this preparation causes much smarting, it may be diluted with water. *Follicular pharyngitis*, *chronic coryza*, and even *syphilitic affections of the mouth*, *throat*, and *nares*, may be much benefited or even cured by the same application. It is said that five to ten drops of the fluid extract, taken by the stomach, will act favorably in the removal of the very troublesome affections named above, but the author is unable to verify these observations.

Hydrastis is very useful as a *stomachic tonic*, and may take the place of calumba in the treatment of *atonic dyspepsia*. A few drops of the tincture or fluid extract (five to fifteen) taken before meals, daily, for some time, will often cure *chronic gastric catarrh*, and remove the distressing headache which frequently accompanies this disease. It is one of the best remedies for the *stomach catarrh of chronic alcoholism*, and is probably the best substitute, if given in sufficient doses, for the alcoholic stimulant when its habitual use is to be abandoned. *Catarrh of the duodenum* is in a similar manner relieved by hydrastis, but this agent has special utility in duodenal catarrh when accompanied by *catarrh of the gall-ducts and jaundice*. Its use should, in these affections, be continued for some time. When a catarrhal state of the cystic duct—often resulting from or aggravated by catarrh of the duodenum—leads to inspissation of the bile and crystallization of the cholesterin, decided benefit accrues from the use of the preparations of hydrastis.

When *constipation* is dependent on deficient secretion, and the stools are dry and hard, it may be overcome by this remedy, but torpor of the muscular layer of the intestine is not affected by it.

Chronic catarrh of the intestine, even when it has proceeded to ulceration, is sometimes remarkably benefited by hydrastis. When the stools are very frequent and there is much pain, it is advantageous to combine a little opium with it. In *fissure of the anus*, *hæmorrhage from the rectum*, and *ulceration of the rectal mucous membrane*, applications of fluid extract of hydrastis to the affected parts promote healing.

The alkaloid hydrastine may be used as a substitute for quinine in many of the conditions for which the latter is now so frequently prescribed, viz., to promote appetite and digestion, and to improve assimilation in cases of *debility*, in *convalescence from acute diseases*, in the various *cachexiæ*, especially the paludal.

As a remedy for *intermittents*, hydrastine ranks below quinine considerably. It should be given under the same regulations as those which govern the administration of quinine, to the physiological and therapeutical action of which it is closely allied. The hydrastine of the eclectics, which is really muriate of berberine, is also a remedy of value in intermittents. The fluid extract of hydrastis contains, of course, both alkaloids. In chronic malarial poisoning (paludal cachexia), hydrastine and berberine may be given with ferruginous preparations, as quinine is so frequently employed. It exerts the same power, though less in degree, which quinine has over enlarged spleen of malarial origin.

The preparations of hydrastis are used with advantage in certain affections of the genito-urinary organs. In *chronic Bright's disease*, it appears to lessen the excretion of albumen. It diminishes the mucus in *catarrh of the bladder*. It is often the most efficacious remedy which we can employ in *gonorrhœa* after the acute stage has subsided, and in *gleet*. Especially in the latter has the author witnessed excellent results from its employment. The local use of hydrastine, or of the fluid extract of hydrastis, should be conjoined with the internal administration. The author has seen no injection so frequently successful in gonorrhœa as hydrastine. ℞ Hydrastinæ, ʒ j ; mucil. acaciæ, ℥ iv. M. A half-ounce as an injection. Better, probably, the fluid extract, diluted properly or in combination, may be used for the same purpose. It is also a useful medicine in the treatment of *spermatorrhœa*, *prostorrhœa*, or *urethral leucorrhœa*, when locally applied.

Uterine and vaginal leucorrhœa, *ulcerations*, and *erosions* of the *cervix uteri*, are quickly improved by the topical application of the fluid extract of hydrastis, which may be used in an undiluted state.

Unhealthy and *sloughing sores*, *chancroid*, old *ulcers* of the leg, are improved in character by the local use of this remedy. To prevent septic decompositions in wounds or cavities communicating with the external air, it may be freely used by local application and injection. It has also been used, apparently with benefit, to the surface of *cancerous growths ;* but the only influence it can have in this disease is to relieve fetor by preventing decomposition.

