Sternberg (G.M.)

RECENT RESEARCHES RELATING TO THE ETIOLOGY AND SPECIFIC TREATMENT OF YELLOW FEVER.

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RECENT RESEARCHES RELATING TO THE ETIOLOGY AND SPECIFIC TREATMENT OF YELLOW FEVER.[1]

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IN a paper read at the Twelfth International Medical Congress at Moscow during August of the present year, and published in the September number of *The American Journal of the Medical Sciences*, I have given my reasons for believing that the bacillus icteroides of Sanarelli, and a bacillus obtained by me from yellow-fever cadavers at Havana, provisionally named "bacillus *x*," are identical. If the identity is not established, the claim of Sanarelli that his bacillus icteroides is the specific infectious agent in yellow fever cannot, in my opinion, be admitted. For this specific infectious agent must be the same in yellow fever occurring at Havana as for that occurring at Rio de Janeiro. My extended and painstaking bacteriologic researches in a series of forty fatal cases occurring in the city of Havana during 1888 and 1889, and three occurring in Decatur, Ala., during the epidemic of 1888, show that no micro-organism, other than my bacillus *x*, develops in the culture media usually employed by bacteriologists, except the colon bacillus and a few other species exceptionally found and excluded from consideration for reasons stated in my report on "The Etiology and

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Prevention of Yellow Fever," published during 1890. In summing up the results of my investigations I refer to the bacillus *x* as follows:

"Among the facultative anaerobics is one—bacillus *x*—which has been isolated by the culture method in a considerable number of cases of yellow fever, and may have been present in all. This bacillus has not been encountered in the comparative experiments made. It is very pathogenic for rabbits when injected into the abdominal cavity. It is possible that this bacillus is concerned in the etiology of yellow fever, but no satisfactory evidence that such is the case has been obtained by experiments upon the lower animals, and it has not been found in such numbers as to warrant the inference that it is the specific infectious agent. All other micro-organisms obtained in pure cultures from yellow-fever cadavers appear to be excluded, either by having been identified with known species, or by having been found in comparative researches made outside of the area of yellow-fever prevalence, or by the fact that they have been found only in small numbers and in a limited number of cases."

The bacillus of Sanarelli readily grows in the culture-media which I employed in my researches, and if present in the blood or tissues of the yellow-fever cadavers examined by me at Havana, I could not have failed to find it. In stating conclusions in my official report I say: "The specific infectious agent in yellow fever has not been demonstrated." It will be observed that I say "has not been *demonstrated.*" I do not say that it has not been discovered, for I sus-

pected at that time that my bacillus *x* was possibly the specific yellow-fever germ.

The name of Eberth is commonly associated with the typhoid bacillus, but Eberth was only successful in finding this bacillus in the lymphatic glands or in the spleen in eighteen out of forty cases in which he searched for it, and it was not until four years later (1884) that Gaffky obtained it from the spleen of typhoid cadavers in twenty-six out of twenty-eight cases examined by him. The demonstration that this is the specific infectious agent of typhoid fever was evidently not made by Eberth, but depends upon the researches of Gaffky, Fränkel, Simmonds, and other more recent investigators.

Klebs is supposed to have first observed or discovered the diphtheria bacillus, but Löffler demonstrated it to be the specific infectious agent in this disease, and this bacillus is spoken of as the Klebs-Löffler bacillus.

Continental bacteriologists have not been so particular in recognizing the discoverer of the micrococcus of pneumonia, which was isolated and described by me in 1880, and was observed in pneumonic sputa by Talamon in 1883, by Salvioli during 1884, and by the author in 1885, before the publication of Fränkel's first paper detailing the results of his investigations. As a matter of fact, the demonstration that this micrococcus is concerned in the etiology of pneumonia depends upon the investigations of Talamon, Salvioli, Sternberg, Fränkel, Weichselbaum, Gameleia, and others, and the common practice of referring to it as Fränkel's pneumococcus is an injustice to the discoverer, and to others

who have had a share in demonstrating its rôle in the etiology of croupous pneumonia.

Neisser discovered the gonococcus, and named it, but he did not present any satisfactory experimental evidence that it is the specific germ of gonorrhea. This demonstration was made by Bumm and others. However, Neisser's name, alone, is usually mentioned in connection with this germ.

