to several days must elapse before the process is repeated. The contraindications to this treatment are the presence of corneal ulcerations and phlyctenular keratitis. The most suitable cases are those in which there is extensive proliferation of the blood-vessels.

A very important property of antipyrin is its power of controlling hemorrhage. When placed in contact with blood at its normal temperature it thickens and condenses it without causing coagulation. When a concentrated solution or the powdered drug is applied to a mucous membrane it causes an anæmia more or less marked, according to the strength of the solution. When applied to an animal's mesentery the blood grows darker in color, the circulation becomes slow and ultimately ceases, and the parts appear almost bloodless after the application of a fifty-per-cent. solution. This styptic action may be secured by applying a plug of cotton saturated with a fifty-per-cent. solution to the bleeding surface, or the powdered drug may be used. This action has been confirmed in numerous cases of epistaxis and of bleeding from the tonsils, or after the extraction of teeth, and even in cases of uterine hemorrhage. In many instances it has been found that a ten-per-cent. solution was sufficient in ordinary hemorrhage from mucous membranes. In hæmoptysis of phthisis its internal administration was thought to prove beneficial, but the large quantities required to produce this effect were accompanied by dangerous symptoms.

To secure the full benefit of antipyrin it requires to be given in doses of ten to fifteen grains, and these should be repeated until the desired effect is obtained, or until forty or fifty grains have been given. These large doses have been given for a prolonged period without any ill effects, and to children much greater quantities in comparison have been given. The drug is generally administered in solution, and it is considered advisable to combine it with alcohol, ammonia, or some diffusible stimulant. The hypodermic injections have been advocated when it is desired to secure a local anodyne action. The effect is noticed in ten or fifteen minutes, and it lasts for six or eight hours. The usual dose is about four grains in ten minims of water, and when the painful area is great a number of injections are required. Cocaine often has to be added, as much pain is sometimes experienced. This method of administering the drug is not without its dangers, as it has produced gangrene of the toes when injected for painful affections of the foot. When the stomach is irritable and rebels against antipyrin, or when a local action on the pelvic organs is wished for, it may be given as an enema: antipyrin, gr. x. to xx., tinct. opii, ɱlv., aquæ, ʒiv. It may also be prepared as a suppository where such can be used with convenience.

Beaumont Small.

[1] The Druggists' Circular, August, 1890.
[2] Notes on New Remedies, 1882.
[3] Johns Hopkins' Bulletin, April, 1890.
[4] British Medical Journal, July 11, 1891.
[5] British Medical Journal, January 17, 1891.
[6] Therapeutic Gazette, December, 1892.

ANTIRHEUMATICUM (Kamm) occurs in the form of blue prismatic crystals which result from the action of sodium salicylate on methylene blue. It is soluble in water and alcohol, and is used in doses of gr. i. to gr. v., three times a day, in acute articular and gonorrhœal rheumatism. Larger doses tend to irritate the kidneys.

W. A. Bastedo.

ANTISEPSINE.—Asepsine, para-brom-acetanilid, para-mono-brom-phenyl-acetamide ($C_6H_4Br.NH.CH_3Co$). Prepared by acting with bromine on a solution of acetanilid in glacial acetic acid. The resulting white precipitate is recrystallized from alcohol. Antisepsine occurs in colorless crystals slightly soluble in water and somewhat more so in alcohol. It is antipyretic, antineuralgic, and analgesic, its action being much like that of acetanilid, but with a tendency to be more sedative. Dose, gr. ij. to x.

W. A. Bastedo.

ANTISEPTICS.—Those agents only which have the power of preventing the putrefactive decomposition of organic material are properly called *antiseptics* (from ἀντί, against, and σηπτικός, putrefying). But inasmuch as these agents have also the power of arresting other forms of fermentation due to the action of micro-organisms of the same class—*e.g.*, the acetic fermentation, the alkaline fermentation of urine, etc.—it will not be necessary to consider antizymotics—a more comprehensive term—separately, and we may accept as satisfactory evidence of antiseptic power the ability of a chemical substance to prevent the development of bacteria of any kind in a medium suitable for their growth. The amount of a given antiseptic agent necessary to accomplish this result is not, however, the same for all species of bacteria, but varies considerably, and can be ascertained for each species only by carefully conducted experiments.

Putrefactive decomposition is a complex process due to the combined or successive action of a variety of micro-organisms, and attended with the formation of a large number of volatile and non-volatile products. The volatile products of putrefaction, many of which are known to us only by their offensive odors, are those which, being recognized by the sense of smell, enable us to distinguish *septic* from other forms of fermentation. An agent which destroys these bad-smelling products of putrefaction is a *deodorant*. It is a popular error to suppose that an *antiseptic* or a disinfectant—terms which are often confounded—is an agent which neutralizes these putrefactive odors.