Authorities referred to :

Porcher, Dr. F. Peyre. *Resources of the Southern Fields and Forests*, Charleston, 1869, p. 15.

CINCHONA AND ITS PREPARATIONS.

Cinchona.—*Cinchona.* The bark of any species of Cinchona (Rubiaceæ) containing at least three per cent of its peculiar alkaloids. (U. S. P.)

Cinchona Flava.—Yellow cinchona (calisaya-bark). The bark of *Cinchona calisaya*. It should contain not less than two per cent of alkaloids which yield crystallizable salts.

Cinchona Rubra.—Red cinchona. The bark of *Cinchona succirubra*. It should contain not less than two per cent of alkaloids which yield crystallizable salts.

Preparations.—*Decoctum Cinchonæ Flavæ.* Decoction of yellow cinchona (℥ j—Oj). Dose, ℥ ss— ℥ j or more.

Infusum Cinchonæ.—Infusion of cinchona (cinchona, yellow bark,

unless specified, 6 parts ; aromatic sulphuric acid, 1 part ; water to make up 100 parts). Dose, ʒ j—ʒ j or more.

Extractum Cinchonæ.—Extract of cinchona (cin. flava). Dose, gr. j—x.

Extractum Cinchonæ Fluidum.—Fluid extract of cinchona. Dose, ♏ x—ʒ j or more.

Tinctura Cinchonæ.— Tincture of cinchona (yellow cinchona, 20 parts to 100 of alcohol, glycerin, and water). Dose, ʒ ss—ʒ ij.

Tinctura Cinchonæ Composita.— Compound tincture of cinchona (red cinchona, 10 parts ; bitter orange-peel, 8 parts ; serpentaria, 2 parts ; alcohol, glycerin, and water, to make 100 parts). Dose, ʒ j—ʒ ss.

Cinchoninæ Sulphas.—Sulphate of cinchonine ; occurs in white, shining crystals ; dissolves in fifty-four parts of cold water, in much less boiling water, in seven parts of alcohol, and very sparingly in ether. Dose, gr. v—ʒ ss.

Quininæ Sulphas.—Sulphate of quinine ; occurs in colorless, very light, and silky crystals ; is entirely dissolved by about seven hundred and forty parts of cold, or thirty of boiling water, is readily soluble in alcohol, and in water acidulated with sulphuric acid, but is insoluble in ether. Dose, gr. j—ʒ j.

Quininæ Valerianas.—Valerianate of quinine. A colorless salt, crystallizable, and having a peculiar odor and bitter taste ; is soluble in one hundred and ten parts of cold, or in forty parts of boiling water, and in six parts of cold alcohol. Dose, gr. j—ʒ j.

Pilulæ Quininæ Sulphatis.—Pills of sulphate of quinine. Each pill contains one grain.

Unofficial Salts of Quinine.—Kinate, tannate, citrate, acetate, tartrate, phosphate, nitrate, hydrochlorate, arseniate, ferrocyanate, picrate, etc. Salicylate of cinchonidine is a really useful addition to these salts. It has therapeutic property only second to the salts of quinine, and may be substituted for the latter in the treatment of malarial affections.

Composition.—Cinchona is remarkable for the number and variety of the principles obtained from it, viz., five alkaloids, two simple acids, two tannic acids, and a resinoid substance. The most important alkaloid is *quinine*, which exists in all varieties of bark, but is most abundant in the yellow or calisaya bark. It occurs in combination with kinic and kino-tannic acids. *Quinidine* is an alkaloid isomeric with quinine, and may be used as a substitute for the latter in the same dose. It is less bitter than quinine, and its sulphate is more soluble in water. *Cinchonine* is found in greatest quantity in the pale barks. It unites with acids to form salts, of which the sulphate is most frequently used. Therapeutically considered, cinchonine has about half the strength of quinine. *Cinchonidine* is an alkaloid isomeric with cinchonine as quinidine is with quinine. *Aricine*, which has close analogies with cinchonine, has been found in the aricia or Cusco bark.

The alkaloids are combined in bark with the acids *kinic* and *kinovic*, chiefly with the former. There are also two kinds of tannic acid, *kino-tannic* and *kinovi-tannic*, and a resinoid substance, *kinovin*. None of these have thus far been applied to therapeutical purposes, except kinic acid, which has been utilized to form a kinate of quinine, under the belief that a combination of quinine in its natural state would be more efficient as a remedy than as combined with a mineral acid.

