malaria as long ago as 1700; but being so inferior to quinine, this use of the drug has been given up. Lately the therapeutic application of salicylic acid has led to the renewed use of salicin, and Maclagan and Ringer, in England, and Senator, in Germany, have made experiments with the drug. The latter observer used it in all those conditions in which salicylic acid was used, and reports the following results: Salicin lowers the temperature in typhoid, phthisis, etc., in doses of from 5 to 10 grms., but not so efficiently or quickly as salicylic acid does, although the effect lasts longer, and the use of this drug is not as often followed by disagreeable complications, such as sweating, collapse, etc. In polyarthritis rheumatica it is also effective. In diabetes it is entirely without any effect, and in malaria it is as uncertain as salicylic acid. Similar results were arrived at by Buchwald. Salicin has not come into general use.

Dosage.—As an antipyretic, salicin is given in very large doses—5.0 to 10.0 grms. at short intervals; in acute rheumatism, from 0.5. to 1.5, every 1 to 3 hours: best given as a powder in capsules, also in solution.

Kresotinic Acid.—Acidum kresotinicum has an antifermentative action like that of salicylic acid. Its sodium salt is also an antipyretic; doses, 5.0 to 8.0 grms. It has not yet been sufficiently used to enable us to express an opinion as to its value.

Gallic and Tannic Acids.

1. Gallic Acid—Acidum Gallicum.

Gallic acid—$C_6H_2(OH)_3.CO.OH$—is a trihydroxybenzoic acid. The assertion that it is present in substance in some fruits, such as the nutgall, is not yet proved. Artificially it can be prepared from tannic acid by boiling with diluted acids and alkalies, or by spontaneous fermentation of tannic-acid solutions, or finally from the salicylic-acid biniodide. It crystallizes in fine shining crystals, dissolves in 100 parts of cold and 3 parts of boiling water, also in alcohol and ether, has a puckery acid taste, and is decomposed at 220° into pyrogallol and carbonic acid.

Physiological Action.—Gallic acid neither coagulates albumen nor is it antifermentative or antiseptic in its action. It does not, therefore, produce the local tanning effect of tannic acid, but dilates, as does the latter, any blood-vessels with which it comes in contact.

It is very readily absorbed, and produces symptoms of poisoning in fifteen minutes after its administration. These symptoms are, according to Schroff, difficult and slow abdominal respiration, irregularity of the heart and pulse, without any change in the passages. From these symptoms even rabbits can recover in a short time, after having taken as much as 5.0 grms.

Men bear from 2 to 5.0 grms. very well.

One of the rabbits with which Schroff experimented passed, in eight hours, 60 grms. of a cloudy, ink-like, dark green urine. After thirty hours the gallic-acid excretion was already finished. As we shall show under tannic acid, it exerts no astringent effect upon distant organs.

Therapeutic Application.—Gallic acid can well be spared from our materia medica. The local effects can be better produced by other means, while we have no certain evidence that it exerts any general effects. Even the action of tannic acid, after its absorption into the blood, is a very doubtful one, so that the idea of substituting this for tannic acid, where we wish to produce general effects, is a futile one.

The dose would be 0.05 to 0.5 in powder or pill.

2. TANNIC ACID—ACIDUM TANNICUM.

Tannic acid (acidum tannicum, or tannin)—$C_{14}H_{10}O_9=C_6H_2(OH)_2.CO.O.C_6H_2(OH)_2.CO.OH$—is one of the constituents of ordinary and Chinese nutgalls, from which it can be extracted by a mixture of four parts of ether and one of alcohol.

Artificially it can be prepared by boiling a solution of gallic acid with arsenic, as well as by treating it with phosphoroxychloride to 120°.

It is an amorphous mass, of a whitish-yellow color, easily soluble in water (1–10), and having a slightly acid reaction.

It can be precipitated from its watery solution by mineral acids and some alkaline salts, such as sal-ammoniac and sodium chlorjde. It also yields precipitates with lead, antimony, and ferric salts (with the latter dark blue ink); also with most alkaloids, forming with these and the metals insoluble salts called tannates. Under the influence of air or fungi, which readily develop in its solutions, a precipitate is formed in its concentrated solution which consists of gallic acid.

PHYSIOLOGICAL ACTION.

The following is what we know of the effect of tannic acid on organic substrata. Gelatinoid matters combine with tannic acid to form insoluble compounds; tissues containing gelatin are converted into leather under the influence of tannic-acid solutions. Soluble albuminoids are precipitated by tannic acid.

The tannates of gelatin and albumen, as well as tissues containing these, are no longer able to undergo decomposition.

The relationship of tannic acid to sugar and other fermentable substances is unknown; but it is very probable that in these it exerts little of its antifermentative action, much less than that of other so-called antiseptic agents.

It is one of the weakest agents for disinfecting cholera excrement (Illisch), and one of the strongest agents to prevent the decomposition of urine (Fleck). Mould-fungus even prefers tannic-acid solutions as its habitat. More accurate investigations concerning these points are necessary.

It has been supposed that tannic acid exerts a similar effect upon the living mucous membranes to that which it exerts upon skins and hides. It has been said that the feeling of dryness, puckering, rawness, and stiffness which follows the moistening of mucous membranes with even a weak solution is dependent upon a contraction of all the tissues, both the individual cells and the blood-vessels; while the latter is supposed to be due to the coagulating and moisture-withdrawing action of the tannic acid.

The following, however, will be found to be the proper view: Organic tissues seem to have the power of absorbing water from dilute tannic-acid solutions, rather than giving any water up to them; for Hennig found that muscles dipped into such solutions swell up, grow thicker, longer, paler, and more watery, and give up to the solution albumen and blood-coloring matter. In strong solutions, according to the experiments of Hennig, Mitscherlich, and Schroff, the tissues take up the tannic acid, while great alterations take place in the cells themselves that resemble the process of tanning skins. Whether during life, however, the tannic acid burrows so deeply as to reach the muscles, as occurs, according to Hennig, after death, is doubtful.

Upon suppurating surfaces tannic acid causes a coagulation of the pus on the surface of the wound, and thus prevents the putrid decomposition of the pus, and thus furthers the healing process.

When brought in direct contact with blood, as in bleeding wounds, it causes a coagulation of the albumen of the blood, so that it can be counted among the strongly coagulating (styptic) agents.

Direct observation shows that, contrary to former opinion, tannic acid, instead of exerting a contractile influence upon the blood-vessels with which it comes in contact, really *dilates* these: this is true of strong and weak solutions. The cross-section (diameter) of all the arteries, veins, and capillaries of a portion of tissue treated by tannic acid is increased to twice (in maximo) the usual size. (Rosenstirn and Rossbach). This dilatation is not the result of a reflex action, but is the direct result of the action of the tannic acid upon the elements of the vascular wall. Vessels thus dilated by tannic acid can be contracted by silver nitrate, so that we cannot explain the dilatation as the result of a total paralysis of the vasor nerves, but rather as a diminished irritability of the musculo-motor apparatus, or an

irritation of the dilator nerves of the vessels. Even in inflamed mucous membranes in the human subject we could not observe any contraction of the blood-vessels from tannic acid, as would follow the application of silver nitrate. We were also unable to observe any diminution in the secretions after the application of medicinal dilutions of tannic acid to the mucous membranes. Indeed there was rather an increased secretion in spite of the feeling of dryness to which the drug gave rise. Anæsthesia of the part painted by the solution always set in, however; taste was almost entirely lost, except to very sharp (acid) substances; while the painting of the pharynx and palate with the solution resulted in an almost complete interruption of the reflex irritability of these parts.

We can therefore ascribe to tannic acid an anæsthetic action upon mucous membranes, a dilating action upon the blood-vessels, a drying and healing (preventing putrid decomposition) upon wounds, and a styptic action upon bleeding surfaces.

Its internal use is followed almost exclusively by local effects upon the mucous membranes with which it has come in contact; small single doses (0.5 grm.) are followed by the puckery taste, dryness of the mouth, and a feeling of heaviness of the tongue. No other symptoms.

It is only after frequent repetition that we have diminished appetite, eructation of wind from the stomach, digestive disturbances from the precipitation of the pepsin, etc.; sometimes gastro-intestinal cramps, but no constipation (at least in healthy people); on the contrary, sometimes diarrhœa. The cathartic action of Glauber's salt is *very little* affected by the simultaneous administration of tannic acid (Wagner, Buchheim), nor is intestinal peristalsis diminished (Hennig). On the other hand, diarrhœa dependent upon an abnormal decomposition of the ingesta would be benefited by the antifermentative action of this drug.

Doses of 1.0 to 5.0 grms. (depending upon the fulness of the stomach) cause serious alterations in the gastric mucous membranes, such as gastric pain, vomiting, fever, and constipation lasting for weeks, due partly to the formation of insoluble, hard fæcal masses and partly to diminution in the intestinal secretion. The fæcal masses may give rise to ulcers, and that may account for their being covered with pus and blood.

The portion of the tannic acid which does not leave the body in insoluble combinations with albuminoids or gelatin derived from the mucous membranes is converted into gallic acid, and appears as such for the most part in the urine, and to a slight extent as pyrogallol. It is highly improbable that tannic acid as such reaches the blood, for nobody has been able to prove its presence there, nor have general tannic-acid poisoning symptoms (which would be coagulation of the blood and its sequelæ) been seen. Only general gallic-acid symptoms, such as weariness, difficult breathing, and weakness of the heart, have been observed. The old idea, therefore, that tannic acid is absorbed into the blood, and that it exerts its effects upon distant organs (such as diminishing secretion, contracting tissues, etc.), is fallacious, first because it does not enter the blood as tannic acid, and secondly because gallic acid does not produce any such effects. Even if tannic acid did circulate as such in the blood, it could not, on account of the great dilution which the medicinal dose would suffer in the blood, exert any such effects (styptic action and contracting vessels: this even strong solutions do not do). Finally, even if absorbed into the blood, its styptic power would immediately coagulate the blood with which it first came in contact, and it could not carry this power latent through the system until it came to the spot where the physician desires the styptic action.

Since gallic acid has no antifermentative or antiseptic power, it cannot be supposed to exert any such power in the urine, by which it is for the most part excreted.

The alteration of the tannic into gallic acid, and the excretion of the latter, take place very rapidly: even twenty-four hours after its administration no more gallic or tannic acid can be found either in the urine, intestinal canal, or in the body.

Mitscherlich's assertion that the use of tannic acid is followed by a diminution in the excretion of the urine, and that the urine is richer in uric and phosphoric acid, requires further proof. According to Schroff, the urine of the herbivora remains strongly alkaline even after large doses of tannic acid.

It goes without saying that the direct injection of tannic acid into the blood causes thrombi and emboli, and thus death.

THERAPEUTIC APPLICATION.

We can only expect tannic acid to be useful in cases where it can be locally applied, and even in such its value is much overestimated. The properties upon which its utility in local affections depends are lost when it passes into the blood. Notwithstanding this it is very much used in practice for conditions in which the effect can only be produced after its absorption. We shall give these various applications for the sake of completeness, but must premise that we ourselves have never seen any utility from the use of tannin in these cases.

Tannin is very much used for hemorrhage of various organs, both locally and internally. When given internally it is certainly entirely ineffective, and no sensible physician would rely upon the internal use of tannin to stop a uterine hemorrhage, for instance. In the slighter cases of pulmonary hemorrhage the drug is just as unnecessary as it is useless in the severer cases. In hemorrhage from the kidneys, and acute hemorrhagic nephritis, tannin is said to be of utility after the first symptoms of severe inflammation (pain in the region of the kidneys, fever, etc.) have subsided and the urine is still bloody. Indeed tannic acid has been very much used in chronic nephritis since the recommendation of Bright and Frerichs. We must, however, acknowledge that we have used tannic acid in all varieties of acute and chronic nephritis without the slightest beneficial results.

As a local hæmostatic it is not as good as liquor ferri, but has the advantage of producing less disagreeable additional effects. It is best applied in severe capillary or small arterial hemorrhage; as in bleeding from the gums, nose, or from ulcers. It is best applied as a powder.

For gastric and intestinal hemorrhage, tannin, next to the liquor ferri sesquichlorate, is one of the most frequently given remedies. Its local styptic action is less than that of the iron preparation, but it is said to have the advantage of being borne in much larger quantities; but even this advantage is doubtful, for tannin in very large doses may cause vomiting. Its utility in gastric or intestinal hemorrhage is, however, doubtful, and here we would refer to what was said under Ferric Chloride; our experience leads us to adopt the opinions of Leube and others, and to con-

clude that its utility here is rather traditional than proved. In rectal hemorrhage we might hope to accomplish a useful result by its local application in large doses.

Tannic acid is very much used in various diseases of the mucous membranes. It is given very much in diarrhœas. Proper cases for its use are chronic diarrhœas, and especially such as are dependent upon an ulcerative process, as in chronic forms of dysentery, follicular enteritis, also in simple chronic diarrhœas, and neglected intestinal catarrhs of children, and the diarrhœa of drunkards. A desirable requisite for the taking of tannic acid is a good digestion and appetite. It should, therefore, not be given in cases in which the maintenance of the appetite is a prime indication; it would thus be contraindicated in the diarrhœa of phthisis. Some authors state that they have seen good results from the use of tannin in certain forms of dyspepsia (with the formation of acid in the stomach and flatulence), but confirmatory experience is still wanting, and this form of dyspepsia rarely occurs in phthisis. Our personal experience does not prompt us to put any particular stress upon the use of tannic acid in diarrhœas of any kind. In catarrh of the bladder it is said to be of utility even upon internal administration; we are positive, however, that its internal administration in leucorrhœa and broncho-blenorrhœa is entirely useless.

The use of tannin as a gargle in chronic catarrhal pharyngitis is, we are positive, without the slightest utility. On the other hand, it is frequently used for painting the throat and larynx (1 : 10–20) to diminish the reflex irritability of these parts and facilitate laryngoscopic examinations.

As to the utility of tannin in inhalation-therapeutics in general, we would suppose that this application of the drug is a very good one, although we cannot speak concerning this point from our own experience. It would be of utility in this way: in the chronic catarrhs of the larynx, trachea, and bronchi, and of the pharynx, these surfaces being covered by a large amount of secretion. It is also of utility in the slighter ulcerations. In the larger ulcerations it is insufficient; in the chronic catarrhs it is sometimes useless; and in acute catarrhs it is always injurious. For the slighter cases of pulmonary hemorrhage it is unnecessary, and even when inhaled for the severer cases it is entirely insufficient.

As to whether tannin or alum should be preferred for

inhalation, Waldenberg says that in some cases it depends upon the idiosyncrasies of the patient. Tannin may be preferred, however, where we wish to affect the secretion (keep it from putrefying), or when the catarrh is a superficial one; while the alum should be preferred where there is much parenchymatous thickening and swelling.

Tannin injections are very much used in gonorrhœa and in leucorrhœa as soon as the acute symptoms have subsided. It is generally believed that tannin is to be preferred to the metallic salts for this purpose, but this is only true in so far as tannin is not apt to produce such injurious effects on the stronger solutions of the metallic salts. Schuster recommends tannin-glycerine bougies (2.0 tannin, 0.12 opium, and 9.1 glycerine) as particularly efficacious in gonorrhœa: these bougies are passed into the urethra, and allowed to stay there from five to ten minutes.

Abnormal sweating is said to be diminished by tannin internally, but this effect is a very doubtful one. When applied directly to the sweating part, however, the effect is more apt to follow. Recently tannic acid has been very warmly recommended in the inflammations of the skin, which are supposed to be the result of cold (boils, etc.), and we think its use is followed by good results.

Tannic acid is of great importance as an antidote to poisoning with alkaloids; it is the best antidote to morphine, strychnine, nicotine, etc., since it enters into almost insoluble combinations with these substances; it is also a good antidote for the antimonial preparations and all metallic poisons. Tannic acid should be administered together with other suitable remedies in the form of an infusion or solution: if we have not the acid itself, we may use substances containing tannic acid, such as tea or coffee; both of the latter, however, should not be given in poisoning from strychniæ.

Dosage.—Acidum Tannicum.—Internally from 0.05 to 0.5 pro dosi (2.0 pro die), in powder, pill, or solution. It is incompatible with all the metallic oxides and vegetable alkaloids.

Externally as a hæmostatic it is used in substance for gonorrhœal injections in solution (½ to 2 per cent), rarely in ointment form (2.0–5.0 to 25.0); for inhalation as an astringent, from ½ to 5 per cent; as a styptic, 1 to 10 per cent solution.

PLANTS AND VEGETABLE SUBSTANCES CONTAINING TANNIC ACID.

There are various tannic acids, according to the plants from which they originate—gallic, oak, rhatany, catechu, kino, and coffee tannic acids, etc. The chemical composition of all of these is still uncertain, but all of them have a coagulating action on albumen and gelatine, turn skins into leather, and form a dark blue or green color with the ferric salts.

On account of this similarity in effects these various tannic acids are supposed to have a similar physiological action, and it is a fact that few variations have hitherto been seen among them, except that as a rule the tannic-acid plants seem to be more powerfully astringent than tannic acid.

It therefore follows that all of these substances are superfluous as long as we can get pure tannic acid from the druggist, and should only be used in travelling in uncivilized lands where tannic acid is not prepared.

We do not here forget that these tannic-acid-containing plants also contain in addition many other substances, such as starches, sugars, fats, and volatile ethereal oils; but either these substances are not necessary where tannic acid is indicated, or if they are necessary they can be given in other forms, where we know how much of them we are using.

This, then, will be sufficient excuse for the brevity with which we treat these substances. We shall first and foremost consider those of them which are indigenous with us, because their cheapness will furnish a sufficient excuse for maintaining them in the materia medica.

Nutgalls—gallæ—are found as outgrowths upon the leaves of various oaks, especially one indigenous in Asia, quercus infectoria, the best of which yield about 70 per cent of gallo-tannic acid. Nutgalls of our own climate yield at most 30 per cent.

Therapeutically, infusions of nutgalls (10.0 — 25.0 : 100.0) are used wherever tannic acid cannot be had for purposes similar to those for which the latter is used. Tinctura gallarum, 1 part of G. to 5 of alcohol, used externally; combined with tincture of iodine (equal parts); this combination prevents the irritant effects of the latter preparation upon the skin.

Oak bark—cortex quercus (the bark of the younger branches of oaks indigenous here)—contains 5 to 20 per cent of another tannic acid, the so-called oak tannic acid, in addition to gums, fats, lime-salts, etc., and has an effect on the whole weaker than that of tannic acid, and more injurious to the digestion. The same is true of the barks of many other trees, such as the horse-chestnut, elm, and many foreign trees. Therapeutically used like nutgalls. Not used internally.

Roasted acorns—glandes s.semina quercus tosta, contain 5 per cent of tannic acid, 40 per cent of starch, 5 per cent of a fatty oil, and sugar, together with a mannite-like body, quercit, and are used for preparing a coffee whose nutritious qualities can well be replaced by other substances. This variety of "coffee" does not, as has been supposed, possess antirachitic properties, but is a good substitute for real coffee for children when the parents insist upon giving something of this kind.

Bilberries—fructus vitis idæae (vaccinium vitis idäa)—contain a considerable amount of tannic acid (1 per cent), vaccinine, and are without any therapeutic value.

Myrtle bilberries—vaccinium myrtillus—(common in our [German] woods) contain, in a fresh state, a considerable amount of sugar and

vegetable acid, such as mallic, tannic, chinic acid, etc., gums, and coloring matters. Therapeutically superfluous.

Butternut-leaves—folia juglandis—contain a tannic acid (which turns ferrous salts green); the unripe butternut-shells—cortex nucum juglandis—contain in addition a body similar to pyrogallol and a coloring matter, nucin.

These have been recently recommended in scrofula. They may influence the digestive disturbances of this condition favorably. They have no especial value except the negative one of being harmless. Dose 1.0 to 3.0 pro dosi (30.0 pro die), in decoction.

Salvia leaves—folia salviæ—have an agreeable spicy odor and bitter puckery taste. Contain in addition to a tannic acid a mixture of several ethereal oils containing oxygen, from which a camphor-like substance is formed if they be retained for a long time. The administration of a cold infusion of 15.0 grms. is followed by psychical excitement, increased frequency of pulse, sweating and heat; the oil seems to be the agent in producing these effects. As an after-effect there is constipation. In the taste tannic acid is markedly felt.

Salvine, used even in the time of Hippocrates, and in the middle ages, has even in the present day been used to arrest sweating. Its action is, however, uncertain, and inferior to that of other remedies. Externally it is used as a popular remedy in the secondary stages of angina catarrhalis. It is generally used as a vehicle for any alum-gargle and where there is a tendency to bleeding from the gums.

Dosage and preparation.—(1) Folia salviæ, 1.0 to 3.0 pro dosi (30.0 pro die), in infusion; (2) Aqua salviæ and, (3) Aqua salviæ concentrata, both in ʒ i-ℨ ss doses.

Bearberry leaves—folia uvæ ursi (arctostaphylos uva ursi)—contain a tannic and gallic acid; in addition to this, physiologically inactive arbutin. These leaves impart a dark color to the urine, although in healthy people they do not act as diuretics. Very large doses are said to produce nausea and vomiting. These leaves had an excellent reputation in chronic catarrh of the bladder. 0.5 to 1.5 pro dosi (10.0 pro die), in infusion.

Rhatany root—radix ratanhae (from Peru: Krameria triandra)—contains 40 per cent of a peculiar tannic acid. Used very much at the beginning of this century as an astringent remedy, but at present very little used.

Dosage and preparation.—1. R. rat., 1.0 to 2.0 pro dosi (15.0 pro die), in infusion or powder. 2. Extract. rat., 0.5 to 1.0 pro dosi. 3. Tinct. rat., 1.0 to 2.0 pro dosi (20 to 40 drops).

Catechu—terra japonica (from east Asia) is the dried watery extract of acacia catechu wood, which contains much catechu, and, as a product of the decomposition of this, catechu tannic acid. This is entirely superfluous.

Dosage and preparation.—1. Catechu, 0.5 to 1.0 pro dosi (10.0 pro die), in powder and solution. 2. Tinctura catechu, from 0.5 to 1.5 pro dosi (10 to 30 drops).

Kino—gummi kino—is the dried juices of various plants of the variety pterocarpus, which contain a kino-tannic acid and gum. It is entirely superfluous. 1. Kino, 0.5 to 1.0 pro dosi (1.0 pro die), in powder and solution. 2. Tinctura kino 2.0 to 4.0 pro dosi, in drops.

In conclusion we will mention radix tormentillæ, lignum campechianum, radix bistortæ, radix rubiæ, radix caryophyllatæ, extractum

monesiæ, and sanguis draconis, as containing tannic acid, although they are superfluous preparations. The same is true of the latest recommended of these, the fruit of myrobalani chebulæ, which is lauded in 4.0 grm. doses in dysentery.

The Volatile Ethereal Oils (Terpenes and Camphors).

The ethereal oils must be considered as benzol derivatives, although their exact composition is not yet determined. Under any circumstances they are closely allied to cymol, which is a parapropylmethylbenzol ($C_6H_4.CH_3.C_3H_7$) which can be prepared from both of the chief groups of ethereal oils: from the terpenes by heating with iodine, and from the camphors by heating with phosphorus pentasulphide. Bruylants explains the composition of the volatile oils by a "derivation law," according to which the mother-substance is said to be a terpene from which the other components of the oil are derived either by hydration, oxidation, or reduction.

The ethereal oils are present in all plants, especially in the odorous plants, where they give rise to the odor. But even in the most odorous of the plants only relatively small amounts of the oil are present. In 36,000 grms. of fresh rose and orange flowers there were only 7 to 8 grms. of volatile oil. They are most plentiful in the flowers and seeds, less in the leaves, bark and wood, mostly dissolved in the juice of the cells, but sometimes filling up cells and vessels. Generally the same ethereal oil is found in different parts of the plant, but to this there are exceptions; thus in orange trees there is one ethereal oil in the flowers, another in the leaves, and another in the seeds or fruit.

These oils are obtained either by pressure (only in citrons, lemons, etc.) or (most frequently) by distillation of the portion of the plant which contains the oil. With the vapor of water the ethereal oils are distilled over much below their boiling point, while without the vapor of water they are accompanied by the many foreign products of decomposition. According to their weight, some oils sink to the bottom of the distilled fluid, others float on top, and others are dissolved in the water, to which they impart their characteristic odor. (These waters are sold under the name of "distilled waters.")

Properties and Composition.—All ethereal oils except the camphors, are fluid at ordinary temperatures; but at low temperatures they separate into two parts, one a crystallized substance, the stearoptene, the other the fluid portion, elæopten. The proportion of these two in various oils differs. In some, like the anise and rose oil, there is so much stearoptene that when cold these oils have a semi-gelatinous and crystalline consistency.

Specific gravity from 0.84 to 1.095; most of these, however, are lighter than water. Boiling point between 120 and 250°, on an average 160°. Some oils cannot be distilled without undergoing decomposition.

Many volatile oils rotate the plane of polarization, either to the left or right.

When dropped upon paper, volatile oils first cause a fat-stain, which gradually disappears; for all volatile oils and camphors volatilize in the air. The volatile oils are used for perfuming, and for concealing offensive odors. The volatile oils are much more inflammable than the fatty or fixed oils.

But very small quantities of volatile oils can be dissolved in water, but

these are sufficient to give to the water the characteristic odor of the oil. They can be withdrawn from their watery solution by the addition of sodium chloride or shaking with ether.

The method of preparing the so-called "distilled waters" of the drug-store is given above. Such are aq. menth. pip., aq. flor. aurant, etc.

Volatile oils are more soluble in dilute alcohol and entirely soluble in absolute alcohol. The oils which are free from oxygen, such as oil of turpentine and citron, are only soluble in absolute alcohol. Liqueurs are prepared by the addition of the volatile oils and strong solutions of sugar to strong alcoholic solutions; although formerly these were prepared by distillation of the plants containing these oils with the alcohol. By the addition of a few drops of ol. flor. aurant, ol. bergamot, lavandulæ, rosmarini, etc., to strong alcohol we obtain very agreeable flavoring agents. Cologne is prepared in this manner.

Ether, concentrated acetic acid, and acetone dissolve ethereal oils.

These oils also mix in all proportions with the fatty oils, talc, fats, (hair-oil, pomade), and with sulphur, bichloride of carbon and the sulphide of carbon.

These oils are also good solvents for the fats, resins, phosphorus, sulphur, etc.

In the air these oils undergo great changes; they quickly absorb oxygen, which they convert into ozone, lose their odor and become thick, form aromatic acids, such as benzoic or cinnamic acid, or are converted into resins. Resins mixed with much ethereal oils are called balsams. When all of the ethereal oil has been converted into acids and indifferent resins, then we have the so-called resins, divided into hard and soft resins, or into gummy and shiny resins.

The ethereal oils have a variable chemical constitution. We can distinguish two varieties:

1. Oils containing no oxygen or terpenes, hydrocarbons of the formula $C_{10}H_{16}$, which are fluid at ordinary temperatures, and exist in plants either ready formed or produced from the natural terpenes by chemical decomposition. The largest number of ethereal oils which are obtained from plants are mixtures of ethereal oils and terpenes with other volatile combinations.

2. Oils containing oxygen or camphor ($C_{10}H_{17}.OH$), which are solid at ordinary temperatures and have a higher specific gravity and boiling point than the first class.

We shall only consider the chief representatives of these two groups, namely, the oil of turpentine and of camphor. The rest of the volatile oils have been too little studied; but it is highly probable that they are allied either to the oil of turpentine or of camphor in their constitution.

PHYSIOLOGICAL RELATION.

Although cymol, when injected under the skin, gives rise only to pain (Binz), yet the ethereal oils do produce characteristic physiological effects; these effects are different for the oils containing oxygen and those not containing oxygen. It is known that the oil of turpentine, free from oxygen, causes in warm-blooded animals increased irritability of the nervous system, and weakens and paralyzes

the respiratory and circulatory apparatus; while camphor, which does contain oxygen, causes in warm-blooded animals increased irritability of the brain and medulla oblongata, but does not sensibly affect the heart's action.

Upon cold-blooded animals the effect of both is similar. Both groups have a lowering effect upon the temperature of warm-blooded animals.

Many of the ethereal oils (myrrh, turpentine, cinnamon, etc.) are said to increase the number of blood-corpuscles, (Hirt, Binz).

The antifermentative and antiseptic action of both groups is weaker than that of the phenols and aromatic acids.

OIL OF TURPENTINE (OLEUM TEREBINTHINÆ).

Oil of turpentine ($C_{10}H_{16}$) is obtained from turpentine, which may be considered as an impure solution of various acids (formic, acetic acid, etc.) in oil of turpentine. By distillation with water the oil of turpentine passes off, and the residue (resin) when melted is turned into colophonium.

Different oils possess different properties of rotating the polarized ray. Most of them turn the polarized ray to the left (pinus maritima), while that of pinus australis rotates it to the right.

Since oil of turpentine has a great affinity for oxygen, which it ozonizes, and through this means becomes converted into resin, it is met in commerce in a state of impurity; when shaken with solutions of the alkaline carbonates it is freed from its acid, and if again distilled in a vacuum it is obtained in a pure state.

Pure oil of turpentine is a colorless fluid, having a characteristic spicy odor. Insoluble in water, although it can impart its odor to the latter, it is soluble in every proportion of alcohol and ether.

PHYSIOLOGICAL ACTION.

