ride (tinctura ferri chloridi). The precipitate is thoroughly washed and then mixed with a rather large amount of water. The directions of Bunsen and Berthold for its preparation are to add a small amount of sulphuric acid to a solution of 100 gm. of ferrous sulphate, then nitric acid, and boil; when cold add an excess of ammonia water, filter and wash, and mix the precipitate with 900 gm. of water. It is rather better, however, to obtain the antidote by the addition of carbonate of magnesium to a solution of ferric sulphate and avoid filtering and washing; one of the products of this operation is sulphate of magnesium, which adds to the value of the antidote by virtue of its cathartic action.

Since the freshly prepared hydrated sesquioxide undergoes gradual changes which lessen its effectiveness in a very material degree, it is advisable when possible to prepare it as occasion demands. The stability is in direct proportion to the care in preparation and the purity of the iron salt. Since all warming is to be avoided in the preparation, the solutions used must be considerably diluted. If the antidote is to be preserved for cases of emergency, it is best kept in a cold place and well stoppered.

In the administration of this antidote there are certain points which are to be kept in mind; the poison should be removed from the stomach as completely as possible by emetics or the stomach tube; the antidote should be freshly prepared if possible, and should be given lukewarm and in large doses (30 to 60 gm.) at first, at intervals of about ten minutes, and later at longer intervals, until the symptoms disappear and iron appears in the stools. It is perhaps needless to say that treatment should be begun as soon as possible. It is well to follow up the treatment with an active cathartic, on account of the poisonous character and slight solubility of the resulting compound. It has been well shown experimentally by Schroff, that when the latter substance is itself administered to animals, arsenic may be detected in the urine.

Basic acetate of iron, dialyzed iron, and saccharated iron (ferrum oxydatum saccharatum solubile) have been used with varying success in poisoning by arsenic and arsenious compounds.

Iron filings and reduced iron have, it is claimed, been used with good effect in poisoning by salts of gold, mercury, copper, and other metals. Dose, 2 to 10 gm. frequently repeated. Sulphide of iron has been proposed as an antidote to mercury, lead, antimony, copper, gold, platinum, tin, arsenic, and other metallic salts, but its value is not proven.

Carbonate of copper in repeated doses of 0.25 to 0.50 gm. with sugar and water has been recommended in acute phosphorus poisoning, following an emetic. It is supposed to act upon the particles of phosphorus in such a way as to prevent their solution by furnishing them first with a layer of phosphide of copper, and later with one of the metal itself. Its use is to be preceded and followed by emetics.

3. The Physiological or Dynamic Antidotes are remedies employed to combat the symptoms or after-effects, and to neutralize the effects of poisons after absorption into the system. As their name implies, they do not act on the poison themselves chemically, mechanically, or otherwise. Consideration of the individual members of this class is beyond the scope of this article and comes more properly under the head of therapeutics.

Charles Harrington.

ANTIDYSPEPTIC AND TONIC SPRINGS.—Nottoway County, Virginia.

Post-Office.—Burkeville.

Access.—Via Norfolk and Western Railroad, thence one half mile to springs. Small hotel and boarding houses.

These springs are located in a fine, salubrious region about 530 feet above the sea level. They are two in number, the flow from the main spring, No. 1, being about 240 gallons per hour. The water was analyzed in 1890 by Prof. E. T. Fristoe, of the Columbian University, with the following results:

One United States Gallon Contains:

Solids.	Grains.
Sodium hydrate (?)	0.51
Sodium chloride	0.23
Magnesium chloride	0.20
Magnesium carbonate	0.94
Magnesium sulphate	1.30
Calcium sulphate	0.46
Iron oxide	Traces.
Aluminum	0.16
Lithium	Traces.
Calcium carbonate	1.65
Nitric acid	Traces.
Organic matter	Traces.
Sulphuric acid	Traces.
Phosphoric acid	0.78
Silica	1.89
Total	8.17

Free carbonic acid gas, large amount.

The acids and elements expressed in the table are undoubtedly in combination. The water has an extensive reputation in the treatment of dyspepsia and intestinal disorders. It is believed to possess useful properties as a tonic. It may be classified as a light sulphated saline. The water of Spring No. 2 contains about ten grains of solid matter per United States gallon, including enough iron to make it a valuable chalybeate. It is warmly recommended as a ferruginous tonic. These waters are bottled and sold, being shipped to any desired point.

J. K. Crook.

ANTIKAMNIA is a proprietary name for a whitish powder which is claimed by the makers to be a mixture of coal-tar products, and found by various analyses to contain acetanilid and sodium bicarbonate, with or without caffeine. Its dose, as an analgesic, is from five to ten grains.

