making the puncture and counter-puncture just at the corneal margin, and I like to make a small conjunctival flap, for I think I am less likely to get prolapse of the iris. In changing over from operating with iridectomy to operating without it I found that I had to learn a new technique, and one of the most essential points to observe is, after making the cystotomy, to make pressure on the lower border of the lens to tip the upper part forward and prevent its sliding up under the iris. In my early career I always practiced on the mask with pig's eyes before attempting an operation, and I think that it is very important for the young operator. I am sure I performed more than a thousand operations on pigs' eyes before I did many cataract operations on the human eye. The young man has plenty of time to do it and it gives him confidence in his hand and forearm, and when he has to operate he will do the operation very much better. I was very much pleased some time ago when I saw a book written on that subject, though I can not recall at this moment the name of the writer.

I used to wash the anterior chamber out when there was any amount of cortex left. I should not hesitate to do that now, although I think there is apt to be some irritation from it, but I do not find the occasion for it as I used to. I think the normal-salt solution sterilized is better than the pure water for this purpose. In dressing the eye I have for a long time been putting cotton over the eye and using isinglass plaster to hold it in place. Fifteen years or so ago I used a shield made of wire and also of pasteboard, but I abandoned them, for in my practice I thought I got more prolapses of the iris when I used them than when I did not. They are apt to become irritating to the patients and they make efforts to move about, causing spasms of the muscles, and, by the way, I think prolapse of the iris is more frequently caused by muscular contractions and spasms than by external violence.

When Dr. Ring brought out his eye shields I tried them, but I again abandoned them for the same reason I had before.

DR. R. L. RANDOLPH, Baltimore—I hope this paper will elicit some discussion as to the technique to be pursued in these cases. I have long maintained that the eye is endowed with natural powers that make it unnecessary to use bichlorid douches before the operation. While I am not prepared to say that its use in Dr. Rogers' case had anything to do with the iritis, I do not think he would have had any more iritis if he had abandoned the use of the bichlorid. I think the eye, more than any other part of the body, is endowed with antibacterial properties, and I make it a rule to use no bichlorid solution whatever. In the first 100 cases I reported I did use it; in the second 100 cases reported a few years ago, I used nothing, but simply sterilized my instruments and used sterile cocain. I would like to ask Dr. Rogers if he sterilized his cocain in these cases.

I am surprised to note the number of cases where he was successful in maturing the cataract. I have tried in ten cases, but succeeded only in one. Lately, I have abandoned cocain also in these cases and never use anything but holocain.

DR. W. B. MARPLE, New York—I should think it would be interesting in connection with Dr. Randolph's remarks to know from the different gentlemen here whether or not they irrigate the eye before operation. Since Dr. Randolph's paper of a few years ago, I have used nothing but the sterile salt solution, and I would like to know if there are many who use no irrigation at all. Irrigation with some sterile non-irritating solution seems to me to be in many respects of decided advantage.

DR. ALBERT E. BULSON, JR., Fort Wayne—Aside from the general interest which a paper on cataract operations excites, this paper becomes of interest because the essayist recounts his failures and successes, with reasons therefor.

The point which I wish to make in discussing the paper is that, with the average operator, a preliminary iridectomy is usually unwarranted. It has always appeared to me to be an unnecessary risk to open the eye twice for the purpose of removing an opaque lens. The average ophthalmologist does not exceed fifteen or twenty cataract operations a year, and as every one of these cases must of necessity carry its weight of praise and blame, and as it is practical results which all patients desire, it behooves the operator to secure the best possi-

ble results as a minimum risk. In spite of the most exacting efforts to have an aseptic operation, occasions will arise in which infection alters what otherwise might prove to be an ideal result, and opening the anterior chamber twice paves the way for such a complication. I have never felt that the results with preliminary iridectomy averaged any better than the results with iridectomy at the time of extraction, and the patient certainly objects to two operations when one may be fairly stated to do as well.

I believe the combined operation for the average ophthalmologist to be, not only the easiest, but the best for securing practical results. It is usually attended with fewer complications, and but few patients will complain of the cosmetic effect, the main desire being to get vision, and it is this which brings out their praise.

DR. J. L. THOMPSON, Indianapolis—These reports appeal to most of us because there are very few of us now that see as many cases as Knapp, or the Baltimore physicians, and very, very few of us get more than twenty-five cataract operations a year. I feel that one of my failures used to be due to the manner in which I used the speculum. That seems to bother a good many of the beginners. I used to open it very widely, but now I open it just as little as possible, to give enough room to work on the eye. Of course, I began when there were no antiseptics in use. In regard to cleaning the wound, I notice, if you go to Knapp's clinic, for instance, the great pains he takes to clean the wound and to put the iris back just as carefully as possible, but the beginner feels that he had better leave well enough alone, and he does not want to work over the eye too much.

I do not recall one case I ever lost where I made a preliminary iridectomy. We have so many cases where just a plain extraction of the cataract is out of the question on account of the small cornea; the deeply sunken eye, the shallow anterior chamber, etc. I would like to advise the beginner to learn to use both hands and to do an iridectomy.

DR. LUCIEN HOWE, Buffalo—I want to call attention to one point in regard to the difficulties with an assistant, and the necessity of having some one who rotates the eye or fixes it without pressing on it. Some years ago I presented a small pair of autofixation forceps, and I want again to call your attention to the advantage of not having another brain to depend on, but in having one's own fingers only involved in the operation. The little forceps on the speculum fixes the eye perfectly, and acts as our third hand.

YELLOW FEVER; ITS NATURE AND CAUSE.*

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From the earliest history of yellow fever in our country there have been evidences of its having been imported from some foreign place, usually the countries to the southward within the tropics. This importation has usually taken place during the prevalence of warm weather in the spring, summer or fall months, and could be traced to one of the intertropic endemic centers. During cold weather, the disease would disappear either entirely or to a great extent.

Its continued presence, however, from year to year in some of our southern cities, and its recrudescence with the advent of the warm weather of the spring, following its epidemic presence during the summer, induced numbers of prominent observers to believe that this disease was indigenous to our southern latitudes, and, like malarial infections, depended on unsanitary conditions.

The cessation of the fever following the institution of an adequate system of maritime quarantine protection for our southern seacoast cities, against such importa-

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tion, was the convincing argument that it was essentially exotic. The continuance of an epidemic invasion of these latitudes depended invariably upon the continuance of heat and moisture, so much so, that close, humid and sultry weather became known as "yellow fever weather," for under such conditions the disease propagated more rapidly and became more fatal; while on the other hand, dry, temperate weather has been known to induce a cessation of the disease before the advent of colder weather. The appearance of the cold season has invariably been followed by a marked diminution in the number of cases at any center, endemic or epidemic; and those instances recorded of this disease, during cold weather, in temperate latitudes must have depended upon some special feature of exposure. As a matter of fact, they have been recorded in cities of the Northern States where the first hint of winter is sufficient to determine the almost perfect closing of houses against cold, and therefore, the enclosure of the specific organism in an atmosphere sufficiently warm to allow the propagation of the disease from person to person. In southern latitudes this barricade against frost is not nearly so complete, and it is not unusual for such communities to be caught unprepared for winter; within the infected homes, therefore, the germ is as much refrigerated as it would be out-of-doors. Isolated recrudescences, however, indicate that through special agencies the organism may pass safely through the season of frost, and produce the disease, under conditions of increased temperature. These deviations from the normal history of yellow fever are so infrequent that it is evident they depend upon such special influences.