Since our knowledge of the physiological effect of the oil of turpentine is very uncertain, because most experimenters have preferred direct injection of the drug into the circulation in their experiments, we have determined to make a thorough examination of the physiological action of the remedy, and have arrived at the following conclusion. First we shall give the effects produced when the drug is taken by the stomach or inhaled. When oil of turpentine is injected directly into the blood, serious lung-affections result, which change the whole picture of the action of the remedy, and hence cannot be set down as resulting from the remedy itself. Furthermore, concentrated solutions produce severe local affections of the gastro-intestinal mucous membrane, with resulting disturbances of

the general health, which cannot, therefore, be looked upon as the general effects of the action of the oil of turpentine.

Since oil of turpentine in strong concentration, when applied externally or internally, produces great pain (frogs are strongly affected even by the odor of the drug), it has been supposed that the restlessness produced by these pains (such as itching of the skin, burning, gastric unrest, etc.) is the result of nervous excitement. From a large number of careful experiments we have come to the conclusion that if the oil of turpentine be administered in a painless manner and deprived of its odor, it will cause, both in small and large doses, not any irritation of the nervous system, but rather a paralysis, especially of the cerebral centres.

All animals, both cold- and warm-blooded, are influenced in a similar manner, although camphor has a different effect upon cold- and warm-blooded animals.

We have only succeeded in determining the fatal dose for rabbits. Upon these, doses of 1.5 to 3.0 grms. have almost no effect; 5.0 grms. under the skin or by the stomach have a decided but not dangerous effect; after a dose of 10.0 grms. death sets in in from five to twenty-four hours. On the other hand, the direct injection into the veins of even small doses (0.15 to 0.28) produces death. Toxicology teaches us that men can bear very large doses by the stomach without fatal effects; children die from 15.0 grms., although the taking of 50.0 to 100.0 grms. has been followed by good results.

Parasites, such as lice, the itch-mite, intestinal worms, etc., are readily destroyed by the oil of turpentine.

LOCAL ACTION.

When rubbed upon the skin, oil of turpentine causes an increased feeling of warmth, pricking, itching, and burning, together with inflammation of the derma with exudation, and even the formation of vesicles. The epidermis becomes dry and white, and later on cracks over the places where vesicles have formed.

In wounds and ulcers the irritating action is even greater, and torpid ulcers can thus be brought to heal more rapidly.

The mucous membranes are more irritated than the skin.

When inhaled in small quantities with the inspired air, the oil of turpentine gives rise only to a not disagreeable odor; in larger quantities it produces a feeling of pain, and

the nasal mucous membrane becomes red and dry. As from other strong-smelling substances, we have as a reflex result, respiratory disturbances, cough, and slowing of the respiration. We allowed rabbits, however, to inhale air bubbled through the oil of turpentine for hours, without observing any noteworthy disturbances either of the tracheal or bronchial mucous membranes.

Upon the buccal mucous membranes the oil of turpentine causes a bitter, burning sensation; a reflex increase in salivary secretion rapidly sets in; a large amount of saliva flows from the mouth of all animals; the mucous membrane of the mouth turns dry and red under the influence of the oil, so that there is a feeling of thirst produced.

It was supposed that this, like many other medicines, produces increased appetite by exciting the secretion of the stomach and the intestinal juices; but impartial observers like Mitscherlich have seen neither an improvement nor a diminution of appetite as a result of the action of the drug. We ourselves found that the subcutaneous injection of 0.5 grm. into the blood in rabbits was followed by a great diminution in the appetite although the general health remained undisturbed.

Small quantities are supposed to increase intestinal peristalsis.

Larger quantities (in rabbits 0.5 grm., cats 5.0 grm., and men 8.0 to 30.0 grms.) are followed by severe irritation of the gastro-intestinal mucous membrane. In dogs and men there is nausea, vomiting, also severe abdominal pains, and diarrhœa (both in carnivora and herbivora).

Only very large doses were found to produce a caustic action upon the mucous membranes (Schubarth and Mitscherlich). In rabbits 10.0 grms. produced gastro-enteritis: in some parts the mucous membranes turned of a dark-brown color. In these animals Mitscherlich also found small hemorrhages upon the mucous membranes, and the intestinal epithelium was shed. The turpentine odor was present as far as the cæcum.

GENERAL EFFECTS.

Disposition of the Oil of Turpentine in the Organism.—Oil of turpentine is absorbed into the blood both from the unbroken skin and all the mucous membranes, whether it is inhaled or taken by the stomach. In the gastro-intestinal

canal it is absorbed both in solution in the fluids of the stomach (fats) and in vapor form.

In the blood and the tissues it remains under its own form, for it is excreted by the sweat, milk, and expired air with its own characteristic odor. These assertions must be taken with circumspection. In the urine there is no turpentine odor present, but rather another odor like that of violets, which would certainly indicate that oil of turpentine undergoes many changes in the body.

Central Nervous System.—Frogs become unconscious in a few minutes and lose all power of voluntary motion, lying in an apathetic condition. The reflex irritability remains preserved much longer, and in this stage strychnine produces tetanus. Finally even the reflex irritability is entirely lost.

The motor nerves and voluntary muscles retain their irritability even in the severest cases of poisoning.

In rabbits, shortly after the administration of large doses in the form of an emulsion, loss of consciousness and voluntary movement set in; after one hour there was also loss of reflex irritability; the pupil was no longer dilated even by the severest painful impressions, and death finally set in, with convulsions, from final paralysis of respiration and CO_2 poisoning.

Cats, after the gastro-enteritic pain and vomiting had subsided, looked drunk; their walk was unsteady; they fell upon the side and could not rise; this was followed by trembling of the limbs, and death set in with clonic and tonic convulsions. We never saw any psychical or motor exaltation.

In men it produces frontal headache, nausea, yawning, noises in the ears, dizziness, weariness, deafness, and sleepiness (Purkinje was so sleepy after taking 4.0 grms. that he could scarcely keep awake), and finally loss of consciousness and coma. The addition of the oil of turpentine to wine increases and quickens the setting in of the stage of unconsciousness (alcoholic intoxication). Fatal doses would also produce opisthotonos.

Respiration.—The ordinary inhalation of the vapor of the oil of turpentine, or when taken through a tracheal canula, or by the stomach, is rapidly followed by a diminution in the number of respiratory movements: in rabbits by 9, in dogs 22 in the quarter-minute. We have never produced any disease of the lungs by these methods of administration.

Circulation.—In all animals experimented on by us (warm- and cold-blooded) even the direct injection of the oil of turpentine into the blood caused no change in the heart's action, or if any, a very slight one. Sometimes the number of pulsations fell, sometimes it rose; when there was an increase, it was owing to the pain produced by administering the turpentine, so that the only change for which the drug itself was responsible was the slight decrease in the number of pulsations. The blood-pressure was in all cases diminished. Even Mitscherlich, who believed oil of turpentine to be a heart-excitant, found that in men 1.0 to 2.0 grm. doses produced only very slight acceleration of the pulse (and even this was not directly due to the drug). In fever-patients Copeland found a diminution in the frequency of the pulse.

Temperature.—No reliable experiments concerning this point have been made. Our own experiments would show that in unbound rabbits 6.0 grms. of the drug in two and a half hours produced a fall of 1.3° C. On another day the fall was 2.0° C., and after a dose of 12.0 grms. given by the stomach the temperature fell 5.2° C. in two and a half hours.

Excretion.—The secretion of the milk and sweat is supposed to be increased, although this is not proved.

As to the excretion of the urine, our own observations agree with those of the older experimenters, so that we are sure that small doses increase the excretion of the urine, while large ones (rabbits 5.0 grms., men 8.0 grms.) very much diminish it. In men, in the latter case, there is a tickling sensation in the urethra, strangury, and painful micturition. Since in our investigations the food and drink were weighed, we feel positive that these variations were not due to any change in the diet.

Microscopic sections showed no alteration in the kidneys.

Oil of turpentine therefore lowers the irritability of the nervous system and diminishes respiration, circulation, and temperature. We have not observed a primary stage of excitement.

When brought directly in contact with the blood, it produces marked blood-changes (turns it reddish brown), and by the deposit of oil emboli in the pulmonary capillaries it causes changes in the lungs, extensive atelectais, and, as a result, increased frequency of the respiration.

THERAPEUTIC APPLICATION.

Oil of turpentine is a much-applied remedy in the most various conditions. A positive and reliable therapeutic effect is not to be expected anywhere. There is scarcely any pathological process in which the oil of turpentine is to be preferred to other remedies. Ordinarily it is only used when other modes of procedure have proved ineffective. Its utility in many conditions, however, cannot be denied.

It has frequently proved effective in neuralgias; and although a satisfactory explanation cannot yet be given for its action, yet this effect loses some of its paradoxical nature when it is shown (Rossbach) that the oil of turpentine allays the irritability of the central nervous system, rather than, as formerly supposed, increasing it. The fact of its curative action in neuralgias has been repeatedly confirmed by reliable observers during the last century (Cheyne, Home, Lentin, Romberg, and others), and we have several times had an opportunity of satisfying ourselves of its reliability in this respect. Most of the cases were sciatica. We are unable to lay down any indications for its use in sciatica, nor can we state the conditions in which the drug is most likely to prove effective; most of the cases treated were old ones, in which other remedies had failed, and the cause of which was either unknown or which were rheumatic in their nature.

Frequently, however, the remedy may be ineffective. Husemann asserts that the drug is sometimes useful in hemicrania. In the neuroses, also, such as hysteria, oil of turpentine has been tried, but without much effect beyond a diminution in the reflex irritability, or in those in whom the nervous excitement was caused by worms: the destruction of these allayed the excitement.

The oil of turpentine is very effective in many of the lung-affections. It was formerly very much given as an expectorant by the English (Stokes, Graves) and French physicians in non-febrile bronchial catarrhs and broncho-blenorrhœa. How the remedy acts in these cases is unknown, but we have many other remedies for these purposes which have none of the disadvantages connected with the use of large doses of turpentine. In recent times the methodical inhalation of turpentine vapors in putrid processes in the lungs (bronchitis putrida and pulmonary gangrene) has been recommended, and with good results; that is, the odor

of the sputa was diminished under its influence, and the cavities healed. Upon what this favorable effect depends has not yet been positively determined. The bacteria which are the cause of the putrid process are not interfered with by the vapors (Leyden and Jaffe). Possibly the good effect is due to the fact that oil of turpentine is a good carrier of ozone, and that the ozone exerts a beneficial action by acting as a stimulant to the wall of the gangrenous cavity, and thus producing a cure.

It was recommended only to use the inhalations during the period when the fever had subsided; but our experience teaches us that the best time is at all times, for often the fever subsides as the gangrenous process subsides. Nor do physiological indications point to the fact that fever is a contraindication. Inhalations of turpentine are also used in diphtheria and non-putrid catarrhs. Waldenberg recommends its use in these cases, although Stokes had long before used a liniment containing oil of turpentine and acetic acid. The best method of inhaling is by the spray apparatus diluted with vapor of water.

Oil of turpentine has also been used as an anthelmintic, especially in tape-worm. Direct experiments have shown that it is injurious to the life of the entozoa; and although clinically it is a successful anthelmintic, yet we have remedies that are more active and less disagreeable (for large doses are necessary).

No person to-day would use oil of turpentine as a cathartic, so that we shall say nothing further concerning this use of the drug.

This drug has quite a reputation in the treatment of colic from biliary calculi, given in the form of Durand's mixture (1 of oil of turpentine and 3 of ether), but the result has sometimes been ascribed to the ether and sometimes to the turpentine.

In addition there is another series of affections in all of which the oil of turpentine has been used. But the results are so doubtful and the indications so uncertain that we shall not enter upon a discussion of all of these conditions, but only mention the names of the principal of them; thus it was formerly given as a diuretic in "atonic hydrops;" it is decidedly contraindicated in recent inflammatory conditions of the parenchyma of the kidneys, and yet we have found in several cases of subacute and chronic nephritis that under the oil of turpentine there

was a decided increase in the diuresis, without any injurious effect upon the general course of the disease. Is it propter or post hoc? Edlefsen has again recently recommended the remedy in catarrh of the bladder. In England turpentine has been used in typhoid fever and puerperal septicæmia as a stimulant, but our knowledge of the physiological action would certainly not prompt any such use of the drug. It has also been used as a hæmostatic in metrorrhagia and intestinal hemorrhages.

Turpentine is no longer given as an antidote to opium or hydrocyanic-acid poisoning. Recently it has been warmly recommended in phosphorus poisoning. There are, of course, but few observations upon men, but the gap can be filled up by studying the action upon animals. Köhler concludes that the oil of turpentine acts as an antidote to phosphorus in animals, if taken by the stomach at least within two hours after the poison has been taken; in men even eleven hours after: but twenty-four hours after it is entirely ineffective. A hundred times as much oil should be given as there was phosphorus. According to Köhler the good effect is due to the formation of the turpentine-phosphorous acid. To produce this effect oil of turpentine containing oxygen (old) must be used.

For external use oil of turpentine is also a favorite remedy, although possessing no advantages over other substances. We have already spoken of its use by inhalation. As an antiparasitic it had an excellent reputation until very recent times, but to-day the balsams are used. It is an excellent cutaneous counter-irritant. In neuralgias the internal administration of the remedy is well combined with its external application. Oil of turpentine is very popular externally in rheumatism and muscular affections. The drug is also used as a dressing in burns of the second degree (formation of blisters). Lücke observed a decline in temperature and arrest of the disease in several cases of erysipelas. In meteorism oil of turpentine is used as a clyster, and as an external application to the abdomen. We cannot state that we have ever gained any very great results from this method of treatment.

Dosage and Preparation.—1. Oleum terebinthini rectif. Internally, from 0.3 to 1.0 pro dosi (5.0 pro die), 5 to 20 drops, in pill, emulsion, or gelatin capsule. As an inhalation, from 0.5–2.5 to 10.0–20.0 : 100.0 of distilled water. Externally it is given either pure, mixed with fatty oils, or in the form of an ointment (in various proportions, 1 part of turpen-

tine to 1–4 of fat); as an addition to clysma, 4.0 to 8.0 (mixed with egg-albumen).

2. Oleum terebinthinæ. As an antidote to phosphorus poisoning.

3. Oleum terebinthinæ ozonisatum—oil of turpentine laden with ozone.

4. Oleum terebinthinæ sulphuratum—sulphur balsam. 1 part of ol. lini sulphuratum and 3 parts of ol. terebinth. rectificat. Is entirely superfluous.

5. Unguent. terebinthinæ—turpentine ointment. 1 part each of turpentine, oil of turpentine, and yellow wax.

6. Sapo terebinthinatus. 6 parts of sapo oleaceus, 6 parts of ol. terebinthinæ, and 1 part of kalium carbonicum.

Turpentin—terebinthina. A thick fluid obtained from the bark of many of the conifera, which is really only a solution of resins in oil of turpentine. Is used externally as a counter-irritant, and as a constituent of irritating plasters, ointments and liniments.

Preparations.—1. Terebinthina communis. 2. Terebinthina laricina s. veneta: only externally. 3. Ung. basillicum: 6 parts of olive-oil, 1 part of turpentine, and 2 each of yellow wax, colophonium and sevum. 4. Cerat resinæ pini: 4 parts of cera flava, 2 parts of resina pini, and 1 part each of sevum and terebinthina. 5. Charta resinosa s. antirheumatica—gout-paper: 6 parts of picis nigra, 6 of terebinthina, 4 of cera, and 10 of colophonium. 6. Emplastrum picis irritans: 32 parts of res. pini, 12 each of tereb. flava and terebinthina, and 3 of euphorbium. 7. Ung. terebinth. camp.: 32 parts of tereb. laricina, 4 of vitel. ovorum., 1 each of myrrha and aloë, and 8 parts of ol. olivarum.

Camphor. Camphora.

Of the various camphors, Japan camphor ($C_{10}H_{16}O$), alone has been investigated and is used. It is derived from the wood of laurus camphora in Japan, but can be prepared artificially from valerian and other oils with nitric acid.

This solid ethereal oil is found in commerce in large transparent cakes, having a penetrating, spicy odor. When slowly sublimed or evaporated from its alcoholic solution it forms octahedral crystals, is only slightly soluble in water (1 : 1000), easily soluble in alcohol, ether, acetic acid, fats and ethereal oils.

PHYSIOLOGICAL ACTION.

Camphor retards fermentation and decomposition (Pringle).

Upon the higher animals it acts in various ways, while it is very poisonous to insects. In cold-blooded animals it produces paralysis, and in warm-blooded animals convulsions. Rabbits and cats are much more sensitive to its influence than dogs; but even among the latter there are some who fall into convulsions after doses of 0.5 grm., while others can bear 15.0 to 20.0 grms. without any bad results. Men are strongly affected even by doses of 0.5 to 2.0 grms.

Disposition of Camphor in the Organism.—Camphor is ab-

sorbed both through the skin and mucous membranes, and excreted by the sweat as well as with the expired air. Even the best observers found no traces of it in the urine or fæces (Buchheim, W. Hoffmann). This fact, and also the fact that some animals can bear very large doses of the drug, while in others symptoms of poisoning that may have set in rapidly pass away, show that the drug does not long remain under its own form in the organism.

Schmiedeberg and Meyer indeed found as a result of its decomposition a non-nitrogenous (*a*) and (*b*) camphoglycouronic acid, and also a nitrogenous, uramido-camphoglycouronic acid. Glycouronic acid is probably formed from dextrose, and may be an intermediate product in the oxidation of sugar.

Local Effects.—Upon the skin and cutaneous ulcers camphor causes a burning, smarting pain and inflammatory redness. Upon the mucous membrane of the nose, when inhaled, it produces the impression of a strong spicy odor; upon the tongue a burning, sharp bitter taste, followed by a sensation of cold. The salivary and mucous secretions are increased under its influence. In the stomach and intestinal canal small quantities produce a feeling of warmth which extends over the whole body, produces eructation of gas, but seldom a fæcal passage. Large doses are followed by acute inflammation, gastric pain and nausea and vomiting.

The general effects are principally produced upon the brain and medulla oblongata; but since cold-blooded animals are differently affected from warm-blooded animals and men, it will not be right to make any deductions from the former to the latter. The symptoms in men and the mammalia are similar in kind.

Central Nervous System.—Non-fatal doses are followed by psychical disturbances, so that men and animals act as though insane; the former are seized with headaches, hallucinations, rapid flight of ideas, excessive restlessness—dancing, jumping, etc. (Purkinje)—although there are individual exceptions, as is true in the case of all drugs which effect men psychically. So individuals may be seen who are weary and mentally tired out, who yawn and even become insensible and unconscious under its influence (Alexander, Malewski). Animals become wild and greatly excited, run around as though insane, and before exhaustion become stertorous, unsteady, and reeling.

Convulsions also occur which, according to Wiedemann, bear the greatest resemblance to epileptic seizures, and are due to an irritation in the convulsion-centre of the medulla. These convulsions are not continuous but occur spasmodically, and the larger the dose the more frequently.

W. Hoffmann says it is terrible to see how the animals exerted themselves in these attacks, uttering cries of anguish, and threatening to choke every moment.

In the mammalia even the strongest doses do not produce paralysis of the spinal cord; either they perish during an attack, or if not, the camphor has probably been converted into a product which is physiologically inactive, and the animal recovers spontaneously in about 12 hours (Wiedemann).

In men, in whom the opportunities for study are very limited, paralysis of sensibility follows the stage of exaltation and convulsions (Lemchen). There is also paralysis of the bladder and rectum, coma and death, so that the increased irritability of certain centres has evidently been followed by death. Upon non-fatal but large doses the temporary excitement is followed by complete recovery, which generally sets in very rapidly, or the consequences of the local irritability may set in, especially acute gastric catarrh, with vomiting and nausea, as well as intense headache. Then recovery is retarded for several days. 2.0 to 5.0 grms. may be considered sufficient to produce psychical excitement in men without being dangerous.

It is not true that camphor dulls the sexual appetite. When this does take place, it is rather the result of the disease for which the camphor is given; for all the functions are diminished in disease, and why not this one? In small doses, which do not produce severe disturbances, some have seen even an increased sexual appetite, but even this would be hard to account for.

The effect upon cold-blooded animals is, as we have already said, an entirely different one. In frogs the spinal cord and motor nerves are so rapidly paralyzed by camphor that even if the medulla were irritated this irritation would not be expressed (Carminati and Wiedemann).

This paralytic influence is so strong that it even overcomes that of strychnine poisoning (Grisar—Binz). This, however, is only true of frogs.

The Respiration.—The views of various observers vary concerning this. When inhaled, camphor has a somewhat

slowing effect upon the respiration. During the convulsions, and in consequence of these, the respiration is interrupted, and dyspnœa with anxiety sets in. Directly after the cessation of the attacks the respiration is very much quickened. In the comatose stage and before death it may become superficial and scarcely noticeable.

Heart- and Blood-Pressure.—The heart-muscle of the frog is directly excited by camphor. The vaso-motor centres of the cord are paralyzed (Huebner).

Upon the mammalia the effect is an entirely different one. A direct action upon the heart, either as concerns its frequency or the strength of its contractions, cannot be proved. But there is a steady rise in blood-pressure, partly due to the convulsions and partly to the irritation of the vaso-motor centre (for this is seen even in curarized animals). But this rise in blood-pressure is entirely absent after section of both vagi, a fact which we cannot explain.

In men no accurate investigations have yet been made, and those that we have are contradictory. Pirogoff found in febrile (erysipelas) patients that after six or seven doses of 0.1 grm. each the pulse became smaller and less frequent.

Temperature.—Both in healthy and in feverish animals the temperature is lowered. Especially is this true of cats, as will be seen from the following table of W. Hoffman :

In cats	from	0.6	grm.	after	2	hours	by 1.8° C.
"	"	"	0.9	"	" 5	"	3.4° C.
"	"	"	1.2	"	" 24	"	1.6° C.
" dogs	"	0.9	"	"	5	"	0.7° C.
"	"	"	1.2	"	" 3	"	0.1° C.
"	"	"	1.9	"	" 4	"	1.1° C.
"	"	"	2.2	"	" 6	"	0.8° C.

In men with high fever from erysipelas Pirogoff found a diminution in the temperature under the influence of camphor. The skin and extremities became cool and covered with sweat.

Excretions.—These do not seem to be much affected. Hypersecretion of sweat and urine, sometimes seen, may be due to other causes; in some animals strangury has been seen, and after death cystitis and inflammation of the kidneys.

The exact modus of the production of the above effects is unknown. We do not know the chemical alterations which camphor causes in the organic substrata. But the

old question as to whether camphor is an excitant or a quieting agent we answer as follows:

In medicinal and non-dangerous doses it is a powerful exciting agent upon the brain and medulla, but does not affect the heart's action, while it strongly lowers the temperature.

THERAPEUTIC APPLICATION.

Although camphor no longer occupies the place which it occupied in the beginning of this century, yet it is a very useful remedy. It was formerly given on theoretical principles, sometimes as an excitant, sometimes as an anodyne. But in many cases in which it was formerly given it is no longer used, and rightly so.

There is one of these indications, however, which agrees with our present ideas of the theories of the action of the drug. This is the use of camphor hypodermically in conditions of collapse in the course of acute febrile diseases. It is true that even in this application of the drug there are many things which are uncertain and vague. Conditions of collapse, as a rule, are dependent upon a diminished contractile power of the heart; but camphor does not act as a stimulant to the heart; some observers even state that the pulse becomes weaker under the use of camphor. Notwithstanding this, however, the utility of camphor in these cases cannot be disputed. In what way the collapse is produced does not make any difference, whether it be due to the high temperature and lack of nourishment in typhoid, or in pneumonia through an unwise antiphlogistic treatment, or whether it be dependent upon the normal weak constitution of the patient. The clinical picture of collapse is well known: a frequent pulse, of weak force, while the temperature remains either normal or sinks slightly; paleness of the face and lips, cold extremities, delirum subsultus tendinum, etc. The diseases in which such a picture may be developed are various; acute febrile exanthema, typhoid fever, hospital-fever, puerperal processes, etc. It is not easy to determine beforehand in what cases to give wine and in what camphor, but practically we generally prescribe both together. It is doubtful whether the assertion of the older writers is a proper one, namely, that in diseases of the respiratory apparatus a stimulant is necessary, and hence give camphor. These physicians also state that the utility of

the drug is greater in those who are easily made to perspire than in others; also that it should not be given where there is a tendency to hemorrhage, etc. All of these statements still require investigation, and more so from the fact that in recent times these general symptomatic, and perhaps important indications require further confirmation.

Formerly, as we have already stated, camphor was given as an antipyretic. That this use is not without a physiological basis is shown in the section devoted to physiological action. And although it is questionable whether we shall be able to make use of this antipyretic action, on account of the psychical disturbances which the drug produces, yet we cannot but suppose that fever is no contraindication to the use of the drug.

Camphor is also used as an expectorant, not alone, but almost exclusively with other remedies, especially benzoic acid. The indications are the same as those laid down for the use of the latter drug.

Camphor is also a good stimulant in the toxic narcosis produced by such substances as alcohol, opium, and belladonna.

Very doubtful, however, is its value in a series of other conditions in which it has been praised. To this group belong various neuroses, such as various convulsive affections, whooping-cough, singultus, chorea, epilepsy, nervous dysphagia, etc., also in satyriasis, nymphomania, etc., and the opposite conditions, like impotence, etc.

In chordee, however, it sometimes acts well. If there be any good effect in these disturbances of the genital organs, it is a psychical and not a real one.

In psychopathies, in which camphor was formerly much used, it is again recommended by Wittich (in doses of 0.1–0.2 internally, or subcutaneously as a hypnotic); it is especially recommended in female melancholic patients, in whom there is fear and confusion of mind, and sleeplessness, without any distinct insane emotions.

Externally, camphor is frequently used, first as a dressing for wounds which show no tendency to heal, and which give off a thin pus. Also in injuries, contusions, etc., when no inflammatory process has set in. A good preparation to use in these cases is vinum camphoratum. Camphor is a popular remedy as a derivative in various inflammatory affections: thus pieces of camphor are put in the auditory canal in toothache.

Dosage and Preparations.—1. Camphors, internally from 0.05–0.5 pro dosi (3.0 pro die) in emulsion with gummi mimosæ or yolk of egg. In powder or alcohol, in children, .0075–.01. In alcohol its application is not very agreeable; for powders, camphora trita should be used (that is to say, the same remedy rubbed up with alcohol, which renders it pulverizable). For subcutaneous injection, 1 : 5–10 parts of sulph. ether, or ol. amydal dulc. or simply ol. camphorat; Inject one pravaz syringe full.

Externally for powdering sores; for ointments and liniments use 1 : 10–15 parts. Camphor clysters are no longer used.

2. Vinum camphoratum—camphora trita, and gummi Arabicum, each 1 part to 48 of vin. album., an opaque white fluid seldom used internally (℥i doses), generally externally.

3. Spiritus camphoratus—1 part of camphor, 7 parts of spir. vin. rectificat., and 12 of water. Clear and colorless. From 10–25 drops per dose.

4. Oleum camphoratum—1 part of camphor to 9 parts of olive oil, as an irritant, or for external subcutaneous injection.

5. Carbolized camphor—2.5 grm. of camphor, 1.0 grm. of carbolic acid; given with oils and oily fluids, but not miscible with water.

COMPOUNDS CONSISTING CHIEFLY OF AROMATIC COMBINATIONS EXISTING IN ANIMAL AND VEGETABLE SUBSTANCES.

Most of the drugs to be considered in this chapter belong to the vegetable and not to the animal world; they are not pure chemical substances, but rather mixtures of such, and consists of terpenes, camphors, phenols, aromatic, fatty and other acids, and resins; together with a few alkaloids. Most of these compounds are composed mainly of aromatic combinations, especially terpenes. This is the reason why they are given immediately after these.

Sometimes chemical substances occurring in the same plant or in the same compound (drug) have differing physiological effects. Thus, for example, we find in one vegetable oil terpenes, which are nerve-paralyzers, and camphors, which are nerve-excitants. In addition to this we have the unfortunate circumstance that some of the chemical substances found in these compounds are very little known, so that we do not even approximately know to what chemical group they belong. Furthermore, we do not know the exact quantitative relations existing between the individual components of these compounds, since they vary with the ground upon which the plant has grown, the season, the ripeness, etc.

The question then arises whether it is right to continue using these vegetable matters in the ignorance in which we are necessarily placed, or whether it would be best to discard them all. Under any circumstances a large portion of these substances are superfluous for two reasons: first, because many of these compounds have proved that they are either inactive, or weaker, or have different physiological effects from those which they were supposed to exert; secondly, because it has been possible in recent years to isolate the active ingredients of many of these drugs, which active principles have entirely replaced the old mother-plant in ordinary use, as was shown when discussing phe-

nols, aromatic acids, and ethereal oils. In these cases of course we shall consider not the action of the impure compound, but rather of the pure active principle.

A large number of these substances, however, still remain, which must be retained for physiological as well as for practical reasons. Among these are many of the spices. Here we would suppose that since many of these resemble each other in their action and their active principle (generally a terpene), and have a similar therapeutic effect (improvement of the appetite and digestion), many of them could be dispensed with. But the peculiarity of the human smelling and tasting organ requires a variety, of which it never tires; while others are retained because of their cheapness, ease in preparation, etc. It certainly does not seem right to first extract an ethereal oil from tea which is to induce perspiration, when the tea itself will do as well. Besides, these vegetable remedies are very popular as home remedies; the physician, however, should know whether they are useful or not. We shall, therefore, speak of many unnecessary drugs, but rather from negative critical reasons than otherwise.

