PREFACE.

The results of the work of Maj. Walter Reed, Medical Corps, United States Army, and the Yellow Fever Commission, of which he was president and the masterful mind, have been so beneficial and far-reaching that its importance is considered secondary to no other scientific achievement.

The various publications in regard to Maj. Reed and his work and the reports of the commission, as well as other reports on subjects intimately connected with this work, while all extant and on file in the larger libraries of this country, are not available for the profession in general. Being bound in one volume they will be much more available for general use, and will be less liable to be misplaced.

Many of the younger men in the profession and in the Medical Corps of the Army are not so thoroughly conversant with the various steps of this work as is thought desirable. This work should be a source of inspiration for every medical officer.

In compiling these various publications repetitions have been avoided as much as possible. However, the reports of Maj. Reed and his associates are considered of so much scientific as well as historical interest that they are published in full in chronological order. In this way the various steps in the experiments are more clearly shown.

TABLE OF CONTENTS.

PART I.—WALTER REED—THE MAN, HIS WORK, AND THE APPRECIATION SHOWN OF THE RESULTS ACCOMPLISHED BY HIM AND HIS ASSOCIATES ON THE YELLOW FEVER COMMISSION.

Chapter 1.

WALTER REED.—A MEMOIR.[1]

By Walter D. McCaw, Major, Medical Corps, United States Army.

It is given to but few scientific men to lay bare a secret of nature materially affecting the prosperity of nations, and the lives, fortunes, and happiness of thousands. Fewer still succeed in so quickly convincing brother scientists and men in authority of the truth of their discoveries that their own eyes behold the glorious result of their labor.

Of the 51 years of Walter Reed's industrious, blameless life, 12 only were spent in the study of the special branch of science in which he became famous, but his name now stands with those of Jenner, Lister, and Morton as among the benefactors of humanity.

Walter Reed was born in Gloucester County, Va., September 13, 1851, the son of the Rev. Lemuel Sutton Reed and Pharaba White, his wife.

The circumstances of his family were modest, and some of the years of his boyhood were spent in a much troubled section of the south during the great Civil War. He acquired, however, a good preliminary education, and at an age when most boys are still in the schoolroom he began the study of medicine at the University of Virginia, graduating as M. D. in 1869, when only 17 years old.

A second medical degree was received later from Bellevue Medical College, New York, and then came terms of service in the Brooklyn City Hospital, and the City Hospital, Blackwell's Island.

Before the age of 21 Reed was a district physician in New York City, and at 22 one of the five inspectors of the board of health of Brooklyn.

He entered the Army of the United States as assistant surgeon with the rank of first lieutenant, in 1875, and for the next 18 years, with the usual varying fortunes of a young medical officer of the Army, he served in Arizona, Nebraska, Dakota, and in the Southern and Eastern States.

According to the exigencies of the service he was moved frequently from station to station, everywhere recognized by men of his own age as a charming and sympathetic companion, and by older officers

[1] Washington, D. C. Published by the Walter Reed Memorial Association, 1904.

as an earnest and intelligent physician, whose industry, fidelity to duty, and singularly clear judgment, gave brilliant promise for the future. In the poor cabins and dugouts of the pioneers in the sparsely settled districts where he served his flag, Reed was ever a messenger of healing and comfort. At that time Army posts on the frontier were usually remote and with small garrisons. The young medical officer, generally the only one at the station, was called upon by the settlers for miles around. Without help, and with only such instruments and medicines as could be hastily stuffed in his saddlebag, he was summoned to attend a fractured thigh, a child choking with diphtheria, or, most trying of all, a complicated childbirth.

Such experience schools well in self-reliance, and in the formation of quick and accurate observation.

For a man like Reed, already an earnest student, no better preparation could perhaps have been had. His earlier Army service must have singularly tended to develop in him the very qualities most necessary to his final success. To the end of his life it was noticeable that even when he had long given up the practice of medicine for the work of the laboratory, he was nevertheless unexcelled at the bedside for rapid, unerring diagnosis and sound judgment in treatment. So also were the series of experiments which robbed yellow fever of its terrors especially remarkable for simplicity, accuracy, and completeness, or they never would have so quickly convinced the world of their truth. Too much reverence for accepted teachings, and too little experience in grappling with difficulties unassisted, and they might never have been conceived or carried out.

In 1890 he was assigned to duty in Baltimore and remained there over a year. Here he had the great advantage of working in the laboratories of Johns Hopkins University and the happiness of winning the close friendship of his distinguished teacher, Prof. William H. Welch.

In 1893, Reed was promoted surgeon with the rank of major, and in the same year was detailed in Washington as curator of the Army Medical Museum and professor of bacteriology at the newly organized Army Medical School. Here he worked industriously at his specialty and wrote many valuable monographs, all characterized by accuracy and originality. His excellent judgment made him especially valuable in investigating the causes of epidemic diseases at military posts, and in making sanitary inspections. He was, therefore, frequently selected for such work, which with his duties as teacher and member of examining boards, occupied much of the time that he would otherwise have spent in his laboratory. Here again it seems that duties which must often have been irksome were specially fitting him for his culminating work.

During the Spanish-American war the camps of the volunteer troops in the United States were devastated by typhoid fever, and Maj. Reed was selected as the head of a board to study the causation and spread of the disease. This immense task occupied more than a year's time. With the utmost patience and accuracy the details of hundreds of individual cases were grouped and studied. The report of the commission, now in course of publication by the Government, is a monumental work which must always serve as a basis for future study of the epidemiology of typhoid fever.

The most original and valuable work of the board is the proof that the infection of typhoid fever is spread in camps by the common fly, and by contact with patients and infected articles, clothing, tentage, and utensils, as well as by contaminated drinking water.

In June, 1900, Maj. Reed was sent to Cuba as president of a board to study the infectious diseases of the country, but more especially yellow fever. Associated with him were Acting Asst. Surgs. James Carroll, Jesse W. Lazear, and A. Agramonte.

At this time the American authorities in Cuba had for a year and a half endeavored to diminish the disease and mortality of the Cuban towns, by general sanitary work, but while the health of the population showed distinct improvement and the mortality had greatly diminished, yellow fever apparently had been entirely unaffected by these measures. In fact, owing to the large number of nonimmune foreigners, the disease was more frequent than usual in Habana and in Quemados near the camp of American troops, and many valuable lives of American officers and soldiers had been lost.

Reed was convinced from the first that general sanitary measures alone would not check the disease but that its transmission was probably due to an insect.

The fact that malarial fever, caused by an animal parasite in the blood, is transmitted from man to man through the agency of certain mosquitoes had been recently accepted by the scientific world; also several years before Dr. Carlos Finlay, of Habana, had advanced the theory that a mosquito conveyed the unknown cause of yellow fever, but did not succeed in demonstrating the truth of his theory.

Dr. H. R. Carter, of the Marine-Hospital Service, had written a paper showing that although the period of incubation of yellow fever was only 5 days, yet a house to which a patient was carried did not become infected for from 15 to 20 days.

To Reed's mind this indicated that the unknown infective agent has to undergo a period of incubation of from 10 to 15 days, and probably in the body of a biting insect.

Up to this time the most generally accepted theory as to the causation of yellow fever was that of Sanarelli, who claimed that the *Bacillus icteroides* discovered by him was the specific agent of the disease. Maj. Reed in association with Dr. Carroll had, however, already demonstrated that this bacillus was one widely disseminated in the United States, and bore no special relation to yellow fever.

In June, July, and August, 1900, the commission gave their entire attention to the bacteriological study of the blood of yellow-fever patients and the post-mortem examinations of the organs of those dying with the disease. In 24 cases where the blood was repeatedly examined, as well as in 11 carefully studied autopsies, *Bacillus icteroides* was not discovered, nor was there any indication of the presence in the blood of a specific cause of the disease.

Application was made to Gen. Leonard Wood, the military governor of Cuba, for permission to conduct experiments on nonimmune persons, and a liberal sum of money requested for the purpose of rewarding volunteers who would submit themselves to experiment.

It was indeed fortunate that the military governor of Cuba was a man who by his breadth of mind and special scientific training could readily appreciate the arguments of Maj. Reed as to the value of the proposed work.

Money and full authority to proceed were promptly granted, and to the everlasting glory of the American soldier, volunteers from the Army offered themselves for experiment in plenty and with the utmost fearlessness.

Before the arrangements were entirely completed, Dr. Carroll, a member of the commission, allowed himself to be bitten by a mosquito that 12 days previously had filled itself with the blood of a yellow-fever patient. He suffered from a very severe attack, and his was the first experimental case. Dr. Lazear also experimented on himself at the same time, but was not infected. Some days later, while in the yellow-fever ward, he was bitten by a mosquito and noted the fact carefully. He acquired the disease in its most terrible form and died a martyr to science and a true hero.

No other fatality occurred among the brave men who, in the course of the experiments, willingly exposed themselves to the infection of the dreaded disease.

A camp was especially constructed for the experiments about 4 miles from Habana, christened Camp Lazear in honor of the dead comrade. The inmates of the camp were put into most rigid quarantine and ample time was allowed to eliminate any possibility of the disease being brought in from Habana.

The personnel consisted of three nurses and nine nonimmunes, all in the military service, and included two physicians.

From time to time Spanish immigrants, newly arrived, were brought in directly from the immigrant station; a person not known to be immune was not allowed to leave camp, or if he did was forbidden to return.

The most complete record was kept of the health of every man to be experimented upon, thus eliminating the possibility of any other disease than yellow fever complicating the case.

The mosquitoes used were specially bred from the eggs and kept in a building screened by wire netting. When an insect was wanted for an experiment it was taken into a yellow fever hospital and allowed to fill itself with the blood of a patient; afterwards at varying intervals from the time of this meal of blood it was purposely applied to nonimmunes in camp.

In December, 5 cases of the disease were developed as the result of such applications; in January, 3, and in February, 2, making in all 10, exclusive of the cases of Drs. Carroll and Lazear. Immediately upon the appearance of the first recognized symptoms of the disease, in any one of these experimental cases, the patient was taken from Camp Lazear to a yellow-fever hospital, 1 mile distant. Every person in camp was rigidly protected from accidental mosquito bites, and not in a single instance did yellow fever develop in the camp, except at the will of the experimenters.

The experiments were conducted at a season when there was the least chance of naturally acquiring the disease, and the mosquitoes used were kept active by maintaining them at a summer temperature.

A completely mosquito-proof building was divided into two compartments by a wire-screen partition; infected insects were liberated on one side only. A brave nonimmune entered and remained long enough to allow himself to be bitten several times. He was attacked by yellow fever, while two susceptible men in the other compartment did not acquire the disease, although sleeping there 13 nights. This

demonstrates in the simplest and most certain manner that the infectiousness of the building was due only to the presence of the insects.

Every attempt was made to infect individuals by means of bedding, clothes, and other articles that had been used and soiled by patients suffering with virulent yellow fever.

Volunteers slept in the room with and handled the most filthy articles for 20 nights, but not a symptom of yellow fever was noted among them, nor was their health in the slightest degree affected. Nevertheless they were not immune to the disease, for some of them were afterwards purposely infected by mosquito bites. This experiment indicates at once the uselessness of destroying valuable property for fear of infection. Had the people of the United States known this one fact 100 hundred years ago, an enormous amount of money would have been saved to householders.

Besides the experimental cases caused by mosquito bite, four nonimmunes were infected by injecting blood drawn directly from the veins of yellow-fever patients in the first two days of the disease, thus demonstrating the presence of an infectious agent in the blood at this early period of the attack.

Even the blood serum of a patient, passed through a bacteria-proof filter, was found to be capable of causing yellow fever in another person.

The details of the experiments are most interesting, but it must here suffice to briefly sum up the principal conclusions of this admirable board of investigators of which Reed was the master mind:

1. The specific agent in the causation of yellow fever exists in the blood of a patient for the first three days of his attack, after which time he ceases to be a menace to the health of others.

2. A mosquito of a single species, Stegomyia fasciata, ingesting the blood of a patient during this infective period is powerless to convey the disease to another person by its bite until about 12 days have elapsed, but can do so thereafter for an indefinite period, probably during the remainder of its life.

3. The disease can not in nature be spread in any other way than by the bite of the previously infected Stegomyia. Articles used and soiled by patients do not carry infection.

These conclusions pointed so clearly to the practical method of exterminating the disease that they were at once accepted by the sanitary authorities in Cuba, and put to the test in Habana, where for nearly a century and a half, by actual record, the disease had never failed to appear annually.

In February, 1901, the chief sanitary officer in Habana, Maj. W. C. Gorgas, Medical Department, United States Army, instituted measures to eradicate the disease, based entirely on the conclusions of the commission. Cases of yellow fever were required to be reported as promptly as possible, the patient was at first rigidly isolated, and immediately upon the report a force of men from the sanitary department visited the house. All the rooms of the building and of the neighboring houses were sealed and fumigated to destroy the mosquitoes present. Window and door screens were put up, and after the death or recovery of the patient, his room was fumigated and every mosquito destroyed. A war of extermination was also waged against mosquitoes in general, and an energetic effort was made to diminish the number bred by draining standing water, screening tanks

and vessels, using petroleum on water that could not be drained, and in the most systematic manner destroying the breeding places of the insects.

When the warm season returned a few cases occured, but by September, 1901, the last case of yellow fever originated in Habana, since which time the city has been entirely exempt from the terrible disease, that had there kept stronghold for 150 years. Cases are now admitted into Habana from Mexican ports, but are treated under screens with perfect impunity, in the ordinary city hospitals. The crusade against the insects also caused a very large decrease in malarial fevers.

The destruction of the most fatal epidemic disease of the Western Hemisphere, in its favorite home city is but the beginning of the benefit to mankind that may be expected to follow the work of Reed and his associates. There can be no manner of doubt should Mexico, Brazil, and the Central American Republics, where the disease still exists, follow strictly the example set by Habana, that yellow fever will become extinct and the United States forever freed from the scourge that has in the past slain thousands of our citizens and caused the loss of untold treasure.

More recent investigations into the cause and spread of yellow fever have only succeeded in verifying the work of Reed and his commission in every particular and in adding very little to our knowledge of the disease.

Later researches by Guiteras in Habana, by the Public Health and Marine-Hospital Service in Vera Cruz, and lastly by a delegation from the Pasteur Institute of Paris in Rio de Janeiro, all confirm in the most convincing manner both the accuracy and comprehensiveness of the conclusions of the American commission. It has been well said that Reed's experiments "will always remain as models in the annals of scientific research, both for the exactness with which they were adapted to the points to be proved, and the precautions taken that no experiment should be vitiated by failure to exclude all possible sources of error."

Appreciation of Reed's work was instant in the scientific world. Honorary degrees from Harvard University and the University of Michigan were conferred upon him, learned societies and distinguished men delighted to honor him, and after his death Congress voted a special pension to his widow.