Within the tropics the disease is endemic under similar atmospheric conditions to those which determine its epidemicity, i. e., heat, moisture and unsanitary environment, the presence of *témoins* contributing to its endemic duration. In such centers the advent of cold weather, scarcely ever so frosty as 40 F., is followed by a notable cessation of yellow fever; and it is a clinical fact that during such seasons of cessation, as in the city of Havana, the cases which do occur are well marked and frequently have a fatal termination.

Such is the natural history of this scourge of the tropics, *bête-noire* of the southern states contiguous to them; it is that of an acute infectious malady, dependent upon an etiologic entity which exhibits a marked susceptibility to changes of temperature, this susceptibility finally causing the disappearance of the disease.

Yellow fever has also presented a uniform complex of symptoms which has served to distinguish it clinically from the other infections. Its onset may be either precipitate, or heralded by a series of prodromes such as are common to these infections. The course and termination of the disease do not seem to be in direct sequence to the onset; the precipitate cases becoming benign, and the mild onset frequently followed by the gravest symptoms.

In a characteristic case the temperature rises to its maximum within the first twenty-four to thirty-six hours; the pulse rising at first in proportion to the temperature. This, however, does not continue and there ensues a remarkable reduction of the pulse-rate, at the same time that the temperature continues to rise, or remains at its acme.

This is the first symptom in yellow fever that is of intrinsic value in the diagnosis of the disease. It was clinically recognized by early observers, but it was not until the introduction of the clinical thermometer enabled the elder Faget to accurately chart the temperature

range, that this remarkable phenomenon was fully recognized to be of diagnostic importance. Faget established *avec l'aide de la montre et du thermomètre* the law of the non-correlation of the pulse and temperature, and it has been recognized, by all conversant with the disease, as of inestimable value in its diagnosis.

The prodromal symptoms of the infection, such as cephalalgia, rachialgia, pain in the eyeballs, the slight yellowing of the conjunctiva and scleræ, can be of only slight differential value. However, with the undoubted presence on the clinical chart of the phenomenon of Faget, the case assumes a more serious aspect, and the diagnosis will probably be confirmed by the later symptoms.

The next clinical feature of importance is also connected with the temperature chart. Upon the second or third day of the disease, it is usual for the temperature to decline, and there is a more or less marked remission, at times an intermission, of fever. There is no fixed time for the appearance of this fall in the temperature, but it is so confidently anticipated by clinicians of epidemic and endemic centers, that its non-appearance has often caused them to diagnose the malady as an infection of an allied nature.

The fall in temperature may be of one or two degrees, or it may reach the normal, or pass below it. Under all circumstances it is accompanied by a notable alleviation of the distressing symptoms, the patient entering a period of comparative calm, which may last from one to many hours. Indeed, it is possible that convalescence may be established at this stage, but in the characteristic type under consideration it is soon followed by an exacerbation of the temperature, which may rise even higher than during the "first paroxysm," and an exaggeration of other symptoms. The patient enters now upon the "third stage" of the disease, or into the "second paroxysm" of the fever, the paroxysms being separated by the "period of calm," or "second stage" of the disease.

This phenomenon presenting the two accessions of temperature, with a decline, the period of calm, separating them, has been recognized by southern clinicians as the most characteristic of all the symptoms of yellow fever; and it may be recognized, as outlined here, in all cases lasting from three to eight days. These variations of the temperature forming the three periods, or stages, of the fever have heretofore been regarded as inexplicable from a clinical standpoint, although many clinicians have advanced theories which did not satisfactorily account for them.

Among the clinical phenomena should be mentioned the "black vomit" encountered in this disease with such constancy as to name the disease in some countries "*vomito negro*;" also that phenomenon encountered post-mortem, the extreme steatosis of the liver cells, which transforms the organ into a friable, yellow tissue incapable of performing its functions, and from which arises the icterus, or yellow skin, giving the well-known name to the disease. Other organs are involved but in them there is no special change characteristic of the malady.

Cases of yellow fever have been divided into three classes or varieties, the ephemeral, the grave, and the *siderante* or fulminantly fatal cases. The first class comprises cases exhibiting a slight toxic attack, ending in recovery in from two to three days or less. They are with difficulty diagnosed because of their resemblance to other infections of less gravity, and have been likened to a "slight cold." To this class belong the acclimatization fevers of the tropics. The second class embraces all grave cases of the type already described as presenting

the characteristic symptoms. The third class are those rapidly fatal cases in which death ensues before the appearance of many of the characteristic symptoms, but in which acute fatty degeneration of the liver is always found, together with a most pronounced paralysis of the vasomotor constrictors, as evidenced in the marked visceral congestions and the intravisceral hemorrhages. These are the clinical and pathologic peculiarities which, with the natural peculiarity of the disease mentioned above, must be correlated with the phenomenal powers of the organisms said to be the cause of the disease.

THE CAUSE OF THE DISEASE.

Since the bacterial origin of yellow fever became a probability through the discoveries of Koch, Fränkel, Löffler, Eberth and others in the domain of the acute infections, there have been numerous organisms announced as its cause. In 1885 Domingo Freire, of Brazil, and Carmona y Valle, of Mexico, announced the discovery of the infecting organism, and in 1887 two announcements were made from Havana, by Finlay and Gibier, who isolated totally dissimilar organisms from the cadavers of yellow-fever patients.

The proofs advanced in support of these claims were not convincing, and during 1888-9 the question was thoroughly investigated by Dr. G. M. Sternberg, of the army medical corps, who was detailed to this duty through the Surgeon-General M. H. S. His report¹ was made in 1890, in which he stated, after careful and exhaustive research into the merits of these claims, that "among the micro-organisms encountered there is not one which, by its constant presence and special pathogenic power, can be shown to be the specific cause of the disease," and further, that with the most approved facilities at his command he had not been able to discover an organism in the blood of those ill from yellow fever, and expressed the decided opinion that the infectious germ, if a bacterium, would require for its detection other aids than those which he had employed. Incidentally, he suggested the possible etiologic value of his bacillus "X," isolated at Havana, since it had proved pathogenic to animals, with the production of the morbid anatomy found in men dead from the disease.