To properly classify these compounds of aromatic combinations will hardly be possible, for they consist of several varying bodies, belonging to a different chemical class. While a physiological classification is also impossible, because most of them have about the same physiological effect. We shall, therefore, classify them according to the purposes for which they are used, whether this use be a proper one or only an imaginary one.

Flavoring Agents.

Used especially for flavoring. This could also be counted among spices, but we shall only speak of those oils, resins, and plants, which are agreeable to the human nostrils, and which for this reason are added to drugs, spirituous fluids, waters, etc., thus in cologne, hair-oils, etc.

Some, such as orange peel, citron rind, etc., are also counted among the bitter principles, but improperly, for most of the effect is due to the ethereal oil.

The effect of the fragrant ethereal oils is very much like oil of turpentine. The headache produced by indulging too much in fragrant odors, as when fragrant flowers are kept in sleeping apartments, is due to the absorption of the ethereal oil by the lungs, and is therefore a mild toxic symptom, like that resulting from oil of turpentine, and the poisoning symptoms following the taking of large quantities of these oils are very much like those produced by the latter.

Most of these agents are used for flavoring waters and ointments used

as cosmetics, or used by physicians to flavor drugs. For the latter purpose, orange and lemon peel are very well liked, although we doubt whether the fact that they have a bitter principle makes them any more useful in dyspeptic conditions; at any rate for the latter purpose we have many superior drugs.

Although all of these oils are somewhat antifermentative and antiseptic, yet for the latter purpose, eucalyptol is especially important.

Since the more diluted the oil, the more delicate the odor, only few drops are used to flavor mixtures or ointments.

Rose oil—oil of roses—is the most pleasing ethereal oil, and is prepared from the leaves of the flowers of Rosa Centifoliâ. These flores rosarum also contain small quantities of gallic acid, tannic acid and gnm.

Preparations: 1. Oleum rosæ, very dear; 2. Aqua rosæ, used in medicine; 3. Ung. rosatum, made of cera alba, adeps, and aqua rosæ, used very much as basis for ointments on account of its agreeable odor.

Oil of orange flowers—oleum florum aurantii, oleum neroli obtained from the flowers of citrus vulgaria—flores aurantii, and has a very agreeable odor; the small amount of bitter principles in the flowers is of no importance. 1. Oleum florum aurantii; 2. Flores aurantii; 3. Aqua fl. aurantii, aqua naphæ; 4. Syrup fl. aurantii.

Oil of orange peel—oleum corticis aurantii—is isomeric with oil of turpentine, and is obtained from the fruit of orange trees. Unripe oranges—fructus aurantii immaturi—orange peel—cortex aurantii; orange leaves—folia aurantii.

The bitter principle, aurantiin, in the peel and leaves is, as will be shown under bitter principles, of very little importance. On the other hand, orange oil has an effect similar to that of the oil of turpentine upon men and animals, while it has the advantage of a much more agreeable odor. The oil is to be found in the outer yellow layer of the peel, and the under surface of the leaves. Workmen who are employed in gathering and peeling the fruit, are affected with an erythematous eruption upon the hands, headache, noises in the ears, burning, vomiting, trembling, and even convulsions (Imbert-Gourbeyre).

Preparations: 1. Oleum corticis aurantii, for oil sugar; 2. Tinct cort. aurantii, from 1.0–3.0 pro dosi (15.0 pro die); 3. Syrup cortex aurantii, by the tea and table-spoon; 4. Ext. cort. aurantii, entirely superfluous; 5. Elixir amarum, by the teaspoonful, prepared from elix. trifol., extr. cort. aur., aqua menth. pip., spirit, and spirit. ether; 6. Elixir aurantiorum composit., also superfluous.

Citron oil—lemon oil; oleum fructus citri, prepared from the fruit (peel) of lemon trees (citrus limonum), cortex fructus citri, and resembling oil of turpentine. Lemon peel also contains a bitter principle. Oleum citri is one of the most agreeable flavoring agents.

Oil of bergamot—oleum bergamottæ; obtained from the peel of the fruit of Citrus Bergamia, is a mixture of various terpenes, and takes up oxygen gradually, thus being converted into a camphor.

Resin of benzoin—resina benzoes; flows out of cuts made in the bark of styrax benzoin; consists chiefly of four resins, whose chemical and physiological properties are still unknown, and contains also the above-mentioned benzoic acid, as well as cinnamic acid, and an ethereal oil.

Benzoin resin has a strong vanilla-like odor, agreeable in strong dilutions, induces sneezing, a feeling of roughness in the throat, a burning sensation in the stomach, and slight redness upon the skin. Benzoin

is not used medicinally; tinctura benzoes (1:5) is used as an addition to washes for comedones, freckles, etc., usually mixed with aqua rosarum.

Violet root—radix iridis; from iris Germanica and Florentina—not to be confounded with the poisonous radix violae odoratæ—contains as yet an unknown ethereal oil, tannic acid, and starch. Used on account of its agreeable odor as an addition to powders and pills, especially tooth-powders.

Oil of lavender—oleum lavendulæ; prepared from the flowers and leaves of lavendula officinalis, is composed of an oil free from, and one containing oxygen, has an agreeable odor, and is still unknown in its effect; exceedingly poisonous upon parasites. Medicinally, only the flowers are used as an addition to the so-called aromatic washes in baths.

Preparations: Flores lavendulæ; 2. Oleum lavendulæ; 3. Spiritus lavandulæ.

Oil of rosemary—oleum rosmarini; from the leaves of rosmarinus officinalis, is a mixture of an oil free from, and one containing oxygen, severely irritant upon the skin and mucous membranes, as well as strongly poisonous to lice and itch mites. The general effect is partly that of camphor, and partly that of oil of turpentine.

Rosmarin is even now very much used externally, although generally the preparations are preferred. They are used as cutaneous counter irritants, as liniments for contusions, muscular rheumatism, etc., but we have never seen any especial virtue in these liniments, and the drug could certainly be spared.

It is also one of the many preparations used as dressing in wounds, and also used for the itch. Folia rosmarini; 2. Oleum rosmarini; 3. Spirit rosmarini (externally); 4. Ung. rosmarini, comp. s. ung. nervinum, ol. rosmarini and juniperi of each, 1 part and 2 parts of oil nucistæ, 2 parts of yellow wax, 8 parts of sebum ovillum, and 16 of adeps suillus, has a yellow color. Externally. 5. Aqua aromatica, a good mixture of many aromatics, herbs, and entirely superfluous. 6. Aqua vulneraria, equally so; 7. Vinum aromaticum, the foregoing preparation with species aromaticæ and red wine.

EUCALYPTOL—EUCALYPTUS LEAVES.—Folia eucalypti globuli, obtained from the giant, rapidly growing Myrtacee Australiens; eucalyptus globulus—a tree that promises to be of great economical and hygienic importance for warm countries, contains in addition to chlorophyll, a resin and a tannic acid, turning black with ferric salts, a large amount (2.75 per cent: 6 per cent) of an etheral oil, which contains oxygen. Eucalyptol—a colorless, movable fluid, which is agreeably refreshing when inhaled in the form of vapor, which has the odor of roses in dilute solution, and whose boiling-point is 175°. It is but slightly soluble in cold water (1–3800); more so in alcohol; it is readily oxidized to resin and ozonizes like oil of turpentine the oxygen which it absorbs (Cloez and Siegen). In fact, according to Faust and Homeyer, eucalyptol is a mixture of a terpene (70 per cent) and cymol, and cannot, as Cloez thinks, be considered a camphor. There is also in the leaves about 10 per cent of ashes (potass. and alkaline carbonates).

Physiological Action.—According to Binz and Siegen, eucalyptol has a more powerful antiseptic and antifermentative action than quinine. The effect upon the unorganized ferments is not as marked as that upon the organized. Eucalyptol also resembles quinine in its effect upon the relations of protoplasm to oxygen.

Upon men and animals the effect is exactly like that of the oil of turpentine (Gimbert, Gubler, Binz, Siegen, Grisar and Schlager.)

It has a sharp, spicy taste, produces burning in the pharynx, and a feeling of warmth in the stomach, without in small doses affecting the appetite. Doses of 2.0–4.0 grms. cause epigastric pains, pressure, and disturbed digestion. Small doses increase the excretion of the urine.

The general effects at first noticed are those of irritation, due rather to the pain of the hypodermic injection, or when given in concentrated solution into the stomach, than to the effects of the drug. A short time after the administration, even when inhaled, the drug is followed by headache, drunkenness, and nervous prostration (after 3.5 grms. according to Siegen), together with paralytic symptoms from the brain and spinal cord (sleepiness, diminished reflex, etc.) Also diminished force of the heart, (Schlager) sinking of the blood pressure and considerable decrease in the temperature. The peripheral nerves are little affected. Fatal doses are followed by death due to paralysis of respiration and dyspnœal convulsions.

The eucalyptol absorbed into the blood is again eliminated with the expired air and urine. The urine has an odor resembling that of violets.

Therapeutic Application.—Of the eucalyptol, introduced into practice during the last ten years, it is reported that it is an energetic antipyretic, especially in malaria intermittens. It is said to be in no way inferior to quinine in the rapidity and certainty of its effects. After many observations concerning this point, we follow those of Keller, because they have a large amount of statistical material. According to Keller, of 432 patients suffering from intermittens, 310 (about 71 per cent) were entirely cured, while 28 per cent were subjected to an after-treatment of quinine. In 118 (27 per cent) of the 432, quinine had been previously used without effect. Of the 122 who were unaffected by eucalyptus, 58 were cured by quinine, 38 remained uncured, and 26 could not be observed to the end of the treatment. Other observers report similar results, and the average time necessary for a cure is said to be not longer than from quinine. The chief advantage of eucalyptus as compared with quinine is its cheapness, (about one half the price of quinine).

It is to be regretted, however, that these favorable reports are contradicted by those of other observers, who have found eucalyptol entirely ineffective in malaria, or very much inferior to quinine. We ourselves cannot express an opinion, for we have had but little opportunity lately to treat malaria in our place of residence; recently, the remedy seems to be losing popularity, for there are no more reports concerning its use.

The recommendations of many other observers (in gastric affections, Bell; in diptheria Bell-Mosler; as a substitute for phenol in the Lister method, Schulz, etc., etc)., have not yet had sufficient time to be confirmed.

Hitherto, tinctura eucalypti has been used almost exclusively in pyrexia, in doses of 3-4 teaspoonfuls.

CLOVER.—HERBA MELILOTI.—Melilotus officinalis contains an extraordinary amount of cumarin, and is used for poultices and plasters (emplastrum meliloti.)

Cumarin, $C_9H_6O_2$, is found in stone clover, in asperula odorata, and in dipteŕix odorata (melilotus officinalis). It crystallizes in colorless prisms, having a highly agreeable odor, and with difficulty, soluble in water.

According to the thorough investigation of H. Kobler, cumarin is a

hypnotic and anæsthetizing agent. It produces paralysis of the cerebrum and of reflex irritability, without at the same time, causing any stage of primary excitement. The inhibitory nerves of the heart are first excited, then paralyzed, and finally, the irritability of the heart muscle itself is diminished to the lowest point. The blood pressure is diminished, owing to paralysis of the vasomotor centre. The respiration is slowed and temperature lowered. The peripheral nerves are not affected. Cumarin reappears as such in the urine. In men, according to Buckheim and Malewski, it produces nausea, vomiting, dizziness, stupor, and headache. To this is due the ill effects of the so-called May wine. Concerning the therapeutic utility of cumarin, we have made no observations.

B. Remedies, Which are Used for their Fragrance and for Their Fatal Effect upon Parasites.

All volatile ethereal oils have a poisonous effect upon the itch parasite because on account of their volatile nature, they easily penetrate into the canals in the skin where the parasites are lodged. The effect upon the higher animals is like that of the oil of turpentine.

Balsam of Peru—Balsamum Peruvianum; has a vanilla-like odor, sharp taste, is soluble in alcohol, and is a thick, dark-brown, non-drying fluid. The oil which it contains, oleum balsami peruviani, contains benzyl cinnamate $C_{16}H_{14}O_2$, and cinnyl cinnamate $C_{18}H_{16}O_2$, (Styracin) and when subjected to dry distillation forms toluol.

Of its physiological action we are certain only of this: that in large doses internally it produces a gastro-intestinal catarrh, and above all causes inflammatory action in the gastric mucous membranes.

Internally balsam of Peru is hardly used, formerly it was used, in addition to other conditions, chiefly as an expectorant in bronchial catarrhs and all inflammations of mucous membranes.

We use the drug very much externally in scabies (Gieffert) in which it has been found a very excellent remedy. Of all remedies for the itch, this is the best; its utility has been shown in thousands of cases, and we ourselves have always found it successful in the most unfavorable hygienic surroundings.

Buchardt has shown that balsam of Peru is a powerful poison for the itch-mite, which dies under its influence in the space of twenty to thirty, at most forty minutes. But the acarus must come in direct contact with the poison, for the vapors from it do not injure it at all. Buchardt also found that the eggs are also killed; beside this it possesses the advantage of being an agreeable substance, which does not cause itching and has a pleasant odor.

The important points in its application are as follows: Before applying the remedy the patient must take a bath, to soften the epidermis; then the whole body (except the head) is covered with the balsam, so that the latter is well applied to the epidermis. Especial attention must be paid to the parts in which the itch-mite is most abundant (penis, scrotum, extensor sides of arms and legs, abdomen, etc.). 50 drops are sufficient for one rubbing, for the whole body. The application may be repeated two, four or six times. During the cure the patient should not change his underclothing; at the end of the second day, another bath should be taken, clothing disinfected, and the cure is complete. The superiority of this method of treatment needs no comment.

Balsam of Peru is also used as an external application in burns,

wounds, ulcers, etc. Recently it is also much used in various skin diseases. The effect in prurigo and pruritus is excellent, also in subacute eczema, Peru balsam has healed when tar was ineffective; but it should never be applied in eczema chronica (crustosa and squamosa). In these cases it acts exceedingly well, and balsam of Peru has frequently succeeded in curing these cases after Theer had failed.

This latter seems more successful on the contrary in old forms with marked infiltration of the derma.

Peru balsam is contraindicated in acute moist eczema previous to the subsidence of the inflammatory action. Even in sycosis rapid improvement is often observed.

Dosage and Preparation.—Bals. peruvianum, internally from 0.3–1.0 in pill and solution; externally pure, in ointments (1–5–10), alcoholic solution (1–1–5); in emulsion with oil or glycerine (1–1–2). 2. Syrupus bals. peruvian s. balsamicus, generally used as an adjuvant to other remedies; internally from 25 to 40 drops. 3. Mist. oleoso balsamica, balsamum vitæ Hoffmani, three parts of balsam of Peru, one part each of oil of lavender, caryophyllum, cinnamoni, cassiæ, thymi, citri, macidis, flor. aurantii, to 240 parts of alcohol. Internally as a stimulant; entirely superfluous.

Tolu balsam—balsamum tolutanum; flows out of cuts into the bark of myroxylon toluiferum, has a fine odor of a terpene, $C_{10}H_{16}$, and contains also cinnamic and benzoic acids, and resins; can be used for flavoring; entirely superfluous.

Styrax balsam—balsamum styracis; obtained from liquid amber oriental, is a thick, fluid, grayish-green, non-drying mass, having a vanilla-like odor, sharp taste and soluble in alcohol. It contains phenol-ethyls C_8H_8, (Styrol); cinnamic acid, and cimmyl cinnamati. Internally this is not used at all, although it has recently been substituted externally for the balsam of Peru in the treatment of itch. But styrax has no advantages over balsam of Peru in the rapidity, agreeability and certainty of the cure. But it is cheaper, and should be used where this element is an important one. This balsam also kills pediculi, just as certainly as the mercury preparations, while it has the advantage of producing no eczema, and is without danger of absorption.

SPICES.

Almost all the vegetable spices used in the kitchen contain as active constituents, oils containing and those not containing oxygen, also aromatic acids, such as cinnamic acid, several carvols and thymols of the phenol series. The peppers contain an alkaloid, but resemble oil of turpentine because they contain an enormous percentage of terpene. Except that they have the advantage over this in a more agreeable taste and odor, and a better effect upon the appetite, they can only be distinguished from each other in the variety of their odors. We can therefore treat of their physiological and therapeutic application together, and briefly.

Physiological Action.—In addition to the agreeable odor, the remedies of this group possess a sharp, spicy, burning, often bitter taste. In consequence of their irritating effect upon the mucous membranes, the salivary and gastric secretions are increased in a reflex manner, they produce a sensation of agreeable warmth in the œsophagus and stomach, increase of the appetite, improved digestion, so that larger amounts and less digestible varieties of food can be taken without injury. How the

intestinal juices are affected by spices, is not known, but we think that these also are increased under their influence. Intestinal peristalsis becomes stronger but not quickened, so that larger quantities of fæces are moved along, with only normal rapidity, and dietetic doses are never followed by diarrhœal stools. On the contrary some varieties of diarrhœa are improved by spices.

Many of the native spices are not used as condiments but rather for the preparation of teas to be taken for colic, gastrointestinal pains and diarrhœas, and generally with very good results. How much of this effect is due to the warm water and how much to the ethereal oil must be judged of by every one for himself, but this much is true, that while warm water alone causes vomiting and nausea, it is well borne and agreeable when taken with these ethereal oils.

What has been said is true only of small doses; large doses cause vomiting, nausea, gastro-intestinal pain, abdominal pains and even diarrhœa; the absorption of the ethereal oil is followed by symptoms of general poisoning, such as headache, dazed condition and paralysis, (Mitscherlich, Binz, etc.), like that effected by the oil of turpentine. In regard to the other substances which occur in the ethereal oils and spices, such as aromatic acids, they have but little effect, and if any, it is similar to that of benzoic and salicylic acid.

Therapeutic Application.—All these drugs belonging to this group, are used for the following purposes: to improve digestion, diminish colic, and to hasten the absorption or expulsion of intestinal gases; they are rarely used for other purposes, and such as are, we shall call attention to in the proper place.

For improving digestion they are used not only medicinally but also in the domestic preparation of the food, and form the so-called "spices" in the kitchen (cinnamon, pepper, ginger and vanilla). It is well known that these spices are misused, and, unless we desire to continue this injury, we must carefully lay down the indications for their use.

In general, it may be stated, that they are indicated where we desire to increase the gastric secretions. But not even in all of these cases should they be used, but only under the following two conditions—first, when, after a sumptuous meal, the gastric juice excreted in normal quantity would not suffice for digesting it; then spices may be used to increase the gastric juice, although if this proceeding be repeated too often it will soon produce a pathological condition; secondly, spices are indicated, where the amount of gastric juice is not only relatively, but actually too small to digest an ordinary meal; this occurs frequently in persons leading a sedentary life. Thus it would be indicated in the atonic forms of dyspepsia, while it is contraindicated in inflammatory affections of the stomach, both acute and chronic.

As "wind-expelling agents" they are not used in the meteorism occurring in typhoid and peritonitis, but in the flatulence, which is the result of fermentative processes in the intestine, which are due to an abnormal quantity of fermenting materials in the stomach, or a diminished supply of gastric and intestinal juices. These agents here act first by increasing the gastrointestinal secretions, and then prevent gas formation, and secondly, by causing the gas already formed to be expelled from the intestine by increased peristalsis.

Finally many of these spices are very much liked in colicky pains and cardialgia, with or without diarrhœa, and also in hysterical attacks of

this kind. What we have already said in the physiological section will sufficiently explain these uses.

The dosage of all these substances, when not used in the kitchen, is, except in exceptional cases to be given below, about the same. Teas are generally prepared with a tablespoonful of the substance to 1 to 3 cups of water. The oils are given in 1 to 3 drop doses. The aquæ from 5.0 to 10.0 grm., and the tinctures in from 20 to 40 drop doses.

DOMESTIC SPICES.

Carraway—Semen Carvi; the fruit of carum carvi contains an ethereal oil of a spicy taste and odor, having a composition similar to that of oil of turpentine, and a body whose molecular constitution is isomeric with thymol (Carvol C_{10} H_{11} O.)

Preparation.—1. Semen carvi; 2. Oleum carvi.

Peppermint—Herba menthæ piperitæ; contains through its oil of peppermint—a mixture of camphors or menthol (C_{10} H_{20} O) and terpenes—its agreeable spicy odor, and sharp, thin, cooling taste. According to Köhler it has a diminishing effect upon reflex action, like that of the oil of turpentine.

Preparations.—1. Folia mentha pip. 2. Oleum menth. pip. 3. Rotulæ menth. pip.; 1 of the oil menth. pip. 200 of rotulæ sacch., and 8 of acetic ether, 4. Aqua menth. pip. 5. Aqua menth. pip. spirituosa, very much used as menstrua; 6. Spirit menth. pip., anglicus; fol. menth. pip., rosmarinus, herb. serpylli, and majoran, flor. lavand., caryoph., and cubebæ; used for fomentations.

Curled Mint—Herba menthæ crispæ; contains a similar, although less spicy ethereal oil.

Preparations.—1. Folia menth. crispæ; 2. Oleum menth. crispæ; 3. Spirit menth. crispæ anglicus; 4. Syrupus menth. crispæ; 5. Aqua menth. crispæ.

Wild Thyme—Herba serpylli; contains chiefly terpenes.

Preparations.—1. Herba serpylli; 2. Spirit serpylli.

Garden Thyme—Herba thymi, from thymus vulgaris, has in addition terpenes, also thymol.

Preparations.—1. Herba thymi; 2. Oleum thymi.

Radix Pyrethri Germanici, from Anacyclus Officinarum—The active ingredients are, according to one authority, ethereal oils and resin; according to others, a veritable base allied to piperin, without odor, but of a burning taste; it finally diminishes the irritability of the terminal nerve filaments of the mucous membranes. Formerly much used in the sensory and motor paralysis of the buccal cavity.

Calamus—Radix calami from the acorus calamus, contains an agreeably-smelling yellow ethereal oil of unknown composition; oleum calami, some benzoic acid, and a glucocide bitter principle, acorin. We have no exact investigations into the physiological actions of this drug. Large quantities of the oil are said to cause headache. Acorin is said to have an effect similar to that of salicin upon malaria.

Calamus is still frequently prescribed in atonic dyspepsia, without however accomplishing any very marked results. Externally it is used as an addition to baths.

Dosage and Preparations.—1. Radix calami, 0.5–2.0 pro dosi (15. pro die).

2. Oleum calami, entirely superfluous, which is also true of 3. Ext. calami; and 4. Tinctura calami. For a bath, ½–2 kgr.

Vermouth Herb—Herba absynthii; from artemesia absynthium, contains a green oil of a spicy odor, and sharp taste, oleum absynthii, also resins, an acid and a bitter principle absyntiin.

Physiological Action.—Absynth oil, according to Bohn and Kobert, has an effect similar to that of oil of turpentine in animals; in moderate quantities it diminishes reflex irritability; very large doses might cause epileptiform spasms. Bohn and Kobert, however, believe that a man could not be placed in such a condition from absynth liquor alone. Absyntiin can be absorbed, and imparts a bitter taste to the flesh of animals who have taken it.

Therapeutic Application.—Vermouth herb is given as a stomachic tonic, but is of no importance, and is of no utility in any of the affections in which it is sometimes used.

Dosage and Preparations.—1. Herba absynthii in infusion (10 to 150.0); also in decoct.; here it acts simply as a bitter tonic.

2. Ext. absynthii, of a thick consistency, dark-brown in color, and soluble in water. Has only the effect of a purely bitter tonic. Internally from 0.3 to 0.5, in pill or solution.

3. Tinct. absynthii; 1 part of herba absynth. to 5 of dil. alcohol, greenish-brown, from 15 to 30 drops; also present in many bitters and cordials.

FOREIGN SPICES.

Foreign spices are the most numerous.

Ginger. Radix Zingiberis, from Zingiber Officinal—Its ethereal oil has a prickling, burning taste, a feeling of warmth in the stomach, increase of appetite and digestion, like that of other spices; used in the kitchen as a spice and appetizer; not necessary in medicine. Tinct. zingiberis.

Ceylon Cinnamon—Cortex Cinnamomi Ceylonici—This rind contains one of the most agreeable ethereal oils, which is easily converted in the air into cinnamic aldehyde, C_9H_8O, and cinnamic acid, $C_9H_8O_2$; the latter is in every way similar to benzoic acid, can be converted into it. The rind also contains tannic acid, sugar, starch and gums. It is one of the best liked of the spices. Whether it causes contraction of the uterus or hemorrhage therefrom is very doubtful. It is also given in chronic diarrhœa and in the second stage of intestinal catarrhs, the result of cold or indigestion. Cinnamon tea is a good vehicle for other remedies. Before ergot was introduced into medicine cinnamon was one of the most frequently used drugs in insufficient labor-pains or in bleeding from the uterus. The circumstances under which it should be used will be given under secale. Since cinnamon is not as effective as ergot, it is to-day superfluous.

1. Cort. c. ceylon, from 0.3 to 1.0 (5.0 pro die) in powder, electuary or infusion; the tea can be prepared at home (1 to 2 teaspoonsful cinnamon to a cup of water); 2. Oleum cinnamomi ceyl.

China Cinnamon—Cortex Cinnamomi Cassiæ; contains an aromatic oil similar to that of Ceylon cinnamon in addition to tannic acid, sugar, starch, and gums.

Dosage and Preparations.—1. Cortex cinnamomi cassiæ (see the preceding drug).

2. Aqua cinnamomi simplex, distilled from 1 part of cinnamon to 10 of water, generally used as a menstruum for mixtures.

3. Aqua cinnamomi spirit. s. vinosa, 1 part of cinnamon, 1 part of water to 10 of spirit vini rectificat.; used like the preceding preparation.

4. Oleum cinnamomi cassiæ.

5. Tinct. cinnamomi, 1 part of cortex cinnamomi to 5 of spirit vini recificat.

6. Syrup cinnamon, 2 parts of cinnamon peel, 12 of aquæ cinnamomi, 2 of aqua rosar, 18 parts of sugar; of a reddish-brown color, and used as a corrigens.

7. Tinct. aromat., 4 parts of cinnamon peel, 1 each of cardamon, cloves, galgant, ginger to 50 of spirit vini rectificat; reddish-brown in color; much used in dyspepsia.

8. Pulvis aromaticus, 5 parts of cinnamon, 3 parts cardamon, 2 parts of ginger, on the point of a knife.

Cloves—Caryophylli, the flowers of Caryophyllis Aromaticus; contains 20 per cent of the oil of cloves, which has a penetrating odor and a burning taste; this is a compound of eugenol, $C_{10}H_{12}O_2$, a body resembling phenol chemically, and a terpene and tannic acid and gums.

Cloves resemble cinnamon in their effects. They are used principally in the kitchen as a condiment and spice. Externally, oil of cloves is used to relieve pain of carious teeth.

Dosage and form like that of cinnamon. 1. Oleum caryophyllorum æthereum, fresh and colorless; later on turns yellow or red. Specific gravity 1.05. 2. Tinct. caryophyllorum, generally used externally in toothache, and as an addition to cosmetic tooth preparations.

Mace—Macis—Myristica fragrans is the outer covering of the so-called nutmegs, nux moschata. Both contain ethereal oils belonging to the group of terpenes, a slight quantity of myristicol and a fatty oil, so-called nutmeg butter.

The action is very much like that of oil of turpentine.

Nutmegs—0.5 to 1.0; little used therapeutically, but a much-used spice, and a popular remedy in diarrhœa.

1. Oleum Nucistæ s. Nucum Moschatarum Expressum—Nutmeg Butter; yellowish in color, and containing a small amount of an ethereal oil; used in popular medicine as an external remedy, especially in cardialgia. But we have never seen any especial utility from its use. 2. Ceratum myristicæ-balsamum, nucistæ, 2 parts of oleum proviciale, 1 part of cera flava; used like the foregoing preparation, but more frequently. 3. Emplast. aromaticum, entirely superfluous. 4. Tinctura macidis, 1 part of mace to 5 of spirits, from 20 to 40 drops. 5. Oleum macidis.

Vanilla—Fructus Vanillæ; the fruit capsules of vanilla plænifolia, contains an extraordinarily agreeably smelling acid, and also ethereal oils, which have not yet been isolated. The cause of the poisonous effects (choleriform) of some varieties of vanilla has not yet been determined (Maurer).

Vanilla is much used on account of its agreeable odor as a spice. Medicinally it is not used, nor has it been proved to increase the sexual appetite, or to be of utility in hysterical or spasmodic attacks. Medicinally, it can be given in powder or infusion, 0.3-1.0.

1. Tinct. vanillæ: 1 part of vanilla to 5 of spirit. vini. rectificat., of a yellowish-brown color and agreeable odor; given in from 25 to 30 drop doses; also, used as an addition to mouth washes and tooth powders.

2. Vanilla saccharata, 1 part of vanilla to 9 of sugar, as a constituent of pills.

Cascarilla Bark—Cortex Cascarillæ; has a sharp, bitter, spicy taste, a pleasant odor, and contains a mixture of ethereal oils and resins, which are known as oleum cascarillæ, and a crystalline, bitter principle, casca-

rillin. The effects are principally due to the ethereal oils. When large quantities of an infusion, for instance, are taken, there results gastric catarrh (nausea and vomiting), and headache; the same symptoms occur when it is smoked with tobacco. The effect of the bitter principle is unimportant.

Cascarilla bark is still quite often administered in atonic dyspepsia, especially where there is at the same time a tendency to diarrhœa.