To the United States the value of his services can not be estimated. Ninety times has yellow fever invaded the country, carrying death and destruction, leaving poverty and grief.

New Orleans, Memphis, Charleston, Galveston, Portsmouth, Baltimore, Philadelphia, New York, and many smaller towns have been swept by the disease.

The epidemic of 1853 cost New Orleans 8,000 lives, that of 1793 wiped out 10 per cent of Philadelphia's population.

The financial loss to the United States in the one epidemic of 1878 was estimated as amounting to $15,335,000, but suffering, panic, fear, and the tears of widows and orphans can never be estimated. Now, however, if yellow fever should again cross our southern border, there need be no disturbance of commerce or loss of property in the slightest degree comparable with that which epidemics in the past have caused.

The death of Maj. Reed took place November 23, 1902, in Washington, from appendicitis. It is gratifying to think that, although his country and the scientific world were deprived of one from whose future services more benefit to humanity might reasonably be expected, nevertheless he was privileged before his life's close to know that his discovery had been tested, and that a great city was freed from her ancient foe, to know that his conscientious work had contributed immeasurably toward the future prospects of an infant Republic, and even more to the welfare of his own beloved country, whose flag he had served so faithfully.

In the national capital and in the great cities of the United States, there are stately monuments to the country's great ones. Statues of warriors, statesmen, and patriots stand as silent witnesses of a people's gratitude. Is there not room for the effigy of Walter Reed, who so clearly pointed out to his fellow man the way to conquer America's worst plague?

Chapter 2.

SKETCH OF THE LIFE OF MAJ. WALTER REED, SURGEON, UNITED STATES ARMY.

By Jefferson R. Kean, Major, Medical Corps, United States Army.

Walter Reed, M. D., LL. D., M. A., major and surgeon, United States Army, was born September 13, 1851, in Gloucester County, Va., and was the son of the Rev. Lemuel Sutton Reed, a leading Methodist divine of that State. His ancestors came from North Carolina, having been among the earliest settlers of that colony. He gave early evidence of the intellectual brilliancy and earnestness of purpose which distinguished him in later years, and graduated in medicine at the University of Virginia in 1869. He afterwards took the degree of M. D. in Bellevue Medical College, New York City. He served as house surgeon in the Brooklyn City Hospital and the city hospital on Blackwells Island, and before the age of 21 was appointed a district physician in New York City. He was also appointed one of the five inspectors of the board of health of the city of Brooklyn at the age of 22. In 1875 he entered the Medical Corps of the Army, and for 18 years thereafter performed the customary duties of a medical officer at various posts in different parts of the United States and in the field. His military service included 15 changes of station, with 4 years in Arizona, 5 in the Department of the Platte, 2 in the Department of Dakota, 3 in the South, and 3 years in the East. He was promoted full surgeon with the rank of major December 4, 1893, and at the time of his death was first on the list of majors in the Medical Department of the Army. In the fall of 1890 he was assigned to duty as attending surgeon in Baltimore, Md., which position he held for a year. He promptly embraced this opportunity to make special studies in bacteriology and pathology, and soon won the attention and esteem of Prof. William H. Welch. This was the beginning of a close friendship with that distinguished scientist which lasted until the untimely death of Maj. Reed, on November 23, 1902.

In 1893 Maj. Reed was placed on duty in Washington as curator of the Army Medical Museum and appointed the professor of bacteriology of the newly organized Army Medical School.

In the 10 years subsequent to this date, in the intervals of his routine duties and others which came to him as a medical officer, such as member of examining boards, teaching, investigation of numerous sanitary questions, and making sanitary inspections, he was able, by immense industry, to obtain a position in the scientific world such as comes to few of those who are able to devote a lifetime exclusively to such pursuits.

Of the numerous monographs which show his scientific work during this time, all are creditable; nor do any show marks of carelessness or haste, in spite of the limited time which he had at his disposal.

In 1898, when typhoid fever prevailed so extensively in the camps of the Volunteer Armies of the United States, Maj. Reed was put at the head of a commission—Dr. Victor C. Vaughan, of the University of Michigan, and Dr. E. O. Shakespeare, of Philadelphia, being the other members—to study the causation and methods of spread of that disease. This investigation, which covered a period of more than a year, was remarkable for the patience and skill with which a vast number of details were assembled and studied, and it marks a great advance in our knowledge of this widespread disease. Among the points of great value brought out were the importance of the common fly as a carrier of infection in camps, and the frequency with which the contagion of typhoid fever is in camp life spread from man to man by immediate contact with each other or with bedding, tents, and implements which have become infected. Strangely enough, this report has never been published in full, but only an abstract of it containing some 240 pages, and, on account of the failure to publish and disseminate the full report, its conclusions are but little known abroad or among the members of the medical profession in this country. Many of the facts contained in it were rediscovered by the English during the Boer War, and it is probable that its prompt publication and dissemination would have saved many thousand lives during that war.

The first work by Maj. Reed bearing on the causation of yellow fever was in 1899–1900, when he overthrew the claim of the distinguished bacteriologist, Sanarelli, to have discovered the bacillus of yellow fever, by his demonstration that the *Bacillus icteroides* (Sanarelli) was an organism widely disseminated in this country and having no causative relation to that disease. He began the special work with which his name will always be inseparably associated as one of the benefactors of mankind in June, 1900, when he went to Cuba as president of a commission to study the infectious diseases of Cuba, with special reference to yellow fever. The other members of this commission were Acting Asst. Surgs. James Carroll, Jesse W. Lazear, and A. Agramonte. The time was most opportune for such investigation, as the disease was at that time prevalent both in Habana and in the little town of Quemados, near the camp of the American troops, and it was plainly evident that the energetic measures of the American military government to clean up the towns, disinfect, and enforce other sanitary measures were without effect in preventing the spread of this particular disease. Maj. Reed became convinced that proper sanitation was not all that was needed, and that some other agent than unclean conditions was responsible for the spread of the disease.

The transmission of malaria by a certain species of mosquito had been recently demonstrated by the English military surgeon, Ronald Ross. The theory had also been advanced both by a Mobile physician and by Dr. Finlay, of Habana, that a mosquito was the agent for the transmission of yellow fever; but these theories, being unsupported by scientific demonstration, received no more attention than the vast number of others which had been at one time or another advanced with regard to this mysterious and deadly disease.

Dr. Reed's attention was attracted by a paper on the spread of yellow fever in Ormond, Miss., by Dr. H. R. Carter, of the Marine-Hospital Service, in which it was shown that although the period of incubation of the disease was 5 days, 15 or 20 elapsed before a house

became infected after a patient sick with yellow fever was carried into it. He inferred that the difference between the time of incubation and the time required to infect a building was due to the fact that the infective agent passed through a stage of development in the body of some biting insect as an intermediate host, and he at once determined to conduct his experiments along that line. It was evident to his mind that the solution of this question, which meant so much for the human race, could never be satisfactorily determined without experiments on human beings, and he went to Gen. Wood, the military governor of Cuba, to ask permission to conduct such experiments, and for a sum of money to liberally reward volunteers who should submit themselves for experiment. Gen. Wood promptly granted both, with a ready appreciation of the importance of the matter and the force of Dr. Reed's arguments, which will entitle him to no small measure of the glory of this discovery.

Meanwhile, during a temporary absence of Dr. Reed in the United States, his assistants, Dr. James Carroll and Dr. Jesse W. Lazear, who had offered themselves as the first volunteers for these experiments, had demonstrated that mosquitoes would convey yellow fever. Dr. Carroll, who was the first experimental case, suffered a very severe attack, but recovered. Dr. Lazear was not infected at this time, due to the fact that the conditions necessary to the transmission of the disease by the mosquito were not yet understood, but he was bitten while working in the yellow-fever ward somewhat later, and died a martyr of science, working in behalf of humanity. This was the only fatality which occurred in these experiments. The fourth member of the commission, Dr. Agramonte, did not participate in the mosquito work of the commission until a later date, nor did he share their dangers, as he was a Cuban and immune.

Immediately upon Dr. Reed's return arrangements were made, with the assistance of the military governor, as stated above, for a series of experiments which, by precision of detail and rigidness of control, would admit of no uncertainity of interpretation and would be a perfect demonstration, carrying conviction to every scientific and unprejudiced mind. These experiments will, as stated by Prof. William H. Welch, always remain as models in the annals of scientific research, both for the exactness with which they were adapted to the points to be proved and the precautions taken that no experiment should be vitiated by failure to exclude all possible sources of error. They were conducted in a camp especially constructed for the purpose, about 4 miles from Habana, and appropriately named "Camp Lazear." The history of the work is best given in Dr. Reed's own words, in an article published in the Journal of Hygiene, Cambridge, England.

Chapter 3.

EXPERIMENTS CONDUCTED FOR THE PURPOSE OF COPING WITH YELLOW FEVER.

[Senate Document No. 10, Fifty-ninth Congress, second session.]

To the Senate and House of Representatives:

The inclosed papers are transmitted to the Congress in the earnest hope that it will take suitable action in the matter. Maj. Reed's part in the experiments which resulted in teaching us how to cope with yellow fever was such as to render mankind his debtor, and this nation should in some proper fashion bear witness to this fact.

THEODORE ROOSEVELT.

THE WHITE HOUSE, *December, 5, 1906.*

[Inclosure 1.]

[Memorandum for the President, through The Military Secretary of the Army.]

WAR DEPARTMENT,
OFFICE OF THE SURGEON GENERAL,
Washington, August 30, 1906.

The persons taking an important part in the investigations in Cuba, which resulted in the demonstration of the fact that yellow fever is transmitted by a species of mosquito, were three members of the board appointed to investigate epidemic diseases in Cuba—Walter Reed, James Carroll, and Jesse W. Lazear—and the individuals who submitted themselves for experimentation by receiving the bites of infected mosquitoes, by receiving injections of blood from yellow-fever patients, and by sleeping in bedding which had been used by yellow-fever patients.

When the Yellow Fever Commission, composed of Walter Reed, James Carroll, Jesse W. Lazear, and A. Agramonte, assembled in Habana they had no thought of investigating the connection of the mosquito with the spread of yellow fever. This idea came to Dr. Reed after the board had demonstrated that the claim of Sanarelli, concurred in by Wasdin and Geddins, that the *Bacillus icteroides* was the cause of yellow fever was without foundation. Dr. Reed then determined to investigate the theory of Dr. Carlos Finlay, that the mosquito was instrumental in conveying yellow fever, which theory Finlay had failed to demonstrate, and which was not then accepted by scientific men. This determination was reached for the reasons which are well stated in Dr. Kelly's biography, and was original with Reed, not being suggested to him by anyone. The final determination to investigate the mosquito theory was arrived at during an informal meeting of the board (Dr. Agramonte being absent) at Columbia Barracks on the evening before Dr. Reed's

departure for the United States, early in August, 1901. It was agreed by these members of the board that in making the experiments on human beings, by which alone the demonstration could be made, that they should submit themselves as subjects for experimentation. To Dr. Lazear, who was familiar with mosquito work, was assigned the duty of breeding and infecting the mosquitoes, while Dr. Carroll was to continue the bacteriological work on which the board had been engaged.

On August 2, 1900, before the mosquitoes were ready for the experiment, Dr. Reed was called back to Washington to prepare for publication the abstract of the report of the board appointed in 1898 to investigate the spread of typhoid fever in the volunteer camps in the United States, of which board he was president. This vast work, of which the full report was published by special authority of Congress about a year after Dr. Reed's death, by the only surviving member of the board, Prof. Victor C. Vaughan, of the University of Michigan, was one of the most valuable contributions to science which has been made by the Surgeon General's Office. The work of preparation of the abstract report had been brought to a standstill by the sudden death of the third member of the board, Dr. Edward O. Shakespeare, of Philadelphia, and Dr. Reed's presence at this time was essential for its completion.

During Dr. Reed's absence the inoculations by means of the mosquito were begun. On August 11, Dr. Lazear made the first experiment, but nine distinct inoculations on persons, including himself and Acting Asst. Surg. A. S. Pinto, were unsuccessful. We know now that these failures were due to two facts—first, that patients after the third day of the disease can not convey the infection to the mosquito, and second, that after having bitten a yellow-fever case the mosquito can not transmit the disease until after an interval of at least 12 days. On August 27 one mosquito was applied to Dr. Carroll, one which happened to fulfill both of these conditions. The result was a very severe attack of yellow fever, in which for a time his life hung in the balance. This was thus the first experimental case. The fever developed on the 31st of August, on which day Dr. Lazear applied the same mosquito which bit Dr. Carroll with three others to another person. This man came down with a mild but well-marked case.

On September 13 Dr. Lazear, while on a visit to Las Animas Hospital (for the purpose of collecting blood from yellow-fever patients for study) was bitten by a mosquito of undetermined species, which he deliberately allowed to remain on the back of his hand until it had satisfied its hunger. Five days thereafter he came down, without other exposure, with yellow fever, which progressed steadily to a fatal termination. These three cases established in Reed's mind the proof of the mosquito theory and made it, in the opinion of his friends, an unnecessary and foolish risk for him, at his age, to submit himself to inoculation. These cases, with his deductions therefrom, were reported by the board in a paper called "The etiology of yellow fever—A preliminary note," read before the American Public Health Association at Buffalo, N. Y., October 22–26, 1900. He then immediately returned to Cuba to undertake a second and more elaborate series of experiments which were made possible by the promise made to him by Gen. Wood on October 12, when told by

Reed of the experiments already made, to assist him with whatever money was necessary. This, the second series of experiments, began November 20 at an experimental camp near Quemados, called Camp Lazear, and embraced 14 cases, of which the last was taken sick February 10, 1901. Of these, 10 were mosquito infections and 4 were infected by injection of the blood of yellow-fever patients. All of these cases recovered.

A third series of 6 cases was produced by Dr. James Carroll the next fall to settle certain undetermined facts as regards the etiology of the disease. The first of these cases came down with the fever September 19, 1901, and the last on October 23, 1901. Of these cases 2 were caused by mosquitoes and 4 by blood injections. None of them resulted fatally. The highly dangerous character of these experiments and the good fortune of the board in its second and third series of cases is shown by the fact that Dr. Guiteras, of Habana, in a series of 7 cases inoculated in Habana lost 3, bringing his experiments abruptly to an end.

No enumeration of unsuccessful cases—namely, those which failed to cause the disease—has been made, although it is obvious that the persons undergoing such experiments exhibited as much courage as those in which the disease was transmitted. This is especially true of the cases occurring after the severe case of Dr. Carroll and the fatal case of Dr. Lazear. Certain ones of these unsuccessful cases deserve special mention, being those made with infected bedding at Camp Lazear. In a specially constructed house at that camp, which was intentionally ill ventilated and kept continually at a summer temperature, was placed a large quantity of bedding taken from the beds of patients sick with yellow fever in Habana and soiled with their discharges. In this house Acting Asst. Surg. R. P. Cook and two privates of the Hospital Corps slept continuously from November 30 to December 19. Each morning they packed the various soiled articles of bedding in boxes and unpacked them at night, when they were used to sleep on.

