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American Public Health Association

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LIMINARY NOTE.**

By WALTER REED, M. D., Surgeon, U. S. A.;
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JESSE W. LAZEAR, M. D.,
Acting Assistant Surgeon, U. S. A.

*Reprinted from the Proceedings of the Twenty-Eighth Annual Meeting, held at
Indianapolis, Indiana, October 22, 23, 24, 25 and 26, 1900.*

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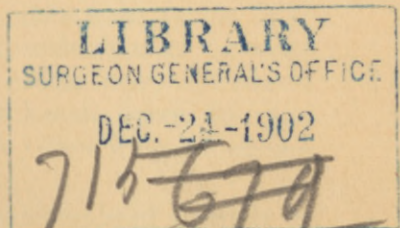
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THE ETIOLOGY OF YELLOW FEVER.—A PRELIMINARY NOTE.

BY WALTER REED, M. D., SURGEON, U. S. A.;
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JESSE W. LAZEAR, M. D.,¹
ACTING ASSISTANT SURGEON, U. S. A.

The writers, constituting a board of medical officers convened "for the purpose of pursuing scientific investigations with reference to the acute infectious diseases prevalent on the Island of Cuba," arrived at our station, Columbia Barracks, Quemados, Cuba, on June 25th of the present year, and proceeded, under written instructions from the Surgeon General of the Army, to "give special attention to questions relating to the etiology and prevention of yellow fever."

Two of its members (Agramonte and Lazear) were stationed on the Island of Cuba, the former in Havana, and the latter at Columbia Barracks, and were already pursuing investigations relating to the etiology of this disease.

Fortunately for the purposes of this board, an epidemic of yellow fever was prevailing in the adjacent town of Quemados, Cuba, at the time of our arrival; thus furnishing us an opportunity for clinical observations and for bacteriological and pathological work. The results already obtained, we believe, warrant the publication at this time, of a preliminary note. A more detailed account of our observations will be submitted to Surgeon General Sternberg in a future report.

The first part of this preliminary note will deal with the results of blood cultures during life and of cultures taken from yellow fever cadavers; reserving for the second part a consideration of the mosquito as instrumental in the propagation of yellow fever; with observations based on the biting of non-immune human beings by mosquitoes which had fed on patients sick with yellow fever, at various intervals prior to the biting.

In prosecuting the first part of our work, we isolated a variety of bacteria, but of these we do not propose to speak at present. It will

¹ Died of yellow fever at Columbia Barracks, Cuba, Sept. 25, 1900.

suffice for our purpose if we state the results as regards the finding of *bacillus icteroides*, leaving the mention of other bacteria to our detailed report.

The cases studied during the Quemados epidemic had been diagnosed by a board of physicians, selected largely by reason of their familiarity with yellow fever. This board consisted of Doctors Nicola Silverio, Manuel Herera, Eduardo Angles and Acting Assistant Surgeons Roger P. Ames and Jesse W. Lazear, U. S. Army.

Those studied in Havana were patients in Las Animas Hospital and had been diagnosed as such by a board of distinguished practitioners of that city.

An examination of Table I will show the character of the attacks.

The milder cases studied, few in number, were attended by jaundice and albumen in the urine.

I.

Bacillus Icteroides (Sanarelli) as the Cause of Yellow Fever.

The claim of Sanarelli for the specific character of *B. icteroides* as the causative agent in yellow fever, has excited such wide attention, since the publication of his observations, that it seemed to us of the first importance to give our undivided attention to the isolation of this micro-organism from the blood of those sick with yellow fever and from the blood and organs of yellow fever cadavers.

(A) *Cultures Taken from the Blood During Life.*

The method followed was that ordinarily used in an attempt to isolate bacteria from the circulating blood; viz., from a vein at the bend of the elbow, a sufficient quantity of blood was taken with an hypodermic syringe, made sterile by boiling, and after careful cleansing of the skin with soap and water, followed by equal parts of absolute alcohol and ether, and 1-2000 bichloride solution.

Exceptionally, the blood withdrawn was plated on agar, but as a rule, it was immediately transferred to sterile bouillon tubes (10 c. cm.) in quantities of 0.5 c. cm. to each of several tubes. These were then incubated at 35° to 37° C. for a period of one week. They were examined daily and if growth was observed, plates in agar or gelatine, or both, were made and the colonies carefully studied by transference to ordinary laboratory media.

Eighteen cases have thus been carefully studied; of these, eleven were designated as "severe" cases of yellow fever with four deaths; three as "well-marked" cases with no deaths, and four as "mild" cases with no deaths.