W. A. Bastedo.

ANTIMONY.—1. General Medicinal Properties of Compounds of Antimony.—As usual with compounds of the heavy metals, all antimonials capable of absorption produce essentially similar constitutional effects. These effects are, in medicinal dosage, depression of pulse in both force and frequency, with fall of arterial tension, diaphoresis, increase of mucous secretions, and, with rise of dosage, nausea and vomiting, with decided muscular debility. In large doses antimonials are powerfully poisonous, causing heart failure, prolonged and violent vomiting and purging, with cramps, and general collapse. Locally, soluble antimonials, such as that most commonly used preparation of antimony, *tartar emetic*, are irritant—much of the emetic effect being evidently due to local irritation of the stomach upon swallowing. Concerning the rationale of the production of the various effects described, the only points of clinical importance are that the effects upon the pulse seem to arise from a direct depressing action upon the heart, and not secondarily from a possible excitation of the restraint influence exerted through the vagus nerve, and that the vomiting seems to be induced partly by direct local irritation of the stomach, and partly by an action upon the nerve centres, after absorption. For tartar emetic vomits when injected into the veins, but yet not so readily as when given by swallowing.

Therapeutically, antimonials generally are used to depress the pulse in sthenic fever, to hasten the secreting stage in respiratory catarrhs, empirically to oppose the inflammatory process—most notably again in respiratory inflammations, such as pneumonia, and, possibly, to determine vomiting.

2. The Preparations of Antimony Used in Medicine.—The antimonials of the United States Pharmacopœia are derived from three compounds of the metal, namely, *antimonious oxide*, *antimonious sulphide*, and *potassio-antimonious tartrate*.

Antimonious Oxide, Sb_2O_3.—Antimonious oxide is official as *Antimonii Oxidum*, Antimony Oxide. It occurs

as "a heavy, grayish-white powder without odor or taste, and permanent in the air. Almost insoluble in water, and insoluble in alcohol. Nitric acid fails to dissolve it, but it is readily soluble in hydrochloric acid without effervescence, and also in a warm solution of tartaric acid, or in a boiling solution of potassium bitartrate" (U. S. P.). Antimonious oxide exerts the general properties of the antimonials, but is uncertain, doubtless because from its insolubility it must undergo chemical conversion in the stomach before absorption is possible. It is rarely prescribed except in the official preparation, entitled:

Pulvis Antimonialis, Antimonial Powder; "James' Powder." This powder consists of thirty-three parts of antimony oxide, intimately mixed with sixty-seven parts of "precipitated calcium phosphate." It is white in color, and from the insolubility of its two ingredients is without taste. It is a generally mild but yet uncertain antimonial, available for the antifebrile purposes of the mineral. Dose, for such use, from 0.20 to 0.50 gm. (gr. iij.–viij.) every few hours.

Antimonious Sulphide, Sb_2S_3.—Under the title *Antimonii Sulphidum*, Antimony Sulphide, the U. S. P. makes official "native antimony sulphide, purified by fusion and as nearly free from arsenic as possible." This is the compound commercially known as *antimony*, or *crude antimony*. It is in conical masses of metallic appearance, which, pulverized, yield a dull, black, odorless and tasteless powder, insoluble in water or alcohol. It is official as the source of the following preparation, which, again, is used only pharmaceutically to yield still another:

Antimonii Sulphidum Purificatum, Purified Antimony Sulphide. The sulphide above described is finely pulverized, the coarser particles separated by elutriation and rejected, and the finer macerated in ammonia water for five days, then washed and dried by heat. By these manipulations impurities in the native sulphide are gotten rid of, the ammonia serving to dissolve out copper, a common contamination. The purified sulphide is a dark-gray powder of the qualities already detailed. It is used to make the following:

Antimonium Sulphuratum, Sulphurated Antimony. "Kermes Mineral." The purified sulphide is boiled in diluted solution of soda, the liquid strained, and while still hot precipitated by diluted sulphuric acid. The precipitate is then washed, dried, and finely pulverized. It appears as a reddish-brown, amorphous powder, odorless and tasteless, and insoluble in water and in alcohol. In composition it is "chiefly" antimonious sulphide, "with a very small amount of" antimonious oxide. Like all the insoluble antimonials, its medicinal action is uncertain, and the preparation is rarely prescribed except as it occurs in the following official pill:

Pilulæ Antimonii Compositæ, Compound Pills of Antimony; "Plummer's Pills." These pills are compounded of one part each of sulphurated antimony and calomel, and two parts of guaiac. Each pill weighs 0.16 gm. (about 2.5 grains). This preparation had an ancient reputation in the treatment of secondary syphilis, scaly skin eruptions, chronic rheumatism, etc. One or two pills constitute a dose, to be given twice a day.

Potassio-antimonious Tartrate, $2K(SbO)C_4H_4O_6+H_2O$. —This salt, so well known by the name *tartar emetic*, is official under the title *Antimonii et Potassii Tartras*, Antimony and Potassium Tartrate. It is commonly made by boiling together in water antimonious oxide and acid potassium tartrate (cream of tartar), and obtaining the resulting double tartrate by crystallization from the solution. Other methods, however, are resorted to by some manufacturers. Tartar emetic occurs as "colorless transparent crystals of the rhombic system, becoming opaque and white on exposure to air; or a white granular powder, without odor, and having a sweet, afterward disagreeable, metallic taste. Soluble in seventeen parts of water at 15° C. (59° F.) and in three parts of boiling water, but insoluble in alcohol, which precipitates it from its aqueous solution in the form of a crystalline powder" (U. S. P.). Aqueous solutions of tartar emetic spontaneously decompose, and are precipitated by acids, alkalies, and alkaline carbonates, soluble salts of lead, and vegetable astringent preparations, such as infusion of galls.

