ORIGINAL ARTICLES.

THE BACTERIOLOGY OF YELLOW FEVER ONCE MORE.

(Translated.)

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THE latest phase of the scientific discussion concerning the causative agent in yellow fever has led us into a path which threatens to last forever. The question at issue is becoming more and more involved, and is being practically lost sight of in the present discussion by many bacteriologists. It seems to me that the recent publication of the Report of the Commission of Medical Officers,[1] detailed by authority of the President of the United States to investigate the cause of yellow fever in Cuba ought to put an end to further controversy. This report, drawn up in the most conscientious manner, definitely substantiates the etiologic value of the bacillus icteroides. There are certain points of interpretation, it is true, though of very secondary importance, with reference to which there still exist some slight differences of opinion between the results of my own investigation and those of that commission. But these do not affect in the slightest degree the fundamental question at issue.

The investigations of the commission, with regard to yellow fever, I may say in passing, have been conducted with such evident seriousness, thorough preparation and scientific exactness that they form a striking contrast to the almost incredible and unpardonable levity with which a number of my opponents have thought it not improper to approach so important and so difficult a question.

It is perfectly true, as Dr. Novy[2] said, in his last article in reply to me that every scientific publication is open to doubt and should be submitted to scientific criticism. But it is also very true that criticism should not go beyond certain limits established by custom and that the discussion should always maintain a high scientific character, otherwise it will not be possible ever satisfactorily to determine a question. After having sustained with an unreasoning obstinacy that is only equalled by the ill success of their efforts the identity of the bacillus icteroides with that of Dr. Sternberg's bacillus X, Dr. Sternberg,[1] and his disciples, Drs. Reed and Carroll,[2] now dispute my discovery from other and entirely different points of view. So much has been said in fact, that in order to defend myself and satisfy every one, I should have to write an article every day, and there would never be an end of the controversy.

As a matter of fact, the arguments advanced by my eminent adversary, when seriously examined, frequently seem either without foundation or paradoxical; while the continuous insistence with which they are brought forward on every possible occasion renders response to them somewhat embarrassing. I am indeed somewhat of the conviction that the whole discussion is a miserable waste of time, and can have no definite scientific importance.

In this, my last paper in the discussion, I shall ignore entirely all the unimportant collateral questions, and shall set forth the arguments for my position as to the specific pathogeneity of the bacillus icteroides in its simplest and clearest terms. I have proclaimed and still proclaim that the bacillis icteroides is the specific causative agent in the etiology of yellow fever. Before my investigations, it had not been isolated nor recognized by any bacteriologist, nor had it been discovered in any malady, and it had never been found in a human cadaver. Since the publication of my investigation it has been isolated by Mendoza,[3] and Ramos[4] in Brazil; by Mesa-Gutierrez and Orvieto[5] in Mexico; by Pothier[6], Archinard and Woodson[7] in New Orleans; by Agramonte[8] in Cuba; by Wasdin and Geddings[9] in Louisiana, in Mississippi, and at Havana, and finally by Gauthier[10] in a case of yellow fever transported to Marseilles from Brazil on the steamer "Provence."

It may therefore be set down as definitely decided: *First, that the bacillus icteroides is undoubtedly found in patients who are ill of yellow fever, and in cadavers of those who have died from the disease.* This is not an opinion. It is a fact.

[1] "Reports," etc., Government Printing Office, Washington, 1899.
[2] MEDICAL NEWS, p. 385, September 23, 1899.

[1] MEDICAL NEWS, August 19, 1899.
[2] MEDICAL NEWS, September 9, 1899.
[3] *Centralblatt für Bakt.*, No. 11, 1899.
[4] *Brasil Medico*, No. 29, 1898.
[5] *Boletin di Consig Supr. de Salubrid*, Mexico, April 30, 1899.
[6] *Jour. of Am. Med. Assn.*, April, 1898.
[7] *N. Y. Med. Journal*, January 28, 1899.
[8] *Centralbl. für Bakt.*, No. 18, 1899.
[9] "Report of Commission," etc., *ut supra.*
[10] *Revue d'hygiene*, October, 1898.