From December 21, 1900, to January 10, 1901, the building was again occupied by two nonimmune Americans under the same circumstances, except that an additional stock of very much fouled bedding and clothing had been added to the collection, and these men slept every night in the very garments worn by yellow-fever patients throughout their entire attacks, besides making use of their much soiled pillow slips, sheets, and blankets. A third couple of Hospital Corps men succeeded these for an equal length of time. None of these seven individuals contracted yellow fever, but the courage and fortitude shown by them certainly equal that of those who submitted to the bites of the mosquitoes, it being borne in mind that belief in the transmission of yellow fever by infected bedding and clothing was at that time practically universal, whereas the mosquito theory had still very few converts.

After this brief history of this great discovery a statement of the part borne by each of the more important participators in it is necessary to a determination of the reward which would be appropriate to each.

Maj. Walter Reed, surgeon, United States Army, president of the commission to investigate and study the epidemic diseases in Cuba, died in Washington from appendicitis, November 23, 1902, at the

age of 51. At the time of his death the Secretary of War had said in his report, which was then in press but not yet given out:

The brilliant character of this scientific achievement, its inestimable value to mankind, the saving of thousands of lives, and the deliverance of the Atlantic seacoast from constant apprehension, demand special recognition from the Government of the United States.

Dr. Reed is the ranking major in the Medical Department, and within a few months will, by operation of law, become lieutenant colonel. I ask that the President be authorized to appoint him Assistant Surgeon General with the rank of colonel.

Gen. Leonard Wood said of him in an address delivered at a memorial meeting of scientific men in Washington, D. C., shortly after his death:

I know of no other man on this side of the world who has done so much for humanity as Dr. Reed. His discovery results in the saving of more lives annually than were lost in the Cuban war, and saves the commercial interests of the world a greater financial loss each year than the cost of the Cuban war. He came to Cuba at a time when one-third of the officers of my staff died of yellow fever, and we were discouraged at the failure of our efforts to control the disease.

In the months when the disease was ordinarily worst the disease was checked and driven from Habana. That was the first time in nearly 200 years that the city had been rid of it. The value of his discovery can not be appreciated by persons who are not familiar with the conditions of tropical countries. Hereafter it will never be possible for yellow fever to gain such headway that quarantine will exist from the mouth of the Potomac to the mouth of the Rio Grande. Future generations will appreciate fully the value of Dr. Reed's services. His was the originating, directing, and controlling mind in this work, and the others were assistants only.

In a letter from Prof. Welch to the Secretary of War he said:

Dr. Reed's researches in yellow fever are by far the most important contributions to science which have ever come from any Army surgeon. In my judgment they are the most valuable contributions to medicine and public hygiene which have ever been made in this country with the exception of the discovery of anæsthesia. They have led and will lead to the saving of thousands of lives. I am in a position to know that the credit for the original ideas embodied in this work belongs wholly to Maj. Reed.

Prof. Welch was Dr. Reed's teacher in bacteriology and was his intimate and confidential friend, with whom he consulted about the details of the work in Cuba.

A bill prepared in this office for a pension for his widow, equal in amount to his monthly pay, was passed, but the amount was so cut down that while it keeps the wolf from the door it does not provide an adequate and comfortable income. It is not probable, however, that Congress would increase this pension, and an effort has been made to supplement it by the raising of a fund of $25,000 by the Walter Reed Memorial Association, incorporated for this purpose in the District of Columbia. The interest on this fund will be given Mrs. Reed during her lifetime, and the principal, after her death, will be devoted to some form of memorial. This fund lacks at present about $6,000 of completion. The existence of this association, should its hopes be attained, does not, however, absolve the nation from the obligation of a fitting recognition for this great work, and it is the opinion of the undersigned, which, it is believed, is shared by the vast majority of physicians in the United States, that Congress should erect a statue to Walter Reed in Washington. The assistance of the President in inducing Congress to do so is requested.

The second member of the commission was Dr. James Carroll, at that time acting assistant surgeon, United States Army.

Dr. Carroll is now 52 years old. He entered the military service June 9, 1874, and served as private, corporal, sergeant, and hospital

steward from that date to May 21, 1898, when he was appointed acting assistant surgeon. He was appointed first lieutenant and assistant surgeon in the Medical Corps October 27, 1902, which rank he still holds.

Dr. Carroll was Dr. Reed's truest assistant and coadjutor from the inception of the work which resulted in the discovery of the method of propagation of yellow fever. As stated above, the third series of experiments were performed by Dr. Carroll alone, Dr. Reed having been refused permission to return to Cuba to complete his work.

Dr. Carroll was the first experimental case of yellow fever, and he suffered a very severe attack, to which he attributes a heart trouble from which he now suffers. At the time of undergoing this experiment he was 46 years old, an age at which the risk from this disease is very great, as its mortality rapidly increases with age of patient. He had at that time a wife and five children who had no other means of support except his pay as an acting assistant surgeon.

It is recommended that Congress be asked to pass a special act promoting Dr. Carroll, on account of his services in connection with this discovery and the courage shown by him in subjecting himself to experiment, to the rank of lieutenant colonel, the number of medical officers in that grade being increased by one for that purpose; also his name and effigy should appear on the monument to Walter Reed.

Dr. Jesse W. Lazear was the third member of the commission.

Dr. Lazear was a native of Baltimore and a graduate of Johns Hopkins University, afterwards getting his professional degree at Columbia University and Bellevue. At the time he incurred his death in the course of these experiments, as above mentioned, he was 34 years old. He left a wife and two young children, the younger a little son born a few months before his death, whom he never saw. Mrs. Lazear received from Congress a pension of $17 a month with $2 additional for each of two minor children until they reach the age of 16. Also a battery in Baltimore Harbor was, by direction of the Secretary of War, named in his honor. It is believed that this recognition on the part of the nation for his services is utterly inadequate. His widow's pension should be increased to $100 a month, and steps should be taken to perpetuate his name in connection with the Walter Reed monument above suggested.

Dr. A. Agramonte was the fourth member of the Yellow Fever Commission. He was a Cuban by birth, an immune to yellow fever, and having been assigned other work, took no part in the first series of experiments with regard to the conveyance of the disease by the mosquito, of which, in fact, he was not at the time cognizant. Being an immune, he ran no risk in connection with this work, and it is believed that his contributions to it have been sufficiently recognized in the association of his name with the other members of the commission who brought about this great discovery.

Twenty-three of the men who submitted themselves for experiment by the board contracted yellow fever, beginning with Dr. James Carroll, who was taken sick August 31, 1900, and ending with John R. Bullard, who was taken sick October 23, 1901.

Conspicuous among them was John J. Moran, a civilian clerk employed at the headquarters of Gen. Fitzhugh Lee, at Quemados, who was one of the earliest volunteers for the second set of experiments, and whose action was dictated by the purest motives of

altruism and self-devotion. Mr. Moran disclaimed, before submitting to the experiments, any desire for reward, and has never accepted any since, although he was offered the $200 which the liberality of the military governor enabled the commission to give to each experimental patient, the members of the board excepted. Such was his modesty that he has made no effort, so far as known to this office, to make known his connection with these experiments and reap the credit which is so justly due him. Mr. Moran was a native of Ohio. His present address is not known to this office. The first inoculations in the case of Mr. Moran were for some reason unsuccessful, on November 26 and 29. He did not suffer an attack until after the third inoculation, on December 21.

The same remarks apply to the first experimental case of the second set, Pvt. John R. Kissinger, hospital corps, who volunteered at the same time with Moran and equally disclaimed any desire for reward. Pvt. Kissinger did not leave Cuba immediately after the experiments, as did Mr. Moran, and therefore the military authorities were able to reward him in some measure along with other enlisted men who volunteered for these experiments. He was promoted acting hospital steward, presented with a gold watch by the chief surgeon of the department in the presence of all the medical officers and hospital corps men on duty at Columbia Barracks, and also received a present of $115 in cash. He took his discharge November 14, 1901, and has since (on December 17, 1903) made application for pension. This was refused for lack of evidence that his ill-health was incident to the service.

Of the other experimental cases, seven were Spanish immigrants who submitted to experiments purely for the money which they were promised. With regard to those who were American soldiers, however, 10 in number, in addition to those already mentioned, it can not be doubted that, although they received pecuniary rewards, a desire to assist in what they appreciated was a great and glorious work, together with a spirit of adventure, was the most powerful motive. The same is true of the last experimental case, Mr. John R. Bullard, a graduate of Harvard, where he was a distinguished athlete and captain of the university crew. The names of these men, with the dates of their attack, is appended with this report.

It remains to mention Dr. Robert P. Cook, acting assistant surgeon, and the six privates of the hospital corps, who were for 20 nights shut up in the infected bedding house at Camp Lazear. These experiments, which were absolutely necessary to demonstrate that yellow fever could not be carried otherwise than by the mosquito, had for these men, so far as they knew, an equal element of danger with the other experiments and had in addition such repulsive and disagreeable features as to test to the full their hardihood and patience. Much of the bedding upon which they slept and which they were required daily to handle, was so soiled with the discharges of the sick as to be very repulsive to the nose and eye, and the last experimenters actually slept in the pajamas and sheets which had been worn by severe cases of yellow fever. The names of these men are appended to the list given below of experimental cases of yellow fever.

It will be observed that three of these men—Folk, Jernegan, and Hanberry—afterwards submitted to the mosquito inoculation or

blood injection in order to demonstrate their nonimmunity at the time of the first experiment.

It is believed that the names of all the Americans on this list should be placed on a tablet in connection with the monument to Walter Reed.

From the foregoing it will be seen that the total disbursements of this great nation in the way of rewards for those who made possible this discovery and their families, amounts to $146 a month. As to its value to the American people attention is invited to the quotations from Gen. Wood and Prof. Welch given above, and others given in the inclosed circulars published by the Walter Reed Memorial Association.

How discreditable appears this niggardly provision when compared with the action of the English Government which more than a century ago, when the purchasing power of money was far greater than at present, gave to Jenner, the discoverer of vaccination, grants amounting to £30,000 sterling. He also received from a subscription in India £7,383 sterling, while the Reed Memorial has so far succeeded in raising only a little over half that sum.

It is believed that if the President would exert his great personal influence in furtherance of the aims of that association its task would be soon completed.

R. M. O'Reilly,
Surgeon General, United States Army.

Names of persons who submitted to experimental inoculation of yellow fever, Cuba, 1900–1901.

		Taken sick.
	Infected by mosquitoes.	
1	James Carroll	Aug. 31, 1900
2	X. Y. (American soldier)	Sept. 6, 1900
3	John R. Kissinger	Dec. 8, 1900
4	Nicanor Fernandez	Dec. 13, 1900
5	Antonio Benigno	Do.
6	Becente Presedo	Dec. 15, 1900
7	John J. Moran	Dec. 25, 1900
8	Jose Martinez	Jan. 3, 1901
9	Levi E. Folk	Jan. 23, 1901
10	Clyde L. West	Feb. 3, 1901
11	James L. Hanberry	Feb. 9, 1901
12	Charles G. Sonntag	Feb. 10, 1901
13	Pablo Ruiz Castillo	Sept. 19, 1901
14	Jacinto Mendez Alvarez	Oct. 13, 1901
	Infected by injection of blood.	
1	Warren G. Jernegan	Jan. 8, 1901
2	William Olson	Jan. 11, 1901
3	Wallace Forbes	Jan. 24, 1901
4	John H. Andrus	Jan. 28, 1901
5	Manuel Gutierrez Moran	Oct. 20, 1901
6	John R. Bullard	Oct. 23, 1901
	Infected by injections of filtered blood serum.	
1	P. Hamann, Twenty-third Battery Coast Artillery	Oct. 19, 1901
2	A. W. Covington, Twenty-third Battery Coast Artillery	Do.
	Exposed to fomites.	
1	Dr. R. P. Cooke, acting assistant surgeon	.....
2	Levi E. Folk	.....
3	Warren G. Jernegan	.....
4	James L. Hanberry	.....
5	Edward Weatherwalks (bitten once, negative; refused after Hanberry came down)	.....
6	James Hildebrand (offered himself, but was declined on account of age)	.....
7	Thomas M. England	.....

Chapter 4.

YELLOW-FEVER COMMISSION.

[Senate Document No. 820, Sixty-first Congress, second session.]

War Department,
Office of the Surgeon General,
Washington, April 29, 1910.

My Dear Senator: It gives me great pleasure to comply with the request contained in your letter of April 20, to furnish you with a report of the occurrences which led to the appointment of the yellow-fever commission, of which Maj. Walter Reed was president, and the names of the persons connected with the experiments of the commission, together with other data which is available concerning them.

Surg. Gen. Sternberg was for many years one of the leading authorities in the world on the subject of yellow fever, and had made, under the direction of the President of the United States, very laborious investigations as to its cause in Habana, Brazil, and Mexico. These investigations were unsuccessful because, as we now know, the organism of yellow fever is invisible to the microscope, but they served a valuable purpose in enabling Dr. Sternberg to disprove the claims of other investigators to have discovered the causative organism and to have prepared protective inoculations against the disease. His attention having been attracted by the claim of Sanarelli, of Buenos Aires, to have discovered the cause of yellow fever in the *Bacillus icteroides*, he ordered Maj. Reed, at that time professor of bacteriology in the Army Medical School, to study this organism in connection with an organism discovered by Sternberg in the bodies of yellow-fever patients in Habana, and named by him bacillus X. This investigation was continued by a board consisting of Maj. Walter Reed, surgeon, United States Army, and Acting Asst. Surgs. James Carroll, Aristides Agramonte, and Jesse W. Lazear, United States Army, which was appointed to meet at Camp Columbia, near Habana, Cuba, in May, 1900. The instructions to Maj. Reed, president of this board, included the following:

> You will naturally give special attention to questions relating to the etiology and prevention of yellow fever. As you are familiar with what has already been done by other bacteriologists in this field of investigation, I do not consider it necessary to give you any suggestions or detailed instructions. But it is evident that the most important question which will occupy your attention is that which relates to the etiology of this disease.
>
> You will also take advantage of such opportunities as may offer for the study of other infectious diseases, and especially of the malarial fevers prevailing in the island of Cuba. An important question in connection with the diseases of tropical and semi-tropical countries relates to the etiology of febrile attacks of short duration, to which strangers are especially subject. Should you have time, there will be ample opportunity for the study of leprosy in the lepers' hospital in the city of Habana. Attention should also be given to the infectious disease of the lower animals, in case any such prevail, the etiology of which has not been definitely determined.