When the mother-liquor, left after the crystallization of the alkaloids, is evaporated, a black residue is obtained, which is called *chinoidine*. This contains amorphous quinine and cinchonine, and probably also quinidine and cinchonidine. It is a very efficient anti-periodic, and may be used with advantage as a substitute for quinine, in doses about twice as large.

With regard to the quantity of the alkaloids contained in the barks, respectively, it may be stated that the three varieties—pale, yellow, and red—differ only in the relative proportions of their constituents. The pale bark contains most cinchonine, the yellow most quinine, and the red an equal proportion of each.

Administration. — The alkaloids of bark are intensely bitter. Quinine being insoluble in the saliva, is less objectionable than its salts. The sweet principle of liquorice covers the taste of the cinchona alkaloids. A sufficient dose of quinine may easily be inclosed in a chocolate caramel. The sugar-coated pill, when freshly prepared and by a reputable maker, is a convenient and suitable form for administration ; but by keeping it becomes hard and insoluble. The most active form is a solution, the quinine being dissolved by the aid of sufficient dilute acid. For hypodermatic use, the following formulæ may be followed : ℞ Quininæ sulphat., ʒ j ; morphinæ sulph., gr. ss ; acid. sulphur. dil., ♏ xl ; aquæ destil., ʒ j. M. Filter. Sig. : Sixty minims contain seven and a half grains. Lente's solution is the following : ℞ Quininæ bisulph., grs. l ; acid. sulph. dil., ♏ c ; aquæ font., ʒ j ; acid. carbol. liq., ♏ v. Solve. The quinine is dissolved by the aid of heat, and after filtration the carbolic acid is added.

Antagonists and Incompatibles.—Substances containing tannic acid in a free state should not be administered with the *infusum* or *decoctum cinchonæ*. The preparations of iodine (tincture and compound solution) are also incompatible, for they form insoluble compounds with the cinchona alkaloids. The alkalies, alkaline carbonates, and alkaline earths, should not be administered with the solutions of the alkaloids, because the latter will be precipitated.

As an agent promoting constructive metamorphosis, cinchona and

its alkaloids are therapeutically antagonized by mercury, the iodides, the salts of copper, zinc, and lead.

As Gubler has shown, morphine and quinine are antagonists in respect to their effects on the brain. As regards their action on the sympathetic system, on the heart, and on the temperature, quinine, and belladonna and its alkaloid, are antagonistic.

Synergists.—All those agents which promote constructive metamorphosis, as the bitters, the ferruginous preparations, arsenic, and the acids, are synergistic to cinchona.

Physiological Actions.—The preparations of cinchona are known as "astringent bitters": they contain, in addition to bitter principles, two tannic acids. As bitters they act as stomachic tonics; that is, promote appetite, the flow of gastric juice, and the digestive power. Long continued, as is the case with all the other bitters, they set up a gastric catarrh, and digestion becomes painful and labored. They differ from the simple bitters in exercising an astringent action on the intestinal mucous membrane, and cause constipation. The red bark is more decidedly astringent than the yellow or pale bark.

Since the time of Sir John Pringle, who made the first experiments on this point, cinchona has been known to possess antiseptic properties. The powdered bark, applied to unhealthy wounds, arrests putrefactive decomposition, and promotes healing. The alkaloids are destructive of the minute organisms, on the presence of which fermentative changes depend, and hence, when added to milk, urine, and other animal fluids, will prevent decomposition (Binz, Herbst, Baxter, etc.). Quinine, the most active of the alkaloids, is not equally destructive of all minute organisms: some, it merely inhibits; others, it kills. The bacteria of septic fluids resist its toxic action to a great extent, and are only inhibited by the largest quantity.

