and shall limit myself in this place to a consideration of the method of Brand, from the stand-point of the physiological pathology of the febrile process.

The refrigerant method comprehends several modes of application. You may use baths, lotions, compresses wet in cold water, bladders of ice, or you may use the ingenious apparatus of Dumontpallier, or even rectal injections of cold water.[2] In all these forms the water may have a variable temperature which is always less than that of the fever patient. But whether you resort to cold affusions, ice bags, or cold lavements, these frigorific means abstract heat

Lyons has deduced from the sum total of Brand's works, this aphorism: "Every case of typhoid fever, treated regularly from the commencement by cold water will be exempt from complications, and will get well."

Huchard, basing himself on the works of French physicians, anterior to those of Brand, maintains that we ought to substitute the term French method, for that of German method (method of Brand) when we speak of the application of refrigeration to typhoid fever.(*a*)

[2] Riegel in studying the action of cold applications on the temperature of fever patients has observed that on applying to the thorax compresses dipped in ice water, the axillary temperature at the end of an hour falls from 0°.2 to 0°.27, and the rectal temperature from 0°.1 to 0°.05. At the same time, Liebermeister observes that in the local applications it is necessary that the refrigeration should be very pronounced, and its application very prolonged.

Riegel has also made some quite interesting experiments in comparing in a typhoid fever patient the effect of baths at 18° C. and renewed every two hours, whenever the axillary temperature exceeded 39.5° C., with the effect obtained by two bladders of ice applied permanently to the thorax. The following are the results which he obtained:

BATHS AT 18°.75 C. EVERY TWO HOURS WHENEVER THE AXILLARY TEMPERATURE EXCEEDS 39.5° C.

	Average of Rectal Temperature.	Average of Axillary Temperature.
1st Experiment.....	39.69	39.18
2d "	39.71	39.69
3d "	39.93	39.55
4th "	40.01	40.03
5th "	39.65	39.51
6th "	39.08	39.84
7th "	40.21	40.09
9th "	39.28	39.34

(*a*) James Currie, Medical Reports of the effects of water, cold and warm, as a remedy in fever and other diseases, whether applied to the surface of the body or used internally, including an inquiry into the circumstances that render cold drinks, or the cold baths, dangerous in health; to which are added observations on the nature of fever, and on the effects of opium, alcohol, and inanition, 5th édit., 2 vol., London, 1814.—Jacquez (de Lure), Bull. de la Soc. méd. de Besançon, No. 2.—Wanner, De l'emploi de la glace comme agent thérapeutique et des lois à observer dans son mode d'administration soit dans les cas de médecine, soit dans les cas de chirurgie (Compt. rend. de l'Acad. des sc., t. XXIX, p. 581, 1849. De la guérison constante, quinze jours au plus tard après l'application du traitment etcela sans nulle convalescence, de toute fièvre typhoïde dont la période d'invasion ne dépasse pas sept jours (Acad. de méd., 1866).

and lower the thermometric curve, on condition, always, that there exist between the temperature of the patient and that of the bath a notable difference.

Liebermeister, in his remarkable researches on calorimetry, has shown us that in a well man the production of heat is in direct relation with the loss of heat. If we apply these data to the refrigerant methods, the result will be that thermogenesis, instead of being diminished, will be increased proportionately to the withdrawal of heat; and reasoning *a priori*, it is not easy to see what good you are accomplishing by this means. Liebermeister, I am well aware, while recognizing that the regulation of heat is the same in the well person as in the febrile individual, has endeavored to prove that in pyrexia cold baths produce much more rapidly a diminution in thermogenesis than in the normal state; but it is none the less certain from the stand point of the physical laws of calorimetry, that as fast as you abstract heat from the fever patient, the same amount of heat is produced anew. So true is this, that to obtain an enduring effect, one is obliged in practice to renew continually the refrigerant applications. Whether the fever patient raise the temperature of the bath, or his own temperature, the effect is the same, and the lesions which you seek to avoid by this means, and which result, not from the elevation of temperature merely, but from the exaggeration of the calorific functions of the economy, will be produced in both cases, and from the strict point of observation of physical laws we should say that the refrigerant method can confer no

TWO BLADDERS OF ICE APPLIED OVER THE THROAX AND ABDOMEN DURING THE ENTIRE DURATION OF THE EXPERIMENT.