In modern medical practice in the United States tartar emetic is practically the only antimonial used, and is available for all the effects of antimony as already described. In doses of about 0.005 gm. (gr. $\frac{1}{12}$) it depresses the heart and promotes secretion; in doses of about 0.01 gm. (gr. $\frac{1}{6}$), repeated, it nauseates, and in doses of from 0.03 to 0.12 gm. (gr. ss. to ij.) it vomits, with the usual prolonged and distressing attendant nausea of the antimonials. In quantities beyond those last mentioned it is a dangerous and easily fatal poison. It may be given in aqueous solution, and if employed to provoke vomiting, should be prescribed in doses of 0.03 gm. (gr. ss.), to be repeated every fifteen minutes until vomiting ensue, or until four doses have been taken. When wanted in small dosage for catarrhs or fevers, the official *Vinum Antimonii*, Wine of Antimony, is more commonly prescribed. To make this wine, four parts by weight of tartar emetic, dissolved in a little boiling water, is added to fortified white wine in such quantity as to yield 1,000 parts by measure of product (about gr. 1.8 to the fluidounce). Wine of antimony keeps far better than aqueous solutions of tartar emetic, but yet will deteriorate in time. From ten to thirty drops is the average dose. Wine of antimony is an ingredient of the *compound mixture of glycyrrhiza* of the Pharmacopœia. (See *Glycyrrhiza*.)

Tartar emetic enters into the composition of the official compound syrup of squill. (See *Squill*.)

Tartar emetic, as a soluble antimonial, possesses local properties wanting in the insoluble compounds hitherto discussed. It is, namely, powerfully irritant, and applied to the skin in ointment or plaster produces after a while an eruption, papular at first, but passing to vesicles or pustules, much resembling the eruption of smallpox, for which it actually has been mistaken. The eruption is painful, and may leave scars. Pustulation by tartar emetic is a possible, but disagreeable method of effecting a continuous counter-irritation. The best mode of application is to prescribe an ointment of one part of tartar emetic to four of simple ointment, to be rubbed, but rubbed lightly, into the skin. Too vigorous inunction may produce an uncontrollable inflammation.

3. General Therapeutics of Antimony Compounds.—*Vascular Depression.*—The power of antimonials to reduce the pulse is unbounded, but in high degree the effect is associated with so much general depression as to be unavailable. Still, in the beginning of a congestion or inflammation, notably of the air passages, in a vigorous subject, a mild antimonial effect is often most happy. Indeed, so marked often is the benefit, that it is probable that depression of undue vascular excitement is but one factor of the curative influence.

Promotion of Secretion in Catarrhs.—Nauseants generally tend to this effect, but none can compete with antimonials in power. Yet again, the use of antimonials should be confined, except in very small dosage, to the fairly vigorous, and particularly should be avoided in subjects at either extreme of age.

Induction of Vomiting.—Although a powerful, antimony is a poor emetic, since it is both slow and unnecessarily nauseant and depressing. Furthermore, the vomiting does not stop when the stomach is empty, as is the case, practically, with the so-called mechanical emetics. For these reasons the emetic operation of antimony is nowadays rarely utilized.

Relaxation of Spasm.—In full antimonial nausea the concomitant muscular debility may determine relaxation of spasm, as in *laryngismus stridulus*, or may be pronounced enough to be of avail in the reduction of a hernia or dislocation. But for all these purposes an even greater degree of paresis is so easily obtainable by medicines less disagreeable and depressing than anti-

monials that the latter are seldom resorted to for the therapeusis. Tartar emetic, in full dosage, has been praised highly by some in the treatment of tetanus.

Edward Curtis.

ANTIMONY, POISONING BY.—Pure metallic antimony is not thought to be directly poisonous. Symptoms of gastro-enteritis occasionally followed its medicinal use in times past, and serious symptoms are said to have been produced by the metal when inhaled in the state of vapor; but the effects in these cases have usually been attributed either to the partial oxidation of the metal or to the presence of arsenic, which is a frequent impurity in commercial antimony. Many of the compounds of antimony are more or less poisonous. The most important of these are tartar emetic and the terchloride of antimony.

Tartar Emetic.—This is a double tartrate of antimony and potassium, and is the most important compound of antimony. It occurs in the form of colorless, slightly efflorescent, crystals, which are usually rhombic octahedrons, or in the form of a white powder obtained by the pulverization of these crystals. It is soluble in about fifteen parts of water at the ordinary temperature, and in less than three parts of boiling water. Tartar emetic may give rise to acute poisoning, as a result of a single large dose, or to chronic poisoning, as a result of small doses frequently administered. Its poisonous properties are due to the oxide of antimony which it contains.