These observations of Sternberg made a profound impression on the professional mind of this country, and, without doubt, acted as a deterrent to further investigation. Indeed, I recall the personally stated opinion of one of the most distinguished bacteriologists of the day, that the disease, in view of that report, was scarcely one of bacterial origin, but that the cause might be a plasmodium, and he suggested freezing the bodies of victims of this disease, immediately after death, in order that section might disclose the pathologic conditions unchanged, and possibly also the infecting cause. When, in 1897, Giuseppe Sanarelli published the account of his work in yellow fever², there at once arose a murmur of surprise and incredulity, so fully had our minds been imbued with the value of the statements made by Sternberg in 1890. Dr. Sternberg himself at once assumed the defensive, and antagonized the statements of Sanarelli as casting reflections upon his own work, and he insisted upon the identity of his bacillus "X" and the bacillus *icteroides*, assumed by Sanarelli to be the cause of yellow fever.

This was the state of affairs when the epidemic outbreak of the disease in Mississippi and Louisiana in the fall of '97 enabled the Surgeon-General of the Marine-Hospital Service to detail officers from his own corps to investigate its etiology. For this purpose he detailed P. A. Surgeon H. D. Geddings and myself to the isola-

tion hospital of the city of New Orleans, and later, at the direction of the President, to Havana, Cuba.

The results of the work of that commission were embodied in a report³ to the President through our Surgeon-General, dated July, 1899. The conclusions arrived at by the commission, as therein stated, are as follows:

1. That the micro-organism discovered by Prof. Giuseppe Sanarelli, of the University of Bologna, Italy, and by him named "*bacillus icteroides*," is the cause of yellow fever.
2. That yellow fever is naturally infectious to certain animals, the degree varying with the species; that in some of the rodents local infection is very quickly followed by blood infection, and that, while in dogs and rabbits there is no evidence of this subsequent invasion of the blood, monkeys react to the infection the same as man.
3. That infection takes place by way of the respiratory tract, the primary colonization in this tract giving rise to the earlier manifestations of the disease.
4. That in many cases of the disease, probably a majority, the primary infection or colonization in the lungs is followed by a "secondary infection," or a secondary colonization of this organism in the blood of the patient. This secondary infection may be complicated by the coinstantaneous passage of other organisms into the blood, or this complication may arise during the last hours of life.
5. There is no evidence to support the theory advanced by Professor Sanarelli that this disease is primarily a septicemia, inasmuch as cases do occur in which the *bacillus icteroides* can not be found in the blood, or organs in which it might be deposited therefrom.
6. That there exists no causal relationship between the bacillus "X" of Sternberg and this highly infectious disease; and that this bacillus, "X," is frequently found in the intestinal content of normal animals and of man, as well as in the urine and the bronchial secretion.
7. That, so far as your commission is aware, the bacillus *icteroides* has never been found in any body other than of one infected with yellow fever; and that whatever may be the cultural similarities between this and other micro-organisms, it is characterized by a specificity which is distinctive.
8. That the *bacillus icteroides* is very susceptible to the influences injurious to bacterial life, and that its ready control by the processes of disinfection, chemical and mechanical, is assured.
9. That the *bacillus icteroides* produces *in vitro* as well as *in vitam*, a toxin of the most marked potency; and that, from our present knowledge, there exists a reasonable possibility of the ultimate production of an antiserum more potent than that of Professor Sanarelli.

Does the *bacillus icteroides*, therefore, fulfil the demands of modern bacteriology; and does it offer an explanation of the clinical and natural history of yellow fever?

In the report of 1899 the Commission affirms the isolation of this bacillus from the blood of 13 of 14 patients in whom the disease was clearly recognized, that is to say, in whom the typical phenomena of the disease were present, or in 92.85 per cent.; in those dead from the disease it was isolated from the blood and organs in 85.7 per cent. Sanarelli had predicated his discovery of the cause of the fever upon the presence of the *bacillus icteroides* in about 55 per cent. of his cases living and dead⁴.

Our cultures thus isolated were pure, and in no instance was a contaminated culture allowed to enter our computations. These cultures were each retained and are still in evidence. Introduced into animals susceptible to them, they each produced illness and death, the morbid anatomy being similar to that of man dead of the disease.

The organism is always found in these artificial infections, as it is in the septicemic cases in man, distributed by the blood-current in the organs.

Moreover, the chemical products of this organism introduced into animals produce the symptoms of the dis-

ease, and furnish the pathologic changes peculiar to it. Sanarelli made use of the soluble toxins of the germ in an experiment carried out upon some nine imbeciles, otherwise healthy, who were under the care of a civic institution. Of these helpless ones nearly all reacted to the intravenous injections of the toxins; in a few there were evident signs of profound toxemia with symptoms of the disease; and in at least one case death must have ensued, the autopsic findings being those of yellow fever.

It would appear therefore that the bacillus *icteroides* would require no further proof of its pathogenicity; that its etiologic rôle is patent, since it has fulfilled the demands of bacteriology as laid down by Robert Koch.

After the Report of 1899, and just prior to its issue, there were a number of voices raised against the acceptance of the bacillus *icteroides* as the cause of yellow fever, mainly because of its close cultural relations to many other organisms known to be infectious in their nature⁵; and because of its behavior in the presence of changes of temperature⁶.

Taking the experimental work of Sanarelli under consideration, during my work in Havana, I soon became convinced that he had fallen short of proving his position in regard to the etiology of the disease, and that the contention of Sternberg, in favor of the specific influence of bacillus "X," was a very valid one, since bacillus "X" was frequently isolated from the yellow-fever cadavers at our disposition, and at times from the living blood, and since this bacillus, and its toxin, acted upon animals in artificial infection in a manner strikingly like that of the bacillus *icteroides*. But Sternberg seemed to have lost faith in his organism, and withdrew it from further consideration before I had fully determined, by experimentation, its lack of specificity.

All that Sanarelli had proved in his *mémoires* was the presence, in one-half of his cases, of an organism not before described in yellow fever; that it possessed powers pathogenic to animals by artificial infection; and that its toxins had proved toxic to man and animals, the lesions produced resembling those of yellow fever.

These facts were applicable to the peculiarly motile, highly pathogenic organism of the colon group, found freely by us in cases of the disease, and which corresponded perfectly to Sternberg's bac. "X." I was therefore compelled to attempt a differentiation of these bacilli. They were both pathogenic in animals; were they infective to them also? Introduced into their tissues, or into their blood, the reactions were very similar; they produced acute sepsis, with a profound influence upon the vasomotor constrictors, the paresis of which was, in all cases, followed by intense congestion of the organs, especially the cavernous ones, in which lack of support tended to free hemorrhages, notably the stomach—"black vomit"—and the intestines—"black stools." The parenchyma of the organs suffered from fatty degenerations, and necrosis. The onset of symptoms and death seemed to be in direct ratio to the amount of culture injected; there could scarcely be determined any cycle of disease in the case of either organism.

The differentiation of the organisms could only be accomplished by a series of experiments with susceptible animals naturally exposed to their infective influence, and to do this I exposed white mice, susceptible to most infections, to bacillus *icteroides*, and bacillus "X," in pure culture, as well as to a common colon organism, and that of Havelberg, who had announced its discovery some time before. The same conditions were maintained for all the mice thus exposed, the organism be-

ing placed in their grain. In a given time—8 to 10 days—all the mice, 19 of them, exposed to the bacillus *icteroides* became infected, and all died except one, which recovered after a severe illness. Of those exposed to bacillus "X" not one sickened or died. Those exposed to bacillus *coli communis*, and to the bacillus of Havelberg remained perfectly well.