	Average of Rectal Temperature.	Average of Axillary Temperature.
1st Experiment.....	37.34	37.49
2d "	37.81	37.65
3d "	37.97	37.62
4th "	39.27	38.83
5th "	39.27	38.97
6th "	37.75	37.47
7th "	40.05	39.95
9th "	38.40	38.12

Foltz, of Lyons, has studied the influence of cold lavements on the heat-fall. According to him, a lavement of one litre of water produces the following thermic depressions:

A lavement of one litre of water at	+ 5°	Diminishes the heat of the body	0°.52
" " " "	+ 10	" " "	0 .52
" " " "	+ 14	" " "	0 .35
" " " "	+ 20	" " "	0 .29
" " " "	+ 32	" " "	0 .14
" " " "	+ 38	" " "	0 .06 (*a*)

(*a*) Riegel, Ueber Warmeregulation und hydrotherapie (Deutsch. Arch. of Klin. Med., t. IX, p. 591, 1872.) Foltz, Du lavement froid (Lyon Médical, janvier 1875).

therapeutic benefit whatever; nevertheless, a real benefit is derived, and you will see when we come to study the therapeutic applications of cold baths, that they produce a marked relief in many cases.

How are we to explain this difference between the result in theory and the result in practice? Simply in this way; the refrigerant applications in fever do not act merely mechanically in removing heat, but they modify profoundly, and often durably, the functions of the nervous system, and particularly of the vaso-motors, all of which, as you know, play so considerable a part in the production of the febrile process, and in this respect Currie seems to me to have rendered a better judgment concerning the action of the refrigerant medication in fever, than even Brand and his pupils.

The action of blood-letting as an antipyretic agent seems to me to belong to that of refrigerants generally, and this, because in withdrawing at a given moment a certain quantity of blood you withdraw also a certain quantity of caloric. Moreover, this antipyretic action produced by sanguineous losses, is one of the most real known, and it suffices to examine what takes place in patients who have had during the course of typhoid fever an intestinal hemorrhage of moderate intensity, to observe the manifest and durable effect of hemorrhages on thermogenesis.

The influence of hemorrhage on pyrexia is complex. The loss of blood has abstracted heat, it is true, but it has also modified the physico-chemical processes which take place in the interior of the tissues, and the functions of the nervous system have also been affected by it. These multiple affections manifest themselves on the elevation of the temperature in pyrexia by effects more enduring than those of cold baths, and we always observe this immediate fall in the febrile heat unless the patient dies in the hemorrhage.

Quite different is the action of the medicaments which constitute the second group of anti-febrile remedies, and their influence is explicable either by a direct action on the nervous system or by morbid changes effected in the blood.

Digitalis is a fair type of anti-febrile agents acting on the nervous system. I have before told you how digitalis acts in diseases of the heart, and the principles there established apply to its antipyretic influence. Hirtz is one of the most earnest partisans of the treatment of fevers by digitalis, and his followers have shown us the benefits which we may derive from this medicine in the divers febrile processes. You obtain from digitalis not only a lowering of the pulse, but also a very evident thermic depression. Nevertheless the precepts of the ancient school of Strasbourg have not been admitted by all, and it is only exceptionally that we see digitalis prescribed in fever; and this results from the fact that this remedy has a powerful emeto-cathartic action on the one hand, and on the other, it is not quite safe to prolong to any extent the action of such a drug in septic and infectious diseases where the heart is prone to undergo fatty degeneration.

It is this same action on the spinal cord and medulla oblongata which explains the anti-febrile effects of colchicine, aconitine, etc., but as in the case of digitalis this influence on thermogenesis is not obtained without serious inconveniences, by reason of the large doses which it is necessary to give and which are not without danger in the case of alkaloids as powerful as those which I have mentioned.

Quinine, whose physiological action I propose to explain more completely when I come to speak of the treatment of intermittent fever—quinine, which is one of the most powerful agents of the antipyretic medication, acts, as you know, not only on the nervous system, but also on the blood; in both modes influencing thermogenesis. This class of medicaments has lately assumed a preponderant importance, since the labors of Pasteur have shown us the important part which the proto-organisms have in the production of infectious and virulent diseases. Chemistry furnishes us under the name of the *aromatic series*, a group of bodies, phenols, or oxy-phenols, which all possess the property of arresting more or less completely the development of micro-organisms. These bodies, such as phenic acid, salicylic acid, kairine, resorcine, etc., were all first employed in the treatment of wounds, as a result of the radical change which Lister had just introduced into the dressing and manipulations of operative surgery; then the idea occurred to give these same *bactericide* medicines internally when there seems to be an indication to destroy the septic agents of disease, these being supposed to be bacilli

But the results were really unexpected, for if there were no direct proofs of the destruction of the micrococcus in the interior of the organism, a most marked antipyretic effect was obtained, and these bodies of the phenol series, became the most energetic agents of the anti-febrile medication.