From these eighteen cases, blood cultures were made, as shown in the following table:

TABLE I.
BLOOD CULTURES DURING LIFE.

Day of Disease.	Character of Attack.	No. of Cultures.	No. of Bouillon Tubes Inoculated.	B. Icteroides.
1st.	Severe.	3	4 (3 agar plates.)	Negative.
"	Well-marked.	1	4	"
"	Mild.	1	3	"
2nd.	Severe.	6	18	"
"	Well-marked.	1	2	"
"	Mild.	1	3 (6 agar plates.)	"
3rd.	Severe.	7	18 (6 agar plates.)	"
"	Mild.	2	4	"
4th.	Severe.	5	14	"
"	Well-marked.	2	6	"
"	Mild.	1	1	"
5th.	Severe.	5	12 (3 agar plates.)	"
"	Well-marked.	1	3	"
"	Mild.	1	1	"
6th.	Severe.	4	6	"
"	Well-marked.	1	2	"
7th.	Severe.	1	2	"
"	Well-marked.	1	2	"
8th.	Severe.	2	6	"
"	Well-marked.	1	2	"
9th.	Severe.	1	2	"

Number of cultures.....	48
" " bouillon tubes inoculated.....	115
" " agar plates.....	15

It will be seen that of 48 separate cultures made from the blood on various days of the disease and representing 115 bouillon inoculations and 18 agar plates, we failed to find bacillus icteroides in any of our tubes or plates.

The results of cultures taken in 18¹ cases of unmistakable yellow fever, on various days of the disease and in some cases on every day from the onset to death or recovery, would seem to exclude the presence of bacillus icteroides in the blood of these cases during life.

It will, therefore, be seen that while Wasdin and Geddings taking cultures from the ear-lobe (Report on the Cause of Yellow Fever, 1899), record that "in the blood of yellow fever cases extracted during life bacillus icteroides has been found in thirteen of the fourteen cases, with one negative," (92.85 per cent.) we, by withdrawing blood from the veins of 18 patients, have to record 100 per cent. of failures.

¹ Cultures from the blood during life had been taken by Dr. Lazear in three other cases of yellow fever, but owing to the death of our colleague, the necessary data as to the day of the disease on which cultures had been taken cannot be ascertained.

These cultures were negative as regards the finding of Sanarelli's bacillus.

We have already stated that we will reserve for a later report a description of the bacteria isolated from the blood in these cases. We now remark that but few organisms were obtained and that, as a rule, our blood cultures gave no growth whatever.

(B) *Cultures from Yellow Fever Cadavers.*

We tried to obtain autopsies very soon after death and sometimes succeeded in doing so. Tubes containing about 10 c. cm. of flesh-peptone bouillon were generally used for the first inoculation direct from the blood and organs. As soon as the laboratory was reached, agar plates were made from these inoculated bouillon tubes, the former as well as the latter being then incubated at 35°-37° C. In nearly every case gelatine plates were, also, made from the recently inoculated bouillon tubes and kept at a temperature of 19°-20° C.

If colonies were found in the agar or gelatine plates, on the following days, the corresponding bouillon tubes were, also, plated on agar and gelatine. The bacteria thus found in our plates were carefully isolated and studied upon the usual nutritive media, so as to enable us to identify them, if possible. We will here content ourselves with giving the results as regards the presence of *B. icteroides* only.

TABLE II.

No. of Case.	Day of Disease.	Time of Autopsy.	Source of Culture.	<i>B. Icteroides.</i>
1	7th.	2 hours after death.	Blood, liver, spleen, kidney.	Neg'tive
2	6th.	13 hours after death.	Blood, liver, spleen, kidney.	"
3	4th.	8 hours after death.	Blood, liver, spleen, kidney.	"
4	8th.	4 hours after death.	Abdominal cavity, blood, liver, spleen, kidney, bile, duodenum.	"
5	4th.	4 hours after death.	Blood, liver, spleen, kidney, bile, duodenum.	"
6	6th.	6½ hours after death.	Abdominal cavity, blood, pericardial fluid, lung, spleen, kidney, liver, bile, duodenum.	"
7	6th.	50 minutes after death.	Blood, lung, liver, spleen, kidney, bile, jejunum.	"
8	6th.	½-hour after death.	Blood, lung, liver, spleen, kidney, urine, small intestine.	"
9	4th.	2 hours after death.	Liver, spleen, small intestine.	"
10	5th.	7 hours after death.	Liver, kidney, spleen, small intestine.	"
11	3rd.	½-hour after death.	Liver, kidney, spleen.	"

Our failure to isolate *B. icteroides* in these eleven autopsies of yellow fever patients was a result which we had not anticipated. One

of us (Agramonte) who, at Santiago, Cuba, during the epidemic of 1898, succeeded in finding *B. icteroides* in 33 per cent. of his autopsies, has been much surprised at the absence of this bacillus in cultures from cadavers sectioned in Havana, during the present year. In two of the eleven cases we had reason to believe that from the character of colonies seen in gelatine plates, we would be able to isolate *B. icteroides*. These colonies, however, when transferred to other media and carefully studied, did not prove to be this bacillus. We wonder whether other observers have occasionally relied upon the appearance of colonies in gelatine plates, without further study. We only mention this as a possible explanation of the large percentage of positive results recorded by some observers.