From those infected by bacillus *icteroides*, it was determined that its incubation took place within five days, the usual incubative period of yellow fever; and that its cycle was that of the septic type of the disease in man, or of 5 to 8 days' continuation. The autopsies in these cases were typical of those in man. Of other animals, guinea-pigs resisted the natural infection, which was a surprise in view of the active reaction of this rodent to artificial infection. Rabbits reacted readily to natural infection, and in case of death gave characteristic autopsies. They developed the fact, however, that in them the blood does not become invaded; that is, that the colony of bacillus *icteroides* remains entirely local to the lung tissue, and sepsis does not take place. Dogs react readily also to the inhalation of the bacillus *icteroides*, and are invincible to the germ placed in their food, or in the small intestine beyond the acid stomach. In them also there is no secondary invasion of the blood, absolutely no sepsis, the necropsies presenting typical pathological appearances. Monkeys are susceptible to the inhalations of bacillus *icteroides*, and present a picture of suffering from symptoms of yellow fever very similar to that of man. In this animal the secondary invasion of the blood on the third day of the disease was demonstrated by careful planting of minute quantities of blood daily from the commencement of the symptoms. There were no deaths in monkeys; all of those infected recovered.

Altogether 44 animals were subjected to the infective influence of the bacillus *icteroides*, exhibited naturally. Of these 34 reacted, showing acute symptoms of disease, and 23 died, a mortality of 67.5 per cent. Recoveries took place among dogs, white mice, rabbits and monkeys, which demonstrates that the domestic animals may enter as a factor in an epidemic of the disease.

During my experimental work we were honored by a visit, at our laboratory in Havana, from Dr. Sternberg, who said to me, while passing through our animal room, that the strongest argument against the acceptance of the specificity of any one of the organisms advanced as the cause of yellow fever, was the fact that no one of them, during experiments in laboratory, had ever communicated this disease by natural infection to the animals of those laboratories; and he asserted that, whenever such infections should occur, the lesions being characteristic, and the organism recovered, he would accept that organism thus demonstrated as the cause of yellow fever, and such demonstration as the proof of its specificity.

In that same room, shortly afterward, I had nine cases of this disease occur among the animals, naturally caught, from the introduction into the atmosphere of the adjoining room, of the bacillus *icteroides*. Eight of these animals died; one recovered; from the necropsies I recovered the bacillus *icteroides* in pure culture from 50 per cent., almost as large a number of cases, and as large a percentage of isolations, as those used by Sanarelli in forming his assumption as to the value of bacillus *icteroides* in the etiology of the disease. These spontaneous infections occurred in dogs, mice, guinea-pigs and rabbits. The first infection, that of rabbit "S. S," was noticed on April 16, 1899, the only known exposure being that of the insufflation of dog "A," in

the adjoining room, on April 7, with the bacillus icteroides in lycopodium powder. Granting 3 to 5 days as the incubating period of this bacillus, we have the disease lasting in this rabbit from 6 to 8 days, and ending in death on the seventeenth. In all these animals the disease was accompanied in the pregnant female by miscarriage, and in the normal female by flooding. Necropsies gave the characteristic morbid anatomy of yellow fever.

I therefore maintain that Sternberg, who has assumed the rôle of censor in this disease, should now be thoroughly convinced, since my work has been crowned with the results which he demanded, and since our commission has proved what Sanarelli did not, that the bacillus icteroides is constantly present in yellow fever, and is the cause of the disease. Sanarelli, in a recent issue of the *Medical News*,⁷ has acknowledged the work of the American Commission, as a confirmation of his own, and he uses its results in formulating several conclusions which were not possible with the information derived from his experience alone.

But the work of that commission was far more important than this. It constitutes the only proof of the specificity of the bacillus icteroides, and without such demonstration the bacillus icteroides would have no better claim to our consideration as the cause of yellow fever than the organisms of Sternberg, Havelberg, or the commoner colons, that of an artificially pathogenic microbe.

The close cultural and biologic relationship which exists between bacillus icteroides and some others, infectious to animals, but not to man, as the micro-organism of American hog-cholera, the hog-cholera of Bavaria, that of the peripneumonia of calves, and that form of colon frequently isolated from the summer diarrhea of children, and also known in acute mucoenteritis epidemic among young pigs, has been noted for some years, and recently resulted in the assertion of one observer that the bacillus icteroides is of the hog-cholera group, and therefore of secondary importance if found in yellow fever in the septic stage. According to this observation the bacillus icteroides, when fed to our domestic pigs, gives rise to disease, and autopsy discloses the characteristic lesions of hog-cholera in their intestines.

This has not been my experience with the most virulent bacillus icteroides, for with a most perfect environment against possible contamination with the bacillus cholerae suis, I was unable to infect the hog in Havana with the icteroides, and later, under conditions equally free from suspicion of contamination with cholera suis, Geddings, upon a group of pigs and controls had a similar experience. Bacillus icteroides in pure culture, and in an environment free from bacillus cholerae suis, does not produce hog-cholera.

When the observations noted above were called to my attention they interested me greatly, not that the conclusion arrived at by the observer was thought to be correct, but the question at once arose in my mind of the possible mutations of these specific organisms with changing environment. Could it be possible for bacillus icteroides to give rise to yellow fever in man and to cholera in the hog? Could environment thus influence results? In so far these observations were of immense interest, but my experience and those of Geddings seemed to properly dispose of the question, and to determine that, however closely allied these organisms might be, the specificity of each one seemed an inherent quality, to be developed under certain environment, and that this quality is immutable. The same observer has

questioned the power of bacillus icteroides, as known in the laboratories of the milder latitudes, to produce constant toxic results, advancing its failure to produce "fatty degeneration" of the liver, when injected under such conditions, as an argument against its specificity. As a matter of fact, the bacillus icteroides, like many other infective pathogens, exhibits at times a most marked quality of septicity, and in proportion as the organism is septic it loses its toxic quality, and consequently the manifestations of toxicity, the fatty liver and renal epithelium, become merged into a condition characteristic of sepsis; that is to say, these organs present then more the appearance of the changes of typhoid fever, with necroses of their parenchyma rather than fatty degeneration. The more acute the intoxication in this disease, typified in the siderant cases, the more typical the fatty degenerations, and the reverse is equally true. We therefore can not expect the same results from this bacillus under conditions which we know will cause its attenuation, as those which we encounter constantly under conditions most favorable to the development of its peculiar powers. An instance in man—cited in the report of the commission,⁸ that of Private Patrick Smith, 8th Infantry U. S. Army, who died of yellow fever at Havana, after an illness of nine days—presented a condition of sepsis or blood invasion by the bacillus icteroides, the most marked that I have ever known. His necropsy revealed a chronic malarial cachexia, upon which a pronounced anemia had depended, and modified changes in the stomach, the intestine and the liver; these modified changes, partaking of the nature of typhoid sepsis, were accepted by some of the attending physicians as diagnostic of typhoid fever, but evidently there was lacking an adequate conception of the quality of septicity in the bacillus icteroides, from which had arisen these modified changes.