One member of the board, Dr. Aristides Agramonte, lived in Habana, and another, Dr. Jesse W. Lazear, was already stationed at Columbia Barracks, having joined there on February 13, 1900. The remaining members of the board arrived in Cuba June 25, 1900. They were able to prove conclusively that in 18 cases of unmistakable yellow fever investigated from beginning to end bacillus icteroides was not present and that this organism could not be the cause of the disease. These conclusions were diametrically opposite to those of Drs. Wasdin and Geddings, of the Marine-Hospital Service, who likewise at that time were studying yellow fever in Habana, and who confirmed the findings of Sanarelli. The board then proceeded to investigate the theory advanced by Finlay, that yellow fever was conveyed by mosquitoes. A full history of these experiments has been published in the reports of the board, and a brief account of it, together with a list of the persons who submitted to experimental inoculation, was given in a memorandum prepared for the President by this office on August 30, 1906, and transmitted as a special message to Congress on December 5, 1906. It was published as Senate Document No. 10, Fifty-ninth Congress, second session, a copy being inclosed.

Before taking up individually the men concerned in these experiments, in order to state what is known about them at the present time, it may be mentioned that the Spaniards who were inoculated did so for the pecuniary inducement offered them. After receiving the reward offered them by the liberality of the military government of Cuba, $200 for each person successfully inoculated, they passed from the scene and nothing further is known concerning them. While their names should be preserved as a matter of historical interest, it is considered that they have been well rewarded for their share in the matter, especially as the idea of assisting in the advancement of science was not a controlling motive for their action. Also it should be stated that it can not be demonstrated that these experiments caused the death or subsequent ill health of any of the participants, with the exception of Dr. Lazear and of three individuals who died in the course of the experiments which were conducted by Maj. Gorgas and Dr. John Guiteras at Las Animas Hospital, Habana, between February and December, 1901, which will be referred to later.

In view of the facts which have come to the attention of this office since the preparation of the memorandum for the President, it is believed that that memorandum does not do justice to the importance of the part which Dr. Agramonte took in these investigations. Dr. Agramonte has made the following statement with regard to the work of the board.

In the investigations of the board with reference to *Bacillus icteroides*, Dr. Carroll had the bacteriological work, Dr. Agramonte the autopsy and gross pathology, Dr. Jesse W. Lazear the microscopical pathology.

In June, 1900, Dr. Agramonte was sent to the city of Santa Clara to investigate the outbreak of yellow fever in that city, and in July he was sent to the city of Pinar del Rio to investigate the outbreak of yellow fever among the American troops, which the surgeons stationed there had failed to recognize as such. Dr. Agramonte promptly recognized the true character of the disease, and was joined there by Maj. Reed a couple of days later. It was there that for the first time the probability of mosquito agency in transmitting the disease was seriously discussed by members of the board, and it was decided to carry out some research in this direction.

As Dr. Lazear had obtained considerable training in mosquito work while in Italy, and none of the other members of the board had any, it was agreed that he take up this part of the work in the beginning. Dr. Carroll continued to investigate the bacteria and Dr. Agramonte the pathological anatomy of yellow fever.

Maj. Reed at this time returned to Washington for the purpose of completing the report upon "Typhoid Fever in the Army," in collaboration with Drs. Shakespeare and Vaughan.

Lazear began to breed, dissect, classify, and infect mosquitoes, in which work Carroll and Agramonte took little or no part. Now and then Lazear would apply them to whoever allowed it. Most of the mosquitoes died early in captivity. Lazear, Carroll, and several other persons had been bitten several times by mosquitoes which previously had fed on yellow fever blood, without result, so that the theory of mosquito transmission was gradually being discredited, until Carroll fell sick, on the 30th of August (1900), entirely innocent of the real nature of his illness.

Suspecting the origin of his infection and its real gravity, Drs. Lazear and Agramonte decided to test the mosquito which presumably had caused Carroll's attack by applying it to the first nonimmune individual who might allow it.

Therefore, on the afternoon of August 31, the same mosquito and three others, were applied to an American soldier who had not left Columbia Barracks (which was free from yellow fever) for 57 days prior to his inoculation; nor did he go out of said reservation before he fell sick with yellow fever, five days afterwards, thus confirming in our minds the fact that he had been infected by the mosquito bites.

Dr. Carroll being at this time still suffering from a severe attack of the disease, Drs. Lazear and Agramonte decided to communicate these results to Maj. Reed, who was yet in Washington.

Before Maj. Reed's arrival in Habana, Dr. Lazear became infected with yellow fever, his death taking place on the 25th of September.

During Carroll's convalescence, the board decided that the results of the investigation were so far sufficiently convincing to justify their presentation, in the shape of a preliminary note, before the coming meeting of the American Public Health Association at Indianapolis, Ind. (October, 1900).

Maj. Reed went north for this purpose, and while Carroll took a short vacation, to recuperate from his recent attack, Dr. Agramonte was charged with breeding and infecting mosquitoes, keeping them at the division laboratory, which was under his care in Habana, in preparation for the work which the board intended to carry out after the Indianapolis meeting.

When Maj. Reed returned from the States, moral and material aid was obtained from Gen. Leonard Wood, commanding the division, and we determined to carry out an investigation exclusively based upon the mosquito theory sustained by Finlay; we knew nothing of Beauperthuy then, who in 1853 had defended practically the same theory.

While the experimental station, afterward named Camp Lazear, in honor to the memory of our deceased colleague, was being established, the care of the mosquitoes and their infection by applying them to yellow-fever cases, was in the hands of Dr. Agramonte, at the division laboratory; when the permanent "mosquito building" was erected at Camp Lazear (Dec. 1, 1900), these mosquitoes were turned over to Dr. Carroll for his care. It devolved then upon Dr. Agramonte to select the mosquitoes from those kept by Dr. Carroll and apply them to nonimmunes, as well as to make all subsequent direct inoculations, and to obtain the nonimmunes (Spaniards) for the purpose, until the end of the work in Cuba.

Let me add that the best friendship existed between all the members of the board, and from the beginning of their work it was agreed that the honor of the results was to be shared by all alike, as the labor was so evenly shared. Unfortunately this has not been the case, let us hope through no fault of the members themselves. Drs. Reed and Carroll had been connected in laboratory work for several years, and Dr. Agramonte had also worked at the Army Medical Museum Laboratory; Drs. Lazear and Agramonte were classmates, having graduated from the College of Physicians and Surgeons, New York, in June 1892.

I certify to the absolute truth of the above statement.

In testimony whereof I affix my signature in the city of Habana, August 31, 1908.

ARISTIDES AGRAMONTE, M. D.

1. Maj. Walter Reed, surgeon, United States Army, died in Washington, D, C., from appendicitis, November 23, 1902, aged 51. His widow, Emilie Lawrence Reed, is receiving a pension of $125 a month.

2. Maj. James Carroll was promoted from first lieutenant to major by special act of Congress March 9, 1907. He died in Washington, D. C., of myocarditis, September 16, 1907. His widow, Jennie H. Carroll, since his death has received an annuity of $125 a month, appropriated from year to year in the Army appropriation bill.

3. Dr. Jesse W. Lazear, contract surgeon, United States Army, died at Camp Columbia, Cuba, of yellow fever, September 25, 1900. His widow, Mabel M. Lazear, since his death has received an annuity of $125 a month, appropriated from year to year in the Army appropriation bill.

4. Dr. Aristides Agramonte is the only living member of the board. He is professor of bacteriology and experimental pathology in the University of Habana and has never received, either directly or indirectly, any material reward for his share in the work of the board.

5. The name of the American soldier, XY, who was the subject of the second experiment, was concealed at the time, because the experiment was made without military authorization. It has been recently ascertained to be William H. Dean, private, Troop B, Seventh Cavalry. He has never received any reward. He was discharged August 17, 1902, by reason of expiration of term of service, and there is no further record of him at the War Department. His residence at enlistment was given as Grand Rapids, Mich. His case has special importance as having been the first experimental case which was complete in the matter of control, for Dr. Carroll's, which came four days earlier, was defective, by reason of his going into the infected zone during the period of incubation.

6. John R. Kissinger, private, Hospital Corps (see p. 6, President's message). Kissinger volunteered for service at the beginning of the Spanish War in Company D, One hundred and fifty-seventh Indiana Volunteers, and after his discharge enlisted in the Hospital Corps. After the first secret experiments of the board, which included the cases of Dr. Carroll and Pvt. Dean, became known and the experimental camp was established and named Camp Lazear, Kissinger and Moran were the first to volunteer as subjects for experiment. Moran was first bitten, but Kissinger was the first to be attacked, on December 8, 1900. He recovered and was afterwards promoted to be acting hospital steward, and discharged November 14, 1901, at Columbia Barracks, Cuba. It is understood that his health afterwards failed so that he became entirely dependent upon the labor of his wife for support. He was pensioned at the rate of $12 per month, by the act of March 2, 1907. This amount is considered quite inadequate either for his support or as a recognition of his services. A bill granting an increase to $125 per month was favorably reported and incorporated in Senate bill 6272 and passed the Senate February 15, 1910, but was objected to by the Committee on Pensions of the House of Representatives. The report of the Senate committee (No. 574) is inclosed.

7. John J. Moran (see p. 6, President's message). Mr. Moran has never received any material reward for his most creditable services. After leaving Cuba he completed his education by a course of study at the University of Virginia, and is at present living at Panama, in the employ of the Isthmian Canal Commission. He is at present an applicant for appointment in the Consular Service for which, by reason of his excellent knowledge of Spanish and other qualifications, he is well fitted.

8. Levi E. Folk, private, Hospital Corps, volunteered to be bitten by infected mosquitoes and was taken with yellow fever January 23, 1901. He is still in the military service, and is a sergeant, Hospital Corps, stationed at the recruit depot, Columbus Barracks, Ohio.

He received a donation of $300 from the appropriation made by Gen. Leonard Wood for these experiments.

9. Clyde L. West, private, Hospital Corps, volunteered to be bitten by infected mosquitoes at Camp Lazear, and was taken sick with yellow fever February 3, 1901. He was discharged from the service July 10, 1902, at Fort Myer, Va., and his subsequent address is unknown. He received a donation of $200 from the appropriation made by Gen. Leonard Wood for these experiments.

10. James L. Hanberry, private, Hospital Corps, volunteered to be bitten by infected mosquitoes, and in consequence, was taken sick with yellow fever at Camp Lazear February 9, 1901. He deserted the service April 4, 1902, at the general hospital, Washington Barracks, D. C. His subsequent address is unknown. He received a donation of $300 from the appropriation made by Gen. Wood for these experiments.

11. Charles G. Sontag, private, Hospital Corps, volunteered to be bitten by infected mosquitoes, and was in consequence taken sick with yellow fever at Camp Lazear February 10, 1901. He was discharged from the service December 12, 1901, at Columbia Barracks, Cuba, and his subsequent address is unknown. He received a donation of $200 from the appropriation made by Gen. Leonard Wood for these experiments.

12. Warren Gadsden Jernegan, private, Hospital Corps, was infected with yellow fever by the injection of blood, and taken sick January 8, 1901. He was discharged November 16, 1901, at Columbia Barracks, Cuba. Address given, care of M. A. Fowler, McMeekin, Fla. He received a donation of $300 from appropriation made by Gen. Wood for these experiments.

13. William Olsen, private, Hospital Corps, was infected with yellow fever by injection of blood, at Camp Lazear, and taken sick January 11, 1901. He was discharged November 15, 1901, at Columbia Barracks, Cuba. Address given, care of C. Olsen, Plum City, Wis. He received a donation of $200 from the appropriation made by Gen. Wood for these experiments.

14. Wallace W. Forbes, private, Hospital Corps, volunteered to be infected with yellow fever by the injection of blood, at Camp Lazear, and became sick January 24, 1901. He was discharged March 1, 1905, at Fort Hancock, N. J. Address given, care of J. W. Forbes, Minneapolis, Minn. This soldier received a donation of $200 from the appropriation made by Gen. Wood.

15. John H. Andrus, private, Hospital Corps, volunteered and was infected with yellow fever by injection of blood, at Camp Lazear, and became sick January 28, 1901. He was discharged April 24, 1902, at Camp Geo. H. Thomas, Chickamauga, Tenn. His subsequent address is not known. He received a donation of $200 from the appropriation made by Gen. Wood.

16. John R. Bullard, native of Massachusetts, a graduate of Harvard University, where he was a distinguished athlete, and engaged in farming in Cuba, volunteered and was infected with yellow fever by the injection of blood. He became sick October 23, 1901.

17. Paul Hamann, private, Twenty-third Company, Coast Artillery, volunteered and was infected with yellow fever by injection of filtered blood serum and became sick October 19, 1901. He was discharged

July 19, 1902, by reason of expiration of term of service. His address given at time of enlistment was care of August Hamann, Moline, Ill. Present address not known. This soldier received a donation from the appropriation made by Gen. Wood for these experiments.

18. Albert W. Covington, private, Twenty-third Company, Coast Artillery, volunteered and was infected with yellow fever by injection with filtered blood serum and became sick October 19, 1901. He is still in the service, and is serving as sergeant, Twenty-third Company, Coast Artillery Corps, at Fort McKinley, Portland, Me. He received a donation from the appropriation made by Gen. Wood for these experiments.

19. Dr. Robert P. Cook (see President's message, p. 7). Dr. Cook entered the medical service June 9, 1900, as contract surgeon, from the State of Virginia. He left the service at his own request, December 22, 1904. His present address is Winchester, Va.

The demonstration made by Dr. Cook and the men with him that yellow fever could not be transmitted by infected clothing and other inanimate objects was of the utmost importance to commerce and has immensely simplified the preventive measures to be taken against this disease. He was shut up in a house with infected bedding for 20 days, together with the following privates of the Hospital Corps, who received a donation of $100 each from the appropriation given by Gen. Wood for these experiments:

20. Edward Weatherwalk. Discharged the service December 12, 1901, at Columbia Barracks, Cuba. Subsequent address not known. He received a donation of $200.

21. James Hildebrand. Still in service as private, first class, Hospital Corps; stationed at the recruit depot, Columbus Barracks, Ohio. He received a donation of $100.

22. Thomas M. England. Still in service as sergeant, first class, Hospital Corps; stationed at Fort Ward, Wash. He received a donation of $100.

In addition to these, Pvts. Folk, Jernegan, and Hanberry underwent the exposure to infected bedding prior to being bitten by the infected mosquitoes.

Additional experiments by Maj. W. C. Gorgas and Dr. John Guiteras, at Las Animas Hospital, Cuba (see vol. 111, p. 386, civil report of Gen. Wood, 1901):

(1) Vergera; Spaniard. Infected by mosquitoes February 23, 1901; recovered.