Portier, of New Orleans, La., only succeeded, however, in isolating *B. icteroides* in three out of fifty-one autopsies (Journal of American Medical Association, April 16, 1896).

Lutz (Revista D'Igiene e Sanita Publica, XI, No. 13, July, 1900, pp. 474-475), says as the result of his extensive observations on yellow fever that bacillus *icteroides* cannot be found by present laboratory methods in more than half of the cases of yellow fever, and that when present, the colonies are few in number.

It is possible that our future autopsies may give more favorable results as regards *B. icteroides*.

II.

The Mosquito as the Host of the Parasite of Yellow Fever.

Having failed to isolate *B. icteroides* either from the blood during life or from the blood and organs of cadavers, two courses of procedure in our further investigations appeared to be deserving of attention, viz., first, a careful study of the intestinal flora in yellow fever in comparison with the bacteria that we might isolate from the intestinal canal of healthy individuals, in this vicinity, or of those sick with other diseases; or, secondly, to give our attention to the theory of the propagation of yellow fever by means of the mosquito,—a theory first advanced and ingeniously discussed by Dr. Carlos J. Finlay, of Havana, in 1881, (*Anales de la Real Academia*, Vol. 18, 1881, pp. 147-169).

We were influenced to take up the second line of investigation by reason of the well known facts connected with the epidemiology of this disease and, of course, by the brilliant work of Ross and the Italian observers in connection with the theory of the propagation of malaria by the mosquito.

We were, also, much impressed by the valuable observations made at Orwood and Taylor, Miss., during the year 1898, by Surgeon

Henry R. Carter, U. S. Marine Hospital Service. A note on the interval between infecting and secondary cases of yellow fever, etc. (Reprint from *New Orleans Medical Journal*, May, 1900). We do not believe that sufficient importance has been accorded these painstaking and valuable data. We observe that the members of the yellow fever commission of the Liverpool School of Tropical Medicine, Drs. Durham and Meyers, to whom we had the pleasure of submitting Carter's observations, have been equally impressed by their importance (*British Medical Journal*, September 8, 1900, pp. 656-7).

The circumstances under which Carter worked were favorable for recording with considerable accuracy the interval between the time of arrival of infecting cases in isolated farm-houses and the occurrence of secondary cases in these houses. According to Carter "the period from the first (infecting) case to the first group of cases infected, at these houses, is generally from two to three weeks."

The houses having now become infected, susceptible individuals thereafter visiting the houses for a few hours, fall sick with the disease in the usual period of incubation one to seven days.

Other observations made by us since our arrival confirmed Carter's conclusions, thus pointing as it seemed to us to the presence of an intermediate host, such as the mosquito, which having taken the parasite into its stomach, soon after the entrance of the patient into the non-infected house, was able after a certain interval to reconvey the infecting agent to other individuals, thereby converting a non-infected house into an "infected" house. This interval would appear to be from nine to sixteen days (allowing for the period of incubation), which agrees fairly closely with the time required for the passage of the malarial parasite from the stomach of the mosquito to its salivary glands.

In view of the foregoing observations we concluded to test the theory of Finlay on human beings. According to this author's observation of numerous inoculations in 90 individuals, the application of one or two contaminated mosquitoes is not dangerous, but followed in about 18 per cent. by an attack of what he considers to be very benign yellow fever at the most.

We here desire to express our sincere thanks to Dr. Finlay, who accorded us a most courteous interview and has gladly placed at our disposal his several publications relating to yellow fever, during the past nineteen years; and also for ova of the species of mosquito with which he had made his several inoculations. An important observa-

tion to be here recorded is that, according to Finlay's statement, 30 days prior to our visit, these ova had been deposited by a female just at the edge of the water in a small basin, whose contents had been allowed to slightly evaporate; so that these ova were at the time of our visit entirely above contact with the water. Notwithstanding this long interval after deposition, they were promptly converted into the larval stage, after a short period, by raising the level of the water in the basin.