Dosage and Preparations.—1. Cortex-cascarillæ, 0.5–2.0 pro dosi (15.0 pro die), in infusion.

2. Extract cascarillæ, 0.3–1.0 (5.10) pro die, in pill or solution.

3. Tinct. C., 1.0–2.0 (20 to 40 drops) pro dosi.

Saffron—Crocus; the dried flower of crocus sativus; contains an ethereal oil, with strong narcotic properties, like those of oil of turpentine, and an intenser coloring matter, crocin, and is only used on account of the latter. Therapeutically, it has no value; is also a constituent of many plasters.

Preparations.—1. Tinctura croci.

2. Syrup cr.

3. Emp. oxycroceum, s. galbani rubrum, contains crocus, olibanum, myrrh, mastich, galbanum, ammoniacum, turpentine, pine resin, colophonium, and cera flava, is a popular "cure all," external remedy for pain. Entirely superfluous; as is also:

4. Emplastrum de Galbano crocatum, Empl. plumbi spl., cera, galbanum, crocus and terebinthina.

Peppers.

Black and white Pepper—Piper nigrum et album; the former the dried, unripe berry, the latter the much weaker seed of piper nigrum. Pepper contains (a) an ethereal oil, isomeric with oil of turpentine, and having a characteristic peppery odor; (b) a resin, which has no local action upon the skin or mucous membrane; (c) Piperin ($C_{17}H_{19}NO_3$), an alkaloid isomeric with morphine (Buchheim counts it among the amides); it is tasteless, although, in commerce, it has a peppery taste, owing to impurities (d); Chavicin (a piperide, in which a hydrogen atom has been replaced by chavicinic acid (Buchheim). Whether the sharp effects of pepper are due to piperin (Buchheim) or to its other constituents, is not yet certain.

Physiological Action.—Pepper, taken in substance, has a powerful effect upon digestion. A feeling of warmth takes place; increased appetite and better digestive powers, even for indigestible substances, such as pickles, etc. All this is probably the result of an increased secretion of the gastric juice, due to the irritation of the mucous membrane by the pepper. The pepper also prevents fermentation of food in the stomach. Large quantities may produce a severe inflammation of the gastric mucous membrane, and the consequences thereof.

Piperin, like quinine, is said to have an anti-febrile and anti-malarial influence. Newmann noticed a large single dose of 2.5 grm. followed by burning in the stomach; later, also, in the lips and eyes, and later, also, in palms of the hands and soles of the feet. In addition to this there was a sensation of prickling in the hands, feet and legs, and also a variable sensation of heat and cold in the affected parts. The heart's action was not markedly affected. According to Buchheim chavicin acts in the same way.

Piperidin, in moderate doses, has no marked effect. Its salts affect the organism in a manner similar to ammonium or ethyl amine salts. Piperinic and chavicinic acid also have no remarkable effect (Buchheim).

Therapeutically, pepper is one of the most useful of the spices. It has long been used as a popular remedy in intermittens, and was even used by physicians for this purpose at the beginning of this century. It cannot be doubted that pepper is often a valuable agent. Its good effect may be due to the fact that it improves digestion, for such improvement is generally seen in cases where there have been digestive disturbances. But against the few cases cured, there are many not cured, and hence the piperin treatment will never come into extensive use.

Dosage.—Piper Nigrum, used in cooking; as an anti-pyretic and anti-malarial agent from 0.3–0.5, in powder or in maceration.

Spanish Pepper—Piper hispanicum fructus capsici; a spice known in Austria by the name of paprika (capsicum annuum). Very much liked; irritates the gastric mucous membrane, as is shown by the feeling of warmth present in the stomach. This irritation is probably due to capsicol (Fleischer and Hogyes), which has not yet been isolated.

Even in very small doses, it causes considerable improvement in the appetite and digestion; but too large doses are followed by gastro-enteritis. Internally it is used therapeutically, to improve digestion. But we should be very careful to individualize the cases in which this strong substance should be used. In the tropics, where pepper is very much used, it is supposed to especially further the digestion of vegetables.

In all other conditions in which capsicum is given, it is useless, especially so in diphtheria of the fauces, in which West Indian physicians have given it as a gargle—a proceeding which may be injurious. The chewing of Spanish pepper in paralysis of the tongue is also an illusory procedure. As a cutaneous irritant, also, it is not indispensable.

Dosage and Preparations.—1. Fructus capsici, internally, from 0.05–0.2 (1.0 pro die), in pill, powder, or infusion, to be taken before meals. As a gargle use the infusion in from 1.0–2.0 : 200–300.0.

2. Tinct. capsici, from 10 to 20 drops.

Cayenne Pepper, from Capsicum Brasiliense, is also a strong spice, having similar effect to that of the preceding.

To this group belong the cardamon fruit, oil of cajeput, pimenta, coriander seed, etc.

AROMATIC DRUGS, EXERTING AN EXPECTORANT ACTION.

Most of these belong to the group of spices, with which they agree in their effect upon the appetite, digestion, and intestinal secretion. It is by no means proved that they hasten the solution of mucus. As an expectorant, they are of very slight importance. It is said that they have a solvent effect upon collected mucus in the air tubes, although they do not increase the amount of mucus or pus formed in the inflammatory stage of a disease, and are contraindicated in such conditions. These preparations are rarely given alone, but generally in combination with other substances; then only in slight laryngo-tracheal catarrhs.

Common Anise—Fructus s. Semina Anisi vulgaris or pimpinella anisum, contains an ethereal oil, known as anethol or anise camphor, con-

sisting of two chemically identical and physically different components, solid and fluid anethol, to which anise owes its agreeable odor. It is only slightly soluble in water, and readily in alcohol.

From the experiments which have been made, it is not possible to determine what the effect of its action is; only this much is certain, that in certain quantities it acts, like the oils of turpentine and camphor, fatally upon the lower and higher animals, causing paralysis. We therefore consider it best to characterize its action as being like that of the oil of turpentine, until we can make more accurate statements.

The *therapeutic application* of the oil of anise is exactly like that of fennel seed; as an eye-wash, however, the latter is preferred. On the other hand, oil of anise has the property of being a much better parasiticide than the latter; it is especially good against pediculi capitis. We must be careful in its application, because the oil can readily cause inflammation of the skin. Chloasma and herpes circinnatus are also cured by anise oil.

Dosage and Preparations.—1. Fructus anisi—from 0.5 to 1.5 in infusion, powder and spirit.

2. Oleum anisi, star anise, fructus s. semina anisi stellate, from illicium anisatum, smells and tastes like ordinary anise, and has the same components (anethol), and has similar effects. It is a constituent of: 1. Species pectorales, ad infusum pectorale. "Brustthee," 8 parts of radix althaeæ, 3 parts of radix glycyrrhizæ, 4 of folia farfaræ, 1 of rhizoma iridis florentinæ, and 2 parts each of florum verbasci and fructus anisi stellati. A much used remedy in non-febrile bronchial catarrhs; 1 tablespoonful to 2 or 3 cups of tea.

2. Species pectorales cum fructibus, 16 parts of species pectorales, 6 of fructus ceratoniæ, 4 of semen hordei excorticati, and 3 of carica used in the same way.

Fennel Seed—Fructus s. Semina Fœniculi, from Fœniculum vulgare; has, like anise seed, an oxidized ethereal oil, containing anetholes, and, in addition, also a terpene. Of its effects we only know that it acts upon the animal body like other ethereal oils, and that it increases the appetite, as well as the milk, sweat, and urinary secretion.

Therapeutic Application.—Fennel seed is very much used. It is generally given for dispelling gas from the stomach and intestines; it is also useful where colic, nausea, etc., are due to wind. It is often added to cathartic mixtures, in order to diminish colicky pains which they would otherwise cause. As an expectorant the preparation is only of slight utility. Fennel should be given with anise and other drugs of the same kind. The fennel tea is also used by the laity to effect the lacteal secretion, but whether it has any such effect is doubtful.

Externally, fennel water is used almost exclusively by the laity as an eye water. That it acts other than as a slight astringent in chronic catarrh of the eyelids is doubtful.

Dosage and Preparations.—1. Fructus fœniculi, internally from 0.5–1.5 in infusion, in powder and as a tea.

2. Oleum fœniculi æthereum, as a carminative, generally in the form of an oil; sugar as a corrective.

3. Aqua fœniculi, in teaspoonful doses alone, or as an addition to mixtures. Externally as an eye water.

4. Syrupus fœniculi, as a carminative and expectorant, with other drugs.

Pimpinella root (from various varieties of the pimpinella) contains an ethereal oil and some sharp substance. Has a disagreeable odor and taste. Tinctura pimpinellæ is a superfluous preparation.

Resin of Ammoniac Gum — Gummi Resina Ammoniacum, from dorema ammoniacum; yellow granules, which, in addition to a little ethereal oil, contain resin and gum; has a strong odor, and sharp taste. Has no well observed effects upon the animal body; the same is true of the resin.

Therapeutically, this formerly much used preparation, is to-day entirely superfluous. Even as an expectorant it does not amount to much. It is said to act well in cases similar to those in which senega is used.

Dosage and Preparations.—1. Gummi Resina Ammoniacum, internally from 0.2–1.0 (5.0 pro die) in pill or emulsion with the yolk of an egg. Externally it is added to irritating plasters.

2. Emplast. Ammoniaci contains, in addition, res. pini. galbanum, terebinthina and cera flava.

Myrrh—Gummi Resina Myrrha; resin obtained from the balsamodendron, contains only 2 per cent of an ethereal oil containing oxygen (myrrhol), and, in addition, contains about equal quantities of resin and gum. We only know that in small doses it improves the appetite; in large doses it causes gastroenteritis.

Therapeutic Application.—What we have said concerning the internal use of ammoniac resin, is also true of myrrh. However, the first should be preferred in broncho blenorrhœa, because it disturbs digestion less, and has a greater influence upon abnormal secretions. The older physicians prescribed it very much in the above-named condition, and certainly with benefit. It not only improves the expectoration, but even diminishes the amount of mucus excreted. In phthisis, in which it was formerly much given in the form of Griffith's mixture, it is to-day no longer used. Tincture of myrrh is used externally as a slightly irritating dressing for wounds; also used as an astringent wash where there is tendency to hemorrhage from the gums.

Dosage and Preparations.—1. Gummi resina myrrhæ, internally from 0.3–1.0, in pill, powder, or mixture. Externally the resin is seldom used, but generally the tincture, in 5–10 per cent solution on a dressing.

2. Tinct. myrrhæ—1 part of myrrh to 5 parts of spir. vin. rectificat., of a reddish-brown color. Not used internally; used as a dressing, and as an addition to tooth mixtures.

3. Extractum myrrhæ—entirely superfluous.

Benzoin resin is also considered an expectorant.

DIURETIC AND DIAPHORETIC AROMATIC DRUGS.

1. Diuretic drugs, although they have the same effect upon urinary secretion as the spices, yet these are preferred (properly) as diuretics. The reason of their diuretic action is probably an irritant effect upon the kidneys, the nature of which we do not know, but which we conclude is irritant, because large doses cause inflammation of the kidneys with excretion of albumen and a bloody urine, just as with oil of turpentine. These drugs are cubebs, copaiba, juniper berries, etc. Some of these are also said to have a good effect upon gonorrhœa.

Cubebs—Fructus Cubebæ, from piper cubeba or cubeba officinalis; contains up to 15 per cent of an ethereal oil (cubeb oil), $C_{10}H_{16}$, polymeric with oil of turpentine; also 2 per cent of an indifferent body (cubebin) $C_{10}H_{10}O_3$, which is insoluble in water, and is odorless and tasteless. Also a resin, together with an acid (cubebenic acid); also, a fatty oil and gum.

Physiological Action.—Cubebs has a favorable effect upon taste and digestion as long as only dietetic doses (0.5–1.0) are given. In medicinal doses (5.0) it causes vomiting, abdominal pains, and diuresis; in large doses (10.0 grm.) gastrointestinal catarrh, or inflammation with severe abdominal pain, vomiting, diarrhœa, and the other general symptoms of a sick stomach; sometimes eruptions have been seen upon the skin.

Birnatzik has seen the same effects from the oil of cubebs as were described under oil of turpentine; even increased urinary secretion. Schmidt has produced gastric disturbances with the acid of cubebs, increased urinary excretion, with increased excretion of uric acid; burning in the urethra and ardor urinæ. No observer has seen any effects from cubebin.

In the urine the acid exists in the form of salts. The good effect upon the mucous membranes of the urinary passages is supposed to be due to acid of cubebs in the urine.

Therapeutic Application.—Piper cubeba is never used to improve digestion, nor is it any longer used in "catarrh of the bronchi," nervous disturbances, etc. Its only application is in gonorrhœa, and here we would refer to what is said under copaiba. The enormous doses (15.0–20.0) formerly used should not be given. It is contraindicated in the acute stage of the disease, and should never be given where there is a tendency to cerebral hyperæmia, palpitation, etc.

Dosage and Preparations.—1. Cubebæ, in gonorrhœa, 1.0–2.0 grms. several times a day, in bolus, capsule, or powder.

2. Ext. cubebarum æthereum, from 0.3–1.0 (5.0 pro die) in pill or capsule.

Matico Leaves—Folia Matico; leaves of piper augustifolium, one of the cubeb varieties of peppers, contains an ethereal oil, a crystallized acid, resins, and tannic acid—superfluous.

Copaiba Balsam—Balsami Copaivæ; from various copaifera, consists of a terpene oil of copaiva, $C_{10}H_{16}$, having a strong taste and odor, and a resin of unknown composition containing copaivic acid.

Physiological Action.—Copaiba oil has an effect similar to that of oil of turpentine; the resin has a much more irritating action upon the mucous membrane of the digestive canal. Copaiba balsam is disagreeable in its effects, even in small doses, producing frequent belching, and in some people nausea and vomiting; sometimes even diarrhœa. There is increased excretion of a urine smelling of copaiba. Large quantities (5.0–10.0) produce gastro-enteritis and its results. There is vomiting, increased temperature, and headache; also, pain in the region of the kidneys, and increased excretion of urine. It gives rise to the presence of albumen and blood in the urine, and still further cutaneous eruption. It also causes strangury.

Balsam of copaiba is used exclusively for the treatment of gonorrhœa. That it is useful in this condition has been proved by an extensive experience; in some cases it causes the entire disappearance of the discharge. It has been a question of dispute as to when it is best to pre-

scribe this excellent remedy—at the onset of the disease, when the symptoms are still acute, or only in the second stage. Good authorities are on both sides. But the large majority of good practitioners use it only after the acute symptoms have disappeared. If given in the inflammatory stage it might make the affection worse or even cause it to spread to the bladder.

It is most probable that the remedy acts by its direct topical astringent action upon the mucous membrane of the urethra, with which it is brought in contact when dissolved in the urine. In favor of this view, is the fact that in females, where gonorrhœa affects the vagina, the remedy is entirely ineffective, and further the interesting observation of Ricord, that in individuals with hypospadias the portion of the urethra over which the urine passed, was cured while the other part (anterior portion) was unaffected.

Although some physicians treat gonorrhœa by internal medication only, yet the large majority use injections as a necessary element in the treatment. It then becomes a question whether internal medication is a necessity in gonorrhœa. We think it is. There are some cases of old neglected gonorrhœa, which remain unaffected by all injections, and yield to internal medication of copaiba (balsam) and cubebs. For ordinary cases they are unnecessary, especially since they give rise to digestive disturbances; when the above-mentioned eruption make its appearance, they must be suspended. Injections of oil of copaiba are decidedly inferior to internal administration. Experience has shown, that the balsam is superior to the oil or resin.

Dosage and Preparations.—1. Balsam copaivæ from ½–1–2 teaspoonsful 2 to 3 times daily, either pure or with lemon juice, or in gelatine capsules or in mixtures.

2. Acidum copaivicum and natrium copaivicum have recently been more frequently used because less disagreeable in taste than the balsam.

Juniper Berries—Fructus Juniperi, from juniperus communis—contain oil of juniper, a strong spicy oil, consisting of a number of terpenes; also a resin and grape sugar. The physiological effect is similar to that of oil of turpentine. The diuretic effect is especially well known, the urine has the odor of violets after its use. In small quantities it is an agreeable spice, and improves digestion.

Therapeutic Application.—Juniper berries are used only as a diuretic, and even for this purpose seldom alone, but generally in combination with other substances. Generally they are used only as popular remedies, or if medicinally only in addition to other diuretic remedies and methods of cure. Experience teaches that the excretion of urine is increased under its use, but its therapeutic utility, as compared with that of other preparations, is very slight. Juniper berries are everywhere to be avoided, where there is an acute or subacute inflammatory affection of the parenchyma of the kidney, as also in every acute nephritis, especially in that of scarlet fever, in which juniper berries are sadly misused by the people. Its application in hydræmic dropsy is not indispensable, especially since its administration in proper doses spoils the appetite of the patient; the same may be said of its use in dropsy due to valvular diseases; but here other drugs are incomparably more beneficial. It may be given in addition to other remedies in anasarca, and in the course of contracted kidney, or where there is a disturbance in the pulmonary circulation. Besides this, juniper berries, and more especially the wood, are use as disinfectants, and for purifying the air. The first expecta-

tion is not fulfilled, the most that is accomplished is that the air is improved in its odor. In patients who have some affection of the respiratory apparatus, these fumigations should be used with great care.

Dosage and Preparations.—1. Fructus juniperi, generally given as a tea (15.0 to 300.0), with radix levistici, ononidia, etc.

2. Oleum juniperi æthereum (e. fructibus), clear, colorless and soluble in alcohol; from 1 to 4 drops in oil, sugar and spirituous solution. Therapeutically not indispensable.

3. Spir. juniperi, internally from 20 to 50 drops externally as a counter-irritant.

4. Ext. juniperi, succus juniperi inspissatus. Roob juniperi—brownish in color and slightly soluble in water, used mostly as an addition to diuretic mixtures.

Parsley Seed—Semen Petroselini; from the well-known petroselinum sativum—a terpene which readily solidifies, has the odor of parsley, and contains another body known as apiol. The latter has an effect similar to camphor (Homolle) upon the brain, while the former acts like the oil of turpentine. Parsley seed is a popular diuretic remedy, used like juniper. Aqua petroselini—entirely superfluous. Radix Levistici, from levisticum officinale, has a peculiar odor, and disagreeable taste, contains an ethereal oil and a resin, and is used by the people as a diuretic remedy.

Pansy—Herba Violæ Tricoloris; contains like the fragrant pansy, an alkaloid, violin; but the small quantity contained in this plant is scarcely sufficient to impart to it its characteristic effects. Is much used in eruption of the skin, dropsy, etc.

Diaphoretics.

The plants used for this purpose are taken only in hot water and in hot infusion. Since the water passes rapidly into the blood, and thus increases the volume of the latter, and increases the rapidity of the blood current, makes the blood warmer and more watery, it increases not only the sweat, but the urine excreted. The ethereal oils of the plants, as such, as far as we know have no particular effect upon the sudoriparous glands. Besides this, diaphoretic teas contain too little of these oils for them to exert such an effect, even if they were able.

If, therefore, we desire to increase the perspiration, without increasing the urine, we should advise local damp warm cloths applied to the skin, and other similar procedures.

Chamomile—Flores Chamomillæ vulgaris; from matricaria chamomilla, contains a mixture of terpenes and camphor, like ethereal oil, a peculiar blue coloring matter, and small quantities of acid, probably valerianic acid.

The odor and taste are not agreeable to the human palate, so that it may cause vomiting in patients with gastric catarrh, otherwise, the physiological action is similar to that of other odorous plants. Upon frogs the effect is a paralyzing one like that of the oil of terpentine and camphor (Grisar). Chamomile is a very popular domestic remedy—it has the advantage of being a harmless remedy; it is used as a diaphoretic, but it is quite certain that the effect is due to the hot water, rather than to the drug (compare above). It is also given to assist an emetic effect, and we think its importance lies in the fact that it distends the stomach and enables the abdominal wall to act in a proper manner on the stomach.

The tea is also given in attacks of cardialgia and colic, but how much of the effect is due to the drug, and how much to the hot menstruum is uncertain.

Externally chamomile is used as a dressing in sluggish ulcers, contusions, as an addition to clysters and baths, and for herb pillows.

Dosage and Preparations.—Flores chamomillæ, internally, generally as a tea, (10—15 : 150—200,) or a tablespoonful to 3 cups of water.

2. Oleum chamomillæ æthureum s. o. rarely used, very dear.

3. Oleum chamomillæ infusum (loco o. ch. cocti) fatty oil of chamomile; 2 parts of chamomile flowers, 1 of alcohol, and 20 of olive oil, externally.

4. Ext. chamomillæ as a vehicle.

5. Aqua chamomillæ concentrata, also a vehicle. 6. Syrupus chamomillæ.

Roman Chamomile—Flores Chamomillæ Romanæ, from authemis nobilis. In this drug, there is no terpene or aldehyde, but a mixture of various compound ethers, a bitter principle, and various acids. It is principally used in southerly countries.

Melissa leaves—Herba melissæ, from M. officinalis, contains a very agreeably smelling terpene which imparts to it its action. It is a popular perfume, and under the form of spirits of melissa it is a popular remedy, which is used also in the form of a tea, for stomachic and diaphoretic purposes. Preparations.—1. Aqua melissae. 2. Aqua melissae concentrata. 3. Spiritus melissa compositus contains a number of aromatic oils.

Sambucus—flores sambuci, from s. nigra; contains a not unknown ethereal oil, valerianic acid, and resins. Very much used for diaphoretic teas. *Preparations.*—1. Aqua sambuci; 2. Aqua sambuci concentrata.

Lime Flowers.—Flores tiliæ, from our lime trees. When dried they lose the volatile oil which they contained, and have very properly, therefore, gone out of use.

Preparations.—1. Flores tiliæ. 2. Aqua tiliæ. 3. Aqua tiliæ concentrata.

Cowslips.—Flores Primulæ; are sometimes added to diaphoretic teas on account of their agreeable odor.

3. Wood Infusions.—Here we give the woods and other substances belonging to the group of aromatic compounds, which have been used in medicine for a long time, in the form of the so-called wood infusions and extracts for the cure of chronic skin diseases and syphilis, and which have hitherto been considered as diuretic and diaphoretic.

Sarsaparilla Root.—Radix sarsaparillæ; contains very small quantities of an ethereal oil, and an unknown sharp body, which Merk has succeeded in extracting, and also smilacin, $C_{18}H_{30}O_6$, which is obtained by boiling the root in alcohol, and which crystallizes in fine colorless needles, which are insoluble in cold, and with difficulty soluble in hot water, when they form a foaming, bitter, sharp-tasting fluid, readily soluble in alcohol and ether.

Physiological Action.—In spite of the frequent use of this agent, we know little of its physiological action. It is true that it is generally received that it excites the action of the skin and kidneys, so that the excretion of the sweat and urine is increased, but according to Böcker, it is probable that this effect is not due to the sarsaparilla as such, but to the warm water with which it is usually taken. Moderate quantities do not

diminish the appetite, while large quantities cause pressure in the stomach and vomiting.

Schroff's brief observations lead us to characterize the effects of the individual components of sarsaparilla as follows: Merk's substance causes nausea, pain in the region of the stomach, increased salivation, and diminished frequency of the pulse. Smilacin seemed to produce no other effects than a disagreeable taste, increased salivation, and rumbling in the abdomen. The sweat and urine were not increased, but the smilacin could be discovered in the latter. Palotta seems to have experimented with impure smilacin, and the hyperidrosis observed was probably due to the impurities which caused nausea and vomiting, and thus sweating.

Therapy.—Sarsaparilla has long been used an anti-syphilitic drug; it is generally given in combination with other drugs (guaiac, senna, etc.), generally also with large quantities of warm water. It is certain that this remedy often produces good results; we shall presently detail when this may be expected; but we do not know in what way these substances cause syphilis to disappear. Indeed, it is even doubtful whether these substances take any part in the effect. The old view that sarsaparilla exerts a specific action upon syphilis is entirely wrong. It is now received, that the vegetable cures act in this manner: that they increase the excretions, and thus hasten tissue metamorphosis; the result of this is that the syphilitic virus is thus excreted from the system. This view has a great deal in its favor, and the fact that syphilis can even be cured by producing sweating with wet cloths and hot teas, would seem to substantiate it. Indeed, the latter facts would seem to say that the sarsaparilla is an unimportant element in the treatment, most of the good effect being due to the menstruum.

Experience teaches that this method of treatment is no more an exclusive remedy than mercury. We have already stated, under mercury, than even the mercurials should not be used as an exclusive method of treatment in syphilis. There we have also shown that in favorable cases syphilis may run its course without drugs; this natural tendency to cure should be assisted by a methodical treatment which increases all the natural excretions. This is therefore indicated in cases with ordinary secondary symptoms, where there are scrofulous, tuberculous, and scarbutic individuals. In the former mercury is superfluous, in the latter even injurious. It is also much used in cases of chronic syphilis, in which mercury has been used without effect, and in severe secondary and tertiary forms; in the latter it is best given in combination with iodine. This method is entirely superfluous in the primary indurated ulcer, for it rarely prevents the occurrence of secondary symptoms; it is useless in syphilitic diseases of the joints, and inapplicable where a rapid effect is desired (iritis, cerebral symptoms, and laryngeal disease).

We cannot here discuss at length the advantages and disadvantages of a non-mercurial treatment. But we would call attention to a few points. The duration of the treatment, as a rule, is longer than that of the mercurial treatment. That relapses are any less frequent is not true; indeed, on the contrary, they occur earlier and more frequently, although milder at each recurrence. There are cases, however, in which relapses never occur. This treatment seems to have the advantage of never giving rise to the terrible symptoms which sometimes follow the use of mercurials. Tertiary symptoms, however, have been observed in some cases, just as after the ordinary mercurial cures.

Sarsaparilla has also been used in the treatment of chronic skin affections; thus in eczema and psoriasis, especially the form which is accompanied by a destructive process such as lupus; also in lepra. Frequently it is found that in these conditions the remedies are invaluable, and successful after other remedies have failed. Sometimes, however, even these are ineffective. Sarsaparilla has also been used in chronic mercurialism, and also in very old cases of rheumatism.

Dosage and Preparations.—Radix-sarsaparillæ, never given in substance, rarely in simple decotion (30–50–200), but generally in the form of an officinal decoction.

2. Decoctum sarsaparillæ compositum fortius (loco decocti Zittmanni fortioris). 100 parts of rad. sarsaparil. are boiled with 2600 parts of water for twenty-four hours, then add 6 parts each of saccharine albissimum and alumen pulverat., and 4 parts each of fructus anisi, and fructus fœniculi, 24 parts of folia sennæ, and 12 parts of radix glycyrrhizæ. The final residuum ought to amount to about 2500 parts. The off. sarsaparilla decoct. contains no mercury, which was contained in the old Zittmann decoct.

3. Decoctum sarsaparillæ comp. mitius (loco decocti. Zittmanni mitioris). 50 parts of sarsaparilla root are boiled for three hours in 2600 parts of water; toward the end 3 parts each of citron peel, cinnamon rind, cardamon and liquorice wood are added; the resulting liquid should contain about 2500 parts.

The methods according to which the sarsaparilla decoction is used are various, and here we must first remark that if the latter are to be useful, they must be used methodically. The patient must remain in his room, at a temperature 15–18° R. The diet should be just sufficient and no more. The large quantities of the decoction formerly used are apt to be injurious, since they readily produce gastric catarrh and digestive disturbances. It is sufficient if the patient takes 1–2 pounds of the decotion, then undergoes a sweating process for two hours. In the evening another pound of the decoction is taken cold.

In addition to Zittmann's decoction, there are a number of other similar decoctions which contain as their chief ingredient sarsaparilla. Such are Feltz decoct., Pollini's decoct., Laffecteur's syrup, Cuisinier's syrup, etc.

4. Syrupus sarsaparillæ comp. 24 parts of rad. sarsaparil., 16 parts each of lign. guaiaci. lign. sassafras, rhiz. chinæ, 8 parts of cort. chinæ fuscus, 3 parts of fructus anisi, with 250 parts of aqua, and 20 parts of saccharum, prepared as a syrup. Entirely superfluous.

China or Cinchona root. — Rhizoma s. Radix Chinæ (not cinchona bark); also from the genus smilax, and is said to contain a balsam-like resin, many starches as well as smilacin. Never used alone, but always in combination with diuretic teas and anti-syphylitic decoct. Used in eczema chronica. Superfluous.

Sassafras Wood.—Lignum sassafras, from sassafras officinale, contains as active ingredients, an ethereal oil, oleum s. æthereum, composed of a camphor and a terpene; also an indifferent crystalline body, sassafrin and resin. Used like the foregoing.

Guaiac Wood.—Lignum Guaiaci from guaiacum officinale; contains a resin, resina guaiaci, which is obtained from the wood by boiling, and forms a brown, brittle mass, with an agreeable aromatic odor, and burning taste. Not soluble in water, but readily in alcohol. It contains three acids (70 per cent guaiaconic acid, $C_{19}H_{24}O_5$, guiac acid, $C_6H_8O_5$,

which resembles benzoic acid, and guiac resin acid),—as well as a bitter-tasting coloring matter. Ozone, hyperoxide, and nitrous acid turn the resin and its yellow solutions a beautiful blue or green.

Its physiological action is not well known, nor are its components. In repeated doses of 0.5 grm., it is said to have an irritating effect upon the vascular system, and upon the various excretory organs. In large doses it produces inflammatory disturbances in the digestive canal; nausea, vomiting, diarrhœa and palpitation, headache, sleepiness, and general weariness. Nervous and full-blooded persons particularly are said to be especially affected.