It is true that an antiseptic or a disinfectant may destroy the volatile products of putrefaction. Many agents properly so called have this power; they are not, however, properly so called for this reason. An antiseptic prevents the development of such volatile products by virtue of its power to arrest the process—putrefactive fermentation—which gives rise to them. (For definition of *disinfectant*, see article under that heading.) So, too, as regards the non-volatile products of putrefaction. Some of these are highly poisonous substances which it may be desirable to destroy, and they may be destroyed by certain of the chemical agents recognized as antiseptics; but this power does not entitle such agents to be ranked as antiseptics any more than does the power to destroy the volatile products of putrefaction. We know, as a result of extended experiments, that those agents which restrain the development of septic organisms also restrain the development of known disease germs, and *vice versa*. We are therefore justified in speaking of those agents as antiseptics which have been proved by laboratory experiments to prevent the development of pathogenic organisms in suitable culture media. Great care, however, must be exercised in drawing any inferences from experiments made upon one organism with reference to the *amount* which may be necessary to prevent the development of another. Thus the bichloride of mercury prevents the development of anthrax spores when present in a culture fluid in the proportion of 1 to 300,000; whereas some micrococci, and certain bacilli, commonly present in putrefying infusions, can multiply in the presence of 1 to 40,000.

It is evident that an agent which has the power of destroying putrefactive organisms must be an antiseptic. *Germicides* (see this heading) are, therefore, antiseptics. But antiseptics are not necessarily germicides, and, as a matter of fact, some of the best-known and most extensively used antiseptics have no germicide power at all, or else destroy the vitality of micro-organisms of this class—bacteria—only when used in a concentrated solution and after a comparatively long exposure; *e.g.*, alcohol, common salt, borax, etc.

Certain chemical agents are antiseptics because of their power in very small amounts to precipitate albuminous matters from organic infusions, and thus to render such infusions unsuitable as pabulum for the development of low organisms. This is especially true of the sulphate of iron, sulphate of zinc, chloride of zinc, and other metallic salts which are extensively used as "disinfectants." It is difficult to determine whether these substances also exert a restraining influence upon the development of germs, inasmuch as their action upon the organic pabulum essential for such development is manifested almost immediately, when they are added in very dilute solution to a culture medium. It is probable, however, that those agents which have been shown to possess germicide power—as, for example, the chloride of zinc, which destroys the bacteria of putrefaction in the proportion of one part to fifty—exert a restraining influence upon the development of bacterial organisms in amounts somewhat less than are required for the destruction of vitality. This inference is based upon our knowledge of the antiseptic action of other germicides which do not destroy our culture media by causing a precipitation of albuminoid matters contained in them.

Certain substances, which in dilute solution have no restraining power upon the development of low organisms, or may even serve as pabulum for them, in a concentrated solution prevent putrefactive decomposition; *e.g.*, sugar, chloride of sodium, sulphate of magnesia, etc. It is probable that these substances, in concentrated solution, prevent the development of putrefactive organisms by giving a density to the fluid containing them, which is incompatible with the performance of physiological processes—osmotic?—upon which vital activity depends.

After this brief account of the *modus operandi* of antiseptics we proceed to consider the comparative value of these agents as established by experimental data.

And first we may refer to certain antiseptics extensively employed in the preservation of food products, the use of which is so general and widely known that a mere mention of them is all that will be required in the present place. The list includes sugar, used largely in the preservation of fruits; vinegar, employed for the preservation of certain vegetables; alcohol, used to preserve fruits, and, very extensively, for the preservation of anatomical, pathological, and natural history specimens; and chloride of sodium, our main reliance for the preservation of meats and fish. All of these commend themselves for use by reason of their cheapness and the absence of noxious properties, rather than because of their antiseptic power, which is comparatively low. Every pathologist knows that his specimens are liable to spoil if the alcohol in which they are kept is not of the strength of fifty per cent. or above, and every merchant knows that his "pickled" pork or fish will become putrid in warm weather if the brine in which they are kept is not very "strong."

Attempts to establish the exact antiseptic value of various chemical agents have been made by numerous investigators, but it is hardly worth while to consider any experimental data published prior to 1875, as the methods adopted prior to that time were not such as could give reliable results, and we have more recent data concerning extended researches which conform more nearly with the exactions of science, upon which we shall base our detailed account of the comparative value of antiseptics.

In conformity with the broad sense in which the term antiseptics is used in the present article we shall report facts relating to the power of the agents named in restraining the development of pathogenic micro-organisms, or of those concerned in various fermentations, as well as those relating to their power to prevent putrefactive decomposition, to which a more strict use of the term would limit us.

In attempting to compare the results of different authors it will be necessary to remember that conformity can be expected only in those cases in which the same test organism has been employed, and in which the conditions, as to the nature of the culture fluid, etc., have been identical.

When the antiseptic agent is volatile it is evident that the result, in a protracted test, will be influenced by the form of the receptacle and the fact of its being open to the air or hermetically closed, as in the culture flasks used by the writer. Again, when the conditions of the experiment are such that the "breaking down" of a flask of beef tea, containing a certain antiseptic in a given amount, as in the experiments of Miquel, depends upon the development of spores or desiccated organisms contained in "dust," or upon accidental inoculation by air-borne spores, the material will be preserved for a longer time than in experiments in which a drop or more of fluid swarming with bacteria is added to the solution at the outset. And the larger the quantity of material containing putrefactive bacteria which is added to a culture fluid protected by an antiseptic the greater will be its liability to "break down."