My first investigations, carried out in the only way that was possible under the circumstances, without any guidance from the labors of others, in the midst of manifold inconveniences and in laboratories improvised from day to day on my journeys, allowed me to isolate the bacillus icteroides in only a little more than half the cases. I made this declaration with perfect sincerity at the time, just as Loeffler in his first communication in 1884 with regard to the discovery of the bacillus of diphtheria confessed that he had not been able to isolate this micro-organism in every case from the throat of diphtheritic patients. The final demonstration of the specificity of the Loeffler bacillus was made only four years later in 1888, when Roux and Yersin were able to demonstrate in animals the specific lesions of the disease, analogous to those which occur in human diphtheria. I was able to definitely demonstrate the specificity of the bacillus icteroides not only as the result of a very large series of comparative observations in animals, but also after having performed a series of decisive experiments on human beings.

I can not ask that this last series of observations be repeated, but I must demand that they should be believed, and I can not permit them to be discussed lightly since I have seen the results recorded with my own eyes, and my observations were confirmed at the time by a number of colleagues who were as familiar as I was myself with yellow fever. When I declare that by means of the toxin of the bacillus icteroides I can reproduce in man the typical picture of yellow fever, I must ask that I shall not be met with the obvious objection that others have been able to obtain the same results by means of other microbic toxins. I am perfectly familiar with the investigations made in this matter by Fraenkel[1] and Rumpf.[2] They produced certain symptoms in man by injections of the toxin of typhoid fever and of the bacillus pyocyaneus, but these authors have never reproduced either yellow fever or its symptoms, nor its anatomical lesions. If I had not been able to reproduce in man genuine yellow fever, I would never have been justified in declaring categorically that I had discovered the specific cause of the disease. I would practically have lost none of the prestige of my discovery had I simply announced the bacillus icteroides as a probable cause of yellow fever, leaving to others the duty of establishing this fact definitively.

The typhoid bacillus to which Eberth's name is usually given was not isolated by Eberth, but by Gaffky. Eberth had simply the distinction of having seen it first, and this of itself alone suffices to establish the priority of a discovery. After all it must be remembered that I was not a novice in the field of bacteriology, nor was I making my first discoveries, and it would have been difficult to persuade me to compromise my reputation as a bacteriologist by the imprudent affirmation of facts that could not be substantiated. But even prescinding from such considerations, which, after all, are of secondary importance, it has come about that when investigations could be made with ample assistance and with every convenience of time and deliberation necessary for such work, the bacillus icteroides has been isolated in every case of yellow fever.

In fact, Archinard and Woodson in Louisiana[1] isolated the bacillus icteroides in eighty per cent. of their cases. Wasdin and Geddings[2] after their lengthy mission of investigation in Louisiana, in Mississippi, and in Cuba declare that the bacillus icteroides can be found in practically every case of yellow fever. The other writers whom I have mentioned above, though they have obtained the bacillus icteroides from yellow-fever patients and from the bodies of such patients after death, have not taken the trouble to calculate the percentage of cases in which it could be isolated. Agramonte,[3] who was sent by Dr. Sternberg to Havana to make control tests of my investigations, alone, protested vigorously that he was able to isolate it only five times in eleven cases. But he himself confesses that he was not able to carry on his investigations as completely as he would like to have done, because of limited supply of laboratory appliances, and because of the arduous and exhausting work which he had to carry on as a member of the medical staff. This confession accounts amply enough, it seems to me, for his partial success in the investigation. Under such arduous conditions of observation no one could hope to secure better results than did Agramonte under the circumstances.