Acute Poisoning, Symptoms.—When a large dose of tartar emetic is taken, the acrid metallic taste of the poison is usually perceived by the patient. After a short time, varying from a few minutes to half an hour, there is nausea and faintness, followed by violent vomiting. There is burning in the throat and œsophagus; sometimes great thirst and difficulty of swallowing; pain in the stomach and abdomen. The vomiting is usually persistent. The vomited matters consist at first of the contents of the stomach, then of mucus, later of mucus mixed with bile, and in some cases blood. Violent and persistent purging is usually an early symptom. The discharges are liquid, resembling those of cholera, and frequently contain blood. Symptoms of extreme depression and prostration, ending in collapse, which is a prominent feature in acute tartar-emetic poisoning, soon appear. The skin is cold and covered with perspiration; the pulse, which appears to be increased in frequency till immediately before vomiting sets in, is at this stage diminished in frequency and force, and may become imperceptible; the respiration is irregular, but for the most part slow, with hasty and forced inspiration and prolonged expiration; the temperature is lowered. Cramps in the extremities, delirium, loss of consciousness, and convulsions, not infrequently precede death. The urine in mild cases is increased in quantity, as it is also in the beginning, even in fatal cases; but in such, toward the close, it is generally scanty and bloody, and even suppressed (H. C. Wood, Jr.). Exceptionally, vomiting is absent; in such cases the other symptoms are said to be, as a rule, more prominent. In some cases a pustular eruption, resembling that produced by the external application of tartar emetic, has appeared on the body on the third, fourth, or fifth day. In fatal cases death may occur within a few hours, but is more frequently delayed for two, three, or more days. Recovery is very frequent.

External Application.—Tartar emetic is occasionally employed externally as a counter-irritant, producing sooner or later a burning pain, followed by a pustular eruption, on the parts to which it has been applied. Its use for this purpose has been followed, in several instances, by symptoms of irritant poisoning as a result of its absorption through the integument. In two cases, at least, death has been caused by its application to the broken skin.

Chronic Poisoning, Symptoms.—The symptoms produced by the repeated administration of small doses of tartar emetic are of the same general character as those which have been described under acute poisoning. They are, however, less severe and less rapid in their progress, varying in these respects with the quantity administered and the frequency of the administration. The most prominent are nausea, retching, vomiting of mucous and bilious matters, soreness and constriction of the throat, a sensation of burning and pain in the stomach, a feeling of uneasiness and sometimes pain in the abdomen, a constant feeling of depression, gradual loss of strength, and progressive emaciation. The nausea and vomiting recur after each administration of the poison. Purging is not so prominent a symptom as in acute poisoning. The stools are at first normal; later, there may be diarrhœa, usually alternating with constipation. The time at which death occurs depends chiefly upon the size of the doses and the frequency of their administration. Taylor collected five cases, four of which were fatal. In three, death took place in six, eight, and nine days respectively; in the fourth, the poison was administered over a period of three months preceding death.

Fatal Quantity.—The quantity of tartar emetic required to destroy life cannot be stated with accuracy, since its effects are variable and frequently depend less on the quantity taken than on other conditions. Owing probably to early and abundant vomiting, recovery has frequently taken place after doses varying from 7.8 to 31 gm. (℥ij. to viij.). On the other hand, as a result probably of idiosyncrasy, alarming symptoms, and even death, have followed the administration of doses which would ordinarily be considered non-fatal. In sixteen fatal cases collected by Taylor, the smallest fatal dose was, in a child, 0.048 gm. (gr. 0.75), and in an adult, 0.130 gm. (gr. ij.); but in the latter case there were circumstances which favored the fatal operation of the poison. Taylor quotes a case in which 0.022 gm. (gr. 0.33), given in divided doses to a child four years of age, produced alarming symptoms. Serious symptoms have followed the administration of 0.032 gm., 0.26 gm. and 0.40 gm. (gr. 0.5, 4, and 6¼ respectively) to adults. Dr. Draper reported a case, at a meeting of the Boston Society for Medical Observation, in 1880, in which 0.26 gm. (gr. iv.), followed in ten minutes by 0.13 gm., proved fatal to a healthy adult woman in fifty-three hours. According to Wakley, 0.195 gm. (gr. iij.) killed an adult in twenty-four hours; 0.65 gm. (gr. x.) and 0.97 gm. (gr. xv.) have proved fatal to children, 2.3 gm. (gr. xxxvi.), 2.4 gm. (gr. xxxvij.), 3.24 gm. (gr. l.), and 3.9 gm. (gr. lx.) to adults. Children, aged persons, and those who are in delicate health are more susceptible to its action than healthy adults. On the other hand, there are certain diseased states of the body in which large and repeated doses have been administered without producing any symptoms of poisoning. Taylor concludes that under favorable circumstances 0.65 to 1.3 gm. (gr. x. to xx.), taken at once, might destroy an adult, and that a still smaller quantity than this might suffice if taken in divided doses.

Appearances.—The mucous membrane of the stomach and intestines is usually more or less inflamed and softened. The inflammatory appearances in the intestines are usually most marked in the duodenum, cæcum, and rectum. The mucous membrane of the mouth, throat, and œsophagus is sometimes inflamed. There are occasionally aphthæ and pustules in the mouth, throat, œsophagus, or stomach; sometimes aphthous ulceration of the glands of the small intestines. The stomach and intestines contain more or less mucus, colored with bile or blood or both. Hypostatic congestion of the lungs has been frequently noticed. A greater or less degree of fatty degeneration of the liver, kidneys, heart, muscular tissue of the diaphragm, and cells of the gastric glands, sometimes recognizable only by microscopic and chemical examination, is a well-recognized result of the action of antimony compounds. This was first pointed out by Saikowsky, who states that there is also a diminution of the amount of glycogen in the liver, and in some cases a total disappearance of it.