When the crude bark is introduced into the stomach, the alkaloids are dissolved out by the acid gastric juice, in which they are freely soluble. Any portion of the bark, or of the alkaloids, escaping solution in the gastric juice, probably, passes out with the other unabsorbed contents of the intestine. The alkaline reaction of the intestinal juices will cause precipitation of the alkaloids, which, forming insoluble combinations with the bile-acids, will not be absorbed. From the stomach the alkaloids diffuse into the blood with facility. In the alkaline blood, it is probable that the alkaloids are held in solution by the carbonic acid (Kerner). No changes visible by the unassisted eye are discernible in the blood, for, notwithstanding the observations of the older writers, who affirm that the blood was dark and uncoagulable, the moderns deny the existence of such alterations (Briquet, Schwalbe). Quinine acts in a definite manner on certain constituents of the blood—on the hæmoglobin, impairing its power to transport active oxygen or ozone, into which the ordinary oxygen of the air is

converted. This is demonstrated in the following manner: Mix with old turpentine, that is, turpentine long exposed to the air, and therefore holding ozone, some tincture of guaiacum; if, now, some hæmoglobin or a drop of blood be added to the mixture, the tincture of guaiacum assumes a blue color, the change of color being due to the oxidation of the guaiacum by the active oxygen or ozone contained in the hæmoglobin (Hermann). The addition of certain substances, notably of quinine, prevents the reaction; in other words, destroys the ozonizing action of the blood. Binz has shown that so small a quantity of quinine as one part to twenty thousand exerts this action to a considerable extent. As soon as the blood is withdrawn from the peculiar influence exerted by the walls of the blood-vessels, as was some time ago shown by Pflüger and Zuntz, its alkalinity begins to decline, and presently it exhibits an acid reaction. Correspondingly with the progress of this acidification, A. Schmidt has shown that the quantity of contained oxygen diminishes and the carbonic acid increases. These changes, leading finally to the death of the blood, are greatly retarded by the addition of quinine (Schulte, Binz, Ransoné, Kerner). From these observations we draw the conclusion that quinine lessens the oxidizing or ozonizing function of the blood.

Binz and his pupils have shown that quinine inhibits or lessens the activity of the white blood-corpuscles, and indeed destroys them, or arrests their production; for, in cats poisoned by this agent, the number of white corpuscles was found to be considerably less than in unpoisoned animals (Scharrenbroich, Martin, Jerusalimsky, Geltowsky). By all the observers just named, by Baxter, who made a series of very carefully conducted experiments, and by Cutter, it has been established that quinine inhibits the amœboid movements of the white corpuscles. These bodies, as other masses of protoplasm, are in constant motion, changing their form and appropriating the materials of their nutrition. Such movements are called amœboid, and they are arrested by quinine, even in so small a quantity as one part to four thousand; hence it is called a protoplasmic poison. Quinine has also the power to prevent or arrest the migration of the white corpuscles from the vessels. This Binz was the first to demonstrate, using the method employed by Cohnheim for exhibiting the phenomena. This is now generally conceded, although denied by Schwalbe; but, as the observations of Geltowsky show, the quantity of quinine necessary to produce the result varies with the animal experimented on, and ranges from one part in four thousand to one part in eight hundred, outside of the body (Appert). No amount, short of a fatal dose, can affect the movements of the white corpuscles in the living warm-blooded animal, according to Geltowsky, who, therefore, holds to the same view as Schwalbe on this point. In opposition to the views of Binz must also be placed Schtschepotjaw, who has studied the effects of small quantities.

Quinine also affects the rate of movement of the heart. An important distinction exists between the action of small and large doses. It is a matter of daily observation that ordinary medicinal doses of quinine (from two to five grains) increase the action of the heart, while experiments with large doses have demonstrated that this agent depresses the circulation. Observations on the intra-cranial circulation, as seen through the retina and drum membrane, have demonstrated that an artificial hyperæmia results from the administration of medicinal doses. On the other hand, as Favier was the first to observe, quinine in large doses depresses the heart, arrests it in the diastole without impairing its contractility, and lowers the arterial tension (Chirone, Briquet). Quinine acts on the cardiac motor ganglia, and hence occur the feebleness of the heart's movements and in part the general lowering of the vascular tension (Lewizky). Besides these effects, it unquestionably depresses the vaso-motor system, after a short preliminary stimulation, probably (Jerusalimsky, Lewizky, Briquet). This depression of the heart from large doses occurs after the vagi are divided (Briquet, Schlockow, Köhler, Lewizky), and is more conspicuous when the agent is introduced into the jugular vein, indicating that the impression made on the heart is not through an increase of inhibition, but on the cardiac ganglia. Immersion of the heart in a quinine solution quickly arrests its movements.