(2) Carro; Spaniard. Inoculated by infected mosquitoes August 8, 1901; died.

(3) Represas; Spaniard. Infected by mosquitoes August 8, 1901; recovered.

(4) Campa; Spaniard. Infected by mosquitoes August 9, 1901; died.

(5) Taylor, John R.; Englishman. Infected by mosquitoes August 13, 1901; recovered.

(6) Miss Clara Louise Maass, of East Orange, N. J., aged 25. Trained nurse in Las Animas Hospital. She served as trained nurse in Medical Department of the Army during the Spanish War. She volunteered and was bitten by infected mosquitoes August 14, and died of yellow fever August 18, 1901.

(7) Varela; Spaniard. Infected by mosquitoes August 14, 1901; recovered.

(8) Alonso; Spaniard. Infected by mosquitoes August 22, 1901; recovered.

(9) Castillo; Spaniard. Infected by mosquitoes September 16, 1901, by Dr. Carroll; recovered.

(10) Semil; Spaniard. Infected by mosquitoes November 17, 1901; recovered.

The amount of the donations received by these volunteers is not known.

There were 22 cases of experimental yellow fever produced by Reed, Carroll, and Lazear, and 10 in the experiments carried on in Habana by Gorgas and Guiteras. There were also 7 persons who underwent the very trying experiment of sleeping in infected bedding.

It has been impracticable to make a complete list of the persons who submitted to the bites of mosquitoes but who failed to become infected, although it must be recognized that in many cases these exhibited as high a degree of courage as those who suffered an attack of yellow fever.

It is hoped that the Senator will be able to obtain the consent of Congress to the erection of a monument which will be worthy of Maj. Reed, who conceived and carried out in so admirable a manner these epoch-making experiments, and to the assistants who shared in his labors and to the persons who offered their bodies for these dangerous experiments.

Very respectfully,

GEO. H. TORNEY,
Surgeon General, United States Army.

Hon. ROBERT L. OWEN,
United States Senator, Washington, D. C.

[Senate Report No. 574, Sixty-first Congress, second session.]

The Committee on Pensions, to whom was referred the bill (S. 7252) granting an annuity to John R. Kissinger, have examined the same and report:

A bill granting an increase of $125 per month to John R. Kissinger, the applicant herein, was favorably reported by your committee and incorporated in Senate bill 6272 at this session and passed the Senate on February 15, 1910.

The Senate report No. 210, which contains a very full statement of the services of this soldier and the grounds upon which his right to increase of pension is recognized, is as follows:

S. 4479. John Kissinger, the claimant, was one of the bravest of soldiers who served in the Spanish-American War. For exhibition of moral courage his submission to inoculation of yellow fever seems unsurpassed. He is now a helpless paralytic, unable to walk, and he is totally disabled for any kind of employment, his ailment being myelitis, or disease of spine, and is the result of experiments made upon him when he volunteered to become a subject for experimental purposes in the yellow-fever hospital in Cuba. At the time he made the sacrifice he was a private in the Hospital Corps of the Army, in which he enlisted November 15, 1898. When he was finally discharged from the hospital, he was appointed an acting hospital steward and served as such until the date of his discharge, November 14, 1901. Previous to his enlistment he served in Company D, One hundred and fifty-seventh Indiana Volunteer Infantry, from April 28, 1898, to November 1, 1898, having enlisted immediately at the breaking out of the war with Spain, and in response to President McKinley's call for troops.

The commission that investigated the mosquito theory of transmission of yellow fever in the fall of 1900 was composed of Drs. Walter Reed, James Carroll, and Jesse W. Lazear. From a book entitled "Walter Reed and Yellow Fever," by Howard A. Kelly, professor of surgery of the Johns Hopkins University, published in New

York by McClure, Phillips & Co., on page 139, is the following paragraph in regard to this soldier:

"The subject of the first experiment was a young private from Ohio, named John R. Kissinger, who volunteered for the service, to use his own words, 'solely in the interest of humanity and the cause of science.' When it became known among the troops that subjects were needed for experimental purposes, Kissinger, in company with another young private named John J. Moran, also from Ohio, volunteered their services. Dr. Reed talked the matter over with them, explaining fully the danger and suffering involved in the experiment should it be successful, and then, seeing they were determined, he stated that a definite money compensation would be made them. Both young men declined to accept it, making it, indeed their sole stipulation that they should receive no pecuniary reward, whereupon Maj. Reed touched his cap, saying respectfully, 'Gentlemen, I salute you.' Reed's own words in his published account of the experiment on Kissinger are: 'In my opinion this exhibition of moral courage has never been surpassed in the annals of the Army of the United States.'"

Dr. Lazear died of yellow fever in Cuba at that time. Dr. Carroll died later of disease resulting from yellow fever contracted during his experiments with that trouble. Dr. Walter Reed is also dead, and the widows of these three men have all been remembered by the Government in an annuity of $125 per month. On account of the death of these doctors, soldier is unable, of course, to furnish any further evidence from them, but his volunteer submission to inoculation from infected mosquitoes is a matter of record in the archives of the War Department.

He is now receiving a pension of but $12 per month, and he can obtain no further relief because he is unable to furnish direct testimony tracing his present grievous condition back to yellow fever in the Army, although there is but little doubt that the relation of the cause and effect exists. Since his discharge he has never been in good health, which he at first attributed to slow recovery from that disease, thinking that with the passing of time his constitution would enable him to throw it off. He continued to fail, however, and is now a helpless paralytic. In the meantime he had married, and is now supported by his small pension and laundry work done by his wife and contributions to his support by a few people who appreciated his services to humanity.

A bill to grant him a pension of $30 per month passed the House during the session of the Fifty-ninth Congress, but by mistake the rate was cut to $12 per month, at which amount it was finally approved. In his present helpless condition it is believed that he is entitled to a highly substantial measure of relief, his disability seemingly being due to causes of service origin.

In view of the fact that a pension or annuity of $125 per month was granted to the widows of Drs. Lazear and Carroll, who conducted these experiments with yellow-fever infected mosquitoes, and who died as a result of being infected by mosquitoes, your committee are of the opinion that as great consideration should be given to the man who braved the danger and who, while he escaped with his life, is so helplessly crippled that he is unable to do anything to care for himself, as to the widows of Drs. Lazear and Carroll. Your committee therefore recommend in this case a pension or annuity of $125 per month.

The bill went to the House and was referred to the Committee on Pensions. There the paragraph increasing the pension to the applicant herein was objected to as carrying a rate in excess of that allowed to any other private soldier and, regarded simply as a pension and without distinguishing language, establishing a vexing precedent.

The facts in this case are exceptional and extraordinary. To meet the exceptional case and obviate the objections the pending bill recites the peculiar circumstances that distinguish the case and proposes an annuity of $125 per month, payable by the Secretary of War in the same manner as the same allowances are now paid to the widows of Drs. Carroll and Lazear. In view of the unprecedented facts in the case and the extraordianry services rendered by the soldier, your committee believe he should receive the same recognition accorded the widows heretofore mentioned. The bill is therefore reported back favorably with a recommendation that it pass.

Chapter 5.

IN MEMORIAM.

DR. WALTER REED, MAJOR AND SURGEON, UNITED STATES ARMY.

Whereas the Medical Society of the District of Columbia has sustained an irretrievable loss by the death of Walter Reed, who died at 2 p. m., November 23, 1902, from appendicitis, for which an operation had been performed five days before:

Be it resolved,[1] That in the death of Dr. Reed, the medical society has lost one of its most distinguished members, whose best efforts were always at its disposal and upon whom it had learned to rely as an able, calm, and accurate exponent of scientific medicine.

Maj. Reed was born in Gloucester County, Va., September 13, 1851, and was a graduate of the medical department of the University of Virginia, 1869, and Bellevue Hospital Medical College, 1872. He was appointed assistant surgeon, United States Army, June 26, 1875; promoted assistant surgeon, with the rank of captain, June 26, 1880; surgeon, with rank of major, December 4, 1893, and at the time of his death was first on the list of majors in the Medical Department.

He served with distinction as medical officer at various Army posts in the Far West, and as his skill and devotion extended to both officers and enlisted men alike, he endeared himself to all classes in the command.

During his service at Fort McHenry, Md., in 1881, and again while attending surgeon and examiner of recruits at Baltimore, from October, 1890, to October, 1891, he made special studies in bacteriology and pathology at the Johns Hopkins Hospital, and after a tour of service at Fort Snelling and St. Paul, he was selected by the Surgeon General, in August, 1893, as curator of the Army Medical Museum, where he continued his studies which ultimately secured for him fame and distinction.

During the Spanish-American War he was president of the board of medical officers to investigate and report on the prevalence of typhoid fever in the Army, and the commission, strongly impressed with the agency of flies as carriers of this disease, recommended the collection of excreta in galvanized-iron tanks, which method was adopted and was followed by a cessation of the disease.

His greatest achievement for science and humanity was his contribution to the cause, spread, and prevention of yellow fever. Starting from Finlay's theory of the agency of the mosquito in the dissemination of this disease, the commission of which Dr. Reed was the head made a series of painstaking experiments and demonstrated conclusively the causal relation of *Stegomyia fasciata* to yellow fever epidemics and disproved the theory that the disease could be conveyed in *fomites*, or that it was contagious in the ordinary acceptation of the term.

[1] The preamble and resolution were adopted December 3, 1902.

The practical value of this discovery, which in point of importance and far-reaching beneficence ranks only second to Jenner's discovery of vaccination, has been proved by the complete eradication of this scourge from Habana.

Maj. Reed has demonstrated how to rid the world of yellow fever, but his studies as to the etiology of the disease were interrupted by his untimely death; he had, however, arrived at the conclusion that the disease was not due to Sanarelli's *Bacillus icteroides*, but was probably caused by some ultramicroscopic organism. Dr. Reed was a clear, forceful writer and speaker; all of his facts were collected with the utmost care and presented in a concise, logical, and convincing manner, and his crowning work shows the highest degree of scientific accuracy, combined with calm judgment and discrimination, qualities which are not only of the utmost importance in searching the causes of epidemic diseases and tracing their progress, but which would have also fitted him for the highest position in his corps.

In every sphere of activity, whether as a medical officer, author, teacher, or investigator, he has acquired a distinction which rightly places him in the first rank of illustrious American physicians. His labors in behalf of science and humanity have been recognized by Harvard, Ann Arbor, and the American Medical Association, and he has borne his honors with accustomed modesty and innate dignity. Dr. Reed was singularly free from all mean self-interest and ambition, and was ever ready to give full credit to his colleagues for their share of the work which made him famous. We have simply to recall his glowing tribute to that brave young soldier Kissinger, from Ohio, who on December 5, 1900, was the first to volunteer to be bitten by infected mosquitoes, with the only provision that he should receive no pecuniary reward, since as he expressed it, he was actuated "solely in the interest of humanity and the cause of science." Such exhibition of moral courage, in the opinion of Dr. Reed, has never been surpassed in the annals of the Army of the United States, and we will add, could never have been inspired except by a man of Dr. Reed's greatness.

His lips are silent; no longer will the sound of his musical but decisive voice be heard within these walls, nor his personal magnetism and discerning mind delight, instruct, and charm his listeners, but his deeds will live and his example will be an inspiration to the present and future generations.

Dr. Reed's death in the prime of life, in the zenith of his distinguished career, is a severe blow to scientific medicine, his corps, and the medical profession which he adorned. This society, while expressing the sincerest grief at the loss of our distinguished associate, whose personal qualities commanded our highest friendship and respect, is not unmindful of the irreparable loss sustained by his beloved family, to whom we beg to offer our heartfelt sympathy in the hour of their great affliction, united with the fervent hope that a grateful Nation will recognize the economic value of Dr. Reed's discovery and make adequate provision for those who were dependent upon him for support.

GEO. M. KOBER,
D. K. SHUTE,
F. S. NASH,
Committee.

79965°—S. Doc. 822, 61-3——3

MEMORIAL MEETING OF THE MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, HELD DECEMBER 31, 1902.

INTRODUCTORY ADDRESS BY SAMUEL S. ADAMS, A. M., M. D., PRESIDENT.

Ladies and gentlemen: Once more we have been called together to pay tribute to the memory of an honored colleague, whose counsel we have enjoyed for nearly a decade. The possessor of a striking personality, unusual reasoning power, an unbiased judgment, and a determination to enforce his convictions, Dr. Walter Reed could not fail to adorn and stimulate this scientific body as well as the military service of the United States Army. The aged die, and we wonder not, believing that they have fulfilled their mission; but when a colaborer in the prime of life, at the height of his usefulness, is cut down before he has had time to enjoy the full fruition of his labors, we marvel, we are lost in wonder.

Dr. Reed was elected a "member by invitation" March 14, 1894. The preceding meeting, however, he made his first appearance in this society, having been invited to open the discussion on Dr. Kinyoun's paper, entitled "The prevention and control of diphtheria." In reverting to this debate, we can recall his modest demeanor, his convincing arguments, and his power to hold his audience throughout a lengthy presentation of the subject. He began by saying that his clinical experience, laboratory work in inoculating animals, and bacteriological studies had led him to certain ideas as fixed convictions:

1. The Klebs-Loeffler bacillus is usually characterized by a deposit of false membrane in the throat and is attended by frequent fatal sequelæ. This bacillus he believed to be the cause of true primary diphtheria.

2. That diphtheria is local in the beginning and by the production of virulent toxins tends to become rapidly constitutional. The bacilli themselves have been found in the internal organs of the human subject, as well as in those of animals. So that we can not any longer say that the bacilli remain local throughout the attack.

3. Diphtheria is not spread by water and food, except by milk and its products, which are infected in transitu. He strongly advocated the bacteriological examination in making the diagnosis.

Two months later, in discussing tuberculosis, he dwelt upon these two points: "The possibility of the transference of tuberculosis by vaccination; and the possibility of its transference from mother to child in utero."

January 9, 1895, in discussing diphtheria and its treatment by its antitoxin, he said he believed the production of antitoxin should be under municipal control and be tested by disinterested parties so as to avoid imposition by unscrupulous men whose desire is gain. He lived to see the enactment of a law to protect this community from spurious viruses. He had witnessed the wonderful immunizing effects of antitoxin, so advised its use as a preventive as well as a curative agent.

His masterly hand struck the death blow to the opponents of antitoxin in the discussion of "The clinical aspects of diphtheria treated by its antitoxin," December 4, 1895.