Absorption and Elimination.—Antimony is quickly absorbed, and after death may be detected in nearly all the organs and tissues of the body. It is rare to find more than a trace in the stomach, since its emetic properties usually secure its early removal. The liver and kidneys probably contain the largest amount. It is eliminated in the urine and bile, also, according to Lewald, in the milk. When tartar emetic is injected into the veins it is said to be rapidly eliminated through the mucous membrane of the stomach (Brinton). The time required for its complete elimination is uncertain. Millon and Laveran detected antimony in the urine of patients as late as twenty-four days after the last administration of tartar emetic. They also found antimony in the fat, bones, and other tissues of dogs, as late as four months after the last administration. They state that there are well-marked intermissions in the elimination.

Treatment.—If vomiting has not occurred, it should be provoked by tickling the throat or by the administration of warm water. The best antidote is tannic acid, which forms with oxide of antimony a compound insoluble in water. A solution of the acid may be used. In the absence of this, an infusion of green tea, decoctions of oak bark, gall nuts, or Peruvian bark, or tincture of kino or catechu, all of which contain tannic acid, may be administered. The stomach should be thoroughly washed out after the administration of the tannic acid. Opium should then be given, to allay pain and irritation. Stimulants, external and internal, may be required. In the treatment of chronic poisoning it is essential to prevent the further administration of the poison. Stimulants, tonics, and nutritious diet are required.

Terchloride of Antimony, Butter of Antimony.—This is a transparent, fusible, crystalline substance, which, on exposure to moist air, rapidly deliquesces to a clear liquid. When pure it is colorless, but it frequently contains more or less chloride of iron, which imparts to it a color varying from yellow to dark brown. It is decomposed by water, with the formation of hydrochloric acid and an insoluble white basic chloride, which may be distinguished from the corresponding basic chloride of bismuth by its solubility in tartaric acid. A concentrated hydrochloric acid solution of the chloride has some uses, and has given rise to a few cases of accidental or suicidal poisoning. It is a violent corrosive and irritant.

Symptoms.—These resemble closely the symptoms produced by the mineral acids. They come on very rapidly, and consist of violent vomiting and severe pain in the throat, stomach, and abdomen, soon followed by symptoms of collapse. Death has taken place in two hours, and has been delayed for ten and one-half, eighteen, and twenty-four hours.

Fatal Quantity.—The smallest quantity required to destroy life is unknown. Ninety cubic centimetres (three fluidounces), approximately, of the solution has proved fatal to adults in three cases. Recovery has taken place after 30 c.c.

Appearances.—The lips, mouth, and throat have usually been found more or less corroded. The interior of the stomach and upper part of the small intestines are intensely inflamed, corroded, and sometimes black, as if charred. In a case related by Taylor, the whole alimentary canal, from the mouth to the middle of the small intestines, presented this black appearance. The mucous membrane was entirely destroyed, and the parts beneath were so soft that they were easily torn with the fingers. Fatty degeneration of the liver, kidneys, heart, muscular tissue of the diaphragm, and cells of the gastric glands, was observed in rabbits to which small doses of terchloride of antimony were administered (Saikowsky).

Treatment.—This consists in the administration of sodic carbonate, chalk, or magnesia, to neutralize the free acid, and of preparations containing tannic acid.

William B. Hills.

ANTINERVIN is a proprietary remedy, which, according to Squibb, contains acetanilid 50 parts, ammonium bromide 25 parts, and salicylic acid 25 parts. It is antipyretic and sedative in eight-grain doses.

W. A. Bastedo.

ANTIPERIODICS.—The various malarial fevers are all characterized by a more or less regular recurrence of their characteristic symptoms, to wit: chill, fever, and sweating; the periods for such recurrence varying according to the life cycle of the particular organism which causes the special type of fever. These phenomena are therefore spoken of as periodical, and the remedies which are known to exert an inhibitive effect upon them are called antiperiodics. The symptoms against which antiperiodics are most commonly employed are those constituting the seizure in the estivo-autumnal, tertian, and quartan types of ague, and consisting of the cold, the hot, and the sweating stages. In the milder forms of intermittent and remittent fever, the breaking up of the recurrent chills as soon as possible is important for the comfort of the patient, but in the so-called "pernicious" malarial fevers, it may be a matter of life or death to stop at once those congestive chills whose effects are so alarming, and it is in such cases that the great value of the antiperiodics is seen. Other chronic manifestations of the malarial cachexia, such as neuralgia, are amenable to antiperiodic treatment, and it is noticeable that the success of quinine in the relief of neuralgia is in proportion to the regular periodicity of the attacks.

By far the most important antiperiodic—of more value, in fact, than all the others taken together—is cinchona, with its derivatives. Ever since the cure of the Countess of Cinchon of an ague at Lima, in the earlier half of the seventeenth century, first gave name and fame to the drug, its value in intermittent fever has been acknowledged. More than any other remedy in the Pharmacopœia it deserves to be considered a specific. Its direct action on the malarial parasite in the blood has been abundantly shown.