What has been said of sarsaparilla in a therapeutic sense, is true of guaiac, which has achieved a reputation through Ulrich v. Hutton.

Dosage and Preparations.—1. Lignum guaiaci in decoction (30.0—50.0: 200.0). 2. Resina g. from 0.2–1.0 in powder, pill, and emulsion. 3. Tinct. resinæ guaiaci, 1 part of r. g., 6 of spir. vin. rectif. Of a greenish-brown color. From 20 to 60 drops. 4. Tinct. guaiaci ammoniata, 3 parts of resin. guaiaci, 10 of spiritus, and five of liq. ammon. caustic.

Radix Ononidis Spinosæ.—Contains no ethereal oil, but only a glucocide ononin, $C_{30}H_{34}O_{13}$, which produces a sharp sensation in the pharynx, but no increase in the excretion of the urine. A very popular remedy in skin diseases and in dropsy.

Species ad decoctum lignorum.—Wood tea. 4 parts of lignum guaiaci, 2 of rad. bardanæ and rad. ononidis, 1 of lignum sassafras and glycyrrhiza. Used as a diuretic under circumstances similar to those in which squill is used. Good digestive powers and healthy kidneys are necessary conditions for its use. ʒ ii. of the tea are cooked in six cups of water, and half of this may be taken in bed in the morning, the other half in the evening cold.

AROMATIC SUBSTANCES USED IN NERVOUS CONDITIONS.

(*a*) From the vegetable world. The plants to be given under this group, also act like the oil of turpentine or the camphors. Their chemical composition is unknown. There is no scientific reason why these plants are used in nervous conditions (hysteria, epilepsy, abdominal pain, etc.). It is peculiar that for nervous conditions the vilest smelling and tasting plants are used. Indeed, the odoriferous assafœtida is used by preference.

Valerian Root.—Radix Valerianæ, from valerian officinalis; its chief constituent is valerian oil; it is a mixture and consists of valerian ($C_{10}H_{18}$ probably) and an oxygenated oil, valerian camphor, $C_{12}H_{20}O$. It has a peculiar odor, and a sharp, spicy taste.

Physiological Action.—Valerian oil, according to Grisar, has an effect similar to that of oil of turpentine upon cold- and warm-blooded animals; it produces a paralyzing effect upon the brain and spinal cord, and can even suspend strychnine convulsions; in men it also produces symptoms similar to those from oil of turpentine; these are headache, dizziness, ringing in the ears, and sleepiness; the root has similar effects. The effect upon the gastrointestinal canal resembles that from oil of turpentine. Valerianic acid does not take part in the nervous effect produced by valerian root.

Therapeutic Application.—Valerian has always been a much-used remedy. Whether it is really useful is another question. We think it could easily be dispensed with without any loss to therapeutics.

Valerian is one of the principal remedies used in daily practice for hysteria, although no physician would assert that hysteria can ever be cured by valerian. On the other hand it is thought to have a favorable effect upon muscular spasm. But this would in no way presuppose a favorable action in hysteria; for it is well known that the most various therapeutic procedures have a temporary effect upon hysteria, but we consider all medicinal (not causal) treatment of hysteria as inactive, and since we have held this opinion, we have always had better results in treatment. Accordingly we doubt that valerian has any specific effect in hysteria.

Valerian has also been much praised in epilepsy. Good observers (e. g., de Hoën, Quarin, Chomel, and others) announce that they have cured several cases by its use; and it is not to be denied that in a few individual cases long intermissions of the paroxysms have been attained under its use. But under what circumstances this good effect may be looked for it is difficult to determine. The older practitioners gave it in the "epilepsy of menstruation," in "worm" epilepsy, or in that sometimes occurring in onanists. We have never used valerian alone in epilepsy, and can therefore express no opinion as to its value.

The administration of valerian as a "stimulating" and "strengthening" agent in the convalescent stage of acute febrile disease, or in "nervous fever" by the older physicians has been proven ineffective. In other conditions its utility is still undemonstrated.

Externally the remedy is used in the form of clysters, especially in hysterical attacks when patients cannot swallow.

Dosage and Preparation.—1. Radix valerianæ, internally, from 0.5 to 1.0 pro dosi; in powder, or best in infusion (10.0 to 15.0 : 150.0 to 200.0.) For clysmata an infusion of 10.0 to 15.0. 2. Oleum valerianæ, from 1 to 4 drops pro dose, as elæosaccharum, or in spirituous solution; best in pill form. 3. Tinct. valerianæ, valerian drops, 1 part of radix valeriana to 5 parts of spiritus vini rectificat; of a brown color; from 20 to 50 drops pure, or as an addition to other mixtures. 4. Tinctura valerianæ ætherea—ethereal valerian drops—1 part of radix valerianæ to 5 of spir. æthereus; when fresh of a yellow color, later it turns brown; from 10 to 30 drops. 5. Ext. valerianæ, entirely superfluous, from 0.2 to 0.5; several times daily.

Radix Angelicæ.—As far as we know its effects are similar to those of valerian root. It contains an ethereal oil with resins and acids (angelica and valerianic acids.)

Therapy.—Same as valerian root. Dose like that of rad. valerian. Preparation: Spiritus angelicæ compositus contains in addition to A. valerian, fruct. juniperi and camphor.

Virginia Snake Root—Radix Serpentariæ, from aristolochia serpentaria; contains an ethereal oil, smells like valerian, has a bitter, spicy taste, and has an effect resembling that of valerian and oil of turpentine.

Radix Artemisia—From Artemisia Vulgaris. Contains an unknown ethereal oil, and is physiologically unknown.

Therapeutically, the drug is used empirically in epilepsy; several observations teach that artemesia diminishes the severity and frequency of the attacks. We think the drug is most beneficial when the epilepsy is in some way connected with disturbances of the genital organs in girls and boys at puberty. But even in these we have seen the remedy inoperative. We give in epilepsy 15.0 grm. pro die in infusion.

Arnica, Flowers and Root—Flores et Radix Arnicæ, from arnica mon-

tana; contains a large number of ethereal oils, tannic acid, and a bitter principle, etc., all of which are not yet thoroughly known.

Physiological Effects of both flowers and root. It is asserted that upon the skin it causes burning and slight redness; in the mouth a like burning sensation; in the stomach a feeling of pain, slight diarrhœa, fullness in the head, dizziness, disturbed sleep, cardiac palpitations, and increase in the perspiration and urine (Jörg.) In very large doses 2.0 (Jörg), 30.0 (Barbier) it is said to cause loss of consciousness, fainting, and convulsions, so that the effect seems to be like that of the oil of turpentine.

Therapeutic Application.—Arnica is quite superfluous. It formerly had an extensive reputation in the torpid forms of typhus and asthenic inflammations of all kinds. But recent investigations do not show any condition in which it is superior to other drugs.

Arnica is very much used as an external application in wounds, contusions, extravasations of blood (and in asthenic inflammations). But our own observations lead us to the conclusion that it can well be dispensed with in these conditions, although it may be used as a slight counter-irritant.

Dosage and Preparation.—1. Flores arnicæ. Here the flowers and leaves are used; from 0.5 to 1.5 pro dose, best given in infusion. Externally it is used in the form of an infusion (15.0 to 20.0 : 200.0.) 2. Tinct. arnica, internally, from 5 to 15 drops, externally, pure, or with water, chamomile tea, and other fluids. Officinally the radix arnicæ is also used.

Assafœtida.—The milky juice from scorodosma assafœtida, which contains 5 per cent of a mixture of ethereal oils containing sulphur and considerable resins (with ferulic acid) and gum.

The odor is sweetish, and very nauseous to noses of Europeans (the Asiatics use it in food as spices). The taste is at first sweetish, then bitter and sharp. According to Trousseau and Semmer both assafœtida and its ethereal oil, even in very large doses, have but slight effects. Eructation of foul gas, and the production of stinking perspiration; and yet one cannot see why this oil in particular should have little effect, and Jörg's experiments show that even in very small doses (1.0 grm.) it causes, for several hours, a burning sensation in the pharynx, pressure and fullness of the stomach, stinking breath, very foul flatus, sometimes diarrhœa, abdominal pain, and a general feeling of discomfort. In large doses (3.0 grm.) it produces, in addition to the above symptoms, vomiting, diarrhœa, fullness in the head, and dizziness. As to any effect upon respiration, circulation, and temperature, nothing has been positively determined. We think it ridiculous to ascribe to the drug any effect upon the male or female sexual desires. The oil is reabsorbed, and reappears in the sweat, saliva, and urine.

Therapeutic Application.—Assafœtida is at present only used in hysteria. As to its utility in this disease we would only refer to what is said under radix valerianæ. In all other conditions the drug is superfluous.

Dosage and Preparations.—1. Assafœtida from 0.05 to 0.5 to 1.0, beginning with small doses in patients whose idiosyncrasy has not been tried. Best given in pill. Emulsions have a vile taste. For clysma from 1.0 to 5.0 with yolk of egg. 2. Aqua assafœtida antihysterica s. Bragensis, contains 12 parts of asafœt., 8 of galbanum, 6 of myrrh, 16 r. valerianæ, 16 rhiz. zedoariæ, 4 of rad. angelicæ, 12 fol. menth. pip., 8 h. serpylli, 8 flor. chamomillæ, 1 castoreum Canadensis with alcohol and water, a mixture worthy of antiquity; dose, ʒi. 3. Tinct. assafœtida

from 20 to 50 drops, pure, or as an addition to mixtures. 4. Emp. fœtidum s. assafœtidæ, 6 of assafœtida, 2 of ammoniæ pulveratum, and 4 each of terebinthina, resina pini, and cera flav. superfluous.

(*b*) Drugs from the animal world, in which on account of the strong odor an ethereal oil has been suspected as being the active therapeutic agent.

These consist of animal secretions and excretions, which necessarily have a bad odor, and cause nausea. Since they are in no way superior as stimulants to the terpenes and camphors, we think they would be much better replaced by the latter.

Moschus—musk is a glandular secretion of the moschus moschiferus, an animal living in Thibet and China. It consists of dark-brown fatty masses, which when dissolved have a penetrating odor and bitter taste. The odorous principle, which is supposed to be the physiologically active one, has not yet been chemically investigated; the remaining components are similar to those found in other secretions (salts, albuminoids, etc.), and take no part in the effect.

Physiological Action.—In addition to disagreeable effects upon the digestive canal, eructation, gastric pressure and vomiting, it has the effect of improving the spirits, and causing in nervous people convulsive muscular movements; the heart's action is also said to be stimulated. This condition however can pass away, leaving headache and drowsiness.

Filehue found the watery extract of the alcoholic extract or the slightly acid watery extract of musk only active. After the injection of 0.05 to 0.1 grm. of musk into the lymph sack of a frog, convulsions of all the muscles of the body followed, which ceased after the motor nerves were cut. Only stronger nerve irritants and the power of the will can prevent these convulsions for a short time. It therefore seems to have an effect similar to guanidin.

Tiedemann found that after injecting 0.3 grm. of musk into the crural vein of a dog the respiration was quickened, although the pulse and temperature were unchanged; then the animal became unconscious, muscular tetanoid spasms set in, there was bloody diarrhœa, and death set in with irregular respiration.

It is hard to determine whether musk passes out with the secretions, such as sweat, urine, etc., because the odor covers everything about the patient

Physiologically, therefore, we see nothing of an especially exciting effect. Since, on the contrary, it seems to produce a depression of the nervous centres very rapidly, we would be disposed to count it among the oil of turpentine group.

Therapeutic Application.—Musk is superfluous. We do not know any condition in which it cannot better be replaced by other drugs, nor do we know any disease in which it cured after other remedies had failed.

Musk has been considered one of our most energetic stimulants, especially when the necessity is to produce a sudden and powerful exciting effect upon the nervous system—less, when such an effect is to be produced upon the heart. It is said to be most effective when the respiratory centre threatens to give out, and there is danger of death; thus it is given in pneumonia, in sudden collapse of typhoid fever, chlorea, acute hemorrhages, disease of the muscle of the heart, etc.

In the first place we would call attention to the fact that the reputation of musk was made at a time when patients threatened with collapse were not treated with champagne, rum, camphor (hypodermically), etc. At

such a time musk may have been indispensable. Then again, in these cases collapse is not due to failure of the respiratory centre; but this is secondary to a weakness of the heart, so that the theoretical indication for the use of musk would not hold good. Finally, we have never seen it proved, that musk was of any utility in cases where other remedies were useless. Indeed, we suspect that grog, champagne, etc., are much more powerful, and have always found that even when musk was given, if the other stimulants did not do good, the patient did not recover from its use alone.

In the other conditions in which musk has been given it is of still less importance. It has been used in various spasmodic affections (cardialgia, [hysterical], globus hystericus, etc.), and such as occur principally in childhood (spasm of the glottis, whooping-cough). Experience, however, teaches that other remedies are cheaper and more effective. Hysterical patients sometimes get an attack when they smell the drug. We must confess, however, that since Wichmann recommended the drug in spasmus glottidis infantum, it has been much used in this malady, and is praised by many practitioners even to-day.

Dosage and Preparations.—1. Moschus—As an excitant the remedy is given in adults not under 0.3, and is increased to 0.5—0.6. Larger doses are unnecessary. In children, from 0.05 to 0.2, according to age. In those one year old, .005 to 0.05; the form is in emulsion or powder, with sugar.

2. Tinct. moschi, of a reddish-brown color: 20 to 50 drops alone or in mixture.

Castoreum.—The præputial secretion of the beaver, when fresh, is of a yellowish brown color, and ointment-like consistency; when dry, a brown, brittle mass, which effervesces with acids, and has a very strong and peculiar odor; that of the Siberian animal is better than that of the Canadian. It contains an unknown ethereal oil, fats, salicin, and phenol; the latter only in very small quantities.

According to Alexander even 6.0 grms. produce no other effect than eructation. Other observers have seen increased frequency of the pulse, warmth of the skin, sweating, dizziness and fullness of the head.

Castoreum has a reputation in the treatment of hysteria. It is certain that it does not cure the disease itself; and as to its effect upon the individual symptoms we would refer to what is said under Valerian. Even less positive is its utility in cardialgia, vomiting, and other conditions.

Dosage and Preparation.—Two varieties of castoreum are officinal. 1. Castoreum Sibericum s. Russsicum s. Europæicum.

2. Castoreum Canadensis s. Anglicum. Only the Siberian should be used; but this is very dear; from 0.1 to 0.5 in powder.

3. Tinctura Castorei Siberici, of a dark-brown color, 5–15–30 drops.

4. Tinct. Castorei Canadensis, 15–30–50 drops.

The following animal secretions have also been used: zibethum; hyraceum; ambra; these are the excrements of various foreign animals, and comment as to their physiological action is unnecessary.

AROMATIC DRUGS USED FOR PLASTERS AND OINTMENTS.

For this purpose only resins can be employed, on account of their adhesiveness to the skin. All others are superfluous.

Pine Resin.—Resina pini Burgundica, pix alba; a resinous exudation

from various pines; a mixture of oil of turpentine with several resin acids (abietin, sylvin, and pimar acids and indifferent resins).

The physiological effect of resin acids and resins is only slight; only in very large doses do they affect the gastro intestinal mucous membrane. The largest portion passes off with the fæces, for only very small quantities can be absorbed. General symptoms cannot therefore be produced.

Resin is used in the preparation of ointments and plasters. It is slightly irritant to the skin, which reddens slightly, and has its sensibility increased. This is more marked in plasters than in ointments, because under them the epidermis softens.

These resinous plasters are used when we wish to produce a slight cutaneous irritation (compare with what was said under tincture of iodine, emp. cantharid., etc.) Used more by the laity than by doctors.

For the preparation of plaster we use oil, wax, talc, and resin; the quantity of the other ingredients varying with the consistency of the resin. Generally the proportions are 1 of resin, 1½ of oil or talc, and 3 of wax.

1. Ung. Resini Pini—Ung. flavum—10 of rhiz. curcumæ 30 each of res. pini and cera flava, 500 of adeps suillus; used as a slightly irritant dressing for sores (popularly known as "althee salve"). 2. Emp. ad fonticulos—3 of res. pini, 1 of sebum, and 36 of emp. lithargyri simplex. 3. Cerat resinæ pini, s. picis—emplast. citrinum, 4 parts of cera flava, 2 parts of resinæ pini, and 1 each of sebum and terebinthina. Resinæ pini occurs in many other and officinal ointments. Colophonium (violin resin), formed by the distillation of turpentine without water; used in medicine only in combination with other substances, as a light hæmostatic powder. Of no particular value.

Galbanum—Mother resin; contains an ethereal oil like oil of turpentine and a mixture of acid and indifferent resins; the latter may cause diarrhœa; therapeutically superfluous. Is a component of several officinal plasters.

Elemi.—West Indian elemi resin; composed of a terpene and an ordinary resin. Entirely superfluous therapeutically. Unguent elemi contains wax, lard, elemi and terebinthina.

Resina Mastich.—Is used as a component of plasters, on account of its agreeable odor.

Resina Dammaræ makes excellent adhesive plasters.

COMPOUNDS OF AROMATIC COMBINATIONS WITH ACIDS, AND ACID ANHYDRIDES OF UNKNOWN CHEMICAL CONSTITUTION.

This group properly follows the foregoing because it also contains many aromatic bodies, and many of the acids or acid anhydrides which exert a large share of the effect are nothing more nor less than aromatic acids. They differ from other aromatic compounds in that they have a distinctly defined and generally local action; this local effect is in some cases due to the acid anhydride. These anhydrides receive the character of acids only after they have absorbed a molecule of water, but many of the acids thus formed no longer have the effect of the anhydride. Buchheim believes that the latter do not only abstract water from the animal body when they are brought in contact with it, but an albuminoid body as well; for otherwise it would be hard to account for the severity of the effect produced by these drugs.

Since we have not sufficient chemical knowledge of these bodies to classify them upon a chemical basis, we have arranged them upon a physiological basis, the physiological effect being well marked and characteristic.

Aromatic Cutaneous Irritants.

To this group belong mustard and cantharides. Both of these exert a severe local, inflammatory, and painful action upon the skin and mucous membranes, as well as general effects upon the animal economy. The latter must be divided under two heads. 1. Those dependent upon the mustard oil, or cantharides itself, their active principles being absorbed, and affect the different organs by being thus brought in contact with them; and 2. Such as are not the direct effect of the mustard, etc., but only the result of the cutaneous irritation and pain produced by these agents.

Every painful nervous excitation and cutaneous irritation produces in a reflex manner a large number of very important functional disturbances. Nor does it make any difference whether these painful impressions are the result of mechanical (pressure, cut, etc.), thermol (severe cold, burning, etc.), electrical (faradization, electric moxæ), or chemical (oil of mustard, cantharides, etc.) agents. All painful irritations have similar effects provided the intensity be the same.

So that although we shall discuss the local effect produced by each agent separately, we shall first consider the general effects of painful impressions, whether produced by fire, electricity, blisters, mustard poultice, etc.

PHYSIOLOGICAL EFFECTS OF PAINFUL CUTANEOUS IRRITATION.

The skin, besides many other functions, is also intended to afford the brain, through its nerves, a communication with the outer world. Here arise impressions of extent, of surfaces, of pain, etc. These when brought to the brain irritate it, and cause it to adopt means and ways for avoiding any injurious effects, etc.; on the other hand, these impressions are also brought to the spinal cord, which, acting as a centre, gives rise to reflex involuntary manifestations in mobility, respiration, temperature, and circulation, all of which also have a purpose. These latter have been well studied and explained by Bezold, Ludwig, Schiff, Heidenhain and Röhrig. The following are the chief facts ascertained by these investigators from experiments upon men and animals:

1. Weak cutaneous irritants of all kinds cause a reflex contraction of many of the peripheral, especially cutaneous, arteries of the body. In consequence of this the blood-pressure rises, and the heart beats more rapidly and forcibly. Furthermore, the respiratory movements become slower. The skin containing less blood, and the lung expiring less air, the amount of heat radiated from the skin, and the warmth given off with the expired air are diminished. In consequence of the increased supply of blood to the inner organs of the body, the oxidation processes in these organs become more energetic, the result is that the internal temperature of the body is elevated. As soon as the slight cutaneous irritation is suspended, then the circulation in the skin is restored, the respiration becomes more fre-

quent, and the deep bodily temperature falls to normal or even slightly below.

2. Severe and very painful cutaneous irritations give rise to effects which may be divided into two stages. In the first stage we find, as from slight irritations, a contraction of peripheral arterioles, increased blood-pressure, and rise in internal temperature. But this stage is only very short in duration. The more severe the irritation, the shorter; indeed, in the case of severe irritants, this stage is so short that for our purposes it may be left entirely out of consideration. In the second stage, which follows very rapidly upon the first, and which, being the lasting one, requires our most careful attention, the opposite condition takes place; dilatation of the peripheral (cutaneous) vessels; whether as a result of paralysis of the contracting vasomotor nerves from over stimulation, or whether, because the dilating vasomotor nerves are only affected by powerful stimulation, is not known. The vessels of the skin become over-filled with blood. The respiratory movements are influenced by strong irritation in a manner similar to that of slight irritants; but the expiration becomes spasmodic in character. In consequence of all this the internal temperature is diminished, while the temperature of the skin is increased, and a larger amount of heat is radiated. The internal temperature would sink even lower were it not that the diminished blood-pressure and the slowing of the heart's action have a somewhat compensatory effect. If the heat-producing function of the body has not been too much injured, the suspension of the cutaneous irritation results in a return of all the functions to the normal.

3. We must not forget that between these two extremes there are many means, and therefore an equal number of variations in the above effects.

4. The results do not always cease with the cessation of the irritant, but may last for a longer or shorter time.

5. In febrile conditions, with elevated internal, and equally elevated external temperature, and high blood pressure, the above effects of cutaneous irritation are not seen, or only very slightly. Indeed, strong irritants may be followed by a lowering of the cutaneous temperature, since the peripheral blood-vessels receive even less blood than before the irritation.

6. Paalzow-Pflüger has shown that in rabbits cutaneous irritation, such as that of mustard poultice, etc., causes an

increase in the amount of oxygen absorbed, and carbonic acid produced, even when no active muscular movements are made. According to Benecke, Röhrig, and Zuntz, slight irritations cause increased excretion of nitrogen, in fact, give rise to increased tissue metamorphosis.

7. Constant pains, such as neuralgia, are diminished or suspended by the production of a new cutaneous pain, by irritation with mustard, blisters, etc. This effect results both when the irritant be applied directly to the painful spot, and when it is applied to distant parts. This effect may be explained by the theory that the irritant causes a derivation of the blood from the deeper parts (painful) to the skin, or that the irritation of the sensitive nerves of the skin is followed by a reflex ischæmia (vascular contraction) of the diseased organ.

8. In very feeble respiration, where there is danger of paralysis of this function, as sometimes happens in chloroform narcosis, strong cutaneous irritants may, in a reflex manner, give rise to deeper inspiratory movements.

THERAPEUTIC APPLICATION OF PAINFUL CUTANEOUS IRRITATION.

In order to prevent repetition we shall discuss in common the therapeutic application of the painful cutaneous irritation produced by the oil of mustard and cantharides. We would here also refer to what was said under caustic alkalies, caustic ammonia, argentum nitricum, and tincture of iodine. Although oil of mustard and cantharides have much in common in their physiological effects as cutaneous irritants, yet a distinction is made in their practical application; this difference depends upon the fact that the irritating effect of the mustard follows much more rapidly than that of cantharides. The mustard is therefore preferred, where the irritating action is desired very rapidly, while where it is more important to have an irritation which will last longer, although it is not produced so quickly, we use cantharides blisters.

The preparations of the oil of mustard generally used as sinapisms are applied where we desire a reflex stimulating effect upon the respiration. Thus in coma, unconsciousness, and in asphyxial conditions. Also when the cutaneous irritant is to be applied to a large extent of surface (mustard baths, etc.); thus mustard is added to foot-baths

to cause a "derivation" of blood to the lower extremities and "draw it away from other organs." In vasomotor neuroses depending upon arterial spasm, we used spirits of mustard and similar preparations to cause a dilatation of the blood-vessels of the skin. In vague, wandering, so-called rheumatic pains, sinapisms are of the greatest utility. The feeling of pressure and anxiety which is often a very troublesome symptom of various diseases of the respiratory and circulating apparatus is often diminished temporarily, at least, by sinapisms. In some cases, mustard or cantharides is used indifferently, the choice resting often upon the circumstance that we wish to avoid if possible the more painful irritation of cantharides. Again, for this latter reason, we often use sinapisms in children, when in adults we would use blisters.

Even more extended is the list of indications for the use of cantharides preparations in the production of cutaneous irritation of a more lasting character. This form of cutaneous irritation is used in inflammation of deep-lying organs, such as pleurisy, pericarditis, meningitis, peritonitis, etc. Most frequently in pleurisy, which we shall therefore discuss most thoroughly. In the stage of acute inflammation with fever, increasing exudation, etc., bloodletting, cold, cataplasms, etc., deserve most attention; although some observers (Gutzeit, J. Meyer, and others) state that even in this stage, vesicants act very favorably; for under their influence not only was the fever diminished but the exudation process was brought to an end. Further experience, however, is necessary as to whether in these cases vesicants possess any advantage in weak and anæmic subjects. We ourselves prefer in such cases dry cupping. Generally in the later stages of pleurisy, vesicants have been applied when the fever has disappeared, in order to hasten the reabsorption of the effusion. Even in this stage, we are not certain of a result, and can only expect it when spontaneous absorption has already begun. We do not think, nor has it been proved, that blisters have the effect of increasing the fever (J. Meyer). Blisters are certainly useful in the pains of the latter stages of the disease; and the same is true of the pains in pleuritis sicca. Indeed the most important application of blisters is the power which they possess of relieving pain in inflammations of serous membranes. The antipyretic effect of such counter-irritation is so slight that we must use other means for accom-

plishing this end. Whether the same may be said of inflammations of other serous membranes as has been said of these is not positive, but such appears to be the case. Recently Mosler praises cutaneous irritants in protracted meningitis. The treatment of acute articular rheumatism by large numbers of blisters, placed in the neighborhood of the affected joints, has been recommended as a mode of treatment by Davies, although Decilly had used it long before, and it had afterward been abandoned. In the subacute and chronic forms of rheumatism blistering plasters are used with favorable results. Cantharides is also used in a number of other conditions with good results; generally in deep inflammatory processes either applied directly over the inflamed part (as in spondylitis chronica) or at some distance from the inflamed spot; (thus in conjunctivitis to the neck or behind the ear). In some cases the blister is kept running by irritating salves. We would warn against the production of such suppurating surfaces in phthisis. It might be permissible to use a temporary blister, but all good observers advise against causing a running sore in these cases.

In the treatment of neuralgias cutaneous irritants play an important part. Valleix thinks that in these cases the vesicants are most useful. It is true that they often diminish the pain, but, on the other hand, it is also true that they are often ineffective. This is the case when the neuralgia is due to malaria, syphilis, or pressure upon the nerves. The utility of the vesicants is best seen in fresh neuralgias due to cold or neuritis. In these cases a cure may result from a few blisters. It is a matter of indifference as to which is the affected nerve (sciatic, trigeminus, etc.). It is best to apply the plasters to the most painful spot (points douloureux, Valleix), and follow one after the other without permitting them to suppurate. In severe cardialgias we often see a diminution of the pain due to the application of a vesicant or sinapism to the epigastrium. We would also add that this has proved useful in severe vomiting, due to a lesion of the stomach or not; but here, also, we are unable to say in advance which cases we may expect to see benefited, and which not. The use of sinapisms in paralysis has been replaced by the galvanic current or faradic brush. The same is true of anæsthesias; there is no form of these, even the peripheral, which is not better treated by electricity.

Cutaneous irritants are also used in other lung affections besides pleurisy. Thus in severe cough, which is the result of a bronchial or laryngo-tracheal catarrh. But these blistering plasters have less influence upon the cough as such than upon the disease process itself. In the febrile stage of these catarrhs blisters are inferior to other remedies (such as cupping, diaphoresis, etc.). They are best used, however, when the patient no longer has fever, and when the secretions become purulent, and the râles coarse. That is, at the end of the first stage.

Blisters are also used in the course of chronic catarrhs, especially when there is a slight subacute exacerbation. Large blisters are also used in the so-called asthmatic attacks of emphysema together with cupping. In nervous asthma chloral and morphine are better remedies. Finally, they are well applied in pulmonary œdema, not such as occurs before death, but that accompanying pneumonia in drunkards; or in broncho-catarrhs of nephritic hydrops. In these cases the blisters must be of some size if they are to have a good effect.

Cutaneous irritants are also used where there is arterial (not passive) hyperæmia; thus they can be placed on the neck in cerebral congestions. But in these cases abstractions of blood are more useful. The results are better when the cutaneous irritant is applied at some distance from the "locus affectus," as we pointed out above. Formerly blisters were also used in typhoid cases with severe cerebral symptoms; also in measles and scarlatina, where severe cerebral symptoms set in simultaneously with the disappearance of the symptoms. We speak of this only for its historic interest.

We would here remark that we should be very careful about giving rise to the formation of large suppurating surfaces in children or aged people. In the former they are apt to cause fever, in the latter they heal badly. They may also remain as persistent ulcers, and in cachetic individuals, or in cases of diphtheria may take on the characters of scrofulous or diphtheritic ulcers.