It is, in fact, by employing the derivatives of this series, carbolic acid, salicylic acid, resorcin, kairine,* and especially with this latter, that we obtain the

* [Karine, thalline and antipyrine are three new antipyretics for which we are indebted to the industry of continental chemists in the application of the synthetical methods to the formation of new compounds. As for Karine, readers of the Therapeutic Gazette will find this antipyretic discussed in the volume for 1884, in the following pages: 46, 105, 95, 129, 142, 153, 164, 254, 313, 285, 335, 378. From Dr. Tangeman's article (Ther. Gaz. 1884, p. 105) we extract the following particulars:

Karine was discovered in 1883 by Fisher, of Munich; (its chemical formula is $C_{10}H_{13}NO$). Fisher has experimented quite largely on animals with thls drug, but Filhene has employed it very extensively on the human subject both in health and disease. Since then the subject has been thorougly studied by Seifert, Drasche and others. If it can be shown that this new antipyretic is equally as good as quinine much has been gained. That it is an efficient drug under certain circumstances nobody will doubt who has ever observed its effects. Two preparations are at present in the market: the sulphate and hydrochlorate of karine; the former is a crystalline substauce of a yellowish-white color, its taste is very unpleasant, and is not much of an improvement on some of the older remedies.

The study of the physiological action of this drug on animals has not produced very satisfactory results. On man in health it does not have any tendency to depress the temperature below normal; the hearts action is somewhat slowed, as is also the respiratory act. In disease its action is more marked. There is no condition in which karine does not manifest its antithermic action if given in sufficiently large doses. This does not say that it is indicated in all febrile conditions, or that its administration can safely be recommended in all cases.

There seems to be a great variance of opinion as to the proper dose of this drug by the different experimenters, but this may be only apparent. I think we can explain this differ-

most considerable depressions of temperature; you will often see the mercury fall two, three, and even five degrees in the course of a febrile state, and I propose in the next lecture to state more particularly the therapeutic effects of each of these substances. But I must tell you once for all that such depressions of temperature are not without danger, and that at the same time that we observe this thermal fall we observe also a general depression of the organism and multiple congestions in the different viscera.

Is it solely by their action on the blood that the medicaments of the aromatic series produce such powerful effects on thermogenesis? Is it only by opposing the progress and development of fermentations, the original cause of the febrile processes, that their antipyretic action is exercised? It is difficult

ence by carefully studying the physiological action of the drug. While its tendency is to reduce the temperature, in every febrile condition the state of the patient physically as well pathologically must be taken in consideration. Its main field of efficiency will undoubtedly be found in diseases where neither the heart nor the lungs are primarily affected; but where the fever is a long-continued pyrexia we may expect more, since its action does not in the least influence or abort the natural course of the disease. The safest method to administer this drug is to begin with a small dose and watch the effect with the thermometer until we have arrived at the correct and safe dose for that individual case—a dose that will keep the temperature at a point almost normal. In this manner we are able to better guard against collapse, and at the same time avoid the objectionable symptom of chilliness that is experienced by patients when the temperature rises again after a large dose of karine. Unpleasant after-effects are met with occasionally, but they are not dangerous to the patient; the remedy is one of the safest powerful antipyretics in our possession, if carefully watched. The adult dose generally varies from 0.3 to 1 and 2 grm. repeated every hour. The effect of a large dose is very rapid sometimes, 20 to 25 minutes being sufficient to cause a decline in temperature; but the effect passes off just as quickly. Therefore, the frequent repetition of the dose becomes necessary. It may range from 12 to 15 grm. per day given in 18 to 20 doses.

The drug is best administered in capsules on account of its bitter taste. My experience with karine has been limited, and in some respects differs from the results of other observers. Altogether I have used it in five cases.

"In many instances the patients absolutely refuse to take the medicine any longer, on account of the bad taste and nausea that it produces. The drug seems to be largely eliminated by the kidneys; it can be found in the urine 30 to 35 minutes after administration. Whenever there is a marked decline of temperature there is profuse perspiration. The drug may become quite valuable in diseases of the kidney, or in cases where a reduction of temperature and an elimination of poisonous material from the blood is desirable.