Quinine, by reason of its more concentrated and convenient form, is now used almost entirely to the exclusion of cinchona as an antiperiodic. For this purpose the dose must be large, corresponding in quantity to the so-called antipyretic dose of the drug. The quinine should be so administered as to produce a saturation of the patient's system at the time when the next seizure would occur. To attain this object we may best give one full dose, 1 to 2 gm. (gr. xv. to xxx.) on the drop of temperature following a given paroxysm in order to abort the following paroxysm. Or it may be given in divided doses through the twenty-four hours before an expected chill, the last dose being six hours before the time the chill is due. If the interval is much shorter than this, the chance of aborting the very next seizure is diminished. If a single administration of the drug anticipates the chill by only four or five hours, the chances are about equal for and against its success. In no other form is quinine more effective than in that of the crystals of the sulphate in an acid solution (bisulphate) or dissolved in lemon juice. The solubility is usually somewhat impaired in the pill form, and the administration in coffee fails to give the best effect because of the imperfect solubility of the tannate. The manufacturing chemists have put upon the market a "compound syrup of licorice," which quite effectually disguises the bitter taste of the drug, without, so far as the writer knows, interfering with its solubility.

When the periodicity of the intermittent fever is irregular, and in cases of remittent fever, cinchonism should be produced as soon as possible after a seizure, and maintained by moderate but sufficient doses for several days. In the cases of pernicious malaria, if there are not ten or twelve hours before the expected time of attack in which to secure complete cinchonism by the oral administration of the drug, it should be given subcutaneously. In order to secure its complete solution, acid must be added, one minim of dilute sulphuric acid to each grain of quinine usually sufficing. But this solution has the disadvantage of being irritating, and

there is some danger of abscess. This risk, however, should be taken in preference to that of a severe congestive chill. The hydrobromate of quinine is especially adapted for subcutaneous use. It may be prepared according to the following formula:

℞ Quininæ sulph..... 10 (gr. clx.)
Acidi hydrobromici (Squibb)... 4 (ʒ i.)
Aquæ (vel spts. frumenti)...ad 30 (ad ℥ i.)

The kinate and the disulphate of quinine are preferred by some for hypodermic use. The dose of quinine subcutaneously is less than by the mouth, and its action is more prompt. When for any reason neither of the foregoing methods is available, the drug may be given by the rectum in doses somewhat larger than by the mouth. For children and others with sensitive stomachs, when haste is not an especial object, quinine may be given by inunction. For this purpose an eligible preparation is the following:

℞ Quininæ sulph ..... 5 (gr. lxxx.)
Acid. oleic. pur ..... 30 (℥ i.)
Ol. olivarum ..... 30 (℥ i.)

Dissolve the quinine in the acid with the aid of gentle heat. Add the oil. The solution should be clear.

There is considerable choice among the various salts of quinine both as to their strength and as to their solubility. For example, the acetate contains 87 per cent. of quinine, the basic and neutral hydrochlorate each nearly 82 per cent., the basic lactate 78, the basic hydrobromate 76, the basic sulphate 74, the neutral sulphate less than 60 per cent., while the tannate, much in favor for administration to children in the form of "chocolate quinine tablets," has only 20 per cent.

The hydrochlorate is the most soluble salt, and as it is one of the richest in quinine, it is, in spite of its slightly greater cost than some others, the most eligible. The neutral hydrobromate is soluble in 6 parts of water, while the basic sulphate is soluble only in 581 parts of water.

In old malarial cases, in many of which the liver is enlarged, we must, in order to get the full and prompt effect of quinine, preface or accompany its exhibition by the use of a mercurial, as calomel or blue pill, followed by a saline.

The other alkaloids of cinchona, quinidine, chinoidine, cinchonidine, and cinchonine, have some antiperiodic value, but are all inferior to quinine, and if used should be given in larger doses. Regarding the dose of quinine, it should be said that it varies much not only with the individual, but with the place. In the tropics and in the habitat of malaria much larger doses are tolerated and are necessary to break up a chill than in temperate climates and non-miasmatic localities. The prophylactic value of quinine against ague is even greater than its curative action. A moderate amount—as, for instance, a grain three times a day—may be taken constantly for years without any ill effects. This precaution is one that should be taken by every one compelled to live in a malarious country. Even in non-malarious districts persons who have contracted ague elsewhere should, after breaking up the chills by the antiperiodic doses, as described above, continue with small quantities of quinine for a fortnight or more, or better, with a full dose once a week.

Next to cinchona, the most useful antiperiodic which we possess is probably arsenic. It is to those chronic cases which have assumed a somewhat irregular type, and in which we hardly know at what time to expect a chill, that arsenic is particularly adapted. It may be given in the form of Fowler's solution, beginning with 0.3 gm. (m v.) three times a day, thence carried up to 0.5 or 0.7, or even 1 gm. three times a day, or the arsenious acid may be given in granules of at first 0.0015 to 0.002 gm. (gr. $\frac{1}{40}$ to $\frac{1}{30}$) three times a day, pushed till the physiological effects are reached. With arsenic we do not attempt to stop the very next paroxysm; hence it is not adapted for pernicious cases. It should always be well diluted and given on a full stomach.