With the mosquitoes thus obtained we have been able to conduct our experiments. Specimens of this mosquito forwarded to Mr. L. O. Howard, Entomologist, Department of Agriculture, Washington, D. C., were kindly identified as *Culex fasciatus* Fabr.

In this Preliminary Note we have not space to refer, at length, to the various interesting and valuable contributions made by Finlay to the mosquito theory for the propagation of yellow fever. In addition to the paper already quoted, his most valuable contributions to this important theory are to be found in the articles designated as follows: *Estadística de las Inoculaciones con mosquitos contaminados*, etc. Reprint, Havana, 1891: *Fiebre Amarilla, Estudio Clínico Patológico y Etiológico*. Reprint, Havana, 1895: and *Yellow fever immunity,—Modes of Propagation: Mosquito theory*, 8th Congress of International Hygiene and Demography, Budapest, 1894.

His present views on this subject may be stated in his own language: "First, reproduction of the disease, in a mild form, within five to twenty-five days after having applied contaminated mosquitoes to susceptible subjects. Second, partial or complete immunity against yellow fever obtained when even no pathogenous manifestation had followed those inoculations." (*Medical Record*, Vol. 55, No. 21, May 27, 1899.)

Without reviewing the cases regarded as mild forms by the author of this theory, we believe that he has not, as yet, succeeded in reproducing a well marked attack of yellow fever, within the usual period of incubation of the disease, attended by albumen and jaundice, and in which all other sources of infection could be excluded.

The experiments made by us on eleven non-immune individuals are embraced in the following table which should be carefully studied.

The mosquito used in all cases was *Culex fasciatus* Fabr.:

TABLE III.
 INOCULATION OF NON-IMMUNE INDIVIDUALS THROUGH THE BITE OF MOSQUITOES (C. FASCIATED).

No. of Case.	Age.	Nativity.	Date of Inoculation.	Character of attack and No. of patients bitten.	Day of Disease.	Time of between infection of mosquito and inoculation.	No. of Mosquitoes.	Result.	Remarks.
1		U. S.	August 11th.	Mild.....1	7th.	5 days.	One.	Negative.	
2		U. S.	" 11th.	Very mild..1	5th.	5 "	"	"	
3	24	U. S.	" 12th.	" ..1	5th.	6 "	"	"	
4	20	U. S.	" 12th.	" ..1	5th.	6 "	"	"	
5	24	U. S.	" 14th.	" ..1	5th.	8 "	"	"	
6	34	U. S.	" 16th.	" ..1	5th.	10 "	"	"	
7	22	U. S.	" 18th.	Severe.....1	2nd.	3 "	"	"	
8	20	U. S.	" 19th.	Very mild..1	5th.	13 "	Two.	"	
				Severe.....1	1st.	3 "			
9	28	U. S.	" 25th.	Fatal.....1	2nd.	6 "	One.	"	
				Mild.....1	1st.	4 "			
				Severe.....1	2nd.	2 "			
10	46	England.	" 27th.	" ..1	2nd.	12 "	One.	Positive.	Severe attack of yellow fever.
				Mild.....1	1st.	6 "			
				Severe.....1	2nd.	4 "			
				Mild.....1	2nd.	2 "			
				Fatal.....1	2nd.	12 "	One.	Positive.	Severe attack of yellow fever.
11	24	U. S.	" 31st.	Mild.....2	2nd.	4 and 10 days.	One.	Positive.	Well marked attack of yellow fever.
				Severe.....2	2nd.	2 and 8 "	One.	Positive.	Well marked attack of yellow fever.
				" ..3	1st, 2nd and 2nd.	2, 8 and 16 "	One.	Positive.	Well marked attack of yellow fever.
				Mild.....2	1st and 2nd.	6 and 10 "	One.	Positive.	Well marked attack of yellow fever.
				Fatal.....1	2nd.	12 "	One.	Positive.	Well marked attack of yellow fever.
				Severe.....1	1st.	2 "	One.	Positive.	Well marked attack of yellow fever.
				Mild.....3	1st, 2nd and 2nd.	4, 6 and 10 "	One.	Positive.	Well marked attack of yellow fever.
				Severe.....3	All on 1st.	2, 4 and 8 "	One.	Positive.	Well marked attack of yellow fever.
				Mild.....1	2nd.	6 "	One.	Positive.	Well marked attack of yellow fever.

It will be seen that we record nine negative and two positive results. It is, we think, important to observe that of the nine failures to infect, the time elapsing between the biting of the mosquito and the inoculation of the healthy subject varied in 7 cases from 2 to 8 days (Nos. 1, 2, 3, 4, 5, 7 and 9) and in the remaining two from 10 to 13 days (Nos. 6 and 8).