In the normal condition of the human subject, quinine does not appreciably affect the temperature. In the course of some carefully conducted experiments a few years ago, I found that the maximum doses caused not more than a half-degree decline in a healthy adult. In fever, however, the influence of antipyretic doses is prompt and decided. This result may be attributed to several factors : to the depression of the heart and arterial tension, to the suspension of the oxidizing power of the blood, and to the inhibition of the white corpuscles. Jürgensen was the first to observe that quinine prevented the rise of temperature produced by certain physiological acts, as, for example, active exercise, but Kerner has more particularly developed the experimental evidence proving this fact. By active gymnastics, the temperature was found to be elevated two to three degrees Centigrade ; but the previous exhibition of a full dose of quinine prevented this rise of the body-heat. Kerner also ascertained that the increased cutaneous secretion, the result of active exercise, was prevented by the administration of sufficient quinine. From all of these facts, it seems evident that the lowering of the temperature by this agent depends on diminished production of heat rather than increased radiation and loss by cooling of the skin. This statement seems confirmed by the experiment of Lewizky, made in Hering's laboratory, by wrapping a rabbit in protective envelopes to prevent loss of heat by cooling, and then practicing the intra-venous injection of quinine ; the result was a depression of temperature as in animals not so enveloped. To such experiments, the author opposes the insuperable objection that the temperature in rabbits kept at rest declines, and to a remarkable extent, without the administration of any medicament. Nevertheless, the fact of the reduction of temperature by quinine is undoubted. By Popow, who admits the diminution of temperature, the influence of quinine over the body-heat is referred to some unknown biological process.

In small doses quinine exerts a distinct stimulant effect on the cerebrum, increases the mental activity, and even exhilarates in some mobile constitutions. As some hyperæmia is caused by it, the resulting cerebral stimulation is probably secondary to this change in the vascular condition. In full medicinal doses, as the quinine accumulates in the brain, a sense of fullness in the head, constriction of the forehead, *tinnitus aurium*, more or less giddiness, even decided vertigo, may be produced. Dullness of hearing results from considerable doses, and deafness has in rare cases been permanent. In a long experience of its use and extended observation, no case has come under my notice of permanently impaired hearing, although the temporary condition is usual. According to Knapp, Moos, and others, amaurosis is produced by very large doses. White atrophy of the optic disks occurs, and most of the vessels disappear from the field. This must be due to strong contraction of the vessels, since this condition is quite curable, the ordinary appearance of the retina being restored in most of the cases. Permanent atrophy of the optic nerve is, however, an occasional result. Amblyopia is frequently produced by the use of considerable doses kept up for some time. It is recovered from readily by suspending the administration of the remedy and taking the necessary steps to improve the intraocular circulation. In actually toxic doses all of the above symptoms have been intensified. There are intense headache with constriction of the forehead, dimness of vision or complete blindness, deafness, delirium or coma, dilated pupils, weak, fluttering pulse, irregular and shallow respiration, convulsions, and finally collapse and death. It is excessively rare to encounter such severe cerebral symptoms.

The influence of quinine over the functions of the spinal cord is yet *sub judice*. Chaperon some time ago demonstrated that quinine lessened and ultimately abolished the reflex function of the spinal cord. This result he decided was due not to immediate action on the spinal cord, but to stimulation of Setschenow's center of inhibition of reflex movements. Brunton, who has repeated Chaperon's experiments, has found them to be correct. The observation of Schlockow, that the first effect of quinine is to increase the sensibility of the reflex function of the spinal cord, has much probability in its favor. Heubach has also, after moderate doses, observed some evidences of

the existence of reflex irritability, but the experiments of Brunton show that these reflex effects decline with the increasing stimulation of the inhibiting center. Brunton's experiments were also directed to ascertain whether the sulphuric acid in combination with the quinine was responsible for the effects observed, but the result proved that quinine is the active agent in stimulating Setschenow's inhibiting center.