When treatment has been delayed until the chill is actually "on," quinine is useless for that seizure. Nothing is so efficacious to check a chill actually in progress as a full dose of morphine subcutaneously. Chloroform is also recommended for this purpose in a dose of from 2 to 4 gm. (ʒ ss. to i.) in sweetened water or mucilage. Good effects have been claimed for the administration, during the chill, of nitrite of amyl by inhalation, and nitrate or muriate of pilocarpine hypodermically.

Nectandra, or bebeeru bark, has met with some success as an antiperiodic. The alkaloid, in the form of the sulphate of beberine, contains whatever of virtue the drug possesses, and may be given in the same doses and at the same times as quinine.

Warburg's Tincture, formerly in much repute, especially in India, as an antiperiodic, contains some sixty-four ingredients, of which the most active is quinine, in the proportion of ten grains to the ounce.

The eucalyptus seems to possess some antiperiodic virtue. Among the peasantry of Southern Europe it has quite a reputation. Careful observation shows that in highly malarious localities it is often without effect. The oil of eucalyptus in doses of 0.1 to 0.3 gm. (m ij. to v.), may be given, or the tincture in doses of 1 to 2 gm. (m xv. to xxx.). That it is of use in the milder cases is made probable by the fact of its undoubted power as a prophylactic. Since the tree was introduced into Southern Europe in 1856, its growth has much improved the healthfulness of many marshy regions. The Trappist monks devoted themselves to cultivating this tree in the most malarious regions of Italy, with the result of making places habitable that were formerly highly unhealthy.

Among the other succedanea of quinine, usually most successful when combined with, rather than entirely replacing, that drug, are salicin and salicylic acid, given in doses of 1.0 to 1.3 gm. (gr. xv. to xx.), repeated frequently until tinnitus is induced; the antipyretics of the coal-tar series, antipyrine, phenacetin, etc. The sulphites, especially the sulphite of magnesia and the hyposulphite of soda, have been recommended by some physicians in this country, in doses of 1.0 to 1.5 gm. every two hours. The ferrocyanide of iron, despite its disagreeable appearance and taste, has been found useful by Flint in doses of 4 to 8 gm. (ʒ i. to ij.). Nitric acid in 0.5 gm. (m vij.) doses, every six hours, through paroxysm and intermission; the chloride of sodium, given to the extent of 10 gm. (ʒ ij.) during the intermission; the chloride of ammonium, the iodide of ammonium, and the iodide of potassium, in 0.3 to 0.5 gm. (gr. v. to viij.) doses, repeated and increased; piperine and narcotine, each in doses of 0.2 gm. (gr. iij.); methylene blue (gr. ij. to iv.) in capsules—these and other drugs have all had their advocates as being of more or less value in preventing the periodic attacks of ague.

Finally, it remains to allude to two or three classes of drugs under which most of the other numberless remedies that have been suggested against intermittent fever may be classed. Emetics and cathartics, when there is time for their administration, sometimes render the system more susceptible to the action of quinine. Alum, ipecac, sulphate of copper, fraxinus, wahoo, Indian hemp, and the like probably owe what reputation they have as antiperiodics to this fact; administered alone they would be quite worthless. Some of the simple and aromatic bitters, on the other hand, may, in mild cases, replace cinchona. Anthemis (chamomile); eupatorium (thoroughwort), ilex (holly), parthenium (feverfew), hydrastis, and cascarilla have a popular repute in the treatment of intermittent fever, by reason of their bitter quality. When it is remembered that the natural tendency of ague is to recovery as soon as the subject is removed from the source of malarial infection, the antiperiodic value of a large number of the drugs last enumerated will appear quite problematical.

Charles F. Withington.

ANTIPYRETICS. See *Appendix, Vol. VIII.*

ANTIPYRIN. — "PHENAZONE," "ANALGESIN," $C_6H_5(CH_3)_2C_3HN_2O$. This popular antipyretic was made known to the profession by Ludwig Knorr in 1884. It is a coal-tar derivative prepared according to a patented process, by the action of acetyl acetic ether upon phenyl-hydrazine, the patent for which expired in 1899. It is a base somewhat analogous to ammonia, and has the property of combining with an acid or an alkali to form salts. It is official in the B. P. under the title *Phenazone*.

It occurs in colorless, scaly crystals, without odor and possessed of a somewhat bitter taste. It is readily soluble in water, alcohol, and chloroform, less so in ether, about one part in fifty. The melting point is 110° C. Ignited with free access of air it burns without residue. It is neutral to test paper.

Antipyrin may be distinguished from all other organic compounds by the action of ferric chloride; this producing a deep red color which is discharged by the addition of dilute sulphuric acid in excess. Other compounds produce various colors and differ in the effect of the sulphuric acid. The bright red color is clearly visible in 1 to 100 solution; in 1 to 100,000 a light brown, and in 1 to 500,000 a light yellow color is produced. Nitrous acid added to a solution forms a green color, and nitric acid a yellow color which deepens to crimson on warming. Both these tests are characteristic of antipyrin. The presence of acetanilid is also detected by the melting point of the suspected salt. The two compounds melt approximately at the same temperature, but a mixture of the two reduces the melting point very decidedly, equal parts melting at 45° C. Many other distinctive tests have been proposed. In 1 to 1,000 solutions, iodine and iodide of potassium produce a reddish-brown, potassio-mercuric iodide a white, and potassio-bismuthic iodide an orange-red precipitate. In 1 to 100 acidulated solutions, Nessler's reagent, mercuric or auric chloride, and tannic acid, produce colorless or yellow precipitates; picric acid a yellow; and ferrocyanide of potassium a bluish-green precipitate.