If my bacillus *x* and the bacillus icteroides of Sanarelli are proved to be identical by the experiments of Sanarelli and this bacillus is demonstrated to be the cause of yellow fever, Sanarelli will deserve full credit for the demonstration, and I shall not be disposed to detract in the least from the praise due him for the success achieved as a result of his investigations. If, as he claims, he has obtained the final proof that this is the yellow-fever germ by producing the disease in man (five cases), as a result of the subcutaneous or intravenous injection of filtered cultures, I think we must accept these results as demonstrating the specific character of the bacillus in question. But without this final proof the demonstration would not be satisfactory, notwithstanding the pathogenic virulence of the bacillus when injected into several species of the lower animals. If it were constantly found in the blood and tissues of yellow-fever cadavers there would be little reason to doubt its specific character. But both my researches and those of Sanarelli show that, notwithstanding the most painstaking investigations, this bacillus has not been found in a considerable proportion of the typical fatal cases of yellow fever examined.

Sanarelli says: "According to the results of my researches, the isolation of the microbes of yellow fever is only possible in 58 per cent. of the cases;" and his paper, published in the *Annales de l'Instit. Pasteur*, shows that his investigations were limited to eleven fatal cases. After having differentiated bacillus *x* from the colon bacillus, which it greatly resembles, I obtained it in about one-half of the cases studied by me in Havana during 1889. Sanarelli says, with reference to his failure to find his bacillus in a considerable proportion of the typical cases: "Its isolation often presents almost insuperable difficulties, due in part to the constant occurrence of secondary infections, and in part to its relative scarcity in the organism."

In the series of cases studied by me secondary infections were extremely rare. The colon bacillus was found in a considerable number of cases, but usually in comparatively small numbers, and there is no good reason for believing that the fatal result depended upon its presence. But for the fact that in the second case studied by Sanarelli, his bacillus was present in considerable numbers in blood extracted from the finger of the patient the evening before his death, and also, after death, in the blood, spleen, liver, and other organs, it is quite probable that his attention would not have been attracted to this particular bacillus. In this regard this case is unique, both in the series of cases investigated by Sanarelli and in those studied by me; and if this is indeed the bacillus of yellow fever, it is evident that it is usually present in the blood or tissues of yellow-fever patients in very small numbers, or not at all.

In my report I suggest the possibility that the yellow-fever germ may multiply in the intestine, as is the case with cholera, and I say: "Finally we remark that many facts relating to the origin and extension of yellow-fever epidemics give support to the inference that the specific infectious agent is present in the dejecta of those suffering from the disease, and that accumulations of fecal matter and of other organic material of animal origin furnish a suitable nidus for the development of the "germ" when climatic conditions are favorable for its growth.

"There is no evidence that yellow fever is propagated by contamination of the supply of drinking-water, as frequently, and probably usually, occurs in the case of typhoid fever and cholera. Moreover, epidemics extend in a more deliberate manner and are restricted within a more definite area than is the case with cholera and typhoid fever. It is usually at least ten days or two weeks after the arrival of a vessel with the disease on board, before cases of local origin occur; and these cases occur in the immediate vicinity of the imported case or vessel carrying the contagion. When the disease has effected a lodgment, the area of infection extends slowly and usually has well-defined boundaries. In towns and cities having a common water-supply one portion remains healthy, while another, usually the most filthy, may be decimated by the scourge."

This hypothesis led me to make the following recommendation: "The experimental evidence recorded and the facts just stated seem to justify the the recommendation that the dejecta of yellow-fever patients should be regarded as infectious material,

and that such material should never be thrown into the privy-vaults or upon the soil until it has been disinfected."

Sanarelli reports his failure to find his bacillus icteroides in the contents of the intestine; but all bacteriologists will recognize the fact that the demonstration of a non-liquefying bacillus which resembles, both in its morphology and in its colonies, the colon bacillus, and which is present in comparatively small numbers in the contents of the intestines, might easily be overlooked even by one skilled in bacteriologic technic, and I cannot admit that Sanarelli's failure to find the bacillus in the contents of the intestine is satisfactory evidence that it was not present.

