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

dangerous stage begins it has been shown that animals can be operated upon without causing them pain. The muscular sense is also lost early, the signs of ataxia being among the first symptoms noticed and the last to pass off; the special senses are at first rendered more sensitive, but this is quickly overcome and depression follows.

The antipyretic properties are considered due to the action of the drug on the heat centres rather than to any influence upon the circulation. It has been shown that it causes a diminution in the production of heat, and continues to act when the secretion of the skin is checked by a previous dose of atropine.

Antipyrin exerts a very decided action upon the respiration. Even in small doses it has been known to greatly accelerate the number of respirations, and in all cases in which toxic doses are given the rapidity is excessive, and, as a fatal termination approaches, the expirations become spasmodic in character. This has been shown not to be influenced by the section of the vagus nerves, and is assumed to be due to a direct action on the respiratory centre in the medulla oblongata.

In moderate doses very little effect is produced on the circulation, but in large doses it weakens the heart and causes depression and collapse. As the result of experimental work, Drs. Cerna and Carter[2] formulate the following conclusions, which, in general, coincide with the work of previous observers: 1. In small and moderate amounts antipyrin produces a rise of the arterial pressure, this stimulating effect being due to an action on the heart. 2. A lowering of the pressure by large and toxic doses is due similarly to a depressant action of the drug upon the cardiac organ. The remedy does not appear to affect the vasomotor system. 3. Antipyrin causes an increase in the pulse rate through paralysis of the cardio-inhibitory centres. The secondary decrease in the number of pulsations is of a purely cardiac origin, the drug exercising a depressant effect upon the heart itself.

Upon the blood there is no effect when moderate doses are administered: in large quantities, however, it produces a chocolate discoloration of the blood which is due to the alteration of the hæmoglobin into methæmoglobin. There is no alteration of the corpuscles caused by the drug itself, but ultimately its administration may lead to a diminution in number and may produce anæmia.

In many instances antipyrin exerts an irritant action on the stomach and causes nausea and vomiting. Another objection to its employment is the copious perspiration which is frequently produced and which generally accompanies a rapid reduction of temperature. A rash of the character of urticaria, in some cases described as resembling measles and scarlatina, is caused in some patients. It generally follows the use of the drug for a length of time, but in many instances a single small dose has had this effect. These rashes are usually accompanied by a burning and itchiness of the skin, and are exceedingly distressing. They rarely continue for more than a few hours and no ill effects remain, but in some cases vesicles, bullæ, and hemorrhagic rashes have been reported, the effects of which persist for some time. Another condition which proves very annoying is an irritation of the mucous membrane of the nose and throat, which may end in an ulcerative stomatitis.

The toxic symptoms produced when the drug has been given in very large doses are convulsive in character, and in accord with the symptoms observed in experimental research upon animals. There are generally marked salivation and lachrymation very quickly following the dose, crying and other signs of distress, and in a short time ataxia. This is followed by a convulsive stage, during which spontaneous convulsions are frequent, and are easily caused by flashes of light, clapping of hands, etc. Subsequently there will be paralysis, insensibility, and death. Respiration and the heart are greatly hurried, and death occurs during a convulsion or from paralysis of respiration. The heart generally continues to beat for some time, and is finally arrested in diastole.[3] When the drug is administered in lesser quantities, and often in ordinary doses, very unfavorable symptoms occur, the result of a depressant action. Collapse of the most alarming character sometimes follows ten and fifteen grain doses, and this is often accompanied by cyanosis and swelling of the eyelids and extremities. The milder symptoms of a toxic action are a rapid and weakened heart, shallow respiration, dyspnœa, oppression in the chest and in the head, giddiness, vertigo, numbness of the surface, irritation of the mucous membranes and skin, and many other symptoms indicating a depression of the circulation and nervous system. This undesirable action is the one great drawback of what is undoubtedly the most efficient antipyretic and analgesic compound that has yet been produced. To this is to be ascribed its decreased employment, as the frequent onset of alarming symptoms, often as sudden as they are unexpected, has caused the profession to avoid its employment in many cases in which it undoubtedly would prove of service. A careful consideration of cases in which the drug has been given will generally enable one to avoid these dangers. That dangerous symptoms are not very common is shown by the result of a collective investigation of the British Medical Association. Of one hundred and sixty-nine observers who reported, no fewer than one hundred and thirty-eight had never observed any ill effects worth mentioning. It is advised to exercise caution in cases of cardiac debility and whenever the respiratory organs or kidneys are affected. The remedy must also be cautiously given to the aged.

Antipyrin is rapidly absorbed, its effects are quickly produced, its elimination from the system begins within a short time after administration, and it is entirely removed within a few hours. In children it has been noticed that there is apparently a tolerance of the drug, as very large doses may be given without producing ill effects. In order to ascertain whether this was or was not due to a rapid elimination of the drug, a series of very interesting observations[4] were made. The urine of children, adults, and aged, to whom eight grains were administered, was systematically examined to determine the first appearance of the drug and the length of time it continued to be excreted. It was found that in the case of all the subjects excretion began within fifty minutes, and that within an hour the drug was present in abundance. The excretion, however, was most rapid in the children, in whom it could not be detected after fifteen or twenty hours; whereas in the adults it was present for twenty-four or thirty hours, and in the case of the aged its excretion was still more slow. When the dose was increased it was found that its first appearance in the urine was not hastened, but its elimination was much prolonged. It is also eliminated by the other secretions, including the milk of nursing mothers.

When antipyrin was introduced as an antipyretic the dose recommended was thirty grains in a single dose, which was to be repeated in four hours if the pyrexia was present, and a third dose of fifteen grains was to be given in another four hours if there were any signs of a rising temperature. This medication produced a decided reduction in the fever, and maintained a condition of apyrexia for from twenty-four to forty-eight hours; it was, unfortunately, often accompanied by profuse sweating and other signs of collapse, and was soon abandoned. It is now given in doses of from ten to fifteen grains, which may be repeated at short intervals if no effect is produced. When it is administered for the first time, it is safer to begin with five-grain doses. The fall of temperature generally begins in from half an hour to one hour, and the lowered temperature is maintained for several hours. In some instances the fall is very rapid, a decline from 103° to 96° F. taking place. Sometimes it is necessary to repeat the dose very frequently before any effect is produced, it apparently being necessary to saturate the system before freedom from fever is secured. In typhoid fever, and in all febrile disorders in which there is a periodic rise and fall of temperature, the time of its administration should be observed, as its action is much more marked when it coincides with the decline of the fever. In typhoid fever it is rarely employed as a mode

of treatment by the continuous administration of the drug; it is considered only of value as a means of reducing hyperpyrexia. Its use in tuberculous troubles is not looked upon with much favor, one great objection being the perspiration that is caused. It has been suggested to combine atropine with it as a means of counteracting this effect. In rheumatic fever it has been advocated by many as a remedy superior to the salicylates; in these cases it is given in fifteen or twenty grain doses five or six times a day. In many instances it has secured relief from pain when salicylate of soda has failed, but it has not proved itself equal to the older remedy in the treatment of rheumatism in any form when accompanied by fever.

Although introduced as an antipyretic, antipyrin was soon found to possess very decided analgesic and anodyne properties, and the latter application of the drug has almost eclipsed its earlier use. In all forms of pain of a neurotic origin, or in nervous diseases accompanied by pain, it has proved itself of especial value. It has been used with success in neuralgia, migraine, pruritus, sciatica, and lumbago, in the pains of tabes dorsalis, in the pains of angina, and in those arising from aneurism. It has been found to replace morphine in renal colic and asthma, and has even proved itself to be superior, as it in no way deranges the secretions. It has been used in all conditions in which the hypodermic use of morphine is generally resorted to, and has been found a very efficient substitute in the greater number of cases. As a remedy for headaches of a nervous origin it is very beneficial. In the forms peculiar to growing children, and in those accompanying anæmia and debility, it has been recommended by Germain Sée, who employed it in a large number of cases with marked success. The same observer also considers it of value in pain of a rheumatic character unaccompanied by fever. Although inferior to the salicylates in the febrile forms, he considers it decidedly superior to all other drugs when there is no fever. In the pains of dysmenorrhœa and other pelvic disorders it has also been employed with success. Its use in such cases is indicated when the suffering is of a nervous character, as the drug exerts no influence on the uterine contractions and fails to relieve the pains that arise from the efforts of the uterus to expel its contents. In obstetrical practice it has allayed much of the suffering that accompanies labor. Its effect resembles that of chloral. In the first stage, in primiparæ and in neurotic patients, it lessens the rigidity of the os and allays the painful spasmodic action. In tedious labor it lessens the exaggerated nervous pain which often in a reflex manner interferes with the efficiency of the uterine contractions. It is useless for the pain of the second stage, which is mechanical in its character. For the after-pains, due to the expulsion of clots, it is without effect, but in those that are of a neuralgic character it affords marked relief. The employment of the drug does not in any way increase the tendency to post-partum hemorrhage. It exercises no ecbolic action, and has proved of service in allaying the pains and checking the progress of threatened abortion. It has been recommended in cases in which it is desired to reduce the secretion of milk. Cases are reported in which doses of eight grains lessened the amount within a day and checked it altogether in three days.

The action of antipyrin on the spinal cord and nerve centres has led to its employment in many diseases of a neurotic character. In chorea it has proved useful, both in cases traceable to rheumatism and in those in which there was no such history. In a report[5] of sixty cases in which it was used, it was found to benefit two-thirds, diminishing the severity of the attack and shortening its duration. Recurrence, however, was noticed in three-fifths of the cases. It was found necessary to give large doses, from 3 to 6 gm. daily being required. This was found to be well tolerated for several weeks, and serious symptoms of poisoning were never noticed. Antipyrin was suggested as a remedy for whooping-cough by Sonnenberger, in 1887, and it has been used for this purpose to a very great extent, with varying results. The dose should be from two grains upward, according to the age of the child. One grain and a half for each year has been advised; for infants of a few months of age one-half to three-quarters of a grain is sufficient. In many of the cases reported remarkable effects have been announced, the disease having been cut short in a few days. This drug has also proved of service for enuresis, when of nervous origin and due to irritability of the bladder. It has also been employed in epilepsy, but not with encouraging results, but more favorable results are reported from its combination with ammonium bromide. From time to time cases have been reported of diabetes that have been successfully treated with antipyrin. The quantity given has ranged from 2 to 6 gm. daily. In some instances the excretion of sugar was wholly checked; in the majority it was lessened in quantity and the patient was relieved of all troublesome symptoms. The most marked effects were noticed in nervous patients and when the polyuria was excessive. The diet must not be neglected.

Antipyrin possesses a decided antiseptic action, and it has been suggested that this should be utilized both by internal administration and as a local application. It has been shown that a two-and-one-half-per-cent. solution prevents the development of the bacillus of diphtheria in various cultures, and a five-per-cent. solution applied to a culture containing the bacillus destroyed it in twenty-four hours. It has also been found to exert a powerful neutralizing action on the toxins of diphtheria. Applications of the remedy to the throat and its internal administration are advocated in this disease, but satisfactory evidences of the beneficial effects of this treatment are still lacking.

In stomachic disorders and diarrhœas of children antipyrin has been employed on account of its effect in checking fermentation. It is given in doses ranging from one-half to one or two grains.

The local application of the drug has proved of decided value as an anæsthetic remedy in various troubles of the nose, throat, and larynx; a solution of the strength of about four per cent., used as a spray or painted directly on the mucous membrane, being found effective in allaying the congestion and lessening the sensibility and irritability of the part. It at first causes a sense of heat and smarting, but this rapidly passes away and is followed by ease and comfort, and freedom from all the painful sensations that may have accompanied the inflamed condition. The sensitiveness of the nasal mucous membrane is more marked than that of the pharynx, and an application of cocaine is often required before the antipyrin can be applied; in such cases it is advisable to begin with a one-per-cent. solution. The powdered drug, or concentrated solutions, have been found to exert an anæsthetic and very astringent action, and have been used for the treatment of tuberculous disease and other painful affections, and in conditions in which there is a reflex element present. When it is applied in these concentrated solutions the resulting anæsthesia is complete, and lasts for one or two hours. A ten-per-cent. solution in a one-per-cent. solution of carbolic acid has been advised in operations upon the urethra.

Antipyrin has also been used in the treatment of certain forms of eye disease. Weak solutions of from one to three per cent. have been used with advantage in simple acute or chronic conjunctivitis. Under the influence of three or four washings a day, the secretion diminishes and a cure is rapidly effected. The solution at first causes a sensation of burning, which may be painful, but this lasts only a few moments and is followed by relief from all distress. Antipyrin[6] has recently been used to replace jequirity in the treatment of scrofulous pannus which has resisted other methods. The eye is to be rendered anæsthetic with cocaine, and a thin layer of antipyrin is deposited on the cornea with a brush, or by means of an insufflator. In spite of the cocaine the patient complains of pain and burning, and there is more or less lachrymation. When this reaction subsides the eyeball is gently massaged through the closed lid. The inflammation that arises varies in intensity, and from one