In rheumatism it has been given with excellent results. The action of karine subsides very rapidly, therefore frequent doses are necessary to maintain a permanent effect; the thermometer is our guide, which must be used frequently; upon the slightest chilliness a half dose should be administered. Absolute laws governing the dose and action of karine in all cases cannot be laid down. In feeble and decrepid individuals it must be given with considerable care, since it may, when given in large doses, suddenly produce collapse."

In the Therapeutic Gazette for February, 1885, is an able aditorial on the subject, from which we cite the concluding portion:

"Guttmann has given karine in cases of pneumonia, measles, phthisis, typhoid fever, scarlatina, pleurisy, peritonitis, erysipelas, ague, septicæmia, and apparently always with advantage. On the other hand, Dr. H. Menche's (of Rheydt) experience with it in the pyrexial stages of pneumonia, pleurisy, and pernicious anæmia was unfavorable, which has been attributed by others to the use of large doses. In rheumatism, he found that its use

to respond categorically to these questions, and without denying the action of these substances on the intimate processes which take place in the blood, I venture to affirm that we must attribute a part of their effect in lowering pyrexial heat, to their action on the nervous system, and particularly the vaso-motors.

In a recent communication to the academy of sciences, Prof. Gosselin has well set forth this action of phenic acid on the capillary net work, and he has shown us that when you apply locally to wounds lotions of carbolic acid, the antiseptic actions of these dressings result much more from the obliteration of

was followed by diminution of the pain, but not by any reduction in the swelling of the joints."

"The cases just reported demonstrate that karine possesses the power of reducing the temperature of the body in fever to an unusual degree, and that it does this with certainty and promptitude, and, it may be added, when moderate doses are used, with safety. One care, however, it is necessary to exercise in its administration, and that is to use fresh specimens of the drug only, as it undergoes change if kept for any length of time. It reduces the temperature much more rapidly than quinine, although the apyrexia produced by it is of much shorter duration than that caused by the latter. It is also capable of depressing the temperature during the evening exacerbations of fever, while the most marked results are obtained, on the other hand, from quinine just before the morning's remission. Its use is also free from some of the objections usually urged against the latter, as it does not give rise to unpleasant effects, such as headache, ringing in the ears, and the like. Although less rapid in its action than the cold bath, it is obvious that it may be administered in many cases in which resort to the latter would be impossible. The excitement and terror which are often occasioned by the use of the bath, even when it is brought to the bedside of the patient, constitute a positive objection to it, which, in the author's opinion, becomes insuperable in cases in which it is necessary to carry him some distance to a bath room. It is said to exert a marked and favorable influence over the brain-symptoms which occur in fevers, possessing, in this respect, an undeniable advantage over several of the other antipyretics."

Thallin has lately been successfully used in a large number of cases in the clinic of Professor Nothnagel. It has the constitution of a secondary quinoline base, being one of a number of quinoline derivatives prepared by Prof. Skraup, and is represented by the systemic name *tetrahydroparachinanisol*. The salts of this base, which have an acid reaction, are freely soluble in water and have the property of forming green compounds when treated with solution of ferric chloride, and oxidizing agents. On account of this peculiarity, the cumbrous systemic name has been dropped, in favor of the shorter designation, "thallin." The hydrochlorate tartrate and sulphate of thallin, and the hydrochlorate of ethyl thallin are the salts which have been employed, and these are said to show great antipyretic activity in doses of half and three quarters of a gramme, a point in which thallin would seem to compare favorably with its competitors. It can be given in wafers, each containing a quarter or half a gramme. It causes a speedy and marked fall in the temperature which lasts several hours. (London Lancet, Dec. 6th, 1884, p. 1018.)

"In the fourth edition of my work" writes Dr. Dujardin-Beaumetz to me, under date, June 10th, 1885, "I have given special attention to antipyrine, karine and thallin. We now divide antithermics into three groups; those which mechanically abstract heat, and of which the cold bath is the type; those which act in the thermogenetic centres, of which the types are quinine, resorcin, salicylic acid, antipyrine, lastly those which act in destroying the respiratory power of the blood, of which karine and thallin are the types. There exists an intermediate class, constituted by phenic acid, which acts at once on the thermogenetic nervous centres and on the respiratory power of the blood."