I obtained bacillus *x* in a certain number of cases from the contents of the intestines of yellow-fever cadavers; but it was present in comparatively small numbers, and I was more successful in obtaining it by inoculation experiments in guinea-pigs than in cultures made directly from material from the intestine. I suggest in my report that possibly yellow fever results from the absorption of a toxin produced during the multiplication of the specific germ in the alimentary canal. This, however, is only advanced as a hypothesis, which has some facts in its favor. If, as stated by Sanarelli, comparatively small quantities of a filtered culture of this bacillus will give rise to yellow fever in man when injected beneath the skin or directly into the circulation, this fact would appear to give additional value to the hypothesis. At all events, I think it would be very unfortunate if, upon the strength of Sanarelli's negative re-

searches, sanitarians should neglect to disinfect the excreta of yellow-fever patients.

The fact that both Sanarelli and myself have failed in a majority of the cases studied to obtain this bacillus in cultures from the liver, the spleen, and other organs, or in thin sections made from portions of these organs preserved in alcohol, does not absolutely prove that the bacillus was not present in these cases. A few scattered colonies might easily escape observation, even in the most painstaking research, just as a few bacilli present in the intestinal contents might not be discovered by a competent bacteriologist after a protracted investigation by the plate method. The isolation of a non-liquefying bacillus is especially difficult on account of the presence of the colon bacillus in large numbers. If, for example, bacillus *x* was present in the proportion of 1–1000 of other non-liquefying bacilli, there would be but little chance of finding it by the use of plate-cultures.

All bacteriologists recognize the difficulty of isolating the typhoid bacillus from the dejecta of typhoid patients, and Gaffky has shown that in fatal cases in which the presence of colonies was not detected in the sections of the spleen, or in which such colonies were extremely rare, the bacillus could always be obtained by means of cultures. I had this fact in view in my researches made at Havana, and habitually introduced a considerable amount of material from the interior of the liver and of blood from one of the cavities of the heart into the various culture-media used in my investigations. I admit that a negative result does not prove the absence of bacteria capable of developing in these culture-media.

Indeed, I obtained proof that the contrary is the case; for I invariably obtained various bacteria from cultures made from portions of liver or kidney preserved forty-eight hours in an antiseptic wrapping. Some of these were well-known bacilli, such as the colon bacillus, bacillus proteus vulgaris, and large anaerobic bacilli. Associated with these was bacillus *x*.

It is evident, then, that notwithstanding the negative results usually attending culture-experiments with blood from the heart or material from the interior of one of the organs principally affected, bacteria of different species were present in the liver and kidney in small numbers, and that they developed abundantly *post-mortem* when portions of these organs enveloped in an antiseptic wrapping were placed in an incubating-oven. This method was followed by Sanarelli, but he neglects to make any reference to the fact that I had employed it in an extended series of cases, or to my bacillus *x*, which is fully described in my official report, to which he apparently had access, although he makes serious mistakes in referring to my work. Thus, he says: "Dr. Sternberg of Baltimore, author of the most recent, the most rich, and the most methodical contribution to this disease known up to present time, declares that the specific microbe of yellow fever is yet to be found, and he affirms that the whole question is to be taken up *ab initio*."

This was not exactly my position, as witness the following quotation from the introduction to my report: "I have now commenced writing a report because I feel that an account of what I have been doing

during the past two years is due, and not because I have brought my investigation to a successful termination, or because I feel that there is nothing more to be done.

"No one can regret more than I do that the question of the etiology of yellow fever is not yet solved in a definite manner, but I at least have not to reproach myself with want of diligence or failure to embrace every opportunity for pursuing the research. The difficulties have proved to be much greater than I anticipated at the outset. If the task before me had been to find an organism in the blood, like that of relapsing fever, or of anthrax, or an organism in the organs principally involved, as in typhoid fever, or leprosy, or glanders, or in the intestine, as in cholera, the researches I have made could scarcely have failed to be crowned with success. But this has not proved to be the case, and among the micro-organisms encountered there is not one which by its constant presence and special pathogenic power can be indisputably shown to be the specific agent in this disease."

Note that I say "among the micro-organisms encountered there is not one which by its constant presence and special pathogenic power can be shown *indisputably* to be the specific infectious agent in this disease." But, as heretofore stated, I carefully described one particular bacillus, and in summarizing my results said: "It is possible that this bacillus is concerned in the etiology of yellow fever." Evidently it was my intention that subsequent investigators should consider this possibility, and if my work was well done, by approved methods, no one

has a right to ignore it, and continued investigations by the same method cannot be considered as taking up the question *ab initio*.