We may set down as a second conclusion then, *that the bacillus icteroides can be isolated from practically every case of yellow fever.*

In spite of the repeated substantiation of my investigations Dr. Sternberg and my other opponents have raised the doubt that the bacillus icteroides may be nothing more than a very commonplace micro-organism present as a secondary infection. As to this I may be permitted a few brief considerations. How can it be conceded even *a priori* that a microbe which is found constantly in patients sick with yellow fever and in the bodies of those who

[1] *Deutsche med. Wochenschrift*, p. 985, 1893.
[2] *Ibidem*, p. 987.

[1] *N. Y. Med. Jour., ut supra.*
[2] "Public Health Reports," No. 33, 1899.
[3] *Centralbl. für Bakt.*, No. 18, 1899.

have died from the disease; which can be isolated during the life of the patient and which constantly produces a perfect specific serum reaction with serum taken from the bodies of yellow-fever patients, from those actually sick of the disease, from convalescents, and from those who have recovered for many years from an attack of yellow fever; which reproduces in animals and in man, by itself and also by means of the toxins elaborated from it in vitro, the symptoms and characteristic lesions of yellow fever, can ever be considered as a simple microbic intruder on a par with all the other micro-organisms of secondary infection, which are well known and have been studied experimentally in every part of the world, because they are practically the same everywhere and in every disease. Besides this we know that careful observation demonstrates that the bacillus icteroides is the only microbe constantly present in yellow fever.

Archinard and Woodson in New Orleans have succeeded in obtaining agglutination in cases of yellow fever in ninety-three per cent. of the cases under observation. I was not able to obtain it in a single instance in eighty-six cases of normal blood, or in patients sick with other diseases than yellow fever, and have never succeeded in obtaining it in a single case in which the patient was either not actually sick with yellow fever or had suffered from it years before. Wasdin and Geddings during their mission in Havana studied carefully the bodies of thirty-one individuals who died from the most diverse maladies known and unknown, but all different from yellow fever and did not succeed in finding in a single case the bacillus icteroides present.

There has been but one discordant voice in the midst of the perfect unanimity in this matter, and that as might have been perhaps, foreseen, belongs to Dr. Agramonte, who was sent to Havana by Dr. Sternberg. I have never attached much importance to Dr. Agramonte's work for the reason given above, but Drs. Reed and Carroll refer to it very confidently and seem to consider it of the highest importance. It will be well for us then to see how things stand in the matter. Dr. Agramonte sent a report to Dr. Sternberg from Havana, which was published during the current year.[1] He describes the case of a soldier who died with suspicious symptoms as he himself says, "a disputed case." At the autopsy he succeeded in isolating, first the bacillus icteroides, second the colon bacillus, and third, a form of typhoid bacillus. Very naturally Dr. Agramonte takes advantage of so promising an opportunity and immediately assumes that this supposed typhoid bacillus was the prime factor in the soldier's illness. He finds a way to make it appear that the patient really died of typhoid fever complicated by a secondary infection with the bacillus icteroides. In order to give more weight to his declaration he affirms that the other members of the yellow fever commission, especially Drs. Wasdin and Geddings, had arrived at the same conclusion. It does not require any hypercritical acumen, however, to decide that the disputed case was in reality a case of genuine yellow fever; and that the supposed bacillus of typhoid could be nothing else than one of the numerous bacilli belonging to the same family as the bacillus of Eberth, whose presence I have frequently demonstrated in the cadavers of patients dead from yellow fever[2] and which two of my students, Puppo and Ottoni[3], have already made the object of lengthy and detailed researches under my direction. Not only can this be presumed to have been the case but Wasdin and Geddings declared explicitly that the case of which so much account was made by Dr. Agramonte (Case No 7 of their report) was without doubt a case of genuine yellow fever.