In giving a detailed account of the comparative value of antiseptics we shall follow the classification of Miquel,[1] to whom we are indebted for a very comprehensive and carefully conducted series of experiments made at the Observatory of Montsouris, Paris, in connection with his extended researches relating to atmospheric organisms. The figures given in the following tables also represent the results reported by this author, unless otherwise stated.

The classification of Miquel is as follows:

	Effective in the proportion of
1. Substances eminently antiseptic....	1 : 100,000 to 1 : 10,000
2. Substances very strongly antiseptic.	1 : 10,000 to 1 : 1,000
3. Substances strongly antiseptic.....	1 : 1,000 to 1 : 200
4. Substances moderately antiseptic...	1 : 200 to 1 : 50
5. Substances feebly antiseptic.....	1 : 50 to 1 : 10
6. Substances very feebly antiseptic...	1 : 10 to 1 : 3.33

In the experiments of Miquel, the amount of each agent tested—in grams—which was required to prevent the putrefaction of one litre of beef tea was determined, thus giving directly the ratio per 1,000. When an agent failed in the proportion of 300 gm. to the litre it was dropped from the list; for, as Miquel says: "In quantities greater than this a substance can scarcely be called an antiseptic, inasmuch as all substances known to chemists, including some of the most fermentable, will preserve indefinitely one litre of bouillon when present in a larger amount than this."

Miquel recognizes the importance of experiments to determine the restraining power of chemical agents upon various species of bacteria, separately, and especially upon "disease germs," but he says: "As to me, faithful to a plan adopted at the outset, I will treat the subject in a more general manner by making known simply the minimum weight of the substances capable of preventing the evolution of any bacteria or germs.

"The method adopted is very simple. To a liquid always comparable to itself it is sufficient at first to add a known weight of the antiseptic and some atmospheric germs or adult bacteria, and to vary the quantity of the antiseptic until the amount is ascertained which will preserve indefinitely the liquid from putrefaction. In order to obtain germs of all kinds in the dry state it suffices to take them, where they are most abundant, in the dust collected in the interior of houses or of hospitals, and to procure a variety of adult bacteria we may take the water of sewers."

In the writer's experiments, published in *The American Journal of the Medical Sciences* (April, 1883), a different plan was adopted, inasmuch as the object in view was to ascertain the restraining influence of various antiseptics upon several different micro-organisms—isolated in pure cultures—for the purpose of determining whether different species of bacteria have widely different vital resisting power to the action of these agents, or whether results obtained with a single test organism could be applied to other organisms of the same class. These experiments, which are included in Table No. IV. of my paper referred to, taken in connection with those of Koch on anthrax spores, those of Arloing, Cornevin, and Thomas on the virus of symptomatic anthrax, those of Salmon on the micrococcus of fowl cholera, etc., show that there are marked differences in the ability of organisms of this class to multiply in the presence of certain antiseptic agents. These differences depend mainly, however, upon the fact that spores are unable to germinate in the presence of very small amounts of certain agents, such, for example, as the bichloride of mercury; and that micrococci and

bacilli in process of active growth may develop in the presence of very much larger amounts of these agents.

In the writer's experiments the antiseptic agent, in a given proportion, was added to a culture fluid; this was then introduced into little culture flasks of the form shown in the figure.* The capillary extremity of the flask was then hermetically sealed in the flame of an alcohol lamp, and the contents of the flask sterilized by long boiling in a water bath. Having now a sterilized culture fluid containing the antiseptic to be tested in known proportion, it is only necessary to introduce into the flask a minute drop of fluid from a similar flask, containing a "pure culture" of the test organism, in order to ascertain the restraining power of the agent under trial with reference to this particular organism. By multiplying the experiments we gradually approach the limit and establish the minimum quantity of each agent required to prevent the development of the several test organisms.

Fig. 219.

The experiments of De la Croix[2] were made by a method which does not differ essentially from that adopted by Miquel.

1. Substances Eminently Antiseptic.

This list, according to the researches of Miquel, embraces:

	Efficient in the proportion of
Mercuric iodide	1 to 40,000
Silver iodide	1 to 33,000
Hydrogen peroxide	1 to 20,000
Mercuric chloride	1 to 14,300
Silver nitrate	1 to 12,500

Of the substances included in this list, the bichloride of mercury (mercuric chloride) is that which has heretofore received the greatest attention, and by reason of its comparative cheapness (it can be bought by the thousand pounds for fifty cents per pound), its solubility, etc., it recommends itself at once as an antiseptic of great practical value.