Again, Sanarelli says: "Sternberg thinks that there is probably a localized infection having its principal seat in the *stomach*." This is a mistake. I have advanced the hypothesis that the germ of yellow fever may perhaps be located in the alimentary canal, as is the case in cholera, and that the symptoms result from the absorption of a very potent toxin produced by it. But this is only a suggestion, and I know of no evidence indicating that there is a localized infection of the stomach. I have carefully studied many stained sections of the walls of the stomach, and have never found any evidence of a localized infectious process, although "in a certain proportion of the cases there is evidence of inflammation, as shown by the presence of an unusual number of leucocytes in the submucous coat."

I say in my report: "The mucous membrane of the stomach is always found to be more or less hyperemic; the congestion commonly is not general, but is confined to smaller or larger spots or districts, in which it is observed to proceed from one or more centers. From these centers it extends or radiates in a lesser degree, either gradually to be lost or to pass over to another congested district. It is owing to this peculiarity of the congestion that it presents no uniformity of character, but is observed to spread irregularly over larger or smaller portions of the membrane (Schmidt).

"The small intestine commonly contains more or less black matter, either fluid and resembling that

found in the stomach, or mixed with mucus and smeared over the mucous coating, especially of the ileum. This, no doubt, comes partly from the stomach, but in other cases is due to passive hemorrhage from the mucous membrane of the intestine itself. This membrane presents arborescent patches of congestion, or portions of the canal may be uniformly red from hyperemia of the mucous coat; the color varies from pale red to a reddish brown, and is usually more marked in the lower portion of the ileum than elsewhere. The large intestine occasionally presents similar arborescent patches of congestion, but it usually has a normal appearance. Finally, we may say that the attention of pathologists has heretofore been so largely taken up with the pathologic histology of the organs which present the most notable changes—liver and kidney—that the histology of the alimentary canal has been somewhat neglected, and further researches in this direction are desirable upon material obtained at the earliest possible moment after death."

If we admit the specific character of the bacillus under consideration, I think we must await further investigations before the question can be considered as definitely settled as to the locality in which it establishes itself in the body of an infected individual —whether in the organs involved, as claimed by Sanarelli, or in the alimentary canal, as suggested by me. But the most important question at present relates to the supposed specific character of this bacillus.

Experiments are now being made under my direction both with bacillus *x* and with cultures of

the bacillus of Sanarelli, which I obtained through the courtesy of Dr. Roux during a recent visit to Paris. While I am not likely to have an opportunity to make experiments on man, I hope to make a careful comparative study of the pathogenic action upon dogs and guinea-pigs of bacillus *x* and the bacillus icteroides of Sanarelli. If identity is established and Sanarelli's results are confirmed, I shall be ready to accept this as the specific infectious agent in the disease under consideration. I desire to express my obligations to Dr. Ezra B. Wilson of the Hoagland Laboratory, Brooklyn, N. Y., for having renewed at regular intervals the cultures of bacillus *x* which I left in that laboratory more than four years ago. I myself maintained the cultures after leaving Baltimore for duty at San Francisco during 1890, until they were placed in the Hoagland Laboratory in 1892.

Serum Therapy.—The writer has long been of the opinion that the discovery of the germ of yellow fever would be likely to be followed by important practical results in prophylaxis and in the treatment of the disease. There was nothing irrational in Freire's method of inoculation but, unfortunately, he did not have at his command cultures of the specific infectious agent, and his statistics are entirely unreliable, as shown in my published report.

It is possible that the bacillus of Sternberg and Sanarelli may have been present in some of his impure cultures, before his visit to France, where these cultures were "plated" by Gibier (1887); but the micrococcus which he declared to be his "crytococcus xanthogenicus" and upon his return from Paris

presented to me as his yellow-fever germ, was the well-known and very common staphylococcus albus. Inoculations made by him in my presence in four individuals resulted only in a slight tumefaction and redness at the point of inoculation without any noticeable febrile reaction.

My own researches and those of Sanarelli show that yellow fever is not an acute septicemia, as might perhaps be inferred from the symptoms and course of the disease, and the inference, therefore, is suggested that the clinical phenomena and pathologic changes in the organs involved are due to the action of some potent toxin, produced by a specific microorganism which has a more or less localized habitat in the body of an infected individual. This is now known to be the case in diphtheria and in cholera, and the deadly effects of the toxins produced by the diphtheria bacillus and the cholera spirillum may fairly be compared with the specific toxemia which we call yellow fever.