Drs Reed and Carroll[3] were imprudent enough, notwithstanding all this, to announce that they had examined the liver of this case histologically and to announce that "from the microscopical findings we are strengthened in the belief that the bacillus icteroides in this case should be considered as a secondary invader" I can only think that in this they were joking at the expense of the suggestibility of their readers. As if they thought for a moment that it could be supposed possible to believe that by means of a microscopic examination they were able to make the bacteriological diagnosis of the bacillus icteroides in the midst of hepatic tissue, and then could afterward affirm that its invasion was primary or secondary. This assumption of theirs can only be the result of a too vivid imagination, and we can scarcely be expected to follow them seriously. From what I have said I think we can deduce the logical conclusion—*third, the bacillus icteroides is found only in those sick of yellow fever, or in the bodies of those dead from the disease. No one has ever succeeded up to this in finding it in a patient sick from any other disease; nor in the cadaver of any but an individual dead from yellow fever.*

We come now to the experiments on animals. As is the case with typhoid fever, with cholera, with infections by the pneumococcus, or the streptococcus, there exists no single lesion that can be said to be absolutely pathognomonic of yellow fever. The catarrhal lesions of the gastric and intestinal mucous

[1] *Centralblatt für Bakteriologie*, No. 18, 1899.

[1] *Annales de l'Institut Pasteur*, page 440, 1897.
[2] *Annali d'igiene sperimentale*, Roma, 1898.
[3] MEDICAL NEWS, p. 329, 1899.

membranes, the erosions of the stomach, the hyperemia of the meninges, and of the parenchyma of certain organs, the hemorrhagic manifestations, the nephritis, the albuminuria and so forth, have, it is true, a particular importance in yellow fever, but they can be found in a great many other morbid conditions either as essential lesions or as secondary complications. Not even the fatty degeneration of the liver can be strictly said to be absolutely specific for yellow fever, since it is found at times in certain other morbid conditions. Despite all this the lesions of yellow fever when taken altogether, as Jaccoud very well says, constitute a pathological criterion that is more complete and more definite for this disease, than the pathological picture presented by the majority of the infectious diseases.

Now as it is impossible to reproduce the clinical picture of yellow fever in rabbits or guinea-pigs, or in animals generally, because yellow fever, like typhoid fever, cholera, pneumonia, and so forth, is essentially a disease that is limited to human beings, the question of the experimental study of the disease in animals must limit itself to the investigation of the question whether the micro-organism, which is supposed to be the specific causative agent of yellow fever, is capable of producing more or less completely all the principal symptoms and the lesions which are considered as more or less characteristic of the disease. As a matter of fact, we are able to obtain in animals, and especially in dogs, practically the whole anatomical and symptomatological picture of the disease. The modern scientific literature of the characteristics of the bacillus icteroides is unanimous in supporting this declaration. There is especially one lesion, however, which can be considered as of the very greatest value and as of almost pathognomonic importance in the post-mortem recognition of yellow fever in human beings. This is the extreme fatty degeneration of the liver. I would like to make it clear at first that when I speak of fatty degeneration I do not attach to the term in the present instance any vague or generic signification, because it is very well known that in many other infectious diseases, human and experimental, the hepatic cell can be affected by degenerative processes, more or less profound. I wish to designate, as a specific fatty degeneration produced by the bacillus icteroides, the true steatosis of the liver; that is to say, a state of extremely profound fatty degeneration, which is produced acutely and with so much intensity that the liver is affected to such a degree, so far as we know up to the present time, by but two specific morbid processes, namely, phosphorus poisoning and yellow fever I insist upon this point, because I think it can be shown that by this lesion alone the morbific agent that produces it can be distinguished from every other. Its extreme steatogenic power, with regard to all elements of the body in general, but especially with reference to the hepatic cell, distinguishes the bacillus icteroides from all other pathogenic agents.

This important phenomenon can be observed especially and very noticeably in dogs. Foa,[1] Della Rovere,[2] Belfanti[3] and Zenoni, Bruschettini,[4] Wasdin and Geddings[5] have also observed it in a very marked degree in rabbits, and while Bruschettini has seen it also in pigeons and in turtles.