There has been made one other, and apparently the most formidable, argument against the bacillus icteroides as the cause of yellow fever. Novy has shown that the bacillus was not killed by exposure to temperatures below the zero mark, but that after such exposures it gave rise to a septic condition when injected into animals. He therefore concluded that the bacillus could have no etiologic relation with this disease, since epidemics of yellow fever have always subsided and disappeared upon the advent of a temperature of the frost-line, or about 40 Fahrenheit.

Having had no experience with this bacillus under other than tropic and semitropic conditions of temperature, I could make no comment at the time of his publication, but at this time I can say that his position was only apparently well taken, for the bacillus icteroides, although not killed by exposure to extreme cold, is most profoundly influenced by temperatures at and below 40 Fahrenheit. Having had the opportunity during the past fall and winter months to observe these conditions, I tested carefully the facts of the case. While specially engaged at the Institut Pasteur, in Paris, in the matter of the possible production of a serum, curative and preventive, in this disease, I made a series of vaccinations in animals with the "sérum anticoli," of M. Lesage, and with the "sérum antipneumoniæ in calves," of M. Fehrenbach, against virulent cultures of the bacillus icteroides which I had taken with me. Details of these observations are in the addendum.

During the months of September and October these serums seemed to afford but little if any protection to the animals used, vaccinées and controls dying nearly at the same time. With the advent of the colder weather,

however, it was noted that the serums were more potent and now protected the animals, but at the same time it was noticed that the controls, inoculated subcutaneously, did not succumb, the points of inoculation presenting nodules of accumulated leucocytes, something unusual in my experience with the germ in the tropics. At this time I determined to test the influence of cold and heat upon the infecting quality of the germ, since cold had so materially attenuated its pathogenicity; for this purpose I exposed white mice to its infective influence at different degrees of temperature. From the same group of mice, six were selected and two were placed in each of three cages. In each cage there was placed grain mixed with an equal quantity of the same culture of bacillus *icteroides*, originally obtained from the blood of Patrick Smith, which had always proved extremely virulent. One cage was then placed in an incubator temperature of 25 C., or 77 F. One other was placed in laboratory room temperature of 18 C., or about 65 F., and the remaining cage in the open air in an outbuilding, one side of which was entirely open. The temperature in Paris during this outdoor exposure averaged 5 C., or about 40 F., and at times was below zero, ice and snow being present, the record of temperature having been taken from the daily Paris edition of the New York *Herald*.

In the cage at 77 F., one mouse became infected and died on the ninth day, about the usual period in these animals; and one died on the thirteenth day, much beyond the usual period of eight to ten days. In the cage placed at 65 F., one mouse died on the fourteenth day, and the other on the eighteenth day after exposure, or in twice the usual period of time. Two other mice, placed in a fourth cage and exposed to this temperature of 65 F., died on the nineteenth day after their exposure. In the cage placed in out-of-door temperature, the mice at no time, under daily examinations, gave the slightest evidence of disease, and when last examined, two months after their exposure, were perfectly well. To summarize, mice are extremely sensitive to the infection, developing acute septicemia, with death in all cases of my own except one. The mice exposed at summer temperature, 77 F., died in very nearly the time noted in the tropics. Those at 65 F. sickened and died, but at periods of twice the usual length in these animals. The mice exposed at and below 40 F., the "frost-line," with us, did not become infected and remained well. Details are given below. Beside this attenuation of the germ, as shown when inoculated into animals, I found that the attenuated germ does not produce a potent toxin, even when grown at 37 C.; for mice and pigs resist large quantities of the soluble toxin produced when injected into their tissues.

The bacillus *icteroides* was thus shown to attenuate rapidly in the presence of cold, losing its toxic, septic and specific qualities.

During the prevalence of extreme cold in Washington last winter, my confrère, Geddings, remarked that animals inoculated subcutaneously, and intravenously, with the bacillus *icteroides*, in order to revive the organism by its passage through them, failed to succumb to it, and as it was desirable to employ the most virulent germ in his work, he was nonplussed. At this time, in a note from Paris, I stated my observation in regard to the influence of cold upon the bacillus *icteroides*, when, acting upon this information, he placed the inoculated animals at incubator temperatures, with the result that they succumbed and furnished the virulent organism desired. Nothing can be clearer than this demonstration, and it is in consonance with the many

different results obtained by observers in different latitudes with this bacillus.

Reverting now to the natural history of yellow fever, I can most positively assert that the most striking of all of its natural phenomena, its endemic and epidemic cessation with the advent of cold, is thus readily explained by my discovery of this peculiar biological phenomenon while investigating the life history of the bacillus *icteroides*—the loss of its toxic, septic and specific qualities in the presence of a temperature below 5 C., or 40 F.

As to the clinical phenomenon of the "double paroxysm," separated by a more or less well marked interval, or "period of calm," I believe that this can be explained by the consideration of the mode of infection in yellow fever. It has long been conceded that the disease is air-borne and not water-borne; and because of the marked lesions of the liver and intestinal canal, the primary colony of the causative organism has been thought to be in the intestinal tract. Sanarelli but dimly realized the truth, and so did not profit by it. He assumed that the bacillus *icteroides*, entering the body, perhaps by way of the respiratory tract, in some occult manner reached the spleen, there to lay *perdu* until finally, late in the disease, it invaded the blood, producing with other organisms a "secondary sepsis."

This is not true; my observations in the natural infections in animals limit the colony primarily to the respiratory tract. In dogs and rabbits it is totally limited to this tract, there being in them no invasion of the blood from the primary colony. In man and the monkey this secondary invasion takes place some time after the appearance of the symptoms of intoxication from the primary colony.

My observations, therefore, have convinced me that the bacillus *icteroides* is always first colonized at some portion of the respiratory tract; that the intoxication arising therefrom produces the early symptoms of the disease, the "first paroxysm" of the fever; that the injury sustained locally sooner or later permits the passage of the germ into the circulation, with those evidences of sepsis termed the "secondary paroxysm," which has been attributed by the earlier authors to an invasion, from the changed intestinal canal, of bacillus *coli communis* and other organisms; and that this secondary invasion is due to the development of an inherent quality in the bacillus *icteroides*, that of septicity.

The interval of calm is due to the profound impression of the commencement of this second intoxication, from the bacillus in the blood-stream, upon the nerve-centers. This depression, amounting to shock, sometimes ends in death, but if the patient rallies the temperature again rises and sepsis is shown by its chart. It is an uncertain quantity, this interval of calm between the two toxic periods, the first intoxication arising from the primary colony, the second from the lung colony plus the influence of the colony invading the blood; the first a pure toxemia, the second a septicemia.