The figures given by Miquel represent the proportion in which this agent will permanently prevent the development of any of the widely distributed micro-organisms in dust deposited from the atmosphere. In the writer's experiments, which have recently been repeated with similar results, it was found that 0.003 per cent., or 1 part in 33,000, prevented the development of the test organisms employed, while one-half this amount failed—1 to 66,000. These results are not in conflict with those of Miquel, in which the test included a great variety of organisms. In my own experiments I encountered a minute bacillus, associated with other putrefactive organisms, which multiplies in solutions containing 1 to 20,000, but the restraining power of the antiseptic is shown in this proportion by the fact that multiplication is delayed, and does not occur during the first twenty-four hours to such an extent as to interfere with the transparency of the culture solution, and it was only after remaining from forty-eight to seventy-two hours in the culture oven, at 38° C., that the fluid became clouded and was found to swarm with this minute actively moving bacillus. On the other hand, the development of the spores of certain bacilli was prevented by a much smaller proportion. Thus I am able to verify the statement of Koch as to the astonishing power of this agent to prevent the development of anthrax spores. A decided restraining power is shown when it is present in the proportion of 1 to 600,000, inasmuch as in a sterilized culture medium containing this amount, anthrax spores produce only a few flocculi of filaments at the end of forty-eight hours, while in the same medium, without the bichloride, an abundant and luxuriant development occurs in less than twenty-four hours.

In one experiment, in which anthrax spores were introduced into two culture flasks containing 1 to 100,000, two containing 1 to 200,000, and two containing 1 to 400,000, no development occurred during the first twenty-four hours in any of the flasks, while an abundant development had taken place in another flask containing the same culture medium, without any bichloride, which was inoculated at the same time to test the purity of my stock solution. At the end of forty-eight hours a feeble development of anthrax bacilli had taken place in the two tubes containing 1 to 400,000, while the others still remained clear.

According to De la Croix, the development of bacteria in beef tea is prevented by 1 to 10,250. This is something more than the amount fixed by Miquel, but it must be remembered that these results are all only approximate, and the statement that 1 to 10,250 prevents development is not to be interpreted as meaning that 1 to 14,300 will not. No intermediate experiment may have been made, for example, between 1 to 10,250 and 1 to 20,500 (referring to De la Croix's experiments). Thus in the writer's experiments, published in *The American Journal of the Medical Sciences*, the standard solution was commonly diluted one-half after each experiment; and, starting with one per cent., we have the following series in experimenting with this agent: 0.1 per cent., 0.05 per cent., 0.025 per cent., 0.012 per cent., 0.006 per cent., 0.003 per cent., 0.0015 per cent.—in which failure occurred only when the proportion was reduced to .0015 per cent., equal to 1 to 33,333; which proportion may be stated in round numbers, on the safe side, as 1 to 30,000 in the case of the micrococci of pus. Recent experiments made by the same method, and with the same test organism, have fixed the limit between 1 to 30,000 and 1 to 40,000. The field is open for those who desire greater exactness to make the experiments for themselves.

To the list of substances "eminently antiseptic" we must add *formaldehyde* gas, or an aqueous solution of this gas—it is also an excellent deodorant and powerful germicide. In the experiments of Slater and Rideal[7] formaldehyde in the proportion of 1 to 20,000 was found to inhibit the development of most bacteria, but Staphylococcus pyogenes aureus developed in the presence of 1 to 5,000. Walter[8] found that 1 to 10,000 absolutely prevents the development of anthrax spores, of the typhoid bacillus, of the diphtheria bacillus, and of Staphylococcus pyogenes aureus.

2. Substances Very Strongly Antiseptic.

In this table we have:

	Efficient in the proportion of
Osmic acid	1 to 6,666
Aluminum acetate (De la Croix)	1 to 6,310
Aluminum acetate (Kuhn)	1 to 5,350
Chromic acid	1 to 5,000
Chlorine	1 to 4,000
Iodine	1 to 4,000
Chloride of gold	1 to 4,000
Bichloride of platinum	1 to 3,333
Oil of mustard (De la Croix)	1 to 3,353
Hydrocyanic acid	1 to 2,500
Picric acid (De la Croix)	1 to 2,005
Bromine	1 to 1,666
Cupric chloride	1 to 1,428
Thymol	1 to 1,340
Cupric sulphate	1 to 1,111
Salicylic acid	1 to 1,000

We notice first in this group the haloid elements, chlorine and iodine, which by the experiments of Miquel are given the same value—1 to 4,000. This is exactly the value obtained for iodine in my experiments heretofore referred to, in which three different test organisms were used. According to Buchholz,[3] 1 to 5,714 of iodine prevents the development of bacteria in tobacco infusion. De la Croix fixes the antiseptic power of this agent at 1 to 2,010 for boiled beef infusion, and 1 to 10,020 for unboiled. This would indicate that the nature of the culture medium employed largely influences the result. In the case of agents which destroy organic matter by oxidation, or which cause the precipitation of albuminoid materials held in solution in our culture fluids, this must evidently be the case. It is therefore necessary that experiments shall have been made upon organisms contained in culture media of identical composition, in order that the experiments of one observer may be compared with those of another. And in protracted experiments with chlorine and other gaseous or volatile substances we must take into account the possibility of loss when the receptacle containing the culture fluid is not tightly closed. Differences of this nature in the conditions may perhaps account for the wide discrepancy of the results by Miquel and by De la Croix with reference to *chlorine*.