In the dog, all the observers who have investigated the subject carefully with the necessary experimental ability and without preconceived prejudices, have succeeded in finding this pathogenic action of the bacillus icteroides. To deny it now would seem the veriest absurdity. It suffices to read the experiments of any of the investigators of the bacillus icteroides, of course with the exception of Drs. Sternberg, Reed, and Carroll, and Novy, to find a description of an intense steatosis which has always been obtained with the bacillus icteroides, and never with any other micro-organism. I must, of course, concede to my opponents that not all the races of dogs are possessed of hepatic elements which are equally sensitive to the toxin of the bacillus icteroides. The age of the animal, and especially the race to which it belongs, exercise undoubtedly an important influence in the modification of the phenomena. If the experiments are continued, however, the observer will always succeed in obtaining such examples of acute steatosis of the liver as cannot be obtained experimentally, even when the animals are poisoned by large quantities of phosphorus. The liver appears absolutely yellow. It is anemic, and its density is greatly increased. The picture which I have had drawn and reproduced in my monograph is the only thing that can give a proper idea of its appearance to those who have not actually seen it. It must be remembered that in cases which run a very acute course the dark yellow color characteristic of the fatty degeneration is masked by the congestion, which has been set up in the organ by the intense irritation of the toxins of the disease. It suffices, however, to produce a slight superficial ischemia, by simple compression with the finger, for instance, to produce an immediate return of the dirty yellow color, and this at once discloses the profound steatosis of the organ that has taken place.

[1] *Giornale di real Accad. de médic. di Torino*, No. 3, 1898.
[2] *Riforma Medica*, July, 1898.
[3] *Giornale di real Accad. di médic. di Torino*, Nos. 5 and 7, 1898.
[4] *Gazetta degli ospedali*, No. 64, 1899.
[5] "Report of Commission of Medical Officers, sent out by the President of the United States, etc., Washington, 1899."

I have not myself seen, nor have any of the well-known investigators who have repeated and confirmed my experiments, ever observed anything similar to this important lesion in animals dead from any other microbic infection. This demonstrates that the steatosis, the true and complete steatosis, which transforms, as I have often seen, the whole liver into a compact mass of fatty degenerated material, is peculiar to the bacillus icteroides.

I have made a great many observations in this matter and the number of dogs that have been killed in my laboratory runs up into the hundreds. As a detail in my last article in the MEDICAL NEWS I have even carefully calculated by mechanical methods the amount of fatty material contained in the liver of dogs killed by the bacillus icteroides in order to compare it with that obtained from the livers of animals killed by other methods of experimental infection. Our experiments included microbes as varied as the cholera vibrio, the colon bacillus, the bacillus pyocyaneus, the bacillus of diphtheria, and the bacillus icteroides. The last mentioned bacillus was capable of producing in a shorter period of time a much larger quantity of fatty material than any of the others. I am myself almost convinced that in Dr. Sternberg's laboratory they have never succeeded in obtaining this steatosis, for it is so peculiarly characteristic that it would at once have attracted attention and convinced even the most skeptical of the specificity of the agents producing it because its appearance is not only extremely peculiar, but because it has an absolute analogy with the appearances which are so well known in human cadavers after yellow fever. This convinces me that perhaps in the Army Medical Museum experiments are devoid of value as far as regards yellow fever, because they are working with a bacillus which is not the bacillus icteroides. It is not possible to admit that in Washington the bacillus icteroides seems to be endowed with characteristics very different from those which have been found repeatedly and indisputably in other cities of the Union, and in all the other countries of the world.

The number of observers who have noted this characteristic steatogenic power of the bacillus icteroides is very large, and is well known by those who follow the literature of the etiology of yellow fever. It is evident then that the negative results obtained by Dr. Sternberg and by those working under his direction are deserving of very little confidence. I think we may without further ado draw the following conclusion: *Fourth, the bacillus icteroides reproduces in animals all the symptoms and all the anatomical lesions which can be considered especially characteristic of yellow fever in human beings.*

Having said this much I may be considered I think rigorously to have fulfilled my duty. Koch's famous laws may seem to have lost some of their primitive and absolute value in our day. Yet, notwithstanding this, it is true that the bacillus icteroides, considered as the specific causative agent of yellow fever, is in all important particulars perfectly in accord with these laws. First, it is found in practically every case of yellow fever. Second, it is never found outside of yellow fever. Third, it can be cultivated in artificial nutritive media. Fourth, it reproduces in animals an anatomical and symptomatic picture analogous to that of yellow fever in the human being.