Should death take place during this primary toxemia the body will be found to be sterile, Sanarelli agreeing with us that the *foudroyante* cases are sterile, excepting the local colony in the lungs, a fact which he did not realize.¹⁰ This explanation correlates the three periods of the disease, the first intoxication lasting from 2 to 4 days, when, if septicity develops, the blood colony becomes a factor in the secondary, septic, or "third period," lasting from 3 to 5 days longer, the "period of calm" being of several hours' duration, or so slight as to barely merit the name. Thus, too, will be explained the

three great varieties of yellow fever. Why should there be three varieties of this disease? Because this bacillus exhibits *par excellence* the dual qualities of toxicity and septicity; if the toxic property is alone developed after an infection, cases of the first and third variety are produced. That is to say, an intense toxemia, resulting in death, is the *siderante* or third type, while the multitude of benign or ephemeral cases, in which only a slight toxic result is noticed, constitutes the first variety. Between these are possibly the majority of cases of diagnosed yellow fever of the second variety, those giving the marked clinical peculiarities mentioned above, and in all there is the phenomenon of the "second paroxysm," "septic invasion," or "third stage" of this peculiar disease.

In regard to the want of correlation between the pulse and temperature I can quote Dr. Bernard E. Baker,¹¹ of Charleston, as noting this phenomenon as due to the soluble toxins of the bacillus *icteroides*.

In regard to the role which domestic animals and vermin encountered in domiciles may play in the retention of yellow fever in their systems after their infection on shipboard, or during the prevalence of the disease on land, and its convection by this means to new areas, which may then become infected, I can but introduce the ready susceptibility of mice, dogs and rats to the infecting influence of the bacillus *icteroides*, and the marked reactions obtained by Sanarelli in his artificial infections, or inoculations, in the horse, in cattle, and in the ass. Domestic animals are therefore susceptible, and if infected, many of them may recover. In all of these the disease, as in man, is accompanied by intravisceral hemorrhages, and, except in the dog, in which there is no blood invasion, the dejecta, as well as any bronchial secretion, may contain the germ, from which the disease may recur in the infection of a resident of the domicile. This mode of entrance from shipboard and from house to house bears the aspect of improbability, but the well-known instances of this fact in the history of plague demand for it respectful consideration in connection with yellow fever. I am reminded also of the fact that during my stay in New Orleans in '97 and '98, I heard well-founded rumors of the presence of some disease at that time frequent among cattle and horses, which resembled epizootic, and which was attributed to yellow fever. I have not had an opportunity of subjecting the greater animals, horses and cattle, to the bacillus *icteroides*, and can not state the facts as to their natural reaction to the germ.

In at least one variety of animal extremely reactive to artificial infection, guinea-pigs, I have not succeeded in inducing a natural infection, although there was one case of natural infection among our animals, and this may apply to horses and cattle.

The danger from infection through animals, especially the rodents, has been illustrated on many occasions of yellow-fever outbreak at points ashore, and adjacent to the nearest landing place of such rodents swimming from an infected ship. Moreover, the recrudescences of the fever, even after quite cold winters, could be attributed to an attenuated form of the disease lasting among these animals during the cold months, and the propagation of the germ in virulent form with the advent of hot weather.

Such convection and propagation of yellow fever deserves the careful consideration of sanitarians in an equal degree as in bubonic plague. I therefore submit to your intelligent body these facts—elicited in my efforts to clear away the obscurities surrounding this American

disease, and although it was the fortune of my friend, Dr. Sanarelli, to first see the germ and name it, it has remained for America, the United States, to furnish the indubitable proofs of the value of the Italian discovery, and further to establish the scientific explanation of this disease which more than any other has occupied our attention. Incidentally also to the establishment of the fact that the infecting pathogens vary in their pathogenic results with the varying preponderance of their two great qualities of toxicity and septicity; and that a proper recognition of the latter will serve to elucidate a number of heretofore obscure problems incident to these infections.

ADDENDUM.

Experiments to test the value of certain serums, known to be protective against the specific organism from which they were produced, on the animals subjected to the influence of closely allied organisms.

The serums used were those termed "*anti-coli*," perfected by M. Lesage, of Paris, France, and the "*anti-peripneumoniæ*" of calves, perfected by M. Fehrenbach in the Institute Pasteur, and the organism the bacillus *icteroides* obtained from cases of yellow fever in Havana, Cuba.

Oct. 26—A full-grown guinea-pig was vaccinated with 2 c.c. serum *anti-coli*, and in 2 hours was given subcutaneously .25 c.c. of a 24-hour bouillon culture of bacilli *icteroides*. A control pig of the same size was given, under the skin, .25 c.c. of the same culture at the same time. Oct. 27, both pigs were ill. Oct. 30, the control was found dead. Oct. 31, the vaccinée was found dead. Autopsy gave hemorrhagic conditions and light colored livers, the blood contained the bacillus *icteroides* in large numbers.

Oct. 28, a large rabbit, 2000 grams, was given .25 c.c. of a bouillon culture of the bacillus *icteroides*, 72 hours old, in the ear vein, two hours after 4 c.c. of the serum *anti-coli* had been given in the other ear vein. A control of the same size was given .25 c.c. of the same culture by the ear vein. Oct. 30, both control and vaccinée were found dead.

Nov. 2, two large guinea-pigs were vaccinated on four successive days with 1 c.c. of serum *anti-coli*. On the fourth day they were also inoculated with .5 c.c. bouillon culture of the bacillus *icteroides*, 72 hours old. Two controls of the same weight were given only the .5 c.c. of the culture of bacillus *icteroides*.

Nov. 6, one vaccinée was dead, no autopsy. Nov. 7, the control was dead, no autopsy. Nov. 8, the other control was dead, no autopsy. Nov. 11, the other vaccinée was dead, the autopsy showing that it had been dead some time. There was an ulceration of the skin at the site of the inoculation 2 cm. long by 1 wide, the peritoneum being laid bare, and covered by a cheesy layer of pus, the margins well defined. The abdominal incision was carried carefully around the ulcer and the peritoneum turned back exposing its inner surface at the site of ulceration. There was no peritonitis, the intestines retaining their brilliance. The outline of the ulcer was seen as a raised border of infiltration on the inner surface, and from this raised border I carefully made cultures on slant agar-agar. The liver was much engorged, with fatty and necrotic areas. The spleen was slightly enlarged. The stomach contained 50 c.c. of fluid containing black flakes of blood; its walls were congested and extravasation had taken place. The kidneys were congested; the heart was full of fluid blood. From all organs cultures were made and in forty-eight hours were sterile; the culture made from the inner surface of the peritoneum gave the bacillus *icteroides* in pure state.