Five individuals out of the nine who failed to show any result (Nos. 2, 3, 4, 5 and 6) were inoculated by mosquitoes that had bitten very mild cases of yellow fever on the fifth day of the disease, and one individual by a mosquito that had bitten a mild case of yellow fever on the seventh day of the disease. (This latter patient was discharged from hospital three days later.) To this fact may possibly be attributed the negative results. Of the remaining three negative cases (Nos. 7, 8 and 9), and which had been inoculated by mosquitoes that had bitten severe cases of the disease, the interval between the bite and the inoculation varied from 2 to 6 days.

In the two cases (Nos. 6 and 8) where the interval was respectively 10 and 13 days, the inoculations had been made with mosquitoes that had bitten very mild cases of yellow fever on the fifth day of the attack. No. 8 was also bitten by a mosquito which had been infected by a severe case of yellow fever 3 days before.

We refrain from commenting further at this time upon the nine negative cases, preferring to record the results obtained rather than to indulge in speculation.

Of the two cases which we have recorded as positive in Table III, we now propose to speak at greater length.

Case 10. Dr. James Carroll, Acting Assistant Surgeon, U. S. Army, a member of this board, was bitten at 2 p. m., August 27, 1900, by *Culex fasciatus*. This particular mosquito had bitten a *severe* case of yellow fever on the *second* day of the disease *12 days* before; a *mild* case of yellow fever, on the *first* day of the attack, *6 days* preceding; a *severe* case of yellow fever, on the *second* day of the attack, *4 days* before, a *mild* case of yellow fever, on the *second* day of attack, *2 days* before inoculation.

Dr. Carroll remained well until the afternoon of the 29th, when he states that he felt tired and for this reason, when on a visit to Las Animas Hospital, the same afternoon (29th), sometime between 4 and 6 p. m., after visiting a few patients, he left the wards and waited outside on the porch, while his companions remained in the wards.

August 30th. During the afternoon, although not feeling well, Dr. C. visited La Playa, distant about one and a half miles from Columbia Barracks, and took a sea-bath.

August 31st, A. M. Dr. C. realized that he was sick and that he had fever, although he refrained from taking his temperature, but did visit the laboratory, distant about one hundred and forty yards, for the purpose of examining his blood for the malarial parasite. The examination was negative. During the afternoon he was compelled to take to his bed. At 7 p. m. temperature

was 102° F. No headache nor backache; only a sense of great lassitude. Eyes injected and face suffused.

September 1st, 7 A. M. T. 102° F. Blood again carefully examined by Dr. Lazear with negative result. 11 a. m., T. 102°.

The case having been diagnosed as one of yellow fever, Dr. C. was at noon removed to the yellow fever wards.

9 p. m., T. 102.8°, pulse 90, 12 o'clock, midnight, T. 103.4°, pulse 84.

September 2d, 3 A. M. T. 103.6, pulse 80. A trace of *albumen* was now found in the urine. The subsequent history of the case was one of severe yellow fever. *Jaundice* appeared on September 3d.

The accompanying chart No. 1 contains all of the necessary data.