The solubility of antipyrin and its action as an alkaloidal base render many drugs and preparations incompatible, and not infrequently some very unsightly as well as inert mixtures are ordered by the physician. E. J. Millard and A. C. Stark[1] describe a series of experiments made for the purpose of testing the compatibility of antipyrin with the whole of the drugs and preparations of the pharmacopœia that are likely to be prescribed in combination, together with many that are unofficial. The following is the list they have prepared and the changes that are produced:

Acid. carbolic.: precipitate.
Acid. hydrocyan. dil.: yellow coloration.
Acid. nitric. dil.: faint yellow coloration.
Acid. tannic.: white insoluble precipitate.
Alumen (ammonia): deep yellow coloration and precipitate.
Amyl nitrite (acid): green coloration.
Arsen. iodid.: precipitate.
Chloral hydras: precipitates in strong solution, no apparent action in dilute.
Cupri sulphas: solution turns green.
Dec. cinchonæ: precipitate.
Ext. cinchon. liq.: precipitate.
Ferri sulph.: brownish-yellow color and precipitate.
Glycer. ac. carbol.: precipitate.
Glycer. ac. tannic.: precipitate.
Hydrarg. perchl.: precipitate.
Infus. catechu conc.: precipitate.
Infus. cinchon. acid.: precipitate.
Infus. rosæ acid.: precipitate.
Infus. uvæ ursi: precipitate.
Liq. arsen. et hyd. iod.: precipitate.
Liq ferri perchlor.: } blood-red coloration.
Liq. ferri pernit.: }
Liq. ferri persulph.: }
Liq. pot. permang.: reduction quickly takes place.
Sodii salicylas: liquefies.
Spts. ætheris nit. (acid): green coloration.
Syr. ferri iodid.: reddish-brown coloration.
Tinc. catechu: precipitate.
Tinc. cinchonæ: precipitate.
Tinc. cinchon. co.: precipitate.
Tinc. ferri perchl.: red coloration.
Tinc. gallæ: precipitate.
Tinc. hamamelid.: precipitate.
Tinc. iodi: precipitate.
Tinc. kino: precipitate.
Tinc. laricis: precipitate.
Tinc. rhei: precipitate.

It was found that with dilute acids no change took place, as with sulphuric, hydrochloric, nitric, and phosphoric acids, soluble salts were formed. The changes that take place with amyl nitrite and nitrous ether occur only when the preparations are acid and contain free nitrous acid, but as this is generally present under ordinary circumstances, these compounds should never be prescribed with antipyrin. Calomel is considered to form a toxic compound when combined with antipyrin, but these observers were unable to notice any change, and mercuric chloride could not be detected in the mixture. Sodium bicarbonate, when triturated with antipyrin, causes a decomposition and disengages the odor of ether. Many substances combine with antipyrin to form stable and definite chemical compounds. Some of them have proved to possess important therapeutic properties and their number is constantly being increased. The most important of these are iodopyrin, salipyrin, and hypnal, information in regard to which may be sought for under their respective titles. The following have also been recommended:

Naphthopyrin is formed when antipyrin is triturated for a length of time with beta-naphthol, one part of the latter with two parts of the former. It assumes the character of a tough mass which gradually forms into crystals when kept for a length of time. It is insoluble in water, soluble in alcohol and ether. A more recent method of preparing the drug is by dissolving 150 gm. of naphthol in ninety per cent. alcohol, and adding to it gradually 190 gm. of antipyrin dissolved in the smallest possible quantity of water. The mixture is to be constantly stirred, and in a few minutes it becomes clouded and then clear; the pure crystals being deposited.

Antipyrin benzoate is formed by the addition of antipyrin to a boiling aqueous solution of benzoic acid. It is slightly soluble in cold and boiling water, but very soluble in alcohol and ether. It has a pungent taste and a slight odor of benzoic acid. A *citrate* and *picrate* may be prepared in the same way.

Phenopyrin is prepared by mixing equal parts of crystalline phenol and antipyrin. It forms an oily liquid, free from color, insoluble in cold and sparingly soluble in hot water.

Pyrogallopyrin is obtained by the interaction of pyrogallol and antipyrin in substance or in solutions. It is a crystalline substance, sparingly soluble in hot or cold water, but soluble in alcohol and ether.

Resopyrin results from the interaction of solution of resorcin and antipyrin; an oily mass is formed which solidifies into a hard, white, opaque body. From an alcoholic solution it forms in crystals. It is not soluble in water, but is so in alcohol, ether, and chloroform.

The physiological effect of antipyrin has received more attention than many of the later derivatives of the same character, and in this country the work of Wood, Reichert, Hare, and Cerna and Carter has done much to advance our knowledge of this remedy. Upon the nervous system the action is similar to that of other antipyretics. There is a short stage of stimulation followed by one of depression. Upon the motor tracts it acts by dulling the power of conducting impressions and inhibits reflex action.

Upon the sensory nerves, antipyrin acts as an anodyne both when administered internally and when locally applied This effect is early manifested, and before any