The recent experiments of Sanarelli appear to give substantial support to the inference that yellow fever is in fact a toxemia. Time and space will only permit a brief summary of the experimental results reported. In *Il Policlinico* of August 15, 1897, details are given of the experiments made upon man (five individuals) with filtered cultures of Sanarelli's bacillus icteroides. The amounts injected varied from 2 to 10 c.cm.

CASE I.—A subcutaneous injection of 2 c.cm. of a filtered culture gave rise to a slight febrile reaction, and to some tumefaction at the point of injection.

CASE II.—A subcutaneous injection of 5 c.cm. of a fil-

tered culture caused a painful swelling at the point of injection, loss of appetite, an elevation of temperature reaching 38.6° C. (101.5° F.). A trace of albumin was found in the urine during several successive days. A second injection of 5 c.cm. after an interval of ten days caused an elevation of temperature and a slight tumefaction at the point of inoculation, which quickly disappeared.

CASE III.—The subject received an intravenous injection of 10 c.cm. of a filtered culture. This was followed within fifteen minutes by nausea and vomiting, general agitation, and pain in the lumbar region. Gradually the abdominal region became painful and the slightest pressure with the hands over the abdomen or in the lumbar region caused severe pain. The temperature, which before the injection was 37.1° C. (98.7° F.), rose within two hours to 101.3° F., and within four hours to 104.5° F. The patient complained of severe headache during the night, and continued to vomit. The following morning the temperature was normal; at 4 P.M. it rose to 101.3° F., and there was slight delirium; there was complete gastric intolerance and anuria. The liquid vomit had a pale coffee color, and upon microscopic examination was found to contain red blood-corpuscles and leucocytes; it had an acid reaction. The anuria continued for two days, when a little turbid urine was obtained from the bladder; this was completely coagulated by heat. Delirium, interrupted by brief periods of coma, continued during the second day, after which the patient's condition improved and recovery took place. On the second day the sclerotics had an evident subicteric tint. On the second day an explorative puncture of the liver and kidney was made and some "juice" was obtained through the aspirating-needle. Under the microscope this was found to contain, from the liver, hepatic cells in a profound state of fatty degeneration and, from the kidney, epithelial cells in a state of intense tumefaction and granular degeneration.

CASE IV.—Five cubic centimeters of a filtered culture was injected into the median cephalic vein. In this case also there resulted persistent vomiting, headache, fever, reaching 106.1°F., cephalalgia, muscular pains, diminished urinary secretion containing an abundance of albumin, and afterwards complete anuria, delirium, a subicteric dis-

coloration of the skin and, on the second day, a condition of collapse developed, the pulse being imperceptible. However, the patient gradually rallied from this grave condition and made a good recovery. "Hepatic juice," obtained as in the previous case by aspiration, contained hepatic cells in a condition of "profound fatty degeneration."

CASE V.—An intravenous injection of 2 c.cm. of a filtered culture was made, November 26th, and two days later was followed by a second injection of 7 c.cm. A third dose of 15 c.cm. was given November 30th, and a fourth of 20 c.cm. December 3d. Each injection was followed by a febrile reaction, but this was greater after the first dose of 2 c.cm. than after the last dose of 20 c.cm.; this was also true as regards the other symptoms, thus showing the immunizing effects of the doses first administered. The initial dose gave rise to general malaise, cephalalgia, and a trace of albumin in the urine. After the second dose (7 c.cm.) there was a decided chill followed by fever, cephalalgia, and severe pains in the back and of the joints of the lower extremities. The third dose was also followed by a violent chill and general prostration and by a febrile movement less intense than after the second dose (7 c.cm.). In this patient a subicteric color of the skin, and especially of the conjunctivæ, was also developed. Blood taken from this patient December 9th, thirteen days after the first intravenous injection, gave a transparent serum having a lemon-yellow color. This serum mixed with a recent culture of bacillus icteroides in the proportion of 1:10 caused an arrest of movement and agglutination of the bacilli.

In a subsequent number (September 15th) of *Il Policlinico*, Sanarelli gives a detailed account of his experiments relating to immunity and serotherapy in the disease under consideration. In this paper the statement is made that blood-serum obtained from a yellow-fever cadaver produces, *in vitro*, when added to a culture of bacillus icteroides, the phenomena of arrest of motion and agglutination ("phenomenon

of Grüber-Durham "), but the intensity of the reaction varies considerably. This serum injected into animals did not manifest any preventive power as regards the pathogenic action of the bacillus.