The last-named author gives the antiseptic value of this agent in *unboiled* beef infusion at 1 to 15,606, while Miquel gives it at 1 to 4,000. My own experiments with *chlorine* relate only to its power as a disinfectant. (See article under this title.)

A discrepancy also exists between the results of Miquel and of De la Croix as regards the antiseptic power of *bromine*; the former author places it at 1 to 1,666, the latter at 1 to 5,597.

Again, we have a discrepancy as regards the action of *chloroform*, one author (Miquel) placing it at 1 to 1,250, and the other at 1 to 103.

Oil of mustard, which is said by De la Croix to prevent the development of micro-organisms in unboiled beef infusion, has been shown by Koch to be capable of preventing the development of anthrax spores in the proportion of 1 to 33,000. According to the same author the *oil of turpentine* destroys the spores of anthrax in five days, and retards their development in the proportion of 1 to 75,000.

Thymol retards the development of these spores in still more dilute solutions—1 to 80,000 (Koch). Buchholz has determined the antiseptic power of this agent in Pasteur's fluid as 1 to 2,000, a result which does not differ greatly from that given by De la Croix for unboiled beef infusion—1 to 1,340.

Sulphate of copper is practically one of the most important agents which appear in this group, and the results of Miquel are in conformity with those of Dougall[4] in giving it a high place as an antiseptic. It is quite extensively used in France, and there can be no doubt of its value from this point of view; but it would be a great mistake to infer from this that it is a reliable disinfectant. (See article under this heading.)

3. Substances Strongly Antiseptic.

	Efficient in the proportion of
Benzoic acid	1 to 909
Potassium bichromate	1 to 909
Potassium cyanide	1 to 909
Muriate of quinine (Ceri)	1 to 900
Aluminum chloride	1 to 714
Ammonia	1 to 714
Zinc chloride	1 to 526
Mineral acids	1 to 500 to 1 to 333
Thymic acid	1 to 500
Lead chloride	1 to 500
Nitrate of cobalt	1 to 476
Sulphate of nickel	1 to 400
Nitrate of uranium	1 to 356
Carbolic acid	1 to 333
Potassium permanganate	1 to 285
Lead nitrate	1 to 277
Alum	1 to 222
Tannin	1 to 207

Benzoic acid is given a higher value by De la Croix than that given in the table, which is taken from Miquel. It is said to prevent the development of bacteria in unboiled meat infusion in the proportion of 1 to 1,439, and to fail in the proportion of 1 to 2,010. According to Koch, 1 to 2,000 retards the development of spores.

The antiseptic power of the salts of *quinine* has been especially studied by Ceri.[5] According to this author the development of bacteria in a culture fluid inoculated with a drop of turbid fluid from malarial soil is prevented by a solution of muriate of quinine of 1 to 1,900; from 1 to 1,000 to 1 to 15,000 non-putrid development begins. In experiments by the writer a minute bacillus associated with the bacteria of putrefaction developed in the presence of 1 to 800, but the results obtained were, in general, sufficiently in conformity with those reported by Ceri to give confidence in the data he has furnished. The power of this agent to restrain the multiplication of germs in the proportion of 1 part to 800 and above indicates that its therapeutic value may depend, in part at least, upon a restraining influence exercised upon the development of germs present in the alimentary canal, but our data scarcely justify the belief that in doses commonly administered it is competent to prevent the multiplication of pathogenic bacteria in the blood and tissues generally.

According to Dougall, the "salts of the alkaline earths" would occupy a comparatively subordinate position as antiseptics were it not for the extremely high preventive point of *aluminum chloride*, which is given at 1 to 2,000 for hay infusion. This is much beyond the value fixed by Miquel (1 to 714), but may be due to a difference in the culture medium used in the two series of experiments. Additional experiments with this agent and with aluminum acetate are desirable.

The antiseptic power of *chloroform* is fixed by De la Croix at a much lower figure than that given by Miquel, and is given at 1 to 103. Evidently experiments with this agent cannot be compared unless we know that loss by evaporation has been prevented in both cases.

Zinc Chloride.—The antiseptic power of this salt, which is fixed by Miquel at about 1 to 500, is no guide to its use as a disinfectant—for which purpose it is frequently recommended,—inasmuch as my experiments show that 1 part in 50 is required to destroy micrococci, and Koch has shown that anthrax spores are not destroyed by exposure for a month to a five-per-cent. solution.

The antiseptic power of the mineral acids is given by Miquel at from 2 to 3 gm. per litre (1 to 500 to 1 to 333). In the writer's experiments *sulphuric acid* prevented the development of all of the test organisms in the proportion of 1 to 800, and according to De la Croix 1 to 3,353 prevented the development of bacteria in unboiled beef infusion. The same author states that sulphurous acid prevents the development of bacteria in the same infusion in the proportion of 1 to 12,649.

Carbolic acid has received special attention from experimenters on account of its extended use, under the teaching of Lister, in surgical practice, and of the popular idea growing out of this, that it is the antiseptic *par excellence*.