I have appended to the lecture on Typhoid Fever a note pertaining to *antipyrine* in which the latest researches on this new medicament are detailed. This is the only one of the series of new antipyretics which is likely to come into favor.—TRANSLATOR.]

of all the capillary openings in the wound, than from the special destructive influence of carbolic acid on the virulent principles. Laborde has completed these researches in showing us that this capillary obliteration is due to an action of carbolic acid on the vaso-constrictors.

It is probable that like effects are produced in fever, and that phenic acid once introduced into the blood acts on the vaso-motor centres either directly or indirectly, and thus modifies the conditions of febrile thermogenesis. As you see, gentlemen, therapeutics confirms in a certain measure, the data furnished us by physiological pathology, and shows us the unbounded and preponderant influence of the nervous system on the febrile processes.

In the next lectures we shall make numerous and practical applications of the deductions which flow from this general survey, and you will see the importance of all these developments into which I have entered.

ON THE TREATMENT OF TYPHOID FEVER.

SUMMARY.—Typhoid Fever—Etiology—Spontaneity—Contagiousness—Theory of Typhoid Contagion—The Microbe of Typhoid Fever—The Virus of Typhoid Fever—Theories of the Contagion—Fecal Matters—Fecal Theories—Sewerage—Aliments—Overcrowding—Experimental Physiology of Typhoid Fever—Public Hygiene—Private Hygiene—Hygienic Treatment of Typhoid Fever—Alimentation—Æration—Cleanliness—Treatments of Typhoid Fever—Divisions—Antithermic Medication—Method of Refrigeration—Cold Baths—Brand's Method—Its Application—Its Results—Its Advantages—Its Disadvantages—Warm Baths—Refrigerant Apparatus—Cold Lotions—Cold Lavements—Antiphlogistic Method—Local Bloodletting—General Bloodletting—Antipyretic Medication—Digitalis—Quinine—Antiparasitic Method—The Aromatic Series—Phenic Acid — Salicylic Acid — Resorcin — Kairine — Evacuant Medication — Purgatives —Calomel — Mercurials — Tonic Medication — Alcohols — Cinchona — Exclusive Medications — Their Dangers — Expectancy — Treatment of Indications — Armed Expectancy—Bases of this Medication—State of the Forces—Intensity of the Fever—Treatment of the Complications—Nervous Complications—Pulmonary Complications—Abdominal Complications—Conclusions.

GENTLEMEN—There is, perhaps, no question in therapeutics which has caused so much discussion as the treatment of typhoid fever, and, if I were to follow out all the lines of inquiry which this subject has opened, I should require, not one lecture, but the entire course. I shall, then, be as brief as possible on points of theory, and dwell rather on practical conclusions. Whether you practise in the country or in the city, you will continually meet with cases of abdominal typhus. Last year (1882) you saw our wards filled with the victims of one of the most severe epidemics that have ever afflicted the population of Paris, and the hall of the Academy of Medicine stills rings with the passionate discussions which were raised by the various questions pertaining to this great problem of hygiene and therapeutics.[1]

Etiology, as I have often told you, has an important bearing on the treatment of disease; you recognize, then, the propriety of considering first the causes of typhoid fever; for, if they were absolutely known to us, we should be able henceforth to establish on a scientific basis the prophylactic treatment of this disease. This particular point in the study of dothinenteritis has been especially investigated during the last few years, and we shall have here to dis-

[1] Read the discussion which was held in 1882 and 1883 at the Academy of Medicine on typhoid fever ; a discussion in which the following gentlemen took part : Marjolin, Proust, Fauvel, Rochard, Lagneau, Léon Colin, Bouchardat, Gueneau de Mussy, on the part of hygiene ; Herard, Germain Sée, Dujardin Beaumetz, Peter, Jaccoud, Vulpian, Bouley, Glenard, on the part of therapeutics. (Bull. de l'Acad. de Méd., 1883.) Read also the discussion which took place at the same Academy in 1876 and 1877, and in which H. Gueneau de Mussy, Bouillaud, Brouley, Bouchardat, Jaccoud, Jules Guérin, Chauffard took part. (Bull. de l'Acad. de Med., 1876, 1877.) Read finally the discussion which was held at the Academy of Medicine *apropos* of the epidemic which broke out in Brussels in 1869, and where Martin, Coussot, Crocq, and Boens had the floor. (Bull. de l'Acad. de Méd. de Belgique, 1875, 1876.)