BLACK MUSTARD SEED.

Semen sinapis nigra; grains about 1 mm. in diam., of an outer dark-brown color, but yellowish from within; comes from brassica nigra, and contains in the fresh, uncrushed state, besides other ingredients, an almost odorless and indifferent oil.

The ethereal allyl, mustard oil ($CH_2.CH.CH_2.N.C.S.$) does not exist

in the seed pre-formed, but is only formed in the mouth upon contact with the water of the saliva, or the water of a poultice; an albuminoid ferment, myrosin, splits up the potassium myronate, $C_{10}H_{19}KNS_2O_{10}$, contained in the seed, into sugar, acid potassium sulphate, and allyl mustard oil, the latter of which gives to mustard seed its sharp taste and odor.

The allyl mustard oil thus obtained can be reformed by fractional distillation. It can be prepared artificially, however, by the decomposition of allyl or bromine iodide, with an alkaline solution of potassium sulphocyanide. It is a colorless and insoluble fluid, miscible with alcohol and boiling at 150°.

Physiological Action.—Mustard and its preparations owe their chief effect to the allyl oil of mustard. It has been most accurately studied.

Effect upon the Skin.—A few minutes after the application of a mustard poultice or painting with the oil of mustard, it is followed by a sharp, prickling, burning pain of the skin, at first punctiform, then affecting the whole surface as far as the oil has been applied; the pain finally becomes so great that it is only with the greatest fortitude that it can be borne. At the same time the affected portion of the skin becomes intensely congested and hot, although there is no swelling; after hours of such action, small and finally large blisters occur, which often leave behind ulcers that heal with difficulty. The more delicate the skin the more intense are the above-described effects. After the mustard poultice has been taken away the pain and redness cease in a few hours, or last for some days.

In spite of the severity of the pains caused by mustard, there is analgesia for other kinds of pain: after these pains have ceased there is still anæsthesia to touch, temperature, and pain. In some cases increased sensibility is noted. In the neighborhood of the part where the mustard has been applied there is usually diminution of sensibility. All this is probably the result of the paralysis following upon the irritation of the sensitive nerves of the skin.

The cause of the vascular dilatation is probably to be sought in the direct action of the oil upon the vascular nerves; that of the pain in the irritation of sensitive nerves by the oil. The fact that redness is just confined to the surface covered by the plaster proves that the effect is not a reflex but a direct one. A reddish discoloration remains long after the mustard has ceased to act. This is probably then due to vascular (red blood corpuscles) extravasation. The general effects resulting from these painful irritations of the nerves have been spoken of in the beginning of this chapter.

Local Effect upon the Mucous Membranes.—Oil of mustard causes pain when inhaled or taken internally by irritating the trigeminus branches. In addition it gives rise to burning pain in the tongue, and a sensation of warmth and burning in the pharynx, in the œsophagus, and in the stomach. The taking of small doses for a short time improves the appetite, but when these are long continued it interferes with the appetite. Large doses cause severe gastrointestinal inflammation, abdominal pain, vomiting, and sometimes purging. But in some way the intensely irritant effect of mustard upon the skin is not seen upon the stomach; for here only very large quantities would produce an effect similar in any manner upon the mucous membrane.

General Effects of Mustard Oil.—That is, those due to the absorption of the oil into the circulation (and not as a reflex result of local irritation), have only been slightly investigated. According to Mitscherlich the gen-

eral effects of mustard-oil poisoning in rabbits are similar to those produced by hydrocyanic acid, only less in severity, and taking a longer time for their production. The symptomatology is complicated by the gastritis which ensues.

Rabbits die of from 3.5 grm. doses in two hours; from 15.0 grm. doses in fifteen minutes, the following symptoms being produced: increased frequency of the heart's action, with a rapid diminution in sensibility; weariness; diminution in the force of the heart's action; difficult respiration; the animals lie upon the abdomen; repeated convulsions occur; there is slow respiration; diminution in the warmth of the external parts and death (Mitscherlich). According to Köhler, there is at first an increase, and later a paralysis of reflex irritability.

After death the stomach and intestines were found somewhat hyperæmic, and denuded of their epithelium; kidneys were hyperæmic. The irritability of the heart and muscles lasted a long time. The mustard-oil odor was easily recognizable in the blood, as well as during life, in the expired air. The urine, on the other hand, had an odor similar to that of horse-radish. (Mitscherlich).

Concerning the main effects of the allyl mustard oil, we only know that when it is mixed with albumen the latter can no longer be coagulated (Buchheim), and that it retards lactic and alcoholic fermentations, and ammoniacal and putrid decomposition (Köhler).

Therapeutic Application.—The external application has already been spoken of.

Internally mustard is used to improve the appetite and digestion, as a condiment with meats. It should not be given in cases of gastric catarrh, and if used in too large quantities is apt to do harm by disturbing digestion. All other conditions in which mustard is used we shall not speak of, since it does not seem to be of much utility. Thus, it has been given in hypochondriasis, especially that accompanied by dizziness and muscæ volitantes; also in asthmatic difficulties. In poisoning with narcotic substances, however, such as opium or belladonna, we should advise its use when vomiting cannot be produced by other substances, and a stomach pump is not at hand. But in these cases apomorphine injections are certainly more useful.

Dosage and Preparations.—Semen sinapis—mustard seed. As an emetic in powder or infusion, 15.0 grm. doses.

Externally the remedy is used in the form of mustard poultice; fresh mustard better than old; it is mixed with a little luke-warm water into a thick paste. Ammoniac is unnecessary.

For a foot or hand bath we take from 50 to 100 grms. of fresh mustard flour, and add it just before the bath to 150 to 250 grms. of water. As an addition to clysters an infusion of 10–20 : 50–100 is used.

3. Oleum sinapis æthereum is entirely superfluous for internal use; externally used as a cutaneous irritant. For this purpose it is rubbed on the affected part, or the part is covered with filtering paper, and the drug dropped upon it.

4. Spiritus sinapis: 1 part of ol. sinapis to 50 of the spirit. This is the form in which to use mustard oil as a cutaneous irritant.

The treatment of mustard oil poisoning is accomplished in a manner similar to that of cantharides poisoning.

BUTYL MUSTARD OIL AND HERBA COCHLEARIÆ.

Butyl mustard oil ($CS.N.C_4H_9$) is the active ingredient of cochlearia

officinalis, and is produced, like allyl mustard oil, by the action of a ferment.

The plant contains quite an amount of alkaline salts.

The plant is said to have a similar but weaker action than the foregoing preparation. More accurate observations are, however, wanting.

It was formerly much used in digestive disturbances, hydrops, etc., but is now no longer used. It is no longer supposed to have a specific action upon scurvy; this reputation was obtained from the fact that it was often the only vegetable obtainable in long sea voyages to the north.

Dosage undetermined.

Spiritus cochleariæ is sometimes used as a mouth wash in various, especially scorbutic, affections of the mouth. Entirely superfluous.

DIALLYL SULPHIDE AND GARLIC.

Radix Allii Sativi, the diallyl sulphide ($CH_2.CH.CH_2.S.CH_2.CH.CH_3$) is the chief constituent of oil obtained by distilling garlic with water, and can be artificially prepared by decomposing allyl iodide with potassium sulphide in alcoholic solution. The oil is colorless, and of an unknown, disagreeable odor and sharp taste.

Diallyl sulphide as well as garlic has an effect similar to that of mustard upon the skin and mucous membrane. In small doses it improves the appetite; in large doses it causes nausea, vomiting, abdominal pain and diarrhœa.

Therapeutically garlic is not used; used more in the kitchen in a manner analogous to mustard. Externally it is used as an injection against the oxyuris vermicularis (5.0 to 10.0 for an injection). Onions have a composition and effect similar to that of mustard and allyl mustard oil; these are the radix s. bulbus cepæ of allium cepa; radish—radix armoracæ—also belongs to this group.

BLISTERS.

Spanish flies—Cantharides.—Cantharides are insects about three centimetres long, of a golden green color (Lytta vesicatoria); their active ingredient, which is destroyed by moisture, is cantharadin ($C_{16}H_{12}O_4$). This can be extracted from the insects by alcohol, ether, or chloroform, together with a greenish oil.

Cantharidin appears in colorless, many-sided prisms, readily soluble in water and cold alcohol; less so in hot alcohol and ether. Concerning the nature of the other ingredients of cantharides, especially of a volatile body which distills over at 100°, and which acts like cantharidin (Dragendorff) little is known.

Cantharidin is found in many other of the insects, such as meloe, mylabris, and these have an action similar to that of cantharades.

Physiological Action.—Since cantharidin is the effective agent of the insects, we shall speak only of its action. The assertion of Schroff that only the whole insect, and not the cantharidin, produces increased sexual desire, needs further confirmation.

Local Effects upon the Skin.—Pure cantharidin, even in quantities of 0.0005 grm., causes a blistering of the skin in fifteen to twenty minutes, while cantharides plasters require as long as five to ten hours to produce the same effect. The effect is even more rapid when oils, etc., are used as solvents for the cantharidin. The order of the symptoms is as follows: A few hours after the cantharides plaster is laid upon the unbroken skin,

there occurs a burning sensation, redness and increased warmth of the affected part. Soon small blisters appear, which gradually run together to form large blisters. Finally the whole of the epidermis, as far as the plaster extends, is raised up in the form of a blister. The serum contained in this is yellow in color, has an alkaline reaction, and contains the cantharidin. For this reason this serum will also cause an inflammation in other parts of the skin. Finally the blister bursts and the dermis is seen underneath; soon the secretion dries over this, and under it a new epidermis is formed. If the plaster be allowed to lie, however, after the blister has burst, the dermis begins to ulcerate, and in weak, strumous individuals these ulcers may take on an unhealthy action.

If in rabbits for four days one and the same portion of the skin be repeatedly painted with cantharidin collodion, we find first, the above-mentioned alteration of the skin; finally the blood vessels in the affected portions of the skin become filled and dilated; so also those of the superficial muscles; on the other hand, the fat disappears, and the deeper lying portions, such as the muscles, inner surface of the chest wall, as well as the affected portions of the lung, become more anæmic than upon the corresponding opposite side (Zülzer).

The inflammation, blistering, and pain in the skin are probably due to an affection of the skin and vascular nerves produced by the cantharidin.

It is uncertain whether cantharidin causes an abstraction of water from the tissues, or a change in the albuminoid bodies.

Its internal administration causes a powerful effect upon the mucous membranes of the digestive canal. Small, greatly dilated doses cause a disagreeable burning taste, a sensation of warmth in the mouth pharynx and stomach, nausea and loss of appetite. Large doses increase the sensation of heat and burning in all of the above-named portions; there is salivation and swelling of the salivary glands. There is great abdominal pain, with passage of blood masses by diarrhœa; there is also bloody vomiting. In extreme cases of poisoning, the drinking of water even is impossible, and we often have the symptoms of hydrophobia and atropia poisoning.

General Effects.—Here we shall consider only those alterations which are dependent upon the cantharidin that has been absorbed. Absorption can take place through the mucous membranes, as well as the inflamed and ulcerated skin; for this reason after the application of cantharides blisters, the general effects of cantharidin poisoning occur, just as after cantharidin poisoning from the internal administration of cantharides. Of the various animals the cold-blooded ones as well as chickens and leeches are least affected. The other warm-blooded animals however (such as rabbits, cats, dogs and men) are very strongly affected. It is not true that after the administration of cantharides dogs suffer less than men. The most that can be said is that in the former somewhat larger doses must be given. The fatal dose of pulverized cantharides for rabbits is 0.05 grm.; for dogs, 0.5 grm.; for men, 2.0 grms. (Orfila, Schroff). The dose of cantharidin is, of course, one hundred times less.

The urinary organs are most affected by cantharides, which is due to the fact that cantharides is excreted from the body through the kidneys, and thus produces in all the urinary passages an inflammatory action, similar to that caused by its direct application to the skin and mucous membranes.

Since the symptoms observed in man are exactly like those observed in the dog, and since the latter have been more thoroughly studied by

Langhans and Schachowa, we shall communicate the results of the latter observers.

Very small doses (0.06 grm.) of cantharides powder given internally, were regularly followed by a cystitis, with hyperæmia and ecchymosis of the mucous membrane of the bladder, as well as great injection of the kidneys, but no other lesion (anatomical) was observed. In men under these circumstances, strangury, tickling in the urethra, and a burning sensation in the region of the bladder and kidneys occur.

Large doses (1.0 grm. almost daily for six weeks) were observed by Schachowa, even on the 3d day, to cause the appearance of many blood corpuscles and mucus in the urine, and in the evening of the same day considerable quantities of albumen appeared. On the 5th day, quantities of bacteria began to appear in the urine, and these persisted in the urine until death; the urine was always examined immediately after it had been passed. On the 8th day a diminution in the quantity of the urine was observed; this appeared due to a suppression of urine rather than a concentration. On the 17th day the urine was reddish and contained red blood corpuscles and triple phosphates, and had an alkaline reaction. On the 18th day changes in the urine, due to a change in the kidney structure, began to appear. There was an increase in the amount of fat. All of these alterations in the urine set in gradually, one after the other, but remained until death, with the exception of the albumen which appeared on the 3d day, and then did not reappear.

Schachowa could follow the various stages of a parenchymatous nephritis in the kidneys of the animals upon which he experimented. The epethelium of the uriniferous tubules appeared as cylinders, and as fatty casts in the urine; the capillaries of the glomeruli, as well as the capillary network proper, and the membrana propria were normal, at most slightly thickened, owing to their saturation with serum.

When only small quantities of cantharidin are contained in the blood they are excreted by the lower part of the looped uriniferous tubules; when larger quantities, the whole extent of the tubes is affected.

In men strangury is common with diminished excretion sometimes amounting even to complete anuria. The pathological changes in the urine and kidneys are similar to those in dogs.

Generative Organs.—It is possible that small quantities of cantharides do produce a tickling sensation in the penis, erection of the organ, and a greater desire for sexual congress; but it is not true that sexual power is thereby increased. Larger doses, according to impartial observers (Pallé), only cause pain and swelling of the generative organs, owing to the local irritation, painful erections, strangury, and other symptoms, which certainly do not encourage sexual congress. In women it is said that hemorrhage from the genital organs sometimes occurs under the influence of the drug and hence it has been used as an abortive agent.

Nervous System.—Is only influenced by very large doses. Smaller doses only produce the above described local effects upon the skin and mucous membranes, and the activity of the generative and urinary organs (Schroff and Henrich).

Large doses produce headache, increased rapidity of respiration, and heart's action and formication; later on stupidity, dyspnœa, and finally paralysis of respiration (paralysis of the respiratory centre in the cord) while the circulation continues. Soon carbonic acid poisoning sets in and hence convulsions and death (Radecki). The temperature is increased owing to the febrile inflammation of the urinary passages.

Cantharidin is an acid which remains in the body for a long time, even after death. Dragendorff obtained it from the body of a cat 84 days after death; Dragendorff killed a cat, with all the symptoms of cantharides poisoning, by feeding her on the flesh of hens killed by cantharides.

Therapeutic Application.—Its internal use is not only of no utility, but very injurious on account of the inflammatory irritation it produces.

Externally it is very much used in the form of blisters, the indications for the use of which have been given above.

Dosage and Preparations.—1. Cantharides pulveratæ internally from 0.01 to 0.05 (ad 0.05 ! pro dosi, ad 0.15 ! pro die) in powder, pill, or with opium in order to diminish the irritant effects of the cantharides. Externally it has been used as a powder upon chronic indolent ulcers, but its use is impracticable.

2. Tinctura cantharidum, 1 of cantharides to 10 of spir. vin. rectifi. yellowish-brown, internally from 2–10 drops (ad 0.5 ! pro dosi, ad 1.5 ! pro die,) in some mucilaginous vehicle. Externally as an irritant component of liniments and for "hair restoring" pomades.

3. Emplastrum cantharidum ordinarium. Ordinary blistering plaster, 2 parts of C., 1 of olive oil, 4 of yellow wax, and 1 of oil of turpentine—dark green. The plaster does not stick, and hence it must be bound on by a bandage. It should be left on until it reddens the skin (in 2–4 hours); sometimes blisters form in this time, but generally it takes from 8 to 10 hours for this purpose. If the blister is not to run, open it and dress with simple salve; if we desire it to keep on running, it should be dressed with an irritating ointment.

4. Emp. cantharidum (vesicatorium) perpetuum, permanent blistering plaster, 50 parts each of colophonium and cera flava, 37 of turpentine, 25 of resin pini, 20 of sebum, 18 of cantharides, 6 of euphorbium; does not stick. As a rule, only produces redness of the skin, and for this reason is only used when we wish a cutaneous counter-irritant effect to last for a long time.

5. Unguentum cantharidum, ung. irritans; irritating salve, 1 part C., 4 of olive oil, and 2 of wax, is of a dark green. Used as an irritating ointment.

6. Ung. acre—contains wax, sebum, cantharides, colophonium, turpentine, and euphorbium.

7. Collodium cantharidatum; collodion which contains cantharides. Used as a convenient blistering agent.

Treatment of Cantharides Poisoning.—Large doses are generally followed by vomiting and diarrhœa. If this is not the case, we must give an emetic; best of all is a subcutaneous apomorphine injection. Also give mucilaginous drinks. Oleosa should *not* be given, for they are solvents for cantharides. The gastroenteritis, collapse and nephritis must be treated on general principles.

Mezereum—Cortex Mezerei—from daphne mezereum, contains as its active ingredient a resin, which, similar to cantharides, must be considered the anhydride of an acid (Buchheim). The fatty oil occurring in the bark owes its power to its containing this acid anhydride. Daphnin, a glucocide, has not yet been studied.

Upon the skin, as well as internally upon the digestive and urinary canals, this drug acts in a manner similar to but much weaker than cantharides. It has not been proved that the drug possesses any advantage over others. The laity use it very much. This drug would be best

stricken from the list. It was formerly used as an irritating local agent (by chewing) to the tongue, in the paralysis of that organ; of course, without effect.

Dosage and Preparation—1. Certix mezerei; internally superfluous; for external use the fresh bark (deprived of its outer layer) is steeped in vinegar or water, and bound upon the portion of the skin to be irritated. If a long-continued effect is desired, the rind may be renewed every 12 hours at first, later on every 24 to 48 hours.

2. Extract mezerei spiritosum, s. æthereum, of a greenish color, not soluble in water.

3. Ung. mezerei, 1 part ext. mezerei and 9 parts of ung. cereum; externally generally as an irritant salve.

4. Emplast. mezerei cantharidatum—Druot's plaster—30 parts of cantharides, 10 of C. mezerei, 100 of acetic ether, 4 of sandaraca, 2 each of elemi and colophonium, 20 of colla piscium, then distilled water and spirits. Used as a blistering plaster.

Cardol—Cardoleum.—Cardol is the blistering agent from the nut-like fruit of anacardium occidentale and semecarpus anacardium, which is generally found in commerce, mixed with cardoleum pruriens and cardoleum vesicans. Pure cardol is a yellowish, odorless mass, not soluble in water, but soluble in alcohol and having the following composition: $C_{21}H_{28}O_2$. Internally and externally it has effects similar to that of cantharides, but in drawing a blister it is said to cause less pain, while it keeps the blistered surface suppurating for a long time (Bartels).

Cardol has hitherto been little used in practice. The advantages which Bartels and Frerichs claim for it are said to be overbalanced by the very severe local effect which it produces. It is only used externally, for local purposes, like cantharides. It is applied to the affected portion of the skin with a brush.

To this group belong the resins of various kinds of euphorbia. They are much weaker in their action than any of the above.

CATHARTIC AROMATIC DRUGS.

To this group belong all of the vegetable cathartics which have been used for a long time, and in which the active ingredient is an acid such as is found in senna; this is a glucocide cathartic acid. In jalap root, the anhydride resinous acid, convolvulin, jalapin, and elaterin; two glucocides, which resemble rheinic acid, and which are probably aromatic bodies, aloin (aloëtin), and colocynthin, and finally castor oil and croton oil acids. All of these acids which have an unknown chemical constitution exert a cathartic effect, owing to their exciting action upon intestinal peristalsis.

The pure acids are never used, although all have been chemically isolated, but always in the natural form in which they occur; here they are mixed with numberless

other ingredients. These natural drugs, then, must receive thorough consideration at our hands.

The older classification into eccoprotica (purgativa, laxantia) and drastica, as well as the classification of Radziejewski into mild and strong, or that of Köhler, according to their solubilty in various fluids, have been proved to be more or less untenable by recent investigations.

GENERAL PHYSIOLOGICAL CONSIDERATION.

1. Concerning the cause of the cathartic action.

According to the present somewhat limited investigations of Liebig, Buchheim, Thiry, Radziejewski, H. Koehler, Moreau, and Lauder-Brunton, we can lay down the following reasons as the cause of the increased quantity and more fluid condition of the fæces, and the more rapid peristalsis which result from the cathartic salts.

The increased strength and rapidity of the peristaltic intestinal movements is probably the chief cause.

Radziejewski made intestinal fistulæ in the ascending colon, in order to compare the intestinal peristalsis as it occurs in the normal condition, as compared with its occurrence in the same animal under the influence of cathartics. He found that in animals in whom no cathartic had been given, the action of the colon began 1½–2½ hours after the first introduction of the food; so that in this time the peristaltic movements have extended from the stomach to the colon. These peristaltic movements last for a half hour, with intervals of five minutes. Later on the intervals become longer, and after six hours the intervals are several hours in length. If strong cathartics were given, the discharge from the fistula set in more quickly, and more often. Radziejewski also found that after a meat diet, in carnivora, where the passages set in quite rapidly in dogs with colon fistula, similar dogs, who had no fistula and no cathartics, had no action from the bowels for three to five days. So that in the normal condition there is a great slowing up of the peristaltic movements in the colon and rectum, while under the use of cathartics, there is even a passage of fæces from the anus in a few hours. Thus it has been positively shown that cathartics hasten the peristalsis in both the small and large intestines, but that the increased and more rapid fæcal evacuations are probably due to increased peristalsis of the large intestine.

It was not determined whether cathartics cause a transudation into the intestinal capillaries, and into the intestine, thus accounting for the fluidity of the fæces when cathartics have been taken. Formerly this was taken as such a matter of course, that no one sought for a proof. It was, therefore, much to the astonishment of all when direct investigation showed that such was not the case. Thiry severed a portion of intestine from the rest of the canal, without disturbing the nervous or vascular supply of this portion. One end was allowed to remain in, sewed up in the abdominal cavity, the other end was fastened to an opening in the abdominal wall. Into this portion of the intestinal canal, both he and Radziejewski and Schiff introduced croton oil, senna, aloes, jalap, and magnes-sulphate and sodium-sulphate, and found that none of these caused a transudation into the intestinal canal, or increased secretion of the normal intestinal juices. Moreau and Lauder-Brunton, however, assert that they did notice such an increase. Moreau saw an increase in the intestinal fluid follow the cutting of the mesenteric nerve supplying the affected portion of the intestine; he was unable, however, to determine whether the fluid was serum or normal intestinal juice. It might be supposed that the stronger cathartics paralyze the same nerves which Moreau cut in his experiments, and thus cause an increase in the fluid of the intestine. Radziejewski repeated Moreau's experiments, and confirmed them; but, on trying croton oil, he came to the conclusion that the watery constitution of diarrhæal stools is not due to transudation or hypersecretion.

Even the analysis of the fæces gave no positive proof, for there did not seem to be any characteristic or decided points of difference between the composition of normal and diarrhœal passages. Normal fæces (flesh) in dogs have an acid reaction, and contain cholesterine, cholalic acid, fat, soaps, indol, and albumen, with properties resembling those of peptone; perhaps, also, leucin, taurin and mucus. The average quantity of water is about 52 per cent, that of ashes on an average 11.9 per cent; that of the potassium is much larger than that of sodium (probably because the diet is richer in potassium). Normal human fæces are also richer in potassium (Fleitmann). Diarrhœal fæces do not differ much from the normal, except that they contain more water (after Epsom salts, 85 per cent), and more sodium than potassium salts. There is seldom any bile in the

fæces, except after calomel—never after senna or Epsom salts. After the use of the latter agents, almost all components which point to some action upon the upper intestinal canal (duodenum) were wanting; while, after calomel, the products of pancreatic digestion, leucin, tyrosin, and peptone, were entirely wanting. Vegetable cathartics gave rise to the presence of a saccharifying ferment; after senna even a peptonizing ferment could be seen. Peptone, leucin, and tyrosin were found even after vegetable cathartics; after castor and croton oil, undigested food materials, such as meat, could be found.

From his many experiments, therefore, Radziejewski concluded that cathartics do not cause increased transudation and secretion, but that the absorption of the normal intestinal fluid is prevented on account of the increased rapidity of intestinal peristalsis. Diarrhœal stools are therefore nothing more nor less than the unchanged contents of the small intestine, and it is proper to consider the matter in this light, namely, that when a mass consisting of fluid and solid portions is rapidly propelled through a long tube of uneven surface, the fluid portion will come out first, while the more solid portions remain in the intestine for a longer time and fastened to the intestinal mucous membrane. In this way, we can account for the fact that even the strongest cathartics do not often bring out with the fæces undigested food substances. The quantity of the fluid cannot be taken as a proof that transudation does take place, for according to Kühne the normal juices secreted by the pancreas and intestine would yield a larger volume of fluid than is passed out in the most profuse diarrhœa. It is because these juices are rich in sodium, that diarrhœal passages have also a predominating quantity of sodium salts. It is true, however, that after diarrhœal passages the blood loses in the amount of water and salts which it contains, but this can just as well be explained by the failure to absorb water and salts from the intestines as by the supposition that these constituents are lost by transudation.

Brieger's recent investigations upon isolated loops of small intestines give the following results: 1. The introduction of 20 per cent solutions of Epsom salts into the loop, was followed in several hours by the filling of the cavity of the loop of intestine with a light yellow, alkaline fluid containing strings of mucus, intestinal epithelium

and undried corpuscles, but no red blood globules; the mucous membrane had retained its normal paleness, so that the cathartic salts would appear to abstract water from the wall of the intestine, when they remain in contact with it for some time; they also stimulate the intestinal glands to increased activity. 2. After the injection of calomel, senna, rhubarb, aloes, and castor oil, the intestine remained empty, and firmly contracted, while the mucous membrane was not congested, so that Brieger, like Radziejewski, believes that the cathartic effect of these salts depends upon the increased peristalsis which they produce. 3. After the injection of croton oil and coloquinten extract, the fluid collected in the intestine was bloody and after the latter cathartic the mucous membrane became strongly diphtheritic. Brieger therefore asserts that the latter acts like group 2 in small doses, while in large doses it produces an inflammatory exudation and hypersecretion.

Increased intestinal peristalsis can be caused by the cathartics in various manners. Every localized irritation of the intestinal nerves causes a reflex irritation of the sympathetic intestinal ganglia, and as a result increased peristalsis (Traube). When croton oil is given internally, diarrhœa is produced even when the croton oil is still in the stomach (Radziejewski), and if both vagi be cut, croton oil no longer acts as a cathartic (Wood). Some of the cathartic drugs therefore do not act locally but through the vagus nerves, in a reflex manner. Other cathartics (jalapæ elaterium, etc.) can only act after having come in contact with the bile, and after having been dissolved by the latter, (Buchheim, H. Köhler); in these therefore the increased peristalsis of the intestine is probably due to a direct irritation of the intestinal wall and its ganglia. Since in isolated loops of the intestine the local irritation also passes from ganglia to ganglia, it is scarcely necessary to conceive here a reflex action of the intestinal ganglia, although we have no proof to the contrary.

The colicky pains produced by laxatives are probably due to a spasmodic contraction of the intestine; this is for many reasons more probable, than the idea that abdominal pain is due to direct irritation of the sensitive nerves of the intestine, or is the consequence of a catarrhal inflammation of the intestinal mucous membrane, for croton oil and other cathartics cause pain before they have reached the intestine, and before, therefore, the sensitive nerves could

have been irritated or the intestinal mucous membrane inflamed.

2. Further effects of cathartics upon other parts of the body are as follows: The stronger cathartics cause loss of appetite and digestion, although it is uncertain whether this is in consequence of a diminution in the amount of gastric juice secreted or an alteration in digestion.

As above stated, the blood becomes poorer in water and salts, in consequence of which it withdraws any water that may be present in the tissues and cavities of the body. The general symptoms resulting from cathartics such as weakness, etc., may be due to the changes produced in the blood.

The long continued use of cathartics was followed by a condition similar to that produced by hunger; there was a dimunition in the fatty deposit of the body; the albuminoid tissues however are unaltered by the cathartic salts (Voit.)

Several vegetable cathartics are also said to have an effect upon the nervous centres after they have been absorbed. We shall say more concerning this point, under the respective cathartics.

THERAPEUTIC APPLICATION.

Here we shall give the circumstances and conditions in which the drastic purgatives are to be preferred to the ordinary cathartics.

First, in certain forms of constipation; thus in so-called habitual constipation, when it is due to deficient peristalsis of the intestines (large); generally caused by the habit of keeping the stool in the rectum, and thus blunting the irritability of the large intestine; also when, although the normal intestinal peristalsis is present, the muscular contractions are not strong enough to propel the contents of the gut downward. In these cases we should prefer, in addition to regulating the diet and using massage, giving those cathartics that have a special irritating action upon the large intestine; such are irritant enemata, aloes and colocynth. Here the methodical use of saline cathartics is just as useful, but the latter have the disadvantage of readily interfering with digestion when taken as a daily laxative.