I have still to reply, however, to certain objections which have been more or less courteously urged against the results of my investigations by Drs. Reed and Carroll. The insistence of these two young bacteriologists of the Army Medical Museum, it strikes me, is due rather to an unfortunate deference which they have for the opinions of their surgeon general than to any special desire for the advancement of scientific truth.

I certainly do not feel that it would be quite proper to force Drs Reed and Carroll into insubordination to what they seem to think their duty, nor do I wish to tire the reader's patience nor take up valuable space in the MEDICAL NEWS in discussing point by point their last article.[1] In that article, while professing a spirit of the greatest courtesy towards my modest person, they get into a most inextricable confusion of experimental results and scientific deductions, but somehow out of it all they emerge at the end with enough energy and self-confidence left to insist that the bacillus icteroides is identical with, or at least is a variety of, the bacillus of hog cholera!

It is only too well known that microbes are like human beings, in this particular at least; seen from a distance they all look alike. Even Drs. Reed and Carroll themselves have furnished an excellent demonstration of this principle when they write: "On the contrary, we wish to state that placed side by side in gelatin we have been unable to detect any differences in the colonies of the two bacilli with the naked eye, and that it is only by means of the microscope that faint differences can be detected."[2]

I do not deny that between the bacillus icteroides and the micro-organisms that cause hemorrhagic lesions (hog-cholera, swine plague, pneumo-enteritis of swine, etc.) there are certain points of resemblance. This family of microbes is, in fact, so extraordinarily pleomorphic in character that the members of

[1] MEDICAL NEWS, September 9, 1899.
[2] MEDICAL NEWS, September 9, 1899, p. 324.

it present some points of resemblance with practically every sort of micro-organism. As the result of this they have been the subject of very great, almost hopeless, confusion in contemporaneous bacteriological literature.[1] Even up to the present time bacteriologists have not succeeded in establishing with anything like unanimity characteristics by which they can be definitely differentiated, so mutable are their qualities under varying conditions. To raise this question, as Drs. Reed and Carroll insist on doing so obstinately, after all that has been said with regard to the isolation and the thoroughly studied characteristics of the bacillus icteroides, may serve as a sport on which to while away time in a laboratory, but it will never assist medical science in the solution of the important problem of the etiology of yellow fever.

Instead of remaining in Dr. Sternberg's laboratory, ever on the hunt for anything that seems likely to hurt the reputation of the bacillus icteroides, laboriously constructing theories that may destroy its significance, Drs. Reed and Carroll would have employed their time much better if they had followed the very practical example of their colleagues of the Marine Hospital Service, who, in order to make control observations on my investigations, went into parts of the country infected with yellow fever. It is at Havana or in New Orleans that a properly critical judgment on my work on yellow fever can be formed, not in the Army Medical Museum in Washington, and especially not under the direction of Dr. Sternberg, who somehow feels himself forced into the unfortunate position of a man, who, not having succeeded in an undertaking himself, pretends to believe that others cannot have been more acute or more fortunate than he was.

As it is now it will evidently be impossible for Doctors Reed and Carroll and myself ever to come to an understanding. Any *rapprochement* of opinions on our part would seem to be precluded by the persuasion that I can not shake off, that Drs. Reed and Carroll either have not been experimenting with the bacillus icteroides at all, or else they do not know how to experiment.

Certain of the expressions they use in their last article would seem to point very clearly to the fact that their experiments were not done with the bacillus icteroides. They say on p. 327 of the MEDICAL NEWS for this year: "True we did state and we wish here to repeat, that, with one exception hereafter to be mentioned, the fatty change found in the livers of the dogs experimented with is not comparable to that found in the liver of human beings who have died of yellow fever, and we may add that there is an almost entire absence of that necrosis of individual liver cells which is so prominent a feature in the human liver."