As quinine depresses the functions of the sympathetic system, its action is opposed to that of agents which have the power to promote uterine contractions, hence, *a priori*, it would not seem to be abortifacient. Very numerous and conflicting statements have been put forth, because there are no exact data. The few cases in which uterine action followed the administration of quinine were, doubtless, due to malarial intoxication or to other causes, and hence the association of uterine action with the effects of quinine was accidental. The innumerable instances in which quinine has been given during the existence of pregnancy, without initiating contractions of the womb, are certainly conclusive against the view of its abortifacient power. While it is not a special uterine stimulant, it may exert such an action indirectly. When uterine inertia is due to depression of the vital forces, quinine, in moderate doses, then becomes a valuable stimulant, and is utilized for this purpose in obstetric practice.

The diffusibility of quinine and its rate and mode of elimination have been studied by Bence Jones, Ciotti and Albertoni, and Kerner. Jones in his researches availed himself of the fluorescent property of animal tissues, possessed also in a high degree by the alkaloids of cinchona, especially quinine. To this substance, as it appears in animal tissues, Jones gave the name "animal chinoidin," but he was not aware that fluorescence is a property possessed by large numbers of animal and vegetable bodies. Nevertheless, he recognized the fact that the diffusibility of quinine could be estimated by the increase in the fluorescence of animal textures, and he thus ascertained that in a half-hour after the administration of quinine a positive gain in fluorescence of the crystalline lens is observed. It is probable that under some circumstances—a catarrhal state of the mucous membrane, for example—a portion of the quinine taken fails to be absorbed, and is consequently excreted by the intestines (Byasson). The effect of this agent on the secondary assimilation is involved in more or less doubt. Opposing opinions have arisen from the different points of view taken. In the normal condition quinine, in small quantity, stimulates the nutrition, and increases the excretion of waste products—urea, uric acid, creatinin, extractives, etc.; but, in considerable doses, the opposite condition obtains—the decrease in the quantity of uric acid is especially well marked (Ranké, Kerner)—and when administered in malarial fevers all the products of waste are greatly increased. The conditions attending the use of the remedy, therefore, influence the result. Considerable doses in the normal state diminish the excretion of urea, uric acid, creatinin, and phosphoric and sulphuric acids (Kerner). Strassburg, however, failed to find any change in the carbonic acid. According to the observations of Cutler and Bradford, quinine has an obvious effect on the globular richness of the blood, increasing the relative proportion of the white, and diminishing the red globules. The action of quinine on the spleen is still *sub judice*. Piorry was the first to note a reduction in the size of the organ produced by quinine, but he had an exaggerated notion of the nicety by which a difference in the size of an organ could be made out by the plessimeter and hammer. Küchenmeister examined the subject experimentally in 1851, with negative results, but afterward, operating with larger doses, obtained confirmation of Piorry's view. Mosler, after dividing all the nerves of the spleen, ascertained that quinine in large doses still acted on the contractile elements, and reduced the size of the organ. Jerusalimsky, in an elaborate research, has established the same fact. That the enlarged spleen of malarial infection is reduced by quinine is an undoubted clinical fact. From these positive observations it must be concluded that quinine does act on the spleen, notwithstanding there are numerous negative statements. It follows, hence, that the diminution in the red and increase of the white corpuscles may be due to this action.

Quinine diffuses out of the blood into the urine, chiefly, but also into the sweat, saliva, milk, and pathological exudations (Kerner, Briquet, Binz). Jürgensen found quinine in the urine in ten minutes after the hypodermatic injection. Thau had evidence of its presence in the urine in a half-hour after the ingestion of a half-drachm dose each by two persons, and he holds that the maximum elimination takes place in about eight hours, but the excretion is not completed until two days after the administration. According to De Renzi, quinine remains in the organism a variable number of days, and may indeed be discovered in the urine on the third day; in a special case, as late as seven days. Binz also finds that the elimination of quinine is variable and rather slow, the maximum being excreted within forty-eight hours. From the time the agent appears in the urine, the systemic action is manifest, and the maximum effect of any given dose must be experienced in advance of the period of maximum elimination, which Thau places at eight hours. According to Kerner, quinine appears in the urine in a somewhat modified form.

The action of quinine has occasionally been attended by the appearance of an eruption on the skin. Sometimes the exanthem has been in the form of an erythema, sometimes it has assumed the appearance of urticaria; again, it has seemed to be herpetic. There is, in fact, no constant and invariable eruption, and many of the reported