A further application of the very strong cathartics (croton oil) is when the constipation is due to a contraction of the lumen of the intestinal canal; (such as is caused by internal and external hernia, intussusception, organic clos-

ure by new growths, etc., etc.). But this method of treatment requires great care; often it cannot be used on account of a doubtful diagnosis; often because of vomiting. It should be avoided when the obstruction has lasted some time, and strong peristaltic movements are apt to tear the gut.

Indeed, experienced physicians have even prohibited the use of these cathartics in ileus, intussusception, etc., first, because their utility has not been proved in the former disease, while there is liability of the intussusception being increased by their use. We can also add that for many years we have acted in a similar manner, and have had no more evil results than when we did use croton oil, etc.

Drastics are used with excellent results when the constipation is due to large collections of hard fæces in the bowel. The constipation which accompanies chronic diseases of the cord and brain, is well treated by drastics, while croton oil especially has gained a great reputation in the treatment of the constipation of chronic lead poisoning.

Certain forms of diarrhœa, such as those accompanying acute intestinal catarrh which are due to and kept up by abnormal ingesta, are sometimes treated at first by purgatives; for this purpose we should use castor oil, rhubarb, or calomel and the salines.

The drastic purgatives are very much used in the treatment of inflammatory affections, or simple congestive conditions of certain organs. Here they answer many indications: first, like the salines, they prevent (by more rapid peristalsis) the absorption of certain assimilable materials and secretion products, thus exerting an anti-inflammatory action. Secondly, they diminish the blood pressure by diminishing the water of the blood (see above), and finally they exert an effect similar to that of the epispastics upon the skin, namely, a counter-irritant action exerted upon the intestine. They are thus used in inflammatory affections, especially of the brain and spinal cord, when there is constipation which can only be relieved by these cathartics. They are also used in congestions and hemorrhages of the brain. The milder drastics—e. g., senna—are given in the earlier stages of acute nephritis, and also in the phlegmonous, (parenchymatous) puerperal peritonitis, as the experience of recent times has taught, in order to produce a thorough evacuation. In the inflammatory affections of the respiratory organs, we can generally succeed with the saline remedies, and calomel and castor oil.

Drastics are often given in combination with the cathartic salts in order to withdraw fluids from the body. Thus in dropsies, when the kidneys do not excrete the water at all, or in insufficient quantities; in these cases, however, diaphoresis is much more effective. Also when we wish to reduce an abnormally high pressure in the vascular system in chronic nephritis with uræmic symptoms and their consequences; also in acute inflammatory effusions. In all these cases, as we have shown above, the drugs act by causing increased peristalsis and thus preventing the absorption of intestinal fluids; as a result of which, the abnormal collections of fluids are absorbed in order to supply the necessary fluidity to the blood.

Drastics are used in all other cases wherever an energetic laxative is necessary; also in the purgative treatment of lues veneri, etc.

Experience has taught many circumstances in which these remedies must not be used at all, or only under very great precaution. These conditions are all acute inflammatory affections of the digestive canal; menstruation; a tendency to uterine hemorrhage; pregnancy; hemorrhoidal tumors, which readily bleed; collapse and great anæmia; finally also a tendency to diarrhœa.

Senna leaves and cathartinic acid.—The chief active cathartic principle of senna leaves, (folia sennæ, from cassia lenitiva) is, according to Kubly, a non-dialyzable, non-crystallizable body resembling a glucocide, and being an acid, cathartinic acid ($C_{188}H_{192}N_2SO_{92}$) which occurs in the leaves, partly free, but for the most part combined with calcium and magnesium. When boiled with acid, the cathartinic acid is decomposed into grape sugar and a new acid, cathartogenic acid. In addition to cathartic acid senna leaves contain a coloring matter allied to chrysophanic acid, also a sweet, non-fermentable body, cathartomannite; also several unknown glucocides, sennapicrin and sennacrol (Ludwig's), also salts of the vegetable acids.

The addition of alkalies to senna preparations weakens them, while acids strengthen the senna action (Kubly.)

Physiological Action.—Pure cathartic acid at first has no acid taste, but later on a puckering acid taste, and causes abdominal pain and diarrhœa in even very small doses 0.1 grm. Its further disposition in the organism is unknown; but it appears to be absorbed into the blood, and thence into the milk, for the milk of women who have taken senna has a cathartic effect upon their children at the breast.

The coloring matter, which is similar to chrysophanic acid, according to Martius, passes into the urine fifteen minutes after it has been taken.

The effects of senna leaves are best known; they have a bitter taste and peculiar odor.

Senna leaves produce an evident effect only in doses of 0.5 grm. and over. Doses of 5.0 grm. are followed by a discharge of flatus, and five

hours afterward dark fæcal masses, without pain. Doses of 10.0 grm. are followed in some people by nausea and even vomiting; but generally there is only rumbling in the abdomen, discharge of flatus, and after three hours, fæcal passages accompanied by much abdominal pain, followed by several other passages in the course of the next one or two hours. These passages are sometimes fluid, sometimes semi-solid, and in dogs contain on an average eighty-five per cent of water, and sodium salts and albumen, but never bile (Radziejewski). The pain in the abdomen and the diarrhœa may last twenty-four hours, and during that time there is disturbed appetite. The peristalsis of the small intestine is diminished, while that of the large is increased (Nasse). Inflammatory conditions of the intestinal mucous membranes have not been observed. When the cathartic effect has passed over, there is generally only normal movement from the bowels, and not as after many other cathartics, constipation.

Martius asserts that senna temporarily slows the pulse.

Large doses are said to increase hemorrhoidal or menstrual hemorrhage, and even to produce contraction of the pregnant womb.

The direct injection of senna infusions into the blood of men or animals causes vomiting and diarrhœa.

Therapeutic Application.—Senna is one of the most frequently used cathartics, because it possesses the advantage of not causing after-constipation, acts certainly, and does not, like many of the drastics, cause inflammation of the intestine or hypercatharsis. We have already given the general indications for the use of this drug, and when it should be preferred to other cathartics.

Dosage and Preparations.—Acidum cathartinicum e senna. It has been possible to isolate this acid with about four per cent of potassium and magnesium salts; its therapeutic effects are certain, and not disturbed by any extraneous symptoms. It is in the form of a powder, easily soluble in water, tasteless, and is always given to adults (from 0.25–0.4 grm.) Children from 0.12–0.2 grm. internally. 2. Folia sennæ, from 0.5–1.5, to cause a simple movement from the bowels; for a strong purgative action, given in infusion or powder, and often combined with other agents. 3. Folia sennæ spiritu extracta, one part of senna and four of alcohol; said to give least pain in its action; dose like that of senna. 4. Species laxantes St. Germain, St. Germain tea, sixteen parts of No. 3, ten of flores sambuci, five each of fructus fœniculi and anise, and three parts of potass. bitart. purum. In infusion, one teaspoonful to a cup of water. 5. Pulvis glycyrrhizæ compositus, pulvis pectoralis Kurellæ, two parts of senna leaves, two of radix glycyrrhizæ, one part each of fructus fœniculi and sulphur depur, six parts of sacch. albissimum; a good cathartic even in children up to a teaspoonful. 6. Electuarium e senna, ten parts of folia sennæ, one of fructus coriandri, fifty of syrup simp., fifteen of pulpa tamarindorum depur.; also much used; of a greenish-brown color; best given pure in teaspoonful doses, or in mixtures. 7. Infus. sennæ compositum aqua laxativa Viennensis, two parts of folia sennæ, twelve of water, with the addition of three of natro-kalium tartaricum and three of manna; nauseous in taste, of a brown color—dose ℥ ss—in children ʒ i–ʒ ii. 8. Syrupus sennæ cum manna contains folia sennæ, manna, fructus fœniculi and saccharum; in children, ten drops to a teaspoonful.

Rhubarb root, radix rhei—the root of many forms of rheum (palmatum, undulatum, compactum, emrodi, etc.) growing in China; the best kind

was formerly imported from Russia or China, now only from China. The active principle is an amorphous acid, very much like if not identical with the cathartic acid found in senna. The chrysophanic or rheinnic acid, which when heated with saltpetre is converted into tetranitrochrysophanic acid, is present in very small quantity, and is not cathartic in its action; it is, therefore, improper to consider this as the active principle in rhubarb. Chrysophan, phoretin and emodin found in rhubarb are of little importance; but the rheum tannic acid which when boiled with mineral acids is converted into grape sugar, and the above chrysophanic acid is of more importance; there is also potassium oxalate.

Physiological Action.—These ingredients produce varying results in different doses.

In small doses (0.05–0.3 grm.) the effect of the rheum tannic acid is most marked; it prevents abnormal decomposition of the food in the stomach, and in catarrhal gastritis prevents nausea, eructation and diarrhœa. In healthy people it does not improve the appetite, although there is very slight constipation,

In larger doses (0.5–1.0 grm. in quickly repeated doses, or 2.0–3.0 grm. in single dose) the effects of the cathartic acid are first felt, producing frequent soft fæculent stools, with colicky pains, in from five to ten hours after the taking of the drug. As soon as this acid has passed out of the intestine the tannic acid which remains subsequently produces a slight amount of constipation.

The absorption of the chrysophan and of the chrysophanic acid into the blood, causes the secretion to become intensely yellow; thus the sweat stains the linen of the patient; the urine takes on an icteroid hue, as does also the milk and fæces. This discoloration of the fæces led to the belief that rhubarb is a chologogue cathartic.

Therapeutic Application.—In small doses rhubarb is very much used as a digestive tonic, and a constipating nremedy in various forms of diarrhœa. Its first application is like that of the bitter aromatic appetizers. If with the dyspepsia there be at the same time diarrhœa, then rhubarb should be preferred. This good effect upon the digestive functions leads to its frequent use in the dyspepsia which accompanies scrofula and rickets; so, also, in the chronic diarrhœas, which sometimes occur in these diseases, rhubarb is a good remedy, although it is useless in acute diarrhœas. It may also be used in the diarrhœa which remains after an acute intestinal catarrh has run its course. It should, of course, be preferred to other remedies when there is at the same time some digestive disturbance. It is, however, only successful in the slighter cases of diarrhœa.

Rhubarb is seldom used in large doses for chronic constipation, but only when we wish a cathartic effect upon a single occasion, and where it is necessary to disturb digestion as little as possible; thus in the constipation of convalescents from acute diseases, also in that of anæmic and cachectic individuals, also in children. Sometimes, however, the drug acts well in cases of chronic constipation, and there are cases of hypochondriacs, who chew pieces of rhubarb root for their habitual constipation. In jaundice, rhubarb is very much used as a cathartic, although we do not believe that in this disease it possesses any extraordinary virtues over other remedies.

Dosage and Preparations.—1. Radix rhei, in small doses from 0.02–0.5 pro dosi, in powder, pill, or infusion. As a cathartic in from 1.0–

5.0 doses. Rhubarb is often taken in substance, either in small pieces or in pills cut out of the root.

2. Extractum rhei—a dark-brown powder—slightly soluble in water. Small doses—0.01–0.25 or 0.3–1.0 in pill form.

3. Extractum rhei compositum (extractum catholicum, s. panchymagogum), 3 of extractum rhei, 1 of aloes, 1 of sapo jalapinus to 4 parts each of water and alcohol; a dark-brown powder soluble in water, used only as a cathartic in doses of from 0.1–1.0 in pill.

4. Tinct. rhei aquosa, infusion rhei aquosum, 100 parts of radix rhei, 10 of kali carbonicum, 20 of borax powder, and 850 of aq. dest., 100 of alcohol, 150 of aq. cinnamomi; reddish-brown drops. Little used and not practicable as a cathartic. Used, however, as a stomachic tonic in children, 10–15 drops; in adults in from 1 to 2 teaspoonful doses.

5. Tinct. rhei vinosa, tinctura rhei Darelii, vini rhei, 8 parts of radix rhei, 2 parts of cortex fructus aurantii, 1 part of fructus cardamoni, 12 of saccharum albissimum, to 100 of vinum xerense; is a yellowish-brown fluid, given only in digestive disturbances, and to be avoided in children in large doses on account of the wine which it contains; from 10 to 20 drops; in adults ½–1 teaspoonful.

6. Syrupus rhei, 12 parts of radix rhei, 3 of cortex cinnamomi, 1 part of potassium carbonicum purum with water and sugar; reddish-brown; used as a cathartic in teaspoonful doses in children.

7. Pulvis. magnesiæ cum rheo, pulvis pro infantibus, pulvis antacidus, Ribke's children powder, 60 parts of magnesium hydricocarbonicum, 40 of olæosaccharum fœniculi, 15 parts of radix rhei; used as a cathartic in children, on the point of a knife.

Appendix—cortex rhamni frangulæ, from rhamnus frangulæ; acts like rhubarb and senna; used in infusion, 15.0 : 150.0, with the cathartic salts (10.0) and in aromatic syrups, tablespoonful doses. Fructus rhamni catharticæ in the form of the syrup rh. c. s. spinæ cervinæ s. domesticus, in tea or tablespoonful doses.

Jalap Root—Radix Jalapæ—Jalap root is from the Mexican convolvulus purga. By extraction with alcohol, the officinal jalap resin (resina s. extractum jalapæ) is obtained. From this again we get the strongly cathartic convolvulin $C_{31}H_{50}O_{16}$, a colorless, odorless, tasteless gummy mass, which is probably the anhydride of an acid convolvulinic acid, into which it is converted when treated with alkalies. The residue of the jalap resin, gamma resin, is also slightly cathartic. In another jalap root, convolvulus orizabensis, there is the jalapin $C_{34}H_{56}O_{16}$, which closely resembles convolvulin.

Physiological Action.—That convolvulin is the chief acting substance, can be seen from the fact that it has a cathartic action in 0.1 grm. doses, while convolvulinic acid and gomma resin have a cathartic effect only in 0.5 grm. doses.

For the production of this effect, the presence of bile is necessary, which acts upon the jalap, (Buchheim, H. Köhler). When injected into the blood it does not occur.

Small doses (0.5 grm. of the root, 0.2 grm. of the resin) at most give rise to a slight cathartic action. Larger doses (1.0–2.0 grm. of the root, 0.5–1.0 of the resin), after 30 minutes, cause nausea, which may even be followed by vomiting, and after two hours, by abdominal pain and catharsis, but not by any tendency to constipation. The liver, and still more the intestinal glands, are excited to stronger secretion (Rutherford).

Very large doses caused death in animals with symptoms of gastro-enteritis.

Therapeutic Application.—The indications for the use of jalap are those generally given for the drastics. It is much used (in combination with calomel), because it leaves behind no constipation, and in chronic constipation because its long-continued use does not result in a diminution of its cathartic power. It has no special advantage in certain conditions, and even in helminthiasis, where it was formerly given as a specific, it only acts like all other cathartics. Jalap must be avoided in inflammatory affections of the intestinal canal even more than senna, because it is more irritant.

Dosage and Preparations.—1. Radix jalapæ, as a purgative in from 0.5 to 1.0. If we wish to produce a strongly cathartic effect 1.0–2.0 grm. in divided doses, at short intervals. In children, half the dose, and often with the addition of aromatics.

2. Resina jalapæ s. extractum jalapæ spirituosum, in half as large doses as the root, in powder or pill.

3. Sapo jalapinus, 4 parts of sapo medicatus and 4 of resina jalapæ, with 8 parts of spirit. vin. rectificat. Given like the resin, but preferred where the jalap is to be continued for a long time. From 0.1 to 0.3 in pill, for long-continued use, to produce a strong effect.

4. Tinct. jalapæ, e resina is superfluous; from 10 to 20 drops.

5. Pilulæ jalapæ, 3 parts of sapo jalapinus, 1 part of tubera jalapæ; 3–6 pills per dose.

Appendix.—Radix scammoniæ, from convolvulus scammonia; the resin contains jalapin, which are chemically and physiologically almost identical with convolvulin, also radix jalapæ orizabensis. Similarly, gutti gambogia (gummi gutti—Siam gutti) acts like the dried milk juice of garcinia morella; contains a resin acid. Gambogic acid produces catharsis (provided there be bile in the intestines) in 0.1–0.2 grm. doses. In larger doses it causes vomiting, and in the largest doses gastrointestinal inflammation. Therapeutically it has no advantages. Dose, from 0.02 to 0.2 (ad 0.3 pro dosi; ad 1.0 pro die), in emulsion or pill.

Aloes.—Aloes is the juice of the fleshy leaves of the various kinds of aloes—aloe capensis, socotrine and hepatica. The cathartic effect is due to aloin, $C_{17}H_{18}O_7$, which can be found by extraction with water and evaporation in a vacuum; it is then formed into small colorless crystals, of a sweetish-bitter taste; the great mass of the aloes is aloëtin, which is also strongly cathartic. Aloin is soluble with difficulty in cold water and alcohol; readily in hot water, in which it is changed to the amorphous aloëtin. Under the continued action of nitric acid, it is converted like rheinic acid (see rhubarb) into tetranitro chrysophanic acid. It belongs to the aromatic compounds, for in melting caustic alkalies, it is converted into paraoxybenzoic, acetic, and oxalic acid. There is also, in aloes, a resin which is soluble in water, namely aloes resin, which also possesses weakly cathartic properties; there are also gallic acid, albuminoid substances, and fat.

In aloes therefore the active ingredients are in excess.

Physiological Action.—Aloes only has a cathartic action when it comes in contact with bile in the intestines (Buchheim). According to Wedekind, it does not cause catharsis when the biliary canals have been closed and the stools are white; Cube also confirms this. Even solutions of aloes injected into the rectum only had a cathartic effect when they were mixed with ox bile. Aloes has a disagreeable taste and odor. We were

never able to confirm the fact that small doses (0.01–0.05 grms.) stimulate the appetite. In larger doses (0.1–0.5 grm.) it causes eructation, a feeling of pressure in the stomach, and, ten to fifteen hours after its absorption, several soft, dark passages with or without abdominal pain. Even 1.5 grm. doses take a half day to produce any effect, and then cause more pain, and the passages are more fluid than from smaller doses. The cathartic action, however, varies in different individuals. It is questionable whether the drug ever increases the biliary excretion. Its long-continued use does not result in the patient becoming accustomed to the drug, but the dose can even be diminished after a time, and yet corresponding effects produced. According to older writers the use of aloes causes a fluxion of blood to the pelvic cavity, especially to the kidneys and true pelvic organs, so that hemorrhoids, menorrhagia, and even abortion, together with increased sexual desire and strangury, may result. The effects of the purely active ingredients of aloes have not yet been well studied, but it appears that the aloin and aloëtin are absorbed into the blood and passed into the secretions, so that then the milk is cathartic after aloes has been taken.

Therapeutic Application.—Aloes is a much used cathartic, and experience has very properly indicated a series of conditions in which it should be preferred to other drugs. First, aloes should be used where we have chronic constipation, because it does not impair digestion (in small doses), and because it can be taken for a long time without any increase in dose. Experience has taught that the existence of hemorrhoids, with tendency to bleeding, general plethora, chronic uterine, and menstrual disorders, which may result in hemorrhages and pregnancy, are contraindications. It is a good cathartic when old hemorrhoids have ceased bleeding, and we have as a result headache, mental depression, feeling of pressure in the epigastrium, etc. Since the time of Stahl aloes was much used, and hence often misused in these conditions. To-day, however, when we no longer attach such importance to the old views of stasis of the portal system and concealed hemorrhoidal affections, aloes is no longer as much used in this direction.

Dosage and Preparations.—1. Aloes from 0.2 to 1.0, best in pill form. 2. Extractum aloes, a yellow-brown powder, but slightly soluble in water; the cathartic effect is somewhat uncertain. The dose is half as large as aloë, 3. Ext. aloës acido sulphurico correctum; superfluous and without advantage. 4. Tinct. aloës, 1 part of aloë in 5 of spirit. vini. rectificat., from 5 to 30 drops. 5. Elixir proprietatis paracelsi contains to 24 parts of spiritus vin. rectificat, and 2 parts of acid. sulphricum dilutum, 2 parts each of aloë and myrrha, and 1 of crocus, a dark brownish red, clear liquid, in from ½ to 1 teaspoonful dose as a stomachic tonic. 6. Elixir ad longam vitam. Tinct. aloes comp. contains 9 parts of aloë, 1 each of gentian, rhubarb, zedoariæ, crocus, and fungus laricis; also in from ½ to 1 teaspoonful.

Colocynth.—2. Fructus colocynthidis, from the cucumber like cytrullus colocythis. This contains an amorphous (but crystallizable), soluble, bitter glucocide colocynthin, $C_{56}H_{84}O_{23}$.

Physiological Action.—Colocynth is one of the strongest cathartics, even in 0.06 grm. doses. It produces exceedingly watery passages. (Rutherford says it increases the excretion of bile and the secretion of intestinal glands). In larger doses it may cause bloody passages and gastrointestinal inflammation. Even nephritis and cystitis, and general narcotism, have been said to have been produced under its use.

Therapeutic Application.—This drug is used therapeutically under the same circumstances as aloes. Colocynth may produce even diarrhœa on account of its strong action, when aloes has been ineffectual. The drug is frequently used in dropsy, especially ascites, in combination with gummi gutti. Not only does it act upon the intestine, but some even ascribe to it a special diuretic effect which has not been positively confirmed.

Dosage and Preparations.—Fructus colocynthidis, from 0.03 to 0.3 (ad 0.3 pro dosi! ad 1.0 pro die!), in powder or pill, often with a narcotic, such as belladonna, to alleviate the pain. 2. Fructus colocynthidis, præparati s. trochisci alhandal is a mixture of 5 parts of colocynth, and 1 of gummi mimosæ; easily pulverizable, and used in same doses as colocynth. 3. Extract colocynthidis, a yellowish-brown powder, slightly soluble in water; up to 0.005 in pill (ad 0.05 pro dosi, ad 0.4 pro die!). 4. Extract colocynthidis composit., 3 parts of ext. colocynth., 10 of aloës, 8 of res. scammony, and 5 of extr. rhei.; from 0.01 to 0.5. 5. Tinctura colocynthidis, 1 part of colocynth to 10 of alcohol, from 5 to 10 drops (ad 1.0 pro dosi, ad 3.0 pro die).

Appendix.—Like colocynth., act bryonia, from radix bryonia of bryonia alba; squirting cucumber, ecballium elaterium.

Preparation.—Elaterium s. extract elaterii, which produces not only abdominal pain and diarrhœa, but nausea, vomiting, and, according to H. Köhler, even narcotic and tetanoid symptoms.

Castor Oil and Croton Oil.—According to Buchheim the acids formed from the glycerides can be divided, from a pharmacological standpoint, into two groups. While the fatty acid and acrylic acid series can be looked upon as food substances, the castor and croton oil acids have no such importance. Of course they possess many chemical characteristics in common with the fatty acids to which they owe their oily constitution and their relationship to the glycerides. Their glycerides are as indifferent as those of the first group; but their free acids possess the same, and their soluble salts have the same active properties. This decomposition is produced by the pancreatic juice, which has the property of decomposing all neutral fats into glycerine and acids. Now the free castor and croton oil acids can act upon the intestinal mucous membrane. Croton oil acts upon the skin and mucous membrane of the mouth, pharynx, and stomach, because in these places its acid is set free by a ferment (Buchheim).

Castor Oil—Oleum Ricini.—This is an oil derived from the seeds of the ricinus communis; it is a thick, odorless oil, soluble in alcohol and ether. The chief constituent of castor oil is the glyceride of ricinolic acid, $C_{18}H_{34}O_3$. In addition, there are traces of stearin, palmatine and cholesterine. The glyceride of castor oil is inactive. It is only when the latter is decomposed in the intestine that it becomes active. Castor oil seeds are much more cathartic than the oil.

Physiological Action.—Castor oil has at first a mild, later, a sharp, oily taste. This bad taste of the oil may cause nausea and vomiting; the addition of flavoring agents may mitigate the bad taste.

A dose of 15.0 to 30.0 grm. is sufficient to produce in adults several fluid fæcal passages without abdominal pain. If much fæces are present in the intestine, then Buchheim finds neither castor oil nor its decomposition products discharged with it; under other circumstances the oil or its derivatives are found in the stools (Golding Bird).

Continued use of the oil interferes with the appetite and digestion. Severe poisoning is generally due to impurities and not to the oil itself.

The cathartic effect is also produced by injection of the drug into the rectum.

Therapeutic Application.—The property which this drug possesses of acting certainly without irritating the intestine is the cause of its frequent use. On account of its ill effect upon digestion it is not a good remedy when it is to be used for a long time as a purgative, but to produce a single evacuation it is the remedy par excellence. Its chief value consists in that it can be used not only in metrorrhagia but in inflammation of the genital organs, kidneys, and direct inflammatory conditions of the intestines. Thus it is given when foreign substances and indigestible food have irritated the alimentary canal and caused gastroenteritis. The evacuation of the irritating substances causes a cessation of diarrhœa and catarrh. When a cathartic is necessary in dysentery or typhoid, then castor oil or calomel are the only ones allowed. It is also often given when in the simple constipation of pregnancy or of the puerperal month, a cathartic is necessary. It is also often used in the severe forms of constipation, such as lead colic, etc. Where there is a gastric catarrh it is true that a clyster is preferable, but this condition is not an absolute contra-indication to the use of castor oil.

Dosage.—Internally from ½ to 2 tablespoonsful, pure with meat broth, coffee, tea, or aromatic oil, or an emulsion. Starke gives an agreeable method for its administration: 1. For children add granulated sugar until a thick dough is formed with the oil; 3 parts of sugar are needed to 1 part of castor oil. 2. For adults a mixture of castor oil with 2 parts of pulv. liquir. comp., made into boli, and swallowed with water. For clysters, 1 to 2 tablespoonsful.

Croton Oil.—Oleum crotonis, from the seeds of the tiglium officinale, a yellowish-brown, thick oil, which, when shaken with alcohol, separates into 2 parts (one soluble in alcohol, with a sharp taste, one tasteless and insoluble). The peculiar odor of croton oil is caused by a mixture of volatile acids, acetic, butyric, valerianic, and tiglinic acids, which do not exist in large proportion in croton oil (1 per cent), do not pre-exist in the fresh seeds, but occur as a product of the oxidation of the non-volatile acids present in croton oil. The volatile acids take no part in the effect of croton oil (Genther and Buchheim). The non-volatile acids are present in croton oil, partly in a free state, and partly as a glyceride; they belong to the group of fatty acids, and are, according to Schlippe, stearic, palmatinic, myristinic, and laurinic acids. The acids not belonging to this series are oleic and crotonic. The last is peculiar to croton oil and is the chief agent in the production of its effects upon the skin and intestinal canal. It is probable that crotonol acid and ricinol acid belong to the same group chemically. Schlippe's assertion that croton oil contains a blistering and noncathartic substance, and a nonblistering and cathartic substance, is founded upon an error.

Physiological Action.—Croton oil has a strongly irritant effect upon the skin and mucous membranes.

Skin.—The effect of croton oil upon the skin is very similar to that of tartar emetic and emetin. If a few drops of the oil are rubbed upon the skin, in five or ten minutes they cause a severe burning sensation in the affected part which lasts for hours. The skin is reddened and soon covered with serous, later with purulent pustules, which sometimes run together to form blisters. These dry up in a few days, leaving no ulcers (for croton oil does not, like tartar emetic, cause inflammation of the true skin). This can be caused, however, by the insertion of the oil under the

skin. The portions of the skin into which croton oil has not been rubbed are unaffected, previous statements to the contrary notwithstanding.

Mucous Membranes.—A drop of croton oil taken into the mouth causes a sharp, burning sensation; when swallowed, long-continued roughness in throat, a sensation of warmth and burning in the stomach, and vomiting (in large doses). In the course of the next two hours there is rumbling in the abdomen, abdominal pain, and fæcal passages, followed by 5–10 fluid stools. After twenty-four hours all these symptoms have disappeared, and the appetite only remains affected. Large doses (on an average 2–5 drops in rabbits, 30 drops in dogs, and 20–60 drops in men) are followed by cholera-like vomiting and diarrhœa, and severe inflammation of the stomach and intestine, followed frequently by death. Even croton oil clysters cause diarrhœa, but they can only be used in large doses internally (!).

General Effect.—The general symptoms are not the direct result of the croton oil but of the gastrointestinal inflammation. But if, as has been seen in several cases, croton oil does not cause diarrhœa, but is absorbed, then it produces severe symptoms of general poisoning. Precordial anxiety, palpitation, restlessness, headache, a feeling of dizziness, pain in the limbs, heat and long-continued weariness. The assertion that even after the application of croton oil upon the skin (the abdomen) its effects are seen upon the bowels, is hardly credible, and has not been confirmed by good observers.

The injection of croton oil into the veins cannot contribute to the understanding of its effects; for, like other oils, it is apt to produce emboli in the pulmonary capillaries, as well as other serious disturbances.

The treatment of croton oil poisoning is simply the treatment of the acute toxic gastritis.

Therapeutic Application.—Croton oil is one of the strongest cathartics, and acts, as a rule, only under those circumstances where other materials are ineffective. It is never given for continuous use, but only when a single marked effect is to be attained. It is therefore not a fit purgative for antipyretic purposes or in dropsies, but only in chronic constipation. It can be given when a collection of fæces cannot be gotten rid of by other means; also in mechanical obstruction of the intestine. Also in diseases of the brain and spinal cord when the constipation cannot be overcome by any other remedy; also in insane patients, because it can be so easily administered with the food. Tanquerel prefers croton oil to all other cathartics in lead colic. It is said to act more rapidly, and to guard against relapses. Often a single drop causes a movement from the bowels, sometimes only the second dose. Sometimes the remedy acts well in clysmata.