Conclusion—The serum *anti-coli* appears to be protective to guinea-pigs to some degree. The first of this group to succumb was one of the vaccinées, yet the other vaccinée lived almost twice as long as the témoins, and presented after death a sterile interior. From the fact that these animals are most susceptible to the septic influence of this bacillus, it is clear that the serum *anti-coli* induced a local reaction at the seat of inoculation in this pig, sufficient to limit the organism to the

seat of the injection and to prevent sepsis. The animal died of a toxemia from the localized colony.

Nov. 2 I inoculated a 2000-gram rabbit with 1 c.c. bouillon culture bacillus icteroides, 72 hours old, in the ear vein, and fifteen minutes afterward injected through the opposite vein 18 c.c. of the *serum anti-coli*. It died in 52 hours. At the same time, in another rabbit of the same weight, there was injected the same quantity of the bacillus icteroides, the "normal serum" of the horse being used instead of the serum anti-coli. This rabbit died in 74 hours. A control rabbit was also inoculated with the same quantity of bacillus icteroides alone. The control died in 65 hours. No autopsies were made except in the case of the first that died, the vaccinée with *serum anti-coli*, from which was regained the bacillus in pure culture.

Conclusion—There was no increase of resisting power from the vaccinations with the *serum anti-coli*, since this animal died first, the vaccin exerting a depressing effect at first similar to that known in the use of the "serum antipesteuse" for vaccinations. The horse serum did not exhibit this toxic influence and prolonged the life of the animal somewhat.

A large rabbit was vaccinated intravenously Nov. 11, with 10 c.c. of *serum anti-peripneumoniæ*, obtained from the sheep from subcutaneous injections of the killed cultures of the bacillus which causes this disease in these animals. Nov. 12, the animal was quite sick from this vaccination. Nov. 13, it was better, and 1 c.c. of a 24-hour bouillon culture of the bacillus icteroides was placed in the opposite ear vein. Nov. 15, there was some reaction; the animal was quite sick. Nov. 16, there was some reaction, the animal was still sick. Nov. 18, there was considerable reaction, the animal was quite thin. Nov. 22, it was better and gaining in weight. Nov. 25, there was given 10 drops of a virulent culture of the bacillus icteroides intraperitoneally. Nov. 27, it ate well and was gaining in weight; there was no reaction. Dec. 4, it was given .5 c.c. of a bouillon culture of the bacillus icteroides subcutaneously. Dec. 6, there was no reaction, and the animal seemed well. Dec. 14, the animal was found dead.

Autopsy showed meager body and under the pelt at the seat of the subcutaneous injection there was a solid lymph plaque 2 cm. by 1.5, from the center of which bouillon tubes were planted. The tissues were dry; the peritoneal cavity and its contents were normal; the liver normal in appearance; the spleen was the same; the kidneys were congested; the heart was full of fluid blood; serosæ normal; stomach and intestine normal. Cultures were made from all organs. On the sixteenth the cultures from liver and spleen and from the lymph plaque gave pure growths of the bacillus icteroides.

Conclusion—The vaccin *serum anti-peripneumoniæ* protected this animal against a dose usually fatal in 36 hours, but this protection was evanescent and the animal succumbed finally to a general invasion from the subcutaneous injection of the germ, on December 4.

Nov. 24, a large rabbit was vaccinated with 10 c.c. *serum anti-peripneumoniæ* in the ear vein. During the day it was dull, but not ill. On Nov. 25, it weighed 1960 grams, and the control 1980 grams. They were now injected in the opposite ear vein with 1 c.c. of the bacillus icteroides in bouillon 72 hours old. Nov. 26, the control was dead; Nov. 27, the original was dead; no autopsies were made, as they died of intoxication.

Nov. 21, five fine guinea-pigs were vaccinated with *serum anti-coli*, 1 c.c. being given daily under the skin for 6 days, or in all 6 c.c. were given to each animal. One received 8 c.c. altogether.

Nov. 21, each of these vaccinées received .5 c.c. of a bouillon culture of bacillus icteroides 48 hours old, a control pig receiving the same dose under the skin. Nov. 22, one vaccinée was dead from a perforation of the peritoneum into the abdominal cavity. Nov. 24, several vaccinées showed considerable local swelling at the site of the inoculation, the one to receive the 8 c.c. presenting the largest lump. This was perforated and the serum from it planted. Nov. 27, all the pigs appeared well, there having so far resulted only a local reaction. The planting from the localized swelling had resulted in a good growth of the bacillus icteroides. Dec. 1, these local swellings in vaccinées and controls were diminishing. Again I planted tubes from the serum obtained by puncture from them all.

Also prepared cover-slips which showed the bacilli free and engulfed by the leucocytes. The tubes gave in 24 hours pure and active cultures of the bacillus icteroides. On Dec. 6, the experiment was finished; all the animals were well; the swellings having disappeared. **Conclusion.** There seemed no doubt that the serum had protected these pigs, yet the control had reacted to the inoculation to the same extent as the vaccinées. This was puzzling, but it was finally attributed to the influence of the very cold weather which had prevailed during the experiment, upon the bacillus icteroides.

On Nov. 27 three large guinea-pigs were vaccinated with 1.5 c.c. of the *serum anti-coli* subcutaneously, and this was repeated daily for ten days, each pig receiving 1.5 c.c. of the serum. On Dec. 5 these pigs were inoculated with 1 c.c. bouillon culture of the bac. icteroides, 36 hours old. Two controls were also given the same quantity of the same culture subcutaneously. On Dec. 10 all were apparently well, the vaccinées had developed a distinct tumefaction at the seat of inoculations, tending to suppuration. The controls had large tumefactions, hard, with sharp borders, and no pus. All were eating well and were playful. On Dec. 12, the vaccinées were purulent, the témoins hard, and sharp bordered at the site of the inoculations. At this time having become convinced of the attenuation of the bacillus by the prevalent cold, I placed the cage containing all these pigs in the incubator at 25 C, and removed them to the room temperature the next morning. On the 14th, the cage was again placed in the high temperature incubator. On the 15th, the control was found dead, the others remained permanently well in the room temperature, the vaccinées were purulent and the control was ulcerated at the site of the inoculations; all recovered. From this and the other results it was determined that it was useless to experiment further with these serums in view of the very evident attenuation of the bacillus icteroides by the cold, and all further effort was in the direction of proving the effect of cold and heat on this germ.

On Dec. 12, to test the quality of the soluble toxins of the germ, a bouillon culture in a Fehrnbach flask, 14 days old, was filtered to 5 c.c., and 1 c.c. was given intraperitoneally to a 500-gram pig without appreciable result. The remainder was tested against the highly toxic blood-serum of the eel and without result. It was considered the result of the attenuation of the germ. On Jan. 1, a 25-gram mouse was given .25 c.c. of the freshly filtered culture under the skin, the culture being 6 weeks old. In 15 minutes, there being no reaction, I gave 1 c.c. with no result; in all the mouse received 2 c.c. within the hour and without result.

On Jan. 4, I gave the pig which had received the toxins on Dec. 12, 2 c.c. of a bouillon culture of the bacillus icteroides, intraperitoneally; this culture had been made in a moderately warm temperature, from the bacilli obtained from the spleen of a mouse dead from natural infection after 19 days. There was no reaction. Therefore, it was evident that the bacillus was so changed by the prevalent cold that there was not the normal production of toxins, or that they were much attenuated.