Miquel, in his work published in 1883 (*op. cit.*), has given the antiseptic value of this agent as 3.20 gm. to the litre of *bouillon*. In a later report it is given as 3 gm. per litre (1 to 333). In the writer's experiments 1 to 500 was found to prevent the development of all the test organisms, and all of these organisms multiplied in the presence of 1 to 1,000. De la Croix also states that 1 to 502 prevents the development of bacteria in unboiled beef infusion.

According to Haberkorn[6] the multiplication of bacteria in urine is not prevented by 1 to 100, and Salmon states that the micrococcus of swine plague multiplies abundantly in urine containing 1 to 100. This would indicate that the restraining power of carbolic acid is neutralized by some ingredient in the urine. The germicide power of this agent is also influenced by the nature of the liquid in which it is in solution. Thus Koch states that in solution in oil or in alcohol in the proportion of five per cent. it fails to destroy anthrax spores in one hundred days or more. Anthrax bacilli are, however, destroyed by 1 to 100, while 1 to 850 prevents their development.

* "To introduce a culture liquid into one of these little flasks, heat the bulb slightly, break off the sealed extremity of the tube, and plunge it beneath the surface of the liquid. The quantity which enters will, of course, depend upon the heat employed, and the consequent rarefaction of the enclosed air. Ordinarily the bulb is filled to about one-third of its capacity with the culture liquid, leaving it two-thirds full of air, for the use of the microscopic plants which are to be cultivated in it."—From the writer's work, "Bacteria," Wm. Wood & Co., New York.

4. Substances Moderately Antiseptic.

	Efficient in the proportion of
Bromhydrate of quinine	1 to 182
Arsenious acid	1 to 166
Boric acid	1 to 143
Sulphate of strychnine	1 to 143
Arsenite of soda	1 to 111
Hydrate of chloral	1 to 107
Salicylate of soda	1 to 100
Ferrous sulphate	1 to 90
Caustic soda	1 to 56
Citric acid	?
Acetic acid	?

The antiseptic power of *boric acid* was fixed by Buchholz at 1 to 133, tobacco infusion being the fluid employed in his experiments. This corresponds very closely with the figures given by Miquel. But Kuhn states that it failed to preserve a solution of egg albumen in the proportion of 1 to 101. On the other hand, the writer's experiments gave more favorable results for all of the test organisms employed, and these differed considerably for the different organisms. Thus the micrococci of pus multiplied freely in the presence of 1 to 400, but failed to multiply in 1 to 200; the micrococcus of pneumonia did not multiply in the presence of 1 to 400. It will be noted that, according to Miquel, the antiseptic power of *salicylic acid* (1 to 1,000) is ten times that of salicylate of soda (1 to 100).

The antiseptic power of *ferrous sulphate* is placed by Miquel at 1 to 90. In the writer's experiments it was found to be efficient in the proportion of 1 to 200 for all the test organisms. It is but fair to state, however, that in these experiments the culture solutions were not left in the culture oven longer than forty-eight to seventy-two hours, and it is possible that some of them might have broken down at a later date if the time had been prolonged, for the antiseptic power of certain agents in dilute solutions is often shown by delayed development of micro-organisms subjected to their action, and after a time these organisms may develop freely in the same solution. Whether in this case the agent has been neutralized chemically, or whether the organisms, developing feebly at first, may after a time become habituated to it, is a question not yet definitely settled. The commercial sulphate of iron contains a certain amount of free sulphuric acid which adds to its antiseptic value. The writer's experiments were made with a chemically pure protosulphate, and no doubt Miquel also experimented with the pure salt. It must be remembered that the value of this and other metallic salts as antiseptics is no criterion for their use as disinfectants. In saturated solution the protosulphate of iron does not destroy the vitality of any of the test organisms experimented upon by the writer, and Arloing, Cornevin, and Thomas assert that a twenty-per-cent. solution did not destroy the virus of symptomatic anthrax after forty-eight hours' exposure.

The caustic alkalies—soda, lime, and potash—all have considerable value as antiseptics, but this has not been definitely determined. Their value as "germicides" will be given under that heading.

5. Substances Feebly Antiseptic.

	Efficient in the proportion of
Protochloride of manganese	1 to 40
Calcium chloride	1 to 25
Sodium borate	1 to 14
Muriate of morphine	1 to 13
Strontium chloride	1 to 12
Lithium chloride	1 to 11
Barium chloride	1 to 10
Alcohol	1 to 10

The writer's experiments give a much higher antiseptic value to *borax* than that reported by Miquel, viz., 1 to 200 for two species of micrococcus. De la Croix states that the development of bacteria in unboiled beef infusion is prevented by 1 to 107. But, as heretofore indicated, the *permanent* preservation of a culture fluid, exposed to the air, from all kinds of micro-organisms present in the atmosphere requires a larger amount of this and of other antiseptic agents than is necessary to restrain development for two or three days, when only a few micro-organisms of one of the species mentioned are introduced into a flask such as the writer used in his experiments. The differences in results are probably due, not to error, but to differences in the conditions of the experiments.