Serum obtained by venesection from a yellow-fever convalescent produced "very slowly" the same reaction. The simultaneous injection of this serum and of a culture of the bacillus did not preserve guinea-pigs from death, but when the same dose (2 c.cm.) was injected twenty-four hours before the injection of the culture, death did not result in most of the animals experimented upon—numbers not given. Antidiphtheritic serum, prepared in Dr. Sanarelli's laboratory, very promptly produced the "Grüber-Durham" reaction with bacillus icteroides and "antityphoid serum" produced it in a partial manner, but normal human blood-serum had no effect. Attempts to immunize guinea-pigs by the injection of filtered cultures were not successful, and rabbits were immunized with great difficulty. Dogs were immunized by a series of inoculations with filtered cultures, first subcutaneously and later intravenously. At the end of two months they were able to withstand small doses of unfiltered cultures injected beneath the skin, and later intravenous injections, but at first these gave rise to vomiting, fever, and debility. It was only at the end of seven to eight months that they were able to withstand full doses of unfiltered cultures.

Horses could not be immunized by subcutaneous injections of cultures of the bacillus because these caused enormous tumefaction followed by ulceration at the point of injection. For the immunization of

horses the following method was adopted: Doses of 5 to 10 c.cm. of a filtered culture were first given. These gave rise to a febrile reaction often lasting several days. Small doses of a filtered culture were then injected into a vein. After about two-months' treatment filtered cultures sterilized by ether were employed, and it was only at the end of five to six months that a small dose of an unfiltered culture could be given. The first dose of a living culture caused loss of appetite and a febrile reaction lasting from eight to ten days. The dose was increased by from 5 to 10 c.cm., and repeated at intervals. These experiments show that the immunization of the lower animals against the pathogenic action of this bacillus is attended with great difficulties, and is a tedious process.

At the time of the publication of his paper, Sanarelli had in his possession three dogs which were very well immunized. One of these had received 300 c.cm. of virulent culture in the space of eight months. Blood-serum from this dog caused arrest of motion and agglutination of the bacilli in a fresh culture when added to it in very small quantity. This serum saved eight out of ten rabbits inoculated with lethal doses of an unfiltered culture; but was not successful in saving the lives of inoculated guinea-pigs.

A horse subjected to the experiment received in the course of five months 29 c.cm. of filtered culture, 2640 c.cm. of culture sterilized by ether, and 35 c.cm. of living (unfiltered) culture. Serum from this horse had a "good preventive power for rabbits." To save a rabbit from a lethal dose of a cul-

ture of the bacillus it was necessary to administer twenty-four hours in advance of the inoculation about 5 c.cm. of the serum. Subsequently a serum was obtained which was effective in the amount of 0.5 c.cm., and which in the dose of 2 c.cm. injected forty-eight hours after inoculation, was successful in saving rabbits from the lethal effects of a full dose of a recent culture.

The painstaking experiments detailed by Sanarelli are most important and interesting, but it is evident that they must be followed by carefully conducted experiments upon man before we can be assured that his immunizing serum can be used with success in the prevention and treatment of yellow fever. If it proves to have specific therapeutic power we can scarcely doubt that the bacillus used in immunizing the animals from which the serum was obtained is in truth the yellow-fever germ.

Note.—Comparative experiments already made at the Army Medical Museum, by Major Walter Reed, Surgeon United States Army, show certain cultural differences between the bacillus icteroides of Sanarelli and my bacillus *x*. Whether these are simply due to the fact that bacillus *x* has been cultivated for eight years in artificial media, or are to be considered as evidence that we are dealing with two more or less permanent varieties of a single species, or are to be taken as evidence that the bacillus of Sanarelli is specifically distinct from my bacillus *x* can only be determined by further investigations, and especially by comparative experiments relating to the pathogenic power of the cultures obtained by me from yellow-fever cadavers in Cuba, and by Sanarelli

from yellow-fever cadavers in Brazil. At present bacillus *x* is non-motile, while Sanarelli's bacillus is actively motile. But in my original cultures, as stated in my published report, bacillus *x* was motile. At present Dr. Reed informs me that the presence of flagellæ may be demonstrated by proper staining methods.