On Dec. 12, in each of two sterile cages there were placed two white mice, and given grain inoculated with bac. icteroides, obtained through an African ape from one Patrick Smith. One cage was placed in a temperature of 18 C., and the other in an incubator at 25 C. On Dec. 21, a mouse in the warm cage was very ill; its mate seemed thin and ill. On Dec. 23, one was dead and the other was quite ill. All in the cold cage seemed well. On Dec. 27, the remaining mouse in the hot cage was dead. Autopsies were made on both. In the first the pelt was yellowish on its inner surface; the liver was friable, not fatty to the eye; the spleen was normal. The cultures from the spleen gave pure colonies of the bac. icteroides. In the second mouse the pelt was yellow; the liver somewhat fatty, and the spleen enlarged—something unusual; from it the bacillus was regained in pure culture. On this date all the mice at 18 C. were apparently well, and one of them was transferred to the hot cage. Dec. 30, this mouse was dead. On the same day, the remaining mouse in the colder cage at 18 C. was dead. **Conclusion**—While the elevated temperature of 25 C., induced infection and death in about

the time usual in these animals in the tropics—8 to 10 days—the reduced temperature of 18 C. induced this infection and death only after twice the usual period, or in about 19 days.

On Dec. 29, two fresh mice were placed in one of the infected cages and 1 c.c. of fresh culture bac. icteroides added to their grain, the cage placed in the open air of the animal barn, one side of which was entirely open, the temperature that day averaging 11 C.

Dec. 30, Temp. 8.5 C. (average)	47.3 F.
Dec. 31, Temp. 8.7 C. (average)	47.4 F.
Jan. 1, Temp. 7.2 C. (average)	45 F.
Jan. 2, Temp. 9.5 C. (average)	49 F.
Jan. 3, Temp. 9 C. (average)	47 F.
Jan. 4, Temp. 7 C. (average)	44 F.
Jan. 5, Temp. 5 C. (average)	40 F.
Jan. 6, Temp. 5 C. (average)	41 F.
Jan. 7, Temp. 4.5 C. (average)	40 F.
Jan. 8, Temp. 4.5 C. (average)	40 F.
Jan. 9, Temp. 4.5 C. (average)	
Jan. 10, Temp. 4.7 C. (average)	
Jan. 11, Temp. 5 C. (average)	
Jan. 12, Temp. 4 C. (average)	
Jan. 13, Temp. 2 C. (average)	
Jan. 14, Temp. 2 C. (average)	
Jan. 15, Temp. 2 C. (average)	
Jan. 16, Temp. 3 C. (average)	
Jan. 17, Temp. 8 C. (average)	
Jan. 18, Temp. 7 C. (average)	
Jan. 19, Temp. 7 C. (average)	
Jan. 20, Temp. 6.5 C. (average)	

These give a general average of about 4.5 C., or 40 F., which is the frost-line, to which the animals were exposed without the appearance of any symptom of infection. At the end of this time the animals were transferred to a clean cage and the infected one was sterilized, the animals remaining well two months after the change.

At the same time, from January 5, two other mice were exposed to bacillus icteroides under the same conditions of temperature in the same barn until the 20th, an average of about 4.5 C., or 40 F., without the appearance of any symptom of infection. They were transferred to the clean cage with the other mice and remained permanently well.

These experiences demonstrate that the extreme degrees of cold, below the line of frost and approaching zero C., are extremely hurtful to the bacillus icteroides, attenuating it to such an extent that it failed to infect white mice, the most susceptible of animals, during an exposure of 23 days. Moreover, these are the only exposures of these animals which failed to result in infection in from 3 to 5 days at high temperature, and a longer period as the temperature became reduced.

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DISCUSSION.

DR. SIMON FLEXNER, Philadelphia—I have been much interested in Dr. Wasdin's exhaustive paper. The high value of it is, of course, dear to everyone who has followed the literature of the subject since Sanarelli's discovery. Most bacteriologists believe that Sanarelli has done no more than point out the existence of a hitherto unknown pathogenic micro-organism in the bodies of a certain percentage of persons dead of yellow fever. The complete proof of its relation in a causative way to the disease is yet to be brought. This evidence, Dr.

Wasdin thinks, is supplied by his experiments. He will, I am sure, permit a reasonable amount of scepticism even after his series of experiments. If we are to conclude that animals are subject to accidental infections with the bacillus icteroides, how are we to harmonize the absence of similar infections during the prevalence of the natural disease? Dr. Wasdin doubtless has established that the bacillus icteroides is capable of a high degree of potency; that its diminution in the air may lead to infection in animals; but I fail to see that by those experiments he has proved that he has produced yellow fever.

DR. GERRY, Boston, Mass.—I should like to ask regarding the immunity of patients who have had yellow fever, if they really were immune. During the Cuban war we heard a great deal about the immune, and there seems to be a fixed idea that these people were really immune.

DR. EUGENE WASDIN, closing the discussion—The remarks of Dr. Flexner should carry much weight. It is certainly right to criticize, and I know of nothing that would be more productive of good. We feel convinced that further investigations will prove the value of the observations of Professor Sanarelli. In regard to the question of actual immunity from yellow fever I should like to have some one in the audience reply. I can not do so. I can only state my own observations in the epidemics of yellow fever and what occurs in endemic centers. One attack does not protect absolutely against a second. I have seen several cases in which two attacks were enjoyed. There was black vomit freely ejected. The soldiers in Cuba supposed to be immune sometimes did suffer from a second attack. I regret that the time is so short that it will not permit me to go into details of the paper which would have been interesting and would satisfy some of the inquiring minds showing the amount of work condensed in the report of the commission made in 1899.

DEMONSTRATION OF HOME MILK MODIFIER.*

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The best food for an infant is its mother's milk; in its absence comes milk properly modified. Up to the present, this has been difficult of accomplishment. The Walker-Gordon Company has set a standard of what can be done in this direction, and now the Sheffield Farms Company, of New York, has opened a laboratory for the modification of milk. But such laboratories are situated in only a few of the larger cities, and their product is so expensive that their usefulness must necessarily be limited.

The modification of milk at home entails much elaborate calculation on the part of the physician; much patience and intelligence on the part of mother or nurse; methods so crude for the most part as to render the procedure difficult and inaccurate. However, although modified milk is acknowledged to be the best artificial food for an infant, it is comparatively little used.

The apparatus which I desire to demonstrate today is not intended to replace the laboratory, nor will it supply the needs of every infant. It will, however, if properly used, provide a food for any healthy infant for the entire first year of its life. It was suggested by Dr. Sidney V. Haas, of New York. This apparatus consists of a glass jar showing seven panels, with lip, capable of holding 16 ounces. One of the panels presents an ordinary ounce graduation, the other six panels present six different formulas for the modification of cow's milk, each

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