I do not wish to fill out a long article with excepts from the opinions of well-known bacteriologists who have recently made series of experiments with the bacillus icteroides. I can, however, say at once without more ado that this opinion of Drs. Reed and Carroll is positively contradicted by the results obtained by bacteriologists who live in countries where yellow fever is endemic, and who are therefore in a much better position to know its characteristic anatomical lesions than are my confreres of the Army Medical Museum. De Lacerda, Ramos, Fajardo, Conto, Mendoza, not to mention others, have carefully studied the pathogenic action of the bacillus icteroides on animals and have become completely convinced of the perfect analogy which exists between the hepatic steatosis produced by this micro-organism and its toxins and that which is found in the cadavers of patients who died from yellow fever.

Doctors Reed and Carroll declare in addition that the bacillus icteroides produces in young pigs the characteristic symptoms and pathognomonic lesions of hog-cholera. But in their experiments done at the quarantine station of the Delaware Breakwater, their colleagues of the Marine Hospital service, Wasdin and Geddings, assert precisely the contrary and declare that young pigs are absolutely refractory to inoculation of the bacillus icteroides. I do not wish to doubt their repeated declarations in the matter nor to discredit absolutely all that they have written, but I am becoming more and more convinced that they have been all the time experimenting with the bacillus of hog-cholera, while they have been as constantly under the impression that they have been experimenting with the bacillus icteroides.

The fact reported by them that my serum causes an agglutination even at very high dilution in liquid cultures of the bacillus of hog-cholera demonstrates absolutely nothing. The phenomenon of agglutination has a value only in certain special conditions, even the serum of the normal horse may possess of itself a very high agglutinative power with regard to certain microbes. In place of working with a serum prepared artificially from horses, Drs. Reed and Carroll would have done much better had they followed the example of their confrères in New Orleans—Pothier, Archinard, Woodson, and others. These men demonstrated that the bacillus icteroides is agglutinated only by serum taken either from those who are actually sick of yellow fever, or from those convalescing from the disease. Serum taken

[1] W. Selberschmidt, *Annales de l'Institut Pasteur*, p. 59, 1895.

from such patients, however, they demonstrated to be completely inactive in regard to any appearance of agglutination in cultures of the typhoid bacillus, and especially as far as regards the colon bacillus, although, as is well known, this last is practically the ordinary agent of secondary infection in yellow fever. I think that it is entirely repugnant even to the most elementary common sense to suppose that the specific causative agent of a disease of hogs, which is very well known and widely diffused over the world, should always have been found, precisely and as it were regularly, in the sick and the dead from yellow fever in cases studied at Rio de la Plata, in Brazil, in Mexico, in the United States, in Cuba, and in Europe. The supposition is so paradoxical that, even without the considerations which precede it, it practically is decisive of the question at issue. It suffices by itself to destroy the quaint edifice of theory which has been raised up in opposition to the bacillus icteroides in the laboratory of Dr. Sternberg.

Finally, I must mention that even Wasdin and Geddings have described very exactly the curious and very well known method in which the bacillus icteroides develops when cultivated on agar-agar at different temperatures. While no one among the authorities who have studied accurately the protean morphology of the microbe of hemorrhagic septicemia have ever mentioned anything like it in the cultures of these microbes.