The advantages of croton oil therefore consist in that it is very energetic, and acts when other cathartics fail. The good effect sets in very rapidly. Finally, it only very rarely produces vomiting and colic.

Externally croton oil is used as a cutaneous irritant in the same conditions in which tartar emetic is used, and is less destructive in its effects than the latter.

Dosage.—1. Oleum crotonis, from ¼ to 1 drop (ad 0.05 pro dosi; ad 0.3 pro die), in pill, capsule, or mixed with a fatty oil. Generally 1 drop is given to 30.0 of castor oil (the so-called ol. ricini artificiale) or in coffee. Externally it is rubbed in pure (from 5 to 15 drops) or with olive oil, or mixed with oil of turpentine, 2 to 3 times a day. For a clysma, 1 to 2 drops are added.

2. Collodium crotonatum—that is, equal parts of flexible collodion and croton oil. Excellent for the local application of croton oil, because it distinctly localizes the effects.

Appendix to Cathartics.

Tamarinds—Fructus Tamarindorum.—These act like our domestic fruits, and like these contain vegetable acids and their salts; they alleviate thirst, and are slightly cathartic. The pulpa tamarind. depurat. is used as a mild cathartic in febrile conditions; either pure (2–4 tablespoonsful) or in solution. It is one of the components of the electuarium lenitivum. Serum lactis tamarindinatum, tamarind whey; to 30 parts of milk take 1 of pulpa tamarindorum depurat; more laxative than ordinary whey, and is used when we desire an additional effect. From 1 to 2 pounds are used daily, with regard to the usual rules in the taking of whey.

Manna.—The juice of fraxinus ornus contains 70 per cent of manna sugar, mannite $C_6H_{14}O_6=C_6H_8(OH)_6$, which differs from the other varieties of sugar in that it is markedly cathartic, which Buchheim thinks due to its slight diffusibility. Nausea and abdominal pain are not often seen under its use. For a cathartic effect 30.0 grm. of mannite, or 50.0 grm. of manna are necessary. Syrupus mannæ and syrupus sennæ cum manna in tea and tablespoonful doses.

Aromatic Anthelmentics.

Flores Cinæ—S. sanitonici (improperly termed semina cinæ, or wormseed) are the flowers of several varieties of artemesia. It contains an ethereal oil which is a mixture of non-oxygenated and oxygenated constituents, oleum cinæ æthereum, which acts like camphor upon warm-blooded animals, but possesses no particular anthelmintic properties; it also contains santonin, which has replaced the mother plant in practice as an anthelmintic; and which we shall therefore consider by itself.

1. Flores cinæ, from 0.5 to 2.0 pro dosi, in powder or electuary.

2. Extractum cinæ, from 0.2 to 0.5; not soluble in water.

Santoninum, $C_{15}H_{18}O_3$, presents colorless crystal, which gradually turn yellow in the light; odorless, and almost tasteless, insoluble in cold, soluble (1–300) in hot water, alcohol, and ether. When heated with zinc powder in a stream of hydrogen it is converted into a phenol-like body, santonol, $C_{15}H_{18}O$, by reduction. With alkalies the santonium decomposes to form salts with santonic acid, as, for example, $2\ C_{15}H_{19}NaO_4$ and $6\ H_2O$, from which, by the addition of hydrochloric acid and ether, santoninic acid is formed in the shape of colorless needles, which, at 120°, again decompose into santonin and water.

Physiological Action.—Relatively small doses of santonin destroy thread worms (ascaris lumbricoides). At the present time we know no other anthelmiutics which have an effect at all similar to that of this drug. On the other hand, much larger quantities are needed to kill tape-worms, and these quantities in man also give rise to poisonous symptoms.

The effects of santonin upon man and the higher animals are very remarkable.

Pure santonin is almost insoluble in water, and has only a weak, bitter taste, but in a solvent, such as chloroform, it is intensely bitter.

In the gastrointestinal canal it is converted into a soluble sodium compound and passes off, for the most part, unchanged with the fæces. For

this reason the higher animals cannot, or rather with only great difficulty, be destroyed with pure santonin.

In the blood the santonin compounds are further changed, and appear in the urine as a further oxidation product of santonin. The increased urine acquires a greenish-yellow color from this substance (xantopepsin, Folck), and on the addition of an alkali turns purple-red.

The first general effects produced by the administration of 0.05 grm. in children, or 0.3–0.5 grm. in adults, result in disturbances which have been especially well investigated by Rose. The spectrum is shortened, especially at its violet end. It likewise causes a perversion of the sense of color. At first one sees more blue, so that all the darker shades appear blue. Later on yellow is the predominating tint, and now the most refrangible rays are no longer seen as violet; later on no blue colors are seen; and where there is a poisonous effect patients cannot distinguish even between the most pronounced shades, such as lilac and dark green, or violet and black. Hallucinations of sight supervene, especially in the dark; when the patient is recovering from the effects of the drug he again sees blue.

The "yellow vision" may be looked upon as due to paralysis of the nerves sensitive to violet rays, and the "violet vision" as a hyperæsthesia of the same.

It is uncertain whether M. Schultz is right in the assertion that the yellow vision is due to a yellow discoloration of the retina, or increased pigmentation of the yellow spot.

During all this there is no amblyopia or disturbance of accommodation.

The disturbances of vision only last a few hours. Other special senses —taste and smell—are likewise disturbed.

During these disturbances in vision there is fulness in the head, although the intellect is unaffected. The consciousness of the unreliable state of the senses affects both the will and spirits. There is a certain amount of excitement and a disagreeable feeling of weariness. Headache is only caused when santonin is taken upon a full stomach; it may cause nausea, which disappears when the patient goes into the fresh air. The pulse is diminished, and not increased in frequency (Rose).

Fatal doses of santonin compounds have the following effects:

Frogs, when given doses over 0.1 grm., fall into a condition of general coma; the respiration ceases, and subsequently spontaneous and reflex convulsions of the limbs and trunk set in. These continue even when the brain is taken out, although they cease when the spinal cord is separated from the body. The heart's action remains unchanged for some time; but finally it is paralyzed in diastole. Shortly before the unconsciousness there is an irritability of the pons and medulla, followed finally by paralysis (Binz).

In warm-blooded animals (cats and rabbits) the convulsions are similar in time and place to those seen in men. There is no stage of extraordinary depression as in cold-blooded animals; but suddenly trembling, pricking up of the ears, grinding of the teeth, contraction of half the face, rolling of the eyeballs, opisthotonos, general convulsions, and stoppage of respiration. Finally a remission of all the symptoms, a free interval of longer or shorter duration. The condition of the pupils is not constant. Here, also, therefore the first effect of the poison is seen in the region of the pons from the 2d to the 7th nerve; later on in the spinal cord. The heart and blood-pressure are not affected (Binz).

In men, and especially in children, the same series of symptoms are observed as in warm-blooded animals. The convulsions are similar to those of epileptics (similar to those from camphor). According to Binz, the paralysis of respiration in the intervals between the convulsions is especially dangerous. The heart's action is strong and not slow.

Therapeutic Application.—Santonin is a much-used remedy, especially against ascarides lumbricoides; against these it is used as a specific. Küchenmeister has shown that santonin produces a fatal effect upon ascarides in the space of an hour; while semina santonici in the doses in which they must be taken to produce an effect are nauseous. This drug being more agreeable is used almost exclusively. Santonin may also be given for oxyuris vermicularis, when these cannot be gotten rid of by clysters; but, according to Rose, it appears to be quite ineffective against oxyuris. We should never use poisonous doses of the drug, and we must combine the remedy with a cathartic which will act in two to four hours after the drug has been given.

Dosage and Preparations.—1. Santonin, from 0.01 to 0.05 in children (latter dose only in those who are 8 to 10 years), in powder or pastille (ad 0.1 pro dosi! ad 0.5 pro die).

2. Trochisci santonini consists of cocoa butter and santonin. Two varieties are officinal, one of which contains 0.025, the other 0.05 of santonin in single pastilles.

Sodium Santonate—Sodium Santonicum; crystals readily soluble, containing 70 per cent of santonin. On account of its ready solubility it is absorbed for the most part before it reaches the worms in the deeper portions of the intestines, and hence gives rise to poisonous symptoms in man. It is therefore better to use santonin; dose, 0.1 to 0.3.

Treatment of Santonin Poisoning.—A slightly toxic effect is not at all rare, although no fatal cases have as yet been reported. No antidotes are known. We can only therefore strive to get rid of unabsorbed portions of the poison by vomiting and purging; otherwise the treatment must be conducted on general principles—artificial respiration, and the administration of ether, chloroform, and chloral hydrate in the convulsions.

Oleum Herba, and Flores Tanaceti.—Tanacetum Vulgare; has a disagreeably-smelling, bitter, sharp, ethereal oil, which is composed of a turpene, $C_{10}H_{16}$, and an alcohol, $C_{10}H_{18}O$, and an aldehyde. Tanacetylhydride, $C_{10}H_{16}O$ (the latter a convulsion-producing agent (Putzeys), has a poisonous effect upon round and thread worms, but also upon man, in whom it has often been seen to cause gastro-enteritis, convulsions, and even death. It can readily be replaced by santonin.

Pomegranate Root (Rind)—Cortex Radicis Granati.—The freshest possible rind of the root of punica granatum contains much tannic acid, a mannite like, as well as a crystallizable body, punicin; to what it owes its anthelmintic action is unknown. Recently the rind of the trunk and branches has been recommended as equally active (Marty).

Physiological Action.—Medicinal doses give rise to nausea, vomiting, and diarrhœa, with abdominal pain; larger doses cause fulness in the head, dizziness, sleepiness, indistinct vision, numbness of the limbs, insensibility, and in some cases convulsions, especially in the muscles of the calves.

Therapeutic Application.—This was even in ancient times recognized as a good remedy for tape-worm, and it has maintained its reputation to the present time; it is only excelled in its effects by kusso flowers. The

worm is expelled, in most cases, dead; but, according to Küchenmeister, only seemingly dead. This observer has seen these worms die after being placed in a decoction for three hours.

It is best given in a simple decoction, 30.0–50.0; 300.0 with or without a corrective; this should be taken in two doses, with the usual precautions which are necessary in the treatment of tape worm. Since vomiting may result, it is best to administer one of the substances, which we shall mention under kusso. The root must be fresh, and the decoction should have been carefully and thoroughly made.

Filix Mas—Radix Filicis, the fresh root of polystichum filix mas; this contains ethereal oils, tannic acid, resins, and filix acid. Many of these components seem to be anthelmintic, although none alone have the power of the root.

Physiological Action.—In man in large doses it only causes nausea; small, oft-repeated doses it improves the appetite and digestion.

Filix mas is one of the oldest and most reliable of the agents used to destroy tape-worm, and it forms a component of many tape-worm remedies and cures.

Bremser's assertion that it is only effective against the bothriocephalus, and useless against tænia, has not been confirmed. It should be preferred because it does not disturb the appetite. Ordinarily it is combined with pomegranate root rind. Many observers prefer the ethereal extract of the root itself.

It is given, with the precautions usual in the cure of tape-worm, in 2–3 doses of 5.0 grm. of the powdered root, at a half to one hour intervals. It is given in decoction or mixture.

Extractum Filicis Ethereum.—A greenish mass, insoluble in water, of thin consistency, given in 0.5–1.5 grms. in pills, generally made up with the root itself.

Kosso Flowers—Flores Kosso.—(S. kusso) the flowers of the Abyssinian tree, brayera anthelmintica, contain an ethereal oil, tannic acid, and an indifferent crystallizable body, cossin, $C_{21}H_{38}O_{10}$; the latter is the anthelmintic agent.

Physiological Action.—In men, in 15.0 grm. doses, it yields a bitter taste in the mouth, gives rise to nausea, to vomiting, and at times to rumbling and pain in the abdomen, diarrhœa, and difficult micturition. In rare cases it causes headache, weariness, and psychical depression. It is questionable whether this be a direct effect.

Therapeutic Application.—Kusso flowers are very much used as a remedy for tape-worm, although only introduced during the last twenty-five years. (It is used against all the varieties of tænia). Its failure is generally due to the inferiority of the preparation. It should be preferred to all other tape-worm anthelmintics. Küchenmeister saw the worms die after a half hour soaking in a milky decoction of kusso. This is sooner than from any other anthelmintic. It is true, however, that cases occur in which kusso is useless, and pomegranate rind is effective.

The best method of administration is to give the flores kusso in compressed cakes (1–2.0 grm. pro dosi), repeated from 10 to 20 times in succession. In adults the flowers, in 5.0–10.0–15.0 grm. doses, may be given with water in a mixture, with the addition of lemon juice, or oleosaccharum or rum. After a half to one hour the dose should be repeated. The decoction and extract are generally useless.

Kamala.—The pollen of rottlera tinctoria is a brick-red powder, with

difficulty miscible with water, and contains a resin resembling cossin and a coloring matter.

Physiological Action.—Nausea, vomiting, diarrhœa, and pain in the abdomen.

Kamala, introduced twenty years ago, hss been used as a remedy against tape-worm, but it does not appear to be as effective as kusso; but it has the advantage of being better borne than the latter drug, and not causing nausea and vomiting so readily.

The kamala is given in 10.0–15.0 grm. doses (divided in two at intervals of one-sixth to one hour). It is best used as an electuary with pulpa tamarindorum.

Aromatic Oxytoxics.

ergot, secale cornutum.

By ergot, secale cornutum, we mean the sclerotium of claviceps purpurea (family of pyrenomycetes), which replaces the fruit grain of rye (secale cereale) and other grains by destroying these and taking their place. This corn ergot presents three edged grains, curved and pointed at both ends, 2½ ctm. long and 3 mm. wide. It readily spoils and hardly retains its active properties more than a year; if ergot is gathered before it is ripe, or when it is overripe, it has little effect.

We were for a long time uncertain as to its active components until recently, when Dragendorff succeeded in isolating them. They are: 1. Sclerotinic acid (probably with the formula, $C_{12}H_{19}NO_9$), an entirely tasteless, odorless, light-brown, hygroscopic but insoluble substance, of an alkaloid nature, and having a weak acid reaction; it occurs in ergot as a calcium, sodium, or potassium salt, and is readily soluble in water, both in this form as well as in a free state. In ergot it exists to the extent of 4–4.5 per cent. 2. Scleromucin, which resembles the latter in its qualitative and quantitative action, is a colloid gum-like mass, without taste or odor, which can be extracted from ergot with water, and again deposited by weak alcohol. When dried it dissolves with great difficulty in water. It is more nitrogenous than sclerotinic acid, and in good ergot it is presumably present to the extent of 2–3 per cent. For therapeutic purposes it is less valuable than the former preparation. 3. The coloring matters, sclerothrin, scleroiolin, and scleroxanthin take part in the effect of ergot, if only to a slight extent; so, also, the potash salts.

In addition to these active ingredients there are, according to Dragendorff, several alkaloids which are inactive, also cholesterine (0.036 per cent), mycose, mannite, cellulose, lactic acid, and lactates, 3 per cent of an albuminoid substance, and 30 per cent of a fatty oil, the oxidation of which is the beginning of the decomposition of ergot. Of the leucin, methylamin, trimethylamin, and ammoniac, it is questionable whether they exist in ergot as such, or are the product of the decomposition of other substances.

The older ergot preparations are a watery extract (extract. secalis, cornuti aquosi; that is, the ergotin of Bonjean), and partly an alcoholic extract (extract. secalis, cornuti spirit.; that is, the ergotin of Wiggers); these are only mixtures of the above-mentioned bodies. The most active substances are found only in the watery extract. Wenzell, so-called alkaloids, ecbolin, and ergotin are only mixtures, according to Dragendorff, which, however, do contain alkaloid bodies; the same is true of Tauret's ergotin.

PHYSIOLOGICAL ACTION.

In spite of the frequent use of this drug in obstetrical practice, there is scarcely another concerning whose effects such a variety of opinions is held. This is probably due to the fact that many of these experimenters make use of different preparations, each of which undergoes other changes in the course of time. Recently, however, Nikitin has thoroughly tested the substances isolated by Dragendorff, with the following results which, for the most part, agree with those obtained by Haudelin and Zweifel from the use of good extracts of ergot. Sclerotinic acid has all of the physiological and therapeutic properties of ergot, and must therefore be considered, together with scleromucin, as the chief active constituent of ergot. Sodium sclerotinate acts similarly, but somewhat more feebly, than the free acid. The latter must be kept in a dry place and undissolved, otherwise it loses its effect.

The free acid and the sodium salt are not very toxic in their action. Judging from the effect upon dogs and cats, the poisonous dose for man would be about 10.0 grms.

Their local and general effects can be distinguished.

Local Effects.—The hypodermatic injection of ergot and its preparations, as well as the above-named chief-acting constituents, gives rise to long-continued pain and inflammatory symptoms. Practically, only sodium sclerotinate could therefore be recommended for internal use.

The taste of sclerotinic acid is slightly bitter. Large doses of sclerotinic acid, and its salt of ergot, and its watery extract (1.0–3.0 grm.), given by the stomach, produce nausea and eructation in men and animals, while 5.0 grm. cause vomiting and diarrhœa. Ergot has also been seen to cause gastroenteritis hemorrhagica in men and animals.

General Effects.—The effects upon the nervous system are especially prominent

Nervous System.—Larger doses of the watery extracts of ergot, as well as sclerotinic acid (0.03 grm.), and scleromucin, produce complete paralysis in frogs. This paralysis begins in the hind legs, and gradually takes possession of the whole body. The pulsation of the heart and respiratory movements are unaffected. Only the very largest doses cause a gradual paralysis of the heart. The latter condition, as well as the general paralysis of the body and weakness of the heart, lasts from five to seven days;

after that there is gradual improvement, and sometimes even complete recovery. Frequently, after a few days, there is a second attack of paralysis, which generally ends in death.

Warm-blooded animals, also, after relatively small doses of the watery extract and of sclerotinic acid, are affected by anæsthesia, disturbance in co-ordination, and after larger doses, paralysis, during which the animal cannot feel the severest pain, nor make the slightest voluntary, and only weak reflex, movements.

The peripheral sensitive nerves are unaffected in general toxæmia, although paralyzed when brought in direct contact with the extract. The motor nerves and voluntary muscles are not sensibly affected.

Respiration.—Large doses are followed in dogs by a diminution of the respiratory movements; in cats this is preceded by a temporary increase. A similar diminution in the frequency of the pulse accompanies this change in the respiratory movements until death sets in.

Circulation.—The heart's action in warm-blooded animals is unaffected even by relatively large doses; the blood-pressure is diminished by small doses for a time, by large doses permanently. The vessels of the intestine and uterus contract, so that immediately after the administration of the drug there is anæmia of these organs. A hæmostatic action of sclerotinic acid is observed in pulmonary hemorrhages; this can only be explained by the diminished blood-pressure; while in the intestine and uterus the muscular contraction of these organs, produced by ergot, is the principal cause of the diminished blood supply.

The uterus of animals, pregnant or non-pregnant, contracts from the effects of 0.2 grm. of sclerotinic acid; contractions of the uterus are increased, and a tetanus uteri was never observed under its use; the contractions proceed from the fundus to the os. Even large doses have never produced any poisonous effect upon the fœtus.

The observations upon the human female are somewhat contradictory, because of the difficulty in making accurate observations. Most physicians however are certain that the human uterus also is made to contract under its use.

Chronic Poisoning.—Both from single large doses (8.0 grm.) and gradual poisoning from eating rye, in which ergot has replaced the rye, ergotism may follow. Sclerotinic acid at first gives rise to the above-mentioned local effects

upon the stomach and intestine; later on the following general symptoms set in: there is a feeling of great weakness; formication, furriness, and anæsthesia of the fingers and toes, wandering pains, slight spasms, which may increase to epileptiform convulsions (ergotismus spasmodicus), and to tonic contractures, accompanied by great pain and anæsthesia of the skin. There may occur in other cases an erysipelatous swelling, followed by gangrene of one or more extremities (ergotismus gangrænosus). The cause of these gangrenous affections is hard to state; some (Zwiefel) consider it the result of paralysis, others as due to the diminished blood supply by the contracted vessels. The convulsions cannot be accounted for in any way.

THERAPEUTIC APPLICATION.

Secale cornutum is used chiefly to produce uterine contractions.* The object is either to alter the nutrition of the uterus by alternate contraction and relaxation of its walls, or to stop hemorrhage by the contraction of its muscular fibres over the blood-vessels, or to aid the uterus in expelling its contents. The latter purpose is the one for which ergot is most frequently prescribed.

Ergot has been used to initiate uterine contractions before term, but this method is so inferior to others that it has not become popular for this purpose. But when labor has already commenced then ergot is the best drug to increase and excite uterine contraction. The contractions produced by ergot during labor are distinguished from natural pains in being stronger, occurring at shorter intervals, and lasting longer; so that intense ergot action resembles that of tetanus uteri. Such a condition of the uterus will succeed in expelling the child, provided the fœtus be in good position, the cervix dilated, and no obstacle exists in the pelvis. If this be not the case, the tetanoid contractions will only serve to imprison the child in the cavity of the uterus. Since long-continued contractions of the uterine wall interfere with the placental circulation, the administration of ergot is of great importance in its influence upon the life of the child.

For these reasons, therefore, rationally ergot should only

* The chapter concerning the obstetric and gynæcological use of secale cornutum we owe to Prof. B. Schultze.

be used toward the end of labor, to stimulate the pains or to enable the fœtus to overcome some obstacle for which the natural pains are insufficient. A necessary condition for the safe use of ergot, therefore, is that the pains should be normal in character; when stricture of the uterus, or spasmodic contractions occur, therefore, ergot would only increase the pain. Again, ergot may be used when we only desire to strengthen the normal pains.

Insufficient dilatation of the cervix, or a bad position of the fœtus are absolute contraindications to the use of ergot. If the strongest pains do not succeed in expelling the child, we should be immediately ready to complete labor by operative interference.

These contraindications to, and conditions in the use of ergot are very important, for much harm is done by the ignorant use of ergot by midwives, who neither know when it should be used, nor are able to interfere actively if the ergot fail to cause the uterus to expel the fœtus.

After labor the use of ergot is valuable, tending to arrest hemorrhage, and further the proper involution of the uterus, by its tonic and non-intermittent contraction.

Not only deficient involution of the uterus after labor, and resulting chronic disease, but even acute puerperal diseases are prevented by the use of ergot immediately after labor is completed. For neither in the well-contracted uterus can voluminous coagula form, nor thrombi form in well-compressed veins.

In the obstetric clinic at Jena, ergot is given to every puerperal woman after the labor has been completed.

In the non-pregnant uterus the action of ergot is less marked, and its use less general. Ergot is useful, however, in uterine hemorrhages, and wherever contraction of the uterine wall is capable of diminishing the hemorrhage.

Ergot is also useful for the reduction of conditions of chronic metritis, and old enlargements of the uterus, due to sub-involution.

Ergot has an especial reputation for the cure of uterine myomata (Hildebrandt, Winkel and others). The views and experience of gynæcologists concerning this effect of ergot are widely different. In the clinic at Jena, however, although the palliative hæmostatic action of ergot in uterine myomata has been acknowledged, no contractile effect has been observed upon the myomata themselves.

Ergot is also used in hemorrhage from other organs;

thus in hæmoptysis and hæmatemesis, it is not to be disputed that it is useful, but it has no advantage over other internal remedies. Recent reports (Drasche and others) would seem to show that ergotin injections are able quickly and positively to control hemorrhages when other means have failed. Experience is very limited concerning this point, but sufficient to show that in hæmoptysis at least the remedy is a very good one.

Langenbeck has used ergotin hypodermically over aneurisms to cure them. A few other communications confirm these favorable results. Vogt has caused the disappearance of varicose veins by the direct injection over them of the aqueous extract of ergot.

C. Schwalbe is disposed to account for the results obtained by Langenbeck, Vogt and others from these "hypodermics" of ergotin, by supposing that the effect is due to the local irritant, inflammatory action of the alcohol used as a solvent for the ergot. Even if this view is the correct one, it would only account for the local effect of ergotin, and not for its hæmostatic action in hæmoptysis. For the irritant action of the injection can scarcely be so great as to check considerable hemorrhages.

Of the large number of other conditions in which ergot is given, we would only mention that it has a good effect in the paraplegia due to various spinal maladies (myelitis after acute infectious diseases, etc.); it has been said to produce a cure in these cases, (Barbier, Arnal, Monneret, Brown-Séquard and others). Brown-Séquard thinks it should be avoided in spinal paralyses, in which there are no symptoms of an irritative type, while it should be given in cases where irritative symptoms exist. Of course it should be used in addition to other important measures, such as abstraction of blood, etc.

Since the pathology of "reflex paralysis" has been better understood, we are inclined to support the views of Leyden, and to suppose that it can be but of slight utility in these affections. A series of cases has also been published, in which ergot is said to be of decided utility in simple paralysis of the bladder. It is chiefly recommended in cases in which the paralysis is due to the hyperdistension of the bladder by the urine. It is questionable whether in these cases the malady would not be as soon cured of itself. This doubt is certainly justified in the more recent cases.

We have but little experience in the use of selerotinic acid,

but most of those who have used the preparation speak favorably of it. Stumpf has used it with good effect in gastric and intestinal hemorrhages, and in hemorrhages from the female genital organs, but not in hæmoptysis. It was used in the form of hypodermic injections, in single dose of 0.05–0.5. It produces disagreeable local effects less frequently than the other preparations of ergot. But for internal use, Stumpf believes it will never become popular because of its great price, and because the present mode of administration of the preparation of ergot is sufficient for all purposes.

Dosage and Preparations.—1. Secale cornutum; for obstetric purposes the dose of powdered ergot is 0.5–1.0, 2 to 3 times at intervals of fifteen minutes. The effect should be seen in about ten minutes. Where the ergot is to be used for some time in chronic conditions, the infusion (5.0: 150.0 of water sine colatura) with the addition of 3.0 acid. sulph. dilut. and 30 of syr. rubi. idæi—1 tablespoonful every hour or two.

2. Tinctura sec. corn. (1 part : 10 of spirit. vin. rectif.); 10–30 drops pro dosi; is little used.

3. Extract. sec. corn. æquos (ergotium, extract. hæmostaticum, Bonjean), internally from 0.10 to 0.5, in pill, pastille, or solution.

Where it is possible the extract should be injected subcutaneously in preference to administration by stomach.

Various solutions of the extract have been used for this purpose; we have found the following the best: a filtered solution of 5.0 of the extract to 15.0 of aq. dest., with the addition of carbolic acid; 0.5–1.0 of this solution pro dosi, 1–2 times daily.

4. Sclerotinic acid—acidum sclerotinicum, subcutaneously from 0.05 to 0.3.

Treatment of Secale Poisoning.—First stop the taking of any more ergot in any form. In acute poisoning use emetics and cathartics to get rid of the ergot still in the alimentary canal; here, also, tannin should be given. The symptoms due to the absorption of the drug must be treated symptomatically; thus in cardiac weakness use stimulants, etc.

Sabinæ Tops—Herba S. Summitates Sabinæ, from Sabina Officinalis.—These contain an ethereal oil, isomeric with oil of turpentine, oleum sabinæ æthereum; the physiological action of this is exactly like that of oil of turpentine, except that it is somewhat more irritant to the skin and mucous membranes. The secretion of the urine is increased; the kidneys are inflamed. The laity believe that it has an irritant action upon the uterus, causing hemorrhage, increased uterine contraction, and more plentiful menstruation; also abortion in the pregnant uterus. This effect upon the female genital organs is probably due to its inflammatory action upon the intestines and kidneys. We must not therefore forget that in producing the uterine effects the life of the patient is endangered.

Therapeutic Application.—The drug is very little used and is entirely superfluous. No physician uses it at the present time, even in deficient menstruation. Experience teaches that there is no case of amenorrhœa in which sabine is of use where other remedies have failed. Sabine is often used however in the production of criminal abortion, although never used for the purpose of producing abortion by a physician.

Externally.—Pulvis herba sabinæ is often used as an external application (ointment) to cause the disappearance of venereal warts. In syphilitic condylomata it is of little use; and in no case does it appear to possess any advantage over other irritant substances.

Dosage and Preparations.—1. Herba sabinæ; internally from 0.3 to 1.0 (5.0 pro die), in powder or infusion. Externally in the form of ointments (powder with equal parts of fat).

2. Oleum sabinæ, from ½ to 3 drops pro dosi as an oleosacch.; or in pill or alcoholic solution.

3. Extract. sabinæ, soluble in water, from 0.05 to 0.2 (ad 0.2 pro dosi! ad 1.0 pro die!)

4. Unguent. sabinæ, 1 part of extr. sab. to 9 of ung. cereum; used as an irritant ointment.

Thuja Tops—Herba S. Summitates Thuja.—The leaves of thuja occidentalis; contains an ethereal oil, a glucocide and resin. It causes severe inflammation of the skin and mucous membranes, and is a popular abortive agent.

Folia Taxi, from Taxus Baccata; contains in addition to an ethereal oil a narcotic body—an abortive agent.

Rue—Folia Rutæ, from a cultivated plant, Ruta Graveolens; contains an oxygenated and non-oxygenated ethereal oil. It acts like oil of turpentine as a severe irritant upon the mucous membranes and skin, and is also used by the laity for the production of abortion.

END OF VOLUME II