A clinician of wide experience and recognized ability, while disclaiming any unfriendliness toward its use, had taken a decided stand

against this serum, basing his remarks upon the statistics and arguments of a distinguished English laryngologist and a well-known American pediatrist. It seemed as if the pendulum were swinging toward the opposition when Walter Reed entered the forum—majestic, fearless, determined to conquer. With keen eyes fixed on his principal antagonist, he hurled his weapon of defense in unmistakable language, when he said:

> You are theorizing while we are dealing with facts. If another friend of antitoxin arises and deals it such blows as Dr. ——— has given it, the antitoxin serum will be slaughtered in the house of its friends.

In concluding his remarks, came this appeal:

> I myself almost feel like saying, with the reader of the paper, that the failure to use it in a case of human diphtheria is criminal; and I beg of you, that if you have not yet done so, when you next stand by the bedside of your patient afflicted with this disease, you do not, through any fear of its peculiar action, withhold this invaluable remedy.

It must have been a great satisfaction to him to witness not only the conversion of his opponents, but the universal use of the antitoxin of diphtheria.

His paper entitled "What credence should be given to the statements of those who claim to furnish vaccine lymph free from bacteria?" is worthy of praise. He conducted a series of experiments upon monkeys by vaccinating them with various vaccine matter, and was "convinced that all virus contained bacteria and that bacteria-free lymph did not exist."

It is a singular coincidence that the last appearance of Dr. Reed in this society was at a memorial meeting, when he eulogized as an author his friend and associate, Dr. W. W. Johnston.

The Medical Society of the District of Columbia is proud of having had the friendship of Walter Reed; we gloried in his achievements, and we now mourn the loss of a courteous, industrious, famous, and highly honored member.

HISTORICAL REMARKS, BY MEDICAL DIRECTOR R. A. MARMION, UNITED STATES NAVY.

Mr. President and members of the Medical Society of the District of Columbia: Walter Reed was born in Gloucester County, Va., on the 13th of September, 1851, and was the son of Rev. Lemuel Sutton Reed, who was for 40 years or more an eminent Methodist minister. In his personal appearance Walter was highly favored even in his youth, and to this there were added a gentleness of disposition and a graciousness of manner which won for him the admiration of all who were brought in contact with him—qualities which we know were characteristic of him ever after. Intellectually he was, as a boy, precocious and devoted to study, so that at the age of 15 he had acquired a knowledge of Latin and Greek rarely found in one so young. History, literature, and philosophy were also favorite studies, and his familiarity with them rendered him the peer of many who were his seniors in age by several years.

By a special dispensation he was matriculated in the academic department of the University of Virginia at the age of 16. He quickly attained and held, throughout that first year, the highest standing in his classes. Owing, however, to the limited means of his father, who was maintaining two other sons at the same school, it became evident to Walter that he would not be able to carry out his original plan of completing the academic course; so, at the beginning of the following

year he began the study of medicine, and at the end of one session of nine months he was awarded the degree of doctor of medicine, although he was not yet 18 years of age. This feat he accomplished in spite of the advice of friends who had, in advance, sought to dissuade him from undertaking it. His only reply to such advisers was that "he did not fear the result." In a few months after his graduation at the University of Virginia he went to New York and matriculated at the Bellevue Medical College, and in one session acquired the degree of M. D. Following his graduation at Bellevue he was attached to various hospitals in New York and Brooklyn, conspicuously the Brooklyn City Hospital and the Charity Hospital on Blackwell's Island; at the latter he devoted himself especially to the study of the diseases of women and children. He was also for awhile, one of the physicians to the poor of New York City. During his Brooklyn life he had attracted the attention of Dr. Joseph Hutchinson, one of the most prominent medical men of that city, who urged and secured his appointment as one of the five inspectors of the board of health—a position much sought after in those days. This post he was filling most creditably when his twenty-first birthday dawned. Even at this early date, Dr. Reed had acquired a very enviable standing among the medical men of New York and Brooklyn, among whom he was especially well known for his skill as a surgeon. Within a few years, as we have seen, he had been holding various professional positions of responsibility, but he could not help feeling that there was a point beyond which he could not go on the road toward that success which he coveted, without the influence of wealthy friends and of influential social connections on the spot. Thus it was that in 1874 he began to think seriously of entering the Medical Corps of the Army or of the Navy, and, by the spring of 1875, he had chosen the Army as the field of his future labors.

I can not dismiss this part of my subject without pausing for a moment to weigh certain characteristics of our lamented colleague and, first of all, I would advert to the fact that even in his boyhood years there shone forth so many of the splendid traits which illustrated his after life; he was fired with ambition and sustained by an indomitable energy in his early student days which invariably brought him victory; but his innate tenderness of nature and his exquisite regard for the sensibilities of a disappointed contestant so dominated him at such times that no one ever knew him to boast of his victory. A deference for the opinions of others, too, was always a prominent characteristic; and this we have seen evinced so uniformly in the discussions taking place at meetings of this society. And so I might go on analyzing and dwelling upon other traits, but the limited time prevents me.

Turning to the military history of Maj. Walter Reed, as borne upon the records of the office of the Surgeon General of the Army, we find that he was appointed assistant surgeon with the rank of first lieutenant June 26, 1875; promoted to be assistant surgeon with the rank of captain June 26, 1880; surgeon with rank of major December 4, 1893; and at the time of his death was first on the list of majors in the Medical Department.

He was on duty in the Department of the East from July 23, 1875, to May 21, 1876; in the Department of Arizona from June, 1876, to May, 1880; again in the Department of the East from September,

1880, to November, 1882. From November, 1882, to July, 1887, he was attached to the Department of the Platte, and from August, 1887, to October, 1890, he was on duty at Mount Vernon Barracks, Ala. His next assignment was to duty in Baltimore, Md., from October, 1890, to October 1891, when he was transferred to the Department of Dakota, where he remained until August, 1893, when he was ordered to duty in the office of the Surgeon General of the Army. Under this assignment he was curator of the Army Medical Museum and member of the faculty of the Army Medical School for over nine years and up to the date of his death, which occurred in this city November 23, 1902.

In the meantime, too, he served, at several different periods, as member of the Army Medical Board in this city, was a member of the cholera board in July, 1898; was on detached duty making inspections of camps and field hospitals in August, 1898; was member of the typhoid fever board in August, September, and October, 1898; in October, 1898, he was on inspection duty at Natural Bridge, Va., and again in April and May, 1899, at Puerto Principe, Cuba. In March and April, 1900, he was ordered to investigate and report upon the use of electrozone and germicides at Tampa and Habana, and in June and July, 1900, was a member of a board of medical officers at Camp Columbia, Cuba, for the purpose of scientific investigation with reference to infectious diseases prevalent in Cuba, and, from September 27 to October 13, 1900, on similar duty with regard to yellow fever. These various assignments were of great importance from the standpoint of preventive medicine and did much to solidify the foundation on which he was destined to erect the structure "more lasting than brass" which to-day towers above the many works of a life full of labors for the benefit of his fellow man.

It seems to me that I can not better close this paper than by quoting the language of the official record of Maj. Reed as drawn from the files of the Surgeon General's Office:

Of Maj. Reed's work in the Medical Department and his scientific researches, it is probable a complete history can never be obtained. His eminence as a bacteriologist, and in practical hygiene as applied to military life (as a student of all forms of bacteria) led to his being intrusted with special investigations, which were interrrupted by his death, and which, it is now believed, will never be completed. He was regarded by his associates as a man who combined an unusual degree of scientific accuracy with calm judgment, which rendered him invaluable in searching out the causes of epidemic diseases and tracing their progress.

In 1901 he began the investigation of the cause and the prevalence of yellow fever, conducting his investigations at Quemados, near Habana, where he established headquarters and was given every facility for conducting his experiments.

The conditions in Cuba in 1901 were such as made the investigations of Maj. Reed and his corps of assistants of special moment. An epidemic of yellow fever existed despite the efforts of the sanitary experts, led by Gen. Wood, who were endeavoring to stamp out the disease. The houses of persons infected were subjected to rigid disinfection. Furniture was destroyed and every possible precaution was taken to prevent the spread of the disease under the old treatment. Maj. Reed became convinced that proper sanitation was not all that was needed. He believed that some other agency than accumulations of filth was responsible for the spread of the disease, and his attention was attracted to the fact that it took much longer for a house to become infected than the usual time of incubation. This suggested a biting insect as an intermediate host of the parasite, and he asked and promptly received from Gen. Wood permission to make experiments with mosquitoes as the conveyers of yellow fever, and a liberal supply of money for these experiments. It was thus determined beyond question that through a certain species of mosquito the yellow fever germ was disseminated.

In recognition of this precious work the degree of master of arts was conferred upon Maj. Reed by the Harvard University in June, 1902, because, as President Eliot stated when the degree was awarded, Maj. Reed had demonstrated how to rid the world of yellow fever. About the same time the degree of LL. D. was conferred upon him by the University of Michigan at Ann Arbor, Mich.

MAJ. REED AS A MEDICAL OFFICER, BY MAJ. J. R. KEAN, SURGEON, UNITED STATES ARMY.

In speaking of Dr. Reed as a medical officer we should consider especially that part of his career with which the members of this society are least familiar, namely, from his entrance into the Army in 1875 to his assignment to duty in Washington in 1893. With the latter date began his career as a scientific man, although much of his time during this last decade was given to examining boards and other work of a military rather than scientific character, and the race horse spent much time at the plow.

These 18 years of garrison duty were, we may be sure, not wasted, yet the official records tell but little of them. The records show 15 changes of station (with 4 years in Arizona, 5 in the Department of the Platte, 2 in the Department of Dakota, 3 in the South, and 3 in the East). There are a few brief commendations for professional zeal and devotion to his patients, and that is all.

The work of young Army surgeons claims always little space in the gazettes or in the reports of military commanders, and in the seventies and eighties the life was certainly not stimulating to intellectual effort.

The surgeon shared with his comrades of the line the tedium of long marches and the monotonous sameness of Arizona summers and Dakota winters. And those with whom bonne camaraderie outweighed studious industry shared also the afternoons of bottlepool and beer and the nightly seductions of draw poker. But for medical officers this life was redeemed by the study of our profession, which was then beginning to broaden out from ancient channels into the full flood of recent progress, and it was saved from triviality by those stern responsibilities of life and death which practice brings to all physicians. To lesser minds the limitations of such a life might have been narrowing, but for the eager industry and professional devotion of a Reed they made the roots strike deep; and when we are surprised at the rapid growth and splendid fruit of his career as a scientist we must remember that in the post surgeon's unmarked life the seed was germinated and the roots were firmly set. But for the opportunities given him by his position in the Army, however distinguished he may have become in other ways, it is safe to say that the work with which his fame will always be inseparably connected would never have been accomplished by him. During this long apprenticeship he acquired too that perfect familiarity with the conditions and limitations of Army life which, combined with his scientific knowledge and sound judgment, made him the best sanitary inspector in the Army and the court of last resort on all sanitary questions.

I first learned to know Dr. Reed by reputation when in the spring of 1888 I followed him in station at Fort Robinson, a two-battalion post in the northwest corner of Nebraska. I learned much of his devotion to his patients, and their devotion to him was equally

in evidence. The country about is thinly settled with families locally known as "Grangers," who were attempting to support themselves by farming in a grazing country where the rainfall was not sufficient for good crops except only about one year in three. The crop of babies, however, never failed, and the Klebs-Loeffler bacillus and the pneumococcus flourished perennially in their wretched cabins. To Reed's tender and generous spirit the call of these poor people never came in vain, and the trail was never so long or the night so dark as to deter him. In the winter these rides were really dangerous and a source of much uneasiness to his family and friends for fear of his being overtaken by one of those blizzards in which the staunchest horse turns tail to the wind and the most experienced frontiersman can not see his way, and the danger to the lost traveler is greater than that of a battle.

Again we find him at Mount Vernon Barracks in Alabama, according to the official statement of his commanding officer, devoting himself with the same earnestness and patience to the sick of Geronimo's band of Apaches, then held there as prisoners, and to the sick negroes of the surrounding country, as to his own patients in the garrison.

Of the first years of his service which he spent in Arizona I gained some knowledge when in the summer of 1896 he came to Key West, my station at that time, to study the blood of variola—there being an epidemic of smallpox there at that time. All day he would sit over his microscope, but the evenings we spent on the coolest corner of the porch looking out at the quiet tropical sea, while he told reminiscences, suggested, it may be, by the heat, of his service at Fort Yuma and Camp Apache. These stories were full of that humor which was so characteristic and so pleasing a trait of his daily conversation, and some of these were models of the short story. The history of Sally Ann, a Gila monster (named after the two ladies of the post most conspicuous in church work), which the chaplain captured in his kitchen, and undertook to tame, would have made a perfect magazine article just as Reed told it. His account of his summer at Yuma, the hottest of Army posts, where the daily July maximum was from 112° to 115°, still brings back a clear-cut picture to my memory, and I can see him with his messmate, a captain of infantry, who weighed 250 pounds, and the soldier—or in Army parlance "striker"—who filled the dual rôle of chef and butler. The captain, a vertiable Porthos, sat down to dinner in two garments, with a fan, a towel to wipe his face, and near at hand a pitcher of the largest size full of water from the olla, for there was no ice. Before him was a large roast of range beef, which, after helping Reed, he would consume entirely and likewise empty the water pitcher.

On one occasion Reed took a leave, and, in company with another officer and a lady of the garrison going home, drove in an ambulance 150 miles to the railroad. The other officer was charged with the commission of laying in the food for this trip of nearly a week. After they started they found that the provision consisted simply of crackers and sardines. Reed up to that time had never been able to eat sardines, but he learned on this trip. He had his share also of Indian campaigning, and on one occasion brought into the post a little Indian girl of 4 or 5, who had been so horribly burned that her people had

abandoned her to die. This child he succeeded in saving and brought her up in his family as a nurse for his children in spite of the warning of that keen old Indian fighter, Gen. Crook. When she was grown, the savage Apache blood asserted itself, and she ran away, after giving evidence that 15 years of gentleness and refinement had not modified the cruel and deceitful character of her race.

Memory often holds most fast to trivial things, but they are usually characteristic. So, though what has come into my mind to tell you of our dead friend is not of weighty matters; yet they show the odd vicissitudes of Army life and show him as he was—the pleasant comrade, the eager student, and the devoted doctor, gentle, unselfish, modest, and brave, as the gentle and devoted ever are. Over this earnest spirit and the high purposes of his life played always a merry and kindly humor like the dancing lights and reflections from the surface of a deep, swift river. It was often keen, but never bitter, and was his most striking social characteristic, as was devotion to the duty which was before him the dominant feature of his professional life. For him, as for the great Duke—

> The path of duty was the way to glory.
> He that walks it only thirsting
> For the truth, and learns to deaden
> Love of self, before his journey closes
> He shall find the stubborn thistle bursting
> Into glossy purples, which outredden
> All voluptuous garden roses.
> He that ever follows her commands
> On with toil of heart and knees and hands
> Through the long gorge to the far light, has won
> His path upward and prevailed,
> Shall find the toppling crags of duty scaled
> Are close upon the shining table-lands,
> To which our God Himself is moon and sun.
> Such was he—his work is done.