According to De la Croix, *alcohol* in the proportion of 1 to 20 prevents the development of bacteria in unboiled beef infusion. It is probable that the figures of Miquel are nearer the mark when the experiment is protracted, for pathologists are aware that their specimens are liable to spoil and to develop a putrefactive odor in solutions containing forty to fifty per cent. of alcohol.

6. Substances Very Feebly Antiseptic.

	Efficient in the proportion of
Ammonium chloride	1 to 9
Potassium arsenite	1 to 8
Potassium iodide	1 to 7
Sodium chloride	1 to 6
Glycerin (sp. gr., 1.25)	1 to 4
Ammonium sulphate	1 to 4
Sodium hyposulphite	1 to 3

My experiments correspond with those of Miquel in giving to sodium hyposulphite a very low place in the list of antiseptics, and yet this salt has been extensively prescribed as an antizymotic agent. If it has any such powers as have been ascribed to it by Pollo and others, it must be in consequence of its undergoing decomposition in presence of certain substances with which it comes in contact in the alimentary canal. In this case the sulphurous acid, if set free, would no doubt act as a potent antiseptic and germicide. But the pure salt introduced into culture solutions failed entirely to exhibit any restraining power upon the development of the test organisms up to eight per cent., at which point it was dropped. From Miquel's experiments it appears that when present in more than thirty per cent. the development of micro-organisms in beef tea is prevented. But in this proportion it is probable that any soluble salt would preserve a culture solution by giving it a density incompatible with the development of micro-organisms.

George M. Sternberg.

[1] M. P. Miquel, M.D., Chef du service micrographique à l'Observatoire de Montsouris: Les organismes vivants de l'atmosphère, chap. ix., pp. 289–290, Paris, 1883; also article in the Annuaire de météorologie for 1884.
[2] N. Jalan de la Croix: Das Verhalten der Bakterien des Fleischwassers gegen einige Antiseptica. Arch. f. exper. Path. u. Pharmakol., Leipzig, 1880–81, xiii., 175–225.
[3] Antiseptica und Bakterien. Arch. f. exper. Path. u. Pharmakol., iv., 1–81, 1875.
[4] Medical Times and Gazette, London, April 27, 1872.
[5] L'action de la quinine en rapport avec le développement des germes et des organismes inférieurs. Trans. Internat. Med. Cong., London, 1881, i., 466–472.
[6] Das Verhalten von Harnbacterien gegen einige Antiseptica, Dorpat, 1879, 8vo.
[7] London Lancet, vol. i., 1894, p. 1004.
[8] Zeitschr. für Hygiene, xxi., 421, 1896.

ANTISEPTOL is the trade name for a substance prepared by mixing a solution of 25 parts of cinchonine sulphate in 2,000 parts of water, with a solution of 10 parts each of iodine and potassium iodide in 1,000 parts of water. The precipitate formed is washed and dried and constitutes a reddish or dark brown powder, without odor, almost insoluble in water and freely soluble in alcohol and chloroform. It is an odorless iodoform substitute containing fifty per cent. of iodine, and when used internally is given in dose of gr. i. to v. Antiseptol is also known as cinchonine iodogallate and cinchonine herapathite, although its chemical formula is unknown.

W. A. Bastedo.

ANTISPASMIN is a double salt of sodium salicylate and narceine-sodium, having the formula $C_{23}H_{26}NO_8Na + 3C_6H_4OHCOONa$. It is a reddish, slightly hygroscopic powder, which is readily soluble in water; fifty per cent.

of it consists of narceine. As an antispasmodic and sedative it is given in whooping-cough, laryngismus stridulus, chorea, asthma, etc., especially in children, and is useful in allaying irritating cough or intestinal colic in adults. On account of its affinity for moisture it is preserved with difficulty in the dry state, and therefore may well be kept in five-per-cent. solution; of this, five to eight drops are given to a child of six months, or forty drops to a child of five years; an adult may take one or two drachms.

W. A. Bastedo.

ANTISPASMODICS.—If we are to interpret the term antispasmodic in its literal sense as a means of preventing spasm, nothing so completely fills the requirement as ether or chloroform, pushed to complete anæsthesia. In conducting a careful physical examination, especially in diseases of the abdomen or pelvis, such relaxation of spasm is often secured by anæsthetizing the patient. But as ordinarily used by therapeutists the word antispasmodic is given a somewhat loose and unscientific application to a class of drugs supposed to be of special service in controlling attacks of muscular spasm depending upon functional nervous derangement. The inappropriateness of the name is seen from the fact that it is not alone convulsive phenomena which form indications for their use, but that they are also useful in other of the multiform manifestations of nervousness or of hysteria. The theory of their mode of action—if, indeed, any one method of action is common to all the members usually included in the class—is not sufficiently established to make any discussion of it profitable in this place. Suffice it to say that it is not impossible that at least one important action of these drugs is a local one upon the intestinal tract, where their warming and stimulating character may produce a revulsive effect. For the detailed description of the most important drugs included under this heading the reader is referred to their proper titles.