With reference to the last objection, that raised by Dr. Novy,[1] my reply will be very brief. The question of the resistance to cold is one that can be passed over as of very little importance in the face of the clinical demonstration and the bacteriological and experimental observations which attest that the bacillus icteroides is the true cause of yellow fever. I have already shown how it is possible that an epidemic of yellow fever may become extinguished at the approach of winter, without it being necessary to admit for this reason that its specific causative agent is destroyed by cold. But if Dr. Novy once concedes that the germs of yellow fever can live even during the winter time in clothing, or in the interior of houses, etc., he must admit that the supposition that they always perish because of cold is theoretically undemonstrable. As a matter of fact every time that an epidemic of yellow fever recurs in the same place in which it was raging before an interval of cold, it can be said that while the germ of the disease has perhaps failed to retain its vitality on the streets and in the open places generally, it has been protected from the effect of the winter temperature in houses, in clothes, and clothing, etc., so that the problem becomes practically insoluble. Dr. Sternberg' himself has written: "It is claimed that the epidemic of 1897 in the City of Memphis was not due to a new importation but resulted from the liberation of germs in houses that had become infected during the epidemic of 1878." For cholera also the same law seems practically to hold good. It has often been noted that cholera is more apt to continue during the winter than yellow fever. This is certainly due to the fact that the bacillus of cholera is less fastidious than the bacillus icteroides, either as regards the kind of nutriment it requires, or the conditions of life and of development which it demands. With reference to the other objections urged by Dr. Novy it is not worth while to discuss them in detail. They have an importance entirely secondary, and would, besides, lead to an interminable discussion. The scepticism which Fraenkel expresses with regard to the yellow fever in certain synthetic writings of his cannot be considered to have more value than as a platonic expression of doubt. He does not present the slightest scientific basis to support his gratuitous opinion. In Germany they are a little too much accustomed to very legitimate and very praiseworthy triumphs of German science. They do not easily admit, without a good deal of preliminary delay and restriction, that bacteriologists in other countries may also be able to make genuine bacteriological discoveries.

As to the doubt expressed by Thoinot, it falls practically into the same category. There is, however, one aggravating circumstance in his declaration of opinion. He makes a comparative review of my first monograph on the subject, and that of the well known Dr. Havelburg, but he does not realize that this last is the most ridiculous, most puerile contribution to the contemporaneous literature on yellow fever that has ever been made. He makes abstracts from both works with evident good faith, and makes it clear that he is not gifted with a very highly developed critical sense.[2]

Finally, I wish to correct an inexactitude into which Dr. Novy has fallen. The antitoxic serum

[1] MEDICAL NEWS, September 23, 1899.

[1] "Report of Yellow Fever," p. 49, 1899.

[2] Dr. Havelburg made his experiments by inoculating directly under the skin or into the peritoneal cavity of guinea-pigs the intestinal contents, or the black vomit, of patients sick with yellow fever, or these same substances obtained from yellow-fever cadavers. The guinea-pigs very naturally died almost at once of septicemia, and Dr. Havelburg had the good fortune to succeed in cultivating immediately, and in pure culture, from the heart's blood of these animals, the true specific bacillus of yellow fever! It is useless to add that this extraordinary bacillus had the unfortunate property of behaving itself entirely and under all circumstances just as does the most classic of colon bacilli. In 1897 it might have been possible for a writer to be still somewhat in doubt with regard to the results of my experiments, but surely he should not have been so ingenuous as to take seriously the windbag that issued from Dr. Havelburg.

used by Dr. Foa in his experiments was not always prepared by him, but is the same as that which I prepared and used in my experiments at Montevideo before any one else. I have never ventured myself to declare positively that any anti-amaryllic serum was endowed with antitoxic properties, since I never succeeded in gathering sufficient evidence of that fact to satisfy myself. I was very willing, however, that Professor Foa should attempt to demonstrate it, and very glad that he succeeded.

This fact may serve to prove once more that in all of my work on yellow fever I may, perhaps, have committed faults by excessive reserve. I certainly never did so by making imprudent affirmations with regard to facts of which I was not sure or had not carefully demonstrated. I flattered myself with the thought that my inevitable adversaries would adhere to the same system. It is needless to say that I have in this suffered from a profound delusion.

It may be that there are still intelligent medical men who think that more light is needed on the etiology of yellow fever. For myself, I must say that very few etiological problems have been robbed of their mystery and demonstrated with as much clearness and rapidity as this one. May I add that no work of serious importance so conscientiously performed as was this one has ever been the subject of criticism so superficial and withal so obstinate as my research on yellow fever has called forth.