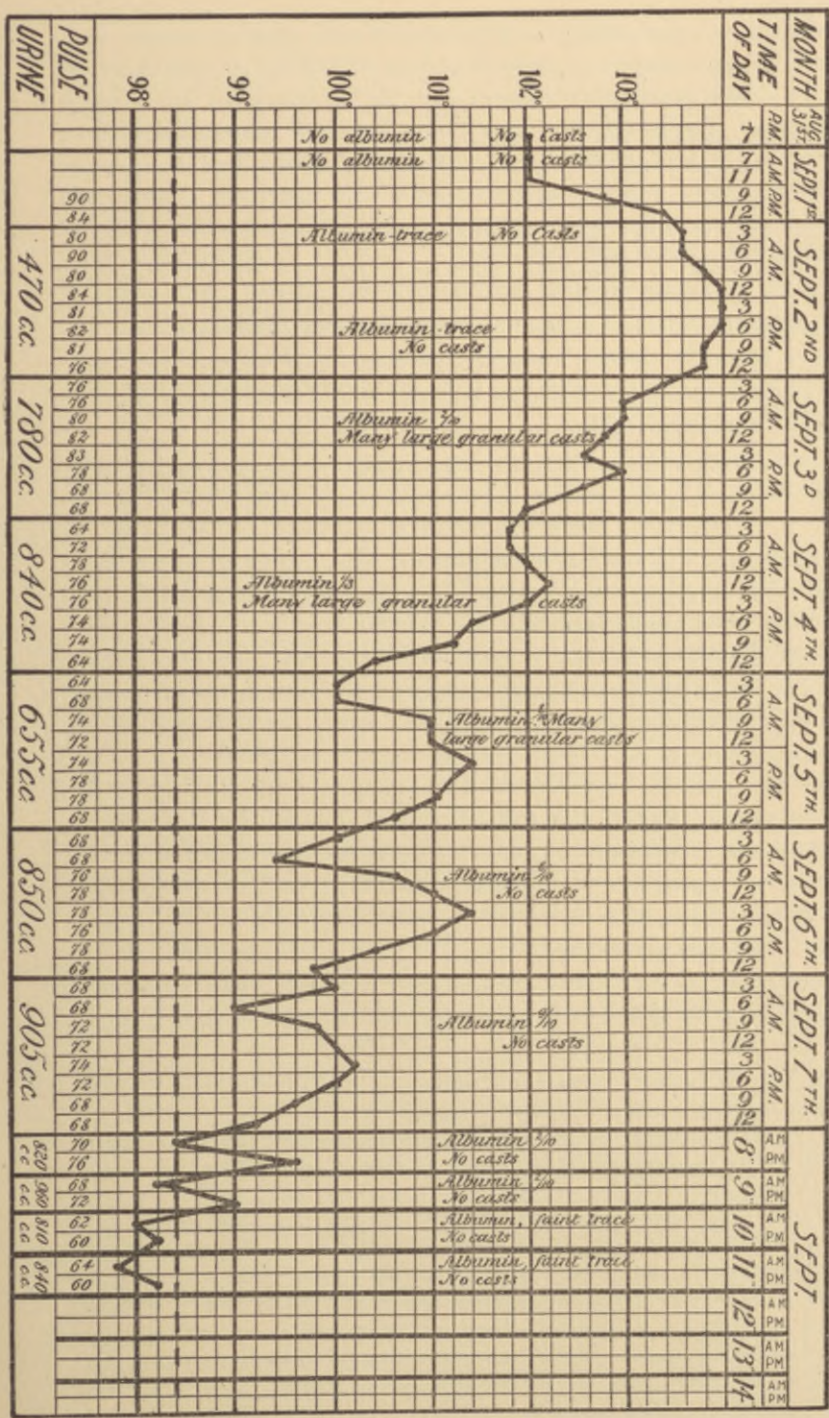
The question of diagnosis having been clearly and easily established, it now becomes important to follow Dr. C.'s movements for a period of ten days preceding the mosquito inoculation, and during the period elapsing from the bite of the insect until the commencement of the attack.

On August 21st, 22d and 23d, Dr. C. was at Columbia Barracks, outside of the epidemic zone. On August 24th he visited the autopsy-room of Military Hospital No. 1, which is situated on Principe hill overlooking the city of Havana. He was present in this autopsy-room while an autopsy was made by Dr. Agramonte on a case of pernicious malarial fever. Dr. C. only took cultures from the blood and organs as the section proceeded. He was there about half an hour and then returned to Columbia Barracks. Subsequent microscopic study of sections of the liver and spleen showed that the case autopsied on the 29th was really a case of pernicious malarial fever.

It should be stated that although cases of yellow fever are not admitted to Military Hospital No. 1, an English sea-captain had been admitted to its wards a few days before, whose case developed into one of yellow fever with fatal result, and the body had been autopsied by Dr. Agramonte in this dead-room on the day preceding Dr. C.'s visit to it.

According to Dr. C. the room was, by no means, in a cleanly condition. As Dr. C.'s visit to this room was made on August 24th, and as he began to complain on August 29th, about the average period of incubation of yellow fever, there is a possible chance for infection in this way. We must call attention, however, to the fact that Dr. Agramonte, whenever he performs an autopsy in this room, is always attended by a young soldier of the Hospital Corps, U. S. Army, who is detailed for that purpose, and whose duty it is to assist and to afterwards tend to the cleaning of the autopsy table. This soldier, a non-immune American, was present when Dr. Carroll was there and remained afterwards to attend to his duties. He has not contracted yellow fever by his duties in this room, from time to time.

Case I. Yellow fever following, within the usual period of incubation, the bite of an infected mosquito, (*Culex fasciatus*)



Our own experience would seem to accord with that of others, viz., that attendance upon autopsies and the handling of portions of organs of yellow fever cases removed to the laboratory is unattended with danger. Certainly the three non-immune members of this board, up to the time of these mosquito inoculations, had during the past three months come in close contact with the dead bodies and organs of yellow fever cases, freely handling and examining these organs, including the small intestine, even kept at thermostat temperature for 24 hours, without contracting the disease. We have, of course, never neglected to cleanse our hands with disinfectants.

Dr. C., upon his visit to the before-mentioned dead-room, only used the platinum loop for taking cultures and did not come in contact with the autopsy table.

The only other opportunity for infection in his case would appear to have been during his visit to Las Animas Hospital, situated in the suburbs of Havana, as here yellow fever patients are admitted in large numbers. We have already pointed out that Dr. C. was complaining of lassitude at the hour of his visit, which was about fifty hours after his inoculation with the contaminated mosquito. We have also called attention to the fact that he remained, for the greater part of his visit outside of the hospital, on the piazza. This would appear to cast doubt upon his visit to Las Animas as the source of his infection.

We do not wish to be understood as unnecessarily seeking to lay too much emphasis upon the exclusion in this case of other sources of infection than the mosquito, as we fully appreciate that Dr. C. had been, on two occasions, within the epidemic zone during the week preceding his attack of yellow fever. His movements on these occasions we have already given.

We will again refer to Dr. C.'s case, after we have given the history of Case No. 11, which we have designated as our second positive result.

Case 11. X. Y., white, American, a resident of the military reservation of Columbia Barracks, was bitten during the forenoon of the 31st day of August, 1900, by the *same mosquito* that had bitten Case 10 (Dr. C.) four days before, and which in the meanwhile had bitten a *mild* case of yellow fever (first day) two days before being applied to X. Y.

X. Y. was, also, bitten by a second mosquito that had been applied to a fatal case of yellow fever (second day) 12 days before, and to two mild cases (second day) 4 and 10 days previously; also, by a third mosquito that had bitten a fatal case of yellow fever (second day) 12 days before; a severe case (first day) 2 days before and three mild cases (first, second and third day) 4, 6 and 10 days before finally by a fourth mosquito that had bitten three severe cases of yellow fever (all on the first day) 2, 4 and 8 days previously, and one mild case (second day) 6 days before. (Vid. Table III.)

It will thus be seen that X. Y. was bitten by *four* mosquitoes, *two* of which had bitten *severe (fatal)* cases of yellow fever *12 days previously*; one of which had bitten a *severe case (second day)* *16 days* before and one which had bitten a *severe case (first day)* *8 days* before.

September 25th, X. Y. began to experience a sense of dizziness and disinclination to work. This was just five days from the time of the mosquito inoculation.

Twenty-four hours later, still dizzy and light-headed in attempting to move about. During the afternoon (sixth day after inoculation), chilly sensations, followed by fever and restlessness during the night.

On the following day (seventh day after inoculation), 8 a. m., T. 102.8° F., eyes slightly injected, face suffused. Patient removed to the yellow fever wards; 9 a. m., T. 103° F., pulse 66. A trace of *albumen* was found in the urine during the afternoon (third day of the attack). This increased during the following days. Conjunctivæ slightly *jaundiced* on the fourth day of disease, which was more distinct and could be plainly seen on anterior aspect of chest on the fifth and following day. *Bleeding* from the gums was noticed on the third and subsequent days after admission. Repeated examinations of the blood failed to show any malarial parasites.

The course of the fever, the appearance of albumen in the urine, with jaundice and hemorrhage from the gums, together with the slow pulse, all pointed distinctly to the diagnosis of yellow fever. His attending physician, Dr. Roger P. Ames, U. S. A., an expert in the diagnosis and treatment of this disease, did not hesitate to diagnose X. Y.'s attack as one of "well pronounced yellow fever." Dr. A. was not cognizant of the method of inoculation in this case. (Vide, Chart II.)

The diagnosis, therefore, not being in doubt, we must follow this patient's movements during the ten days preceding the bite of the mosquitoes and from this time until five days later, when the attack began. It so happens that we can follow X. Y.'s movements for a much longer period. Fifty-seven days prior to his inoculation, he spent a day and night in the city of Havana. Sixteen days before the inoculation, he rode on horseback with six other non-immunes a distance of about one and a half miles towards the seashore and returned to his dwelling, without in the meantime dismounting from his horse. From this time until his complete convalescence was established, he had remained within the immediate vicinity of his home. So that it may be positively stated that X. Y. had not absented himself from the Military Reservation of Columbia Barracks during a period of fifty-seven days prior to his inoculation (with the exception above stated), nor between the date of his inoculation and the establishment of convalescence.

Let us now inquire whether the military reservation of Columbia Barracks is outside of the epidemic zone of yellow fever. To this we answer that since the commencement of the present epidemic

of yellow fever in Havana, dating from May, 1900, the average monthly population of this Station, including civilian employes, has been 1400, nearly all of whom are young non-immunes.

There have occurred amongst this non-immune population from May 1 to October 13, 1900, sixteen cases of yellow fever, all of which have been easily and readily traced to a visit to within the boundaries of the epidemic zone, except Cases 10 and 11 of Table III, and one other case of which we shall presently speak. These cases have been distributed as follows:

May 24th.....	1
June 10th.....	1
“ 17th.....	1
“ 19th.....	2
“ 21st.....	1
“ 29th.....	1
July 9th.....	1
“ 26th.....	1
“ 29th.....	1
August 11th.....	1
“ 12th.....	1
“ 16th.....	1
“ 31st.....	1
Sept'r 7th.....	1
“ 19th.....	1
Total.....	16 cases.

Ten of these cases have occurred amongst an average monthly military population of 1295 men, and six cases in an average civilian population of 105.

Whenever these cases have occurred, as soon as the patient has been removed to hospital most careful measures of disinfection have been immediately carried out by a trained sanitary squad, under the personal supervision of a medical officer. These have consisted of destruction by fire of mattresses, the disinfection of bedding and clothing with 1 to 500 bichloride solution, and the application of the same solution freely to the ceiling, walls and floors by means of a force pump.

We repeat that no case has ever been connected with a preceding case, but that the source of infection has been readily shown to have occurred during the individual's visit to Havana, 6 miles distant, or to some other nearer Cuban settlement.

We now invite attention to the fact that from August 17th to October 13th, a period of fifty-seven days, only three cases of yellow fever have occurred amongst this population of 1400 non-immune

Americans, and we consider it very important to note that *two of these had been bitten, within five days of the commencement of their attacks, by contaminated mosquitoes.*

Taken in connection with Case 11, in which we have been unable to find any other source of infection than the bite of an infected mosquito, five days preceding the attack, the case of Dr. C. (Case 10, Table III) becomes strongly confirmatory of the same origin.

We will now briefly give the history of the third case of yellow fever that has occurred at Columbia Barracks during the period August 17 to October 13, 1900.

In the light of Cases 10 and 11, we consider this case of sufficient importance to be here included, especially as it is one that might be possibly designated as a case of accidental infection by a mosquito.

Case. Dr. Jesse W. Lazear, Acting Assistant Surgeon, U. S. Army, a member of this board, was bitten on August 16, 1900, (Case 6, Table III), by a mosquito (*Culex fasciatus*) which ten days previously had been contaminated by biting a very mild case of yellow fever (fifth day). No appreciable disturbance of health followed this inoculation.

September 13, 1900, (forenoon), Dr. Lazear, while on a visit to Las Animas Hospital and while collecting blood from yellow fever patients for study, was bitten by a *Culex* mosquito (species undetermined). As Dr. L. had been previously bitten by a contaminated insect without after-effects, he deliberately allowed this particular mosquito, which had settled on the back of his hand, to remain until it had satisfied its hunger.

On the evening of September 18th, 5 days after the bite, Dr. L. complained of feeling "out of sorts," and had a chill at 8 p. m.

September 19th, 12 o'clock noon, T. 102.4°, pulse 112. Eyes injected, face suffused; 3 p. m., T. 103.4°, pulse 104; 6 p. m., T. 103.8°, pulse 106. *Albumen* appeared in the urine. *Jaundice* appeared on the third day. The subsequent history of this case was one of progressive and fatal yellow fever, the death of our much lamented colleague having occurred on the evening of September 25, 1900.

As Dr. L. was bitten by a mosquito while present in the wards of a yellow fever hospital, one must, at least, admit the possibility of this insect's contamination by a previous bite of a yellow fever patient. This case of accidental infection therefore cannot fail to be of interest, taken in connection with Cases 10 and 11.

For ourselves, we have been profoundly impressed with the mode of infection and with the results that followed the bite of the mosquito in these three cases. Our results would appear to throw new light on Carter's observations in Mississippi, as to the period required between the introduction of the first (infecting) case and the occurrence of secondary cases of yellow fever.

Since we here, for the first time, record a case in which a typical attack of yellow fever has followed the bite of an infected mosquito,

within the usual period of incubation of the disease, and in which other sources of infection can be excluded, we feel confident that the publication of these observations must excite renewed interest in the mosquito-theory of the propagation of yellow fever, as first proposed by Finlay.

From our study thus far of yellow fever, we draw the following conclusions:

1. *Bacillus icteroides* (Sanarelli) stands in no causative relation to yellow fever, but, when present, should be considered as a secondary invader in this disease.

2. The mosquito serves as the intermediate host for the parasite of yellow fever.