DR. WALTER REED AS A TEACHER, BY A. F. A. KING, A. M., M. D.

At the time of the organization of the United States Army Medical School, in 1893, Dr. Reed was appointed professor of bacteriology and clinical microscopy, and he continued to fill this position and to perform its duties most acceptably until the time of his decease, in November, 1902.

Two years after beginning his work in the Army Medical School he was elected professor of pathology and bacteriology in the medical school of the Columbian University in this city, and he continued to hold this position also until the end of his life.

If we endeavor to ascertain in a general way what are the requirements necessary for anyone to become a really skilled and successful instructor in any department of knowledge, and then ask ourselves how far Prof. Reed possessed these qualifications, it will at once be seen that the particular attributes necessary were preeminently his own.

To teach well one must know well the subject to be taught, and, conversely, he who can not explain a thing clearly to somebody else does not usually know it well himself.

In the whole domain of medical science there is probably no subject more difficult and intricate than that of pathology, especially

when considered in relation with bacteriology, this latter being also a comparatively new departure, and therefore bristling with the unfamiliar terms of a new and labored nomenclature, as every new science necessarily must be.

Notwithstanding these difficulties, Prof. Reed, with his well-trained mind and cultivated powers of observation, inspired, too, with the spirit of research and led on by the charm of discovering new principles and new facts, had devoted himself with so much ardor, earnestness, and industry to the study of his chosen sphere of thought that, it may be said, all difficulties had been trampled under his feet; that he rose, step by step, to higher and still higher planes of knowledge, until reaching an eminence where the whole subject became easily intelligible in one comprehensive view and where he himself attained a complete mastery of his favorite theme.

Having traversed the highways of knowledge himself he was fully able to lead his pupils along the same paths and perhaps point out to them many short cuts which were easier than the longer distances and more laborious journeys originally pursued by himself. It should be remembered also that many of these roads were not always the well-traveled avenues of old lines of thought, but, on the contrary, entirely new, strange, and perhaps lonely ways, far out in the prairies of investigation, where briars of speculation, weeds of error, and the ignes fatui of false theories were liable to obstruct and mislead the honest seeker for truth. It was under these circumstances that Prof. Reed became a trusted guide and counselor. In these trackless wastes of thought he could not easily get lost or take a wrong direction, for in many instances he was able to say: "I made these paths myself," and he well knew whither they would lead.

The successful teacher, however, must not only possess the requisite knowledge and be able to guide his pupils in the best way, and hold out to them the easiest method of obtaining the information for which they are in search, but he should also have the faculty of presenting the subject in such a manner as to hold their undivided interest and attention by pointing out the attractive features and pleasing aspects of the subject under discussion. Dreary, indeed, would be the road to learning were it always through thorns, thistles, and briars, with no flowers to charm and no vistas in the forest through which we might at times obtain a glimpse of pleasant scenes—of sunshine and beauty. Dreary, and dull too, will be the teacher who continues his endless monotony of tiresome propositions, with no touch of humor and no sparkle of wit to vary the irksomeness of continued effort and awaken the flagging power of a strained attention by the pleasant diversion of an occasional happy thought.

In this particular again Dr. Reed was singularly fortunate. One of his latest admiring pupils writes me that—

> his lectures, besides satisfying the zealous seeker for knowledge, were spiced with humor which was most refreshing, and which made the relation between himself and his students a freer and more sympathetic one.—Donnally.

Indeed, in whatever aspect we review Dr. Reed's work as a teacher and however critically we single out the several qualifications required for the best and most successful execution of the teaching art, we find Prof. Reed happily endowed in a more than usual degree with these special gifts and qualifications, and which he knew full well how to utilize to the best advantage.

During the later years of Prof. Reed's work in the medical school of the Columbian University he was assisted by Dr. James Carroll, of the United States Army, who also accompanied Dr. Reed to Habana, and again assisted him in their well-known experiments with mosquitoes and yellow fever. No one, perhaps, was better acquainted with Dr. Reed's methods of teaching than Dr. Carroll, who kindly writes me as follows:

Dr. Walter Reed was respected and beloved by all his pupils. Always kind and courteous, earnest and enthusiastic, he imbued them with the same spirit, and invariably commanded their respect and attention. A thorough master of his subject and of the English language, he treated the driest and most difficult topics in such a manner as to render them lucid and interesting. His marvelous accuracy and clear conception of every detail, his charming personality and polished manner, made him an ideal professor, of whom his students were both fond and proud. Of nervous temperament, he was quick to note and resent the slightest laxity and inattention; and when it became necessary to administer a rebuke it was implied rather than given directly, his delicacy of feeling prompting him to soften the blow by a subtle flash of wit that convulsed the class and diverted attention from the culprit. The lesson was never forgotten by him for whom it was intended, and it was never necessary to repeat it, for the moral effect of the slightest manifestation of his displeasure was far greater than could have been the dread of any other method of reproof. So closely was he in sympathy with his class and so securely had he engrafted himself upon their affections that their inquiries during his illness and manifestations of grief upon his demise indicated the loss of a dear friend, guide, and counselor rather than a teacher of cold scientific facts.

Another pupil, Capt. J. Hamilton Stone, assistant surgeon, United States Army, writes me as follows:

As a teacher Dr. Reed always seemed to me to be, first of all, master of his theme. His information was so much his own—a part of him, as it were—that when it was given to others it flowed forth with unadulterated naturalness, and sparkled with a keen interest which his charming personality could not help but lend it. These qualities would not permit his words to fall upon deaf ears. His kindly and considerate mien, together with his universally acknowledged high scientific attainments, won for him both the respect and admiration of his students. His language was always interesting, eloquent, and well appointed. When at his best his voice would reach a high falsetto note, and this was his characteristic method of impressing important facts upon dull or indurate intellects. His students never feared him, but from the start regarded him with filial affection. Of patience, that special attribute of a good teacher, he possessed an abundance. He was constantly at the side of his pupil in the laboratory, advising, consoling, encouraging, and, above all, instructing.

A student of the Columbian University, Mr. H. H. Donnally, remarks that—

Dr. Reed's lectures were models of order and system. A recital of the various views previously held in the different branches of pathology and bacteriology always led up to and served to emphasize the more recent and generally accepted theories. In these historic reviews the student was constantly surprised at Dr. Reed's remarkable memory for dates and his familiarity with the host of investigators and their several special lines of research, not only those in this country, but others in all parts of the civilized world. This method of unfolding the subject historically, with a final and forcible exposition of the latest current views, was keenly appreciated by the students and gave them a broad and comprehensive picture of the whole subject, which was easily remembered and understood.

Finally, I must express my great regret that it has seldom fallen to my lot to hear Dr. Reed lecture, and I have never witnessed his demonstrations in the laboratory; hence I have supplemented my own remarks by quoting from others who had happily been more favored in these respects, and certainly no statements of mine could more appropriately represent the work of Prof. Reed as a teacher than these eloquent expressions from his own faithful and loving pupils.

DR. WALTER REED AS AN AUTHOR, BY CH. WARDELL STILES, PH. D., ZOOLOGIST, UNITED STATES PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE.

Zoology was once facetiously defined as "The study of the useless." This definition will doubtless appeal to many people as quite applicable; for to persons not in scientific work the practical application of long, detailed, and often tedious accounts of animals is not always evident. In defending such work, many men quote the time-honored expression "Knowledge for knowledge's sake." But seeing little difference in principle between this expression and the phrase "Money for money's sake," and not wishing to pose as a defender of the intellectual miser, I take great pleasure as a professional zoologist in acknowledging the debt which zoology owes to the medical profession for the practical application of zoologic knowledge to the benefit of mankind.

Zoologists have shown how important the insects are from an economic standpoint in making or destroying certain foods upon which we directly or indirectly depend for life. But it is chiefly to the medical profession that this world is indebted for the application of entomologic knowledge in connection with the transmission of the important infectious diseases, hence in connection with saving life.

Dr. Walter Reed, in whose memory we meet here this evening, stands out among medical authors as one who has been particularly prominent in this field of work, and though he was not a zoologist by training, his writings in applied zoology in connection with yellow fever entitle him to rank as among the greatest of applied zoologists.

It was the United States Bureau of Animal Industry which first clearly demonstrated the great importance of arthropods as intermediate hosts of epidemic diseases, and its reports on the tick (*Boophilus*) as a transmitter of Texas fever of cattle will always remain classic. Then the writings of two English physicians, Ross and Manson, and of an Italian zoologist, Grassi, carried the subject further in connection with mosquitoes and malaria.

Finally, the writings of our friend Walter Reed and of his associates demonstrated to us the relation of mosquitoes and yellow fever and showed us how we could protect both life and commerce from this scourge.

It is interesting to note that all three of these discoveries in applied zoology show certain parallels. All deal with diseases which are preeminently tropical or subtropical; all deal with diseases of unusual economic importance; and the actual positive experimental work upon transmission has been done chiefly by English-speaking investigators.

Might I add here, without misinterpretation, that the Texas fever work was done before the days of the Noble prize. The first medical awards of this prize of $40,000 were to Behring in recognition of his work for mankind in connection with diphtheria, and to Pawlow for his work in physiology; the next award was to Ross in recognition of his work for humanity in connection with malaria. Are not Reed, Carroll, Lazear, and Agramonte the natural candidates for the next award because of their work for mankind in connection with yellow fever, and in case the conditions of the grant permit it, should not each of the widows of two of these men receive the share which would have gone to her husband?

Our friend, Dr. Reed, was not what would be called a prolific writer. His numerous routine duties prevented him from furnishing the manuscript which we had a right to expect from a man of his ability. Still, beside short remarks in society discussions, his bibliography contains 27 original articles all printed between 1892 and 1902. Ten of these articles dealt with yellow fever, three or four with typhoid, two each with malaria and erysipelas, and one each with cholera, pneumonia, trikresol, vaccine, artificial immunity against vaccination, amœboid bodies in the blood of vaccinated monkeys and children and in variola, formaldehyde, splenic leukemia, and electrozone. All were in English, and although they were all official Government work, it is a striking fact that only five, so far as I have been able to find, were published by the Government.

Regarding the general style of the articles, there are three points in particular which are striking: First, the attention given to details immediately reminds us of the writings of Dr. Theobald Smith of Harvard University; second, the directness of diction immediately reminds us of Dr. J. McKeen Cattell, professor of experimental psychology, Columbia University. In fact, one of the characteristics for which Dr. Reed was noted among his friends was the absolutely straight line of his thoughts and the orderly, lucid, and logical development of his subject. Third, Dr. Reed was of a judicial temperament, and the judicial manner in which he handled his subject, even in controversy, forcibly reminds us of the same prominent characteristic in Prof. William H. Welch of Johns Hopkins University.

In forecasting the time of the influence of Dr. Reed's writings, it is clear that his articles on yellow fever will far outlive his papers on other subjects. His other writings will be known to men only in certain lines of medical work, but his papers on yellow fever will be known directly or indirectly to both physicians and zoologists, and to both professional men and business men. They will be quoted for decades to come, both by Government officials and by private practitioners, and they will be one of the most important factors in determining the future policy of civilized nations in dealing with yellow fever, a disease which we dreaded only a few years ago, but now one which, thanks to the work of Reed and his colleagues, will soon be little more than a medical curiosity.

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DR. REED'S WORK IN CUBA, BY MAJ. GEN. LEONARD WOOD, UNITED STATES ARMY.

[Abstract.]

The work of Dr. Walter Reed is the most important work in the way of medical research and discovery which has been accomplished by any one who has lived in this hemisphere. There is no other medical discovery to which it can be compared, unless it be that of anæsthesia. The results to humanity are incalculable and far-reaching. It is safe to say that this discovery has resulted in saving each year more lives than were lost in the war with Spain, and in a saving to commerce, and especially to the southern portion of our country, of an amount equal to the cost of the war with Spain.

The following letters and telegrams were received:

WASHINGTON, D. C., *December 29, 1902.*

Dr. S. S. ADAMS,
President District Medical Society.

MY DEAR DR. ADAMS: I regret exceedingly that an engagement made some time since, and from which I can not excuse myself, will prevent me from attending the Reed memorial meeting on Wednesday evening.

No one appreciates more deeply than I do the loss to scientific medicine and to the medical corps of the army caused by Maj. Reed's death. His scientific work was eminently fruitful and far-reaching in its results. As the head of the medical corps during nine years of his most useful work, which was prosecuted under my general direction, I am of course entirely familiar with the results accomplished.

Maj. Reed was endowed by nature and by training with the essential qualifications for engaging in research work in the special field to which he devoted his talents and his energies. Conservative, painstaking, thorough, persevering, and ready in resources, he acquitted himself with credit in every task assigned to him, and has achieved great and deserved distinction by his successful demonstration of the method by which yellow fever is transmitted from man to man. In addition to this, he was a modest and courteous gentleman, who attracted all of those who came in contact with him. His death came to me, as to his other numerous friends, as a great personal grief and irreparable loss.

Very truly, yours, GEO. M. STERNBERG.

BALTIMORE, *December 30, 1902.*

DEAR DR. ADAMS: I have to leave unexpectedly to-day for Canada. Please express my regrets that I can not be at the memorial meeting to Reed.

With kind regards, sincerely yours,

WM. OSLER.

RICHMOND, VA., *December 31, 1902.*

Maj. J. R. KEAN,
Surgeon General's Office, War Department, Washington, D. C.:

Greatly regret I can not attend the meeting to-night in honor of Dr. Reed, whose friendship I prized, whose character I admired, and whose contribution to science and country can not be measured.

FITZHUGH LEE.

TREASURY DEPARTMENT,
PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE,
Washington, D. C., January 5, 1903.

Dr. F. S. NASH,
1723 Q Street, Washington, D. C.

MY DEAR DR. NASH: As you may know by this time, I have been absent from the city for a month and returned Saturday. On opening my mail to-day I find your note of December 9, and I wish to express my great regret that I could not have been here to accept the honor which was conferred upon me of responding at a meeting held in memory of Dr. Reed. It would have been a great privilege to have taken part

in that meeting, and of all the things which I have missed by being away one month I regret this more than any other.

I had, during his life, the highest regard for Dr. Reed as a scientist, and, more than that, I had the warmest feeling of friendship toward him, although we were by no means intimate, and certinly his death was a blow to science and the whole governmental service.

I had a conviction that in the near future the service of which I have charge would find a way of having some official connection with Dr. Reed in his great work, and that through him the bond of union between the medical services of the Government would be materially strengthened.

I have learned that Dr. Stiles took the place which was intended for myself, and I am much gratified that he did.

Very sincerely yours,

WALTER WYMAN.

Chapter 6.

VALUE OF DR. REED'S WORK AND EXPRESSION OF APPRECIATION.[1]

Popular appreciation of the value of the work of the Yellow Fever Commission has been singularly slow and imperfect. While nearly every educated person in the United States is familiar with the name and work of a distinguished Austrian surgeon who has recently demonstrated in this country an operation for the cure of a rather rare deformity in children, only a small fraction of them know anything of Walter Reed, the conqueror of the "yellow plague." And yet distinguished men have not been silent in regard to him. Gen. Leonard Wood said, in a recent address at a memorial meeting of scientific men held in honor of his memory in Washington:

I know of no other man on this side of the world who has done so much for humanity as Dr. Reed. His discovery results in the saving of more lives annually than were lost in the Cuban war, and saves the commercial interests of the world a greater financial loss each year than the cost of the Cuban war. He came to Cuba at a time when one-third of the officers of my staff died of yellow fever, and we were discouraged at the failure of our efforts to control the disease. In the months when the disease was ordinarily worst the disease was checked and driven from Habana. That was the first time in nearly 200 years that the city had been rid of it. The value of his discovery can not be appreciated by persons who are not familiar with the conditions of tropical countries. Hereafter it will never be possible for yellow fever to gain such headway that quarantine will exist from the mouth of the Potomac to the mouth of the Rio Grande. Future generations will appreciate fully the value of Dr. Reed's services. His was the originating, directing, and controlling mind in this work, and the others were assistants only.

In a letter dated November 24 General Wood said:

To Maj. Reed belongs the honor of having led in the greatest medical work of modern times, and the results he accomplished will live for all time.

Prof. William H. Welch, of Johns Hopkins, said in a letter to the Secretary of War:

Dr. Reed's researches in yellow fever are by far the most important contributions to science which have ever come from an Army surgeon. In my judgment, they are the most valuable contributions to medicine and public hygiene which have ever been made in this country with the exception of the discovery of anæsthesia. They have led and will lead to the saving of untold thousands of lives. I am in a position to know that the credit for the original ideas embodied in this work belongs wholly to Maj. Reed. Such work, if done in Europe, would receive substantial recognition from the Government.

He was last year given the degree of LL. D. by the University of Michigan, and the degree of M. A. by Harvard University. In conferring, the language used by President Eliot was:

Walter Reed, graduate of medicine of the University of Virginia, the Army surgeon who planned and directed in Cuba the experiments which have given man control over that fearful scourge, yellow fever.

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[1] "The scientific work and discoveries of the late Maj. Walter Reed, United States Army" (S. Doc. No. 118, Jan. 28, 1903), ordered to be published. Prepared by Maj. Jefferson R. Kean.

Precedents are abundant for State aid to public benefactors and their families. The English Government a century ago, when the purchasing value of money was far greater than at present, gave to Jenner, the discoverer of vaccination, grants amounting to £30,000. He also received £7,383 from a subscription in India.

Pasteur, the founder of the science of bacteriology, besides numerous honors and decorations and money donations from other sources, received from the French Government a pension of 12,000 francs.

Lister, the originator of antiseptic surgery, has, besides numerous honors and decorations, been successively knighted and elevated to the peerage.

In this country a bill to donate $100,000 to the discoverer of anæsthesia was twice passed by the Senate (in 1853 and 1854), but failed in the House, probably because of the uncertainty as to which of the rival claimants was entitled to the credit of that discovery.

The resolutions of various scientific and professional societies are appended as an indication of the standing which Dr. Reed occupied in the scientific world at the time of his death.

The following editorial from a prominent medical journal, American Medicine, is also quoted on account of its pertinence to the question:

DUE REWARDS FOR SCIENTIFIC ACHIEVEMENTS.

The recent death of Maj. Walter Reed directs attention to the self-sacrifice of the medical investigator and the inadequacy of the recognition which is attainable in America by these heroes of science. His demise deprives the country of a citizen whose public spirit, devotion to duty, and splendid achievements justly entitle him to an enduring testimonial. His scientific career, strictly speaking, began about 1890, when, through the stimulating influence of his illustrious teacher, Dr. Welch, of Johns Hopkins, his interest was awakened in the intimate nature and underlying causes of disease, and he took up the special study of pathology and bacteriology. With rare native intelligence, indefatigable industry, high ideals, broad sympathies, and a personality that attracted all who came in contact with him, he soon distinguished himself as a trustworthy, independent investigator, and entered upon a work that was to become a triumph for scientific medicine and a blessing to humanity. Notwithstanding his manifold duties as curator of the Army Medical Museum, Reed never lost his love for pure medical investigation, and was a frequent contributor to medical literature. Yet while his contributions in general to scientific medicine are uniformly as good as the best, they are insignificant when compared with the great work upon yellow fever with which his name will ever be inseparably associated. His was the master mind and he the guiding spirit in an investigation whereby multitudes of lives have been saved, a pestilential malady robbed of its mysteries and terrors, and an annual expenditure of millions of money shown to be in large part, if not entirely, needless. As has been said, his work "means to the United States for the future a saving in life and treasure that is cheaply paid for by the whole cost of the Spanish-American War."

In other countries a man who had done such a work as Reed would at once receive office, honors, and financially security. In ours we leave him unrewarded, to work out his life, to die early, perhaps, and then we offer his family a sum as a pension small beyond ridicule. We appeal to Congress to demonstrate the nation's gratitude in this case. It should act promptly and in a manner commensurate with the magnificient public service rendered by our colleague. This, we are sure, is the wish of everyone conversant with what he has done.

RESOLUTIONS OF MEDICAL SOCIETIES AND LEARNED BODIES WITH REFERENCE TO MAJ. WALTER REED, SURGEON, UNITED STATES ARMY.

At a stated meeting of the New York Academy of Medicine, held December 3, 1902, the following resolution was unanimously adopted:

Whereas in the recent death of Dr. Walter Reed, major and surgeon, United States Army, the science of medicine has lost the one whose brilliant research led first to the

demonstration of the transmission of yellow fever by the mosquito, and later to the practical removal of the disease from a large part of Cuba and the prevention of its transmission to the shores of this country: Be it

Resolved, That the New York Academy of Medicine records its sense of the greatness of the loss to science and to mankind and its sympathy with the friends and relatives of the deceased.

The following minutes and resolutions were adopted at a special meeting of the faculty of the medical department of the Columbian University:

The sudden and unexpected demise of our esteemed friend and colleague, Maj. Walter Reed, United States Army, professor of bacteriology and pathology in the medical school of the Columbian University, is an event that brings to us the most acute regret and overwhelming sorrow.

Taken from us in the prime of manhood and in the zenith of his professional usefulness, at a time when the medical profession and humanity at large were prepared to do him homage for his great work in demonstrating the method of exterminating yellow fever by protection from inoculating mosquitoes and by which that fatal disease has been abolished from some of its most malignant haunts—at a time, too, when his relations with the faculty and students of the Columbian University had become securely united by bonds of mutual affection and esteem—under these circumstances it is with a most earnest and sincere feeling that we, the medical faculty of the Columbian University, hereby desire to express our unreserved admiration for the work, life, and character of Prof. Reed, both as a physician, a teacher, a trusted friend, and a man of science. In testimony whereof, it is hereby

Resolved, That the foregoing note be recorded in the permanent archives of the faculty; that a copy of the same be given to the press for publication and also forwarded to the family of Dr. Reed as an evidence of our sympathy for them in their great sorrow.

Resolved, That, as a further mark of respect for our lamented colleague, the exercises of the medical school be suspended and that the students and faculty attend in a body his funeral obsequies.

The following resolutions were adopted by the medical faculty of the University of Virginia December 8, 1902, and by them reported to the general faculty, which heartily concurred in this expression of regard for the memory of Dr. Reed, of admiration for his work, and of sympathy for his family:

The medical faculty of the University of Virginia have heard with deep sorrow of the death of Maj. Walter Reed, professor of bacteriology and pathology in the Army Medical School, and distinguished graduate of this medical department.

His masterly investigation of the causes of the outbreaks of typhoid fever in the United States Army during the Spanish-American War, and especially his work furnishing conclusive proof of the conveyance of yellow fever by the mosquito, entitle him to a preeminent place amongst scientists and sanitarians and will prove of inestimable service to mankind.

As an alumnus he was true and loyal, manifesting on every appropriate occasion his continued interest in the university, upon which he had reflected great credit.

In testimony of our high appreciation of his character and achievements it is hereby

Resolved, That the foregoing note be spread upon our minutes and a copy be forwarded to the family of Dr. Reed as an evidence of our sympathy for them in their great sorrow.

RESOLUTIONS OF THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE.

Resolved, That the American Association for the Advancement of Science hereby records its sense of the great loss sustained by science in the death of Maj. Walter Reed, surgeon in the United States Army, and its appreciation of the far-reaching and invaluable services which he has rendered to humanity. By solving the problem of the mode of spread of yellow fever, Maj. Reed not only made a great contribution to science, but at the same time conferred inestimable benefits upon his country and upon mankind. To have discovered and demonstrated the methods, which have already been successfully tested in Cuba, of eradicating a widespread and terrible pestilence, is a benefaction of imperishable renown, of incalculable value in the saving of human lives, of vast importance to commercial interests, and deserving the

highest rewards in the power of his countrymen to bestow. This association earnestly urges upon the attention of Congress the duty of making full provision for the support of his family.

Resolved, That the president designate a committee of nine members of this association, with power to increase its number, which shall be authorized and requested to devise and carry out a plan or aid in similar efforts elsewhere instituted, by which a suitable and permanent memorial of this great benefactor of his race may be secured. This committee shall be authorized to prepare and publish a statement of the services of the late Maj. Reed in discovering the mode by which yellow fever may be exterminated.

The following resolution was adopted at the meeting of the American Medical Association at Saratoga, N. Y., on June 11, 1902:

Whereas the members of the American Medical Association believe that the recent work of the United States Army surgeons in Cuba in relation to the discovery of the method of transmission of yellow fever is of such magnitude and far-reaching beneficence as to rank only second with Jenner's discovery of vaccination; and

Whereas the practical value of this discovery has been proven by the complete eradication of this scourge from Habana:

Resolved, That the thanks of this association be tendered the gentlemen who accomplished this brilliant result, and particularly to Drs. Walter Reed, James Carroll, A. Agramonte, W. O. Gorgas, and to Leonard Wood, who recognized the importance of the work and made it possible by his hearty encouragement and assistance.

Resolved, That this association, while deeply deploring the death of Dr. Jesse A. Lazear, who died a martyr to science, admires and gratefully acknowledges the heroic devotion of this physician and some of the members of the Hospital Corps to the cause of humanity.

Resolved, That these resolutions be published in The Journal, and that copies be transmitted to Drs. Reed, Carroll, Agramonte, Wood, Gorgas, and Mrs. Lazear.

RESOLUTIONS TAKEN BY THE INTERNATIONAL CONGRESS OF MEDICINE AT CAIRO, EGYPT, DECEMBER 22, 1902.

Les membres du Premier Congres de Medecine en Egypte apprennant avec le plus profond regret la mort prematurée du Maj. Walter Reed du Corps Medical de l'Armée des Etats Unis d'Amerique.

La part brillante et importante qu'il a pris dans la découverte du moustique stégomyia comme le seul agent transmitteur du parasite de la fièvre jaune, réussessant ainsi a mettre les ravages de cette terrible maladie sous le controle des hygienistes fait de sa mort une perte cruelle pour l'humanité.

Le Congrès decide en consequence d'exprimer a cette occasion toute sa sympathie au Corps Medical de l'Armée des Etats Unis ainsi qu'a la famille du Maj. Reed.

Le Congrès decide en outre de prier le secretaire du Congres d'envoyer officiellement par l'entremise des Autorités compétentes une copie de la presente résolution au Chirurgien en Chef de l'Armée des Etat Unis d'Amerique et une autre égalment a Madame Veuve Reed.

[From an editorial in American Medicine (referring to Maj. Reed).]

His was the master mind and he the guiding spirit in an investigation whereby multitudes of lives have been saved, a pestilential malady robbed of its mysteries and terrors, and an annual expenditure of millions of money shown to be in large part, if not entirely, needless.

[From the resolutions of the American Association for the Advancement of Science.]

By solving the problem of the mode of spread of yellow fever Maj. Reed not only made a great contribution to science, but at the same time conferred inestimable benefits upon his country and upon mankind. To have discovered and demonstrated the methods, which have already been successfully tested in Cuba, of eradicating a widespread and terrible pestilence is a benefaction of imperishable renown, of incalculable value in the saving of human lives, of vast importance to commercial interests, and deserving the highest rewards in the power of his countrymen to bestow.

[From lecture of Sir Patrick Manson, M. D., medical adviser of the British Colonial Office.]

—Dr. Walter Reed did a great and beneficent work. We in England thoroughly appreciate this, and heartily sympathize with America in the loss she and the world

has sustained by his premature death. The best tribute we can pay to his memory is at once to apply his discovery. Let us hope that the good he has done will not be interred with his bones, and that his countrymen and the rest of us will take care to push forward the great and beneficent measures his brilliant labors so clearly indicate.

Similar resolutions have been passed by numerous other scientific bodies. They are not given here because it is not desired unduly to lengthen this report.

INCORPORATORS OF "THE WALTER REED MEMORIAL ASSOCIATION," WASHINGTON, D. C.

R. M. O'Reilly, Surgeon General, United States Army, Washington, D. C.
P. M. Rixey, Surgeon General, United States Navy, Washington, D. C.
Walter Wyman, LL. D., Surgeon General, United States Public Health and Marine-Hospital Service, Washington, D. C.
George M. Sternberg, LL. D., brigadier general, United States Army (retired), Washington, D. C.
Calvin De Witt, brigadier general, United States Army (retired), Washington, D. C.
Daniel C. Gilman, LL. D., president of Carnegie Institution, Washington, D. C.
Chas. W. Needham, LL. D., president of Columbian University, Washington, D. C.
Carroll D. Wright, LL. D., Commissioner of Labor, Washington, D. C.
Henry B. F. Macfarland, president Board of Commissioners, District of Columbia.
H. St. George Tucker, LL. D., dean of school of law and diplomacy, Columbian University, Washington, D. C.
Alexander Graham Bell, LL. D., Columbian University, Washington, D. C.
G. Wythe Cook, M. D., LL. D., Washington, D. C.
A. F. A. King, M. D., dean emeritus medical school, Columbian University, Washington, D. C.
Chas. Wardell Styles, M. D., Chief of Division of Zoology, Hygienic Laboratory, United States Public Health and Marine-Hospital Service, Washington, D. C.
W. J. Boardman, Washington, D. C.
William A. Gordon, lawyer, Washington, D. C.
Maj. J. R. Kean, surgeon, United States Army, War Department, Washington, D