Belladonna has a considerable power of relaxing spasm, as, for instance, in the unstriped muscular tissue of the intestine. It and its congeners, stramonium and hyoscyamus, are also much used in asthma, which is a disease attended by spasm of the bronchi. In the same condition opium is at times of the greatest value, the hypodermic injection of morphine alone causing relief to some asthmatic attacks. In "colic" (meaning spasm of the muscular walls of the intestine) opium is also invaluable. This drug, like the anæsthetics already mentioned, while distinctly antispasmodic, has other and more important therapeutic qualities which lead to its classification in another group (see *Anodynes*), and we pass to those remedies known more specifically as antispasmodics. First, we have a group of animal origin, strongly odorous, but of little therapeutic value. *Moschus*, musk, an oily substance obtained from the preputial glands of the Thibetan musk-deer, is the only one of this class which is used to any extent. In the last stages of adynamic diseases, as typhoid fever, it is given, especially by German physicians, but rather as a forlorn hope than with real confidence. Its former use in hysteria is now quite superseded. *Castoreum*, a corresponding secretion from the *Castor fiber*, or beaver; *ambergris*, a morbid product obtained from the sperm whale, and the source of the *oleum succini*; and the *oleum animale* of Dippel, a substance of disgusting origin and nature, obtained from "trying out" decomposing animal structures, deserve mention only as having been at some time used as antispasmodics.

Another group consists of drugs of generally feeble action, but occasionally useful in infantile hysteria and allied states. Among these are *humulus*, hops, and its derivative, *lupulin*. The former, applied locally in the form of poultices or embrocations, has possibly some virtue, and the latter is somewhat more active internally. *Lactucarium*, derived from the garden lettuce, is even more feeble than hops, but as some persons are made drowsy by eating lettuce, it is not impossible that lactucarium may have in certain cases a useful medicinal effect. The claims which have been made for *celery* as an antispasmodic and anticephalalgic do not seem to rest on reliable grounds. *Cimicifuga*, or black snakeroot, belongs in this group. It has been chiefly used in chorea, and in full doses it has seemed to have some effect. *Dracontium*, the root of the "skunk cabbage," and *Galbanum*, an ingredient with asafœtida and myrrh in the *Pilula Galbani Comp.*, U. S. P., 1880, have also had antispasmodic virtues ascribed to them, but with little reason.

We now come to the group which contains the most important drugs of this class. They are three in number, viz.: *camphor*, *valerian*, and *asafœtida*. They all produce a sensation of warmth in the stomach, and probably stimulate the whole alimentary canal. But that this is not their sole action is proved by their superiority in certain nervous states over the essential oils and other so-called carminatives. The intestinal action of camphor makes that drug a valuable aid in the treatment of cholera and choleraic diarrhœa. In the delirium of adynamic fevers and as a sedative for "nervousness" it is useful. An especially quieting influence has been claimed for it in sexual irritation and excitement. For more distinctively hysterical symptoms, camphor is often combined with bromine in the form of bromated or monobromated camphor, which, despite its disagreeable taste, difficult solubility, and frequent tendency to cause irritation of the stomach, is considerably used for chorea, reflex convulsions, etc. Perhaps no drug is more generally used to combat the true hysterical convulsive seizure than *valerian*, and certainly in many cases it meets the indication better than almost any other agent. The fluid extract and the ammoniated tincture are among the most eligible palliatives of the hysteric attacks, sometimes a single dose serving to restore consciousness. For more protracted use in the countless nervous manifestations of hysteria, hypochondria, and neurasthenia, the salts of valerianic acid, notably the valerianates of zinc and of ammonium, are especially adapted, serving to control at times even such positive and conspicuous symptoms as neuralgia.

Asafœtida, long the synonym for what is most loathsome and offensive to the palate, acts very like valerian in the hysteric attack. The flatus which has been rolling about in the intestine is expelled, and, as has been intimated above, there is some reason to believe that the stimulation of the intestinal mucous membrane and the revulsion so caused may, with the relief of the tympanites, play a prominent part in the alleviation of the hysterical spasm. In cases in which simulation seems to have any part in the attack, the vile taste of the drug may become of service in adding to its effectiveness. In other cases we may give the drug by enema, and its action upon the intestine and also its effect on the convulsions will be nearly the same as if it were administered by the mouth.

While the above-mentioned drugs constitute the more distinctive antispasmodics, there yet remain two groups to which the term is often applied, and of which some part of the action is similar to that above described. The *compound spirit of ether*, Hoffman's anodyne, is very useful in controlling nervous disturbances, as is also the *spirit of chloroform*, formerly known as chloric ether. The substances from which these are derived—sulphuric ether and chloroform—may, administered internally in appropriate doses, be employed for the same purpose, although, of course, their more proper classification is among the anæsthetics. The *bromides* of *potassium*, *ammonium*, and *sodium* and chloral, though in their most prominent action depresso-motors, are yet, in moderate doses, used as antispasmodics.

Finally, we have the group which includes coffee, tea, maté, and guarana, of all which the active principle is practically identical with caffeine. Leaving out of account the important action of this substance upon the heart and circulatory system, and limiting our attention entirely to functional nervous phenomena, we find that in migraine, which in the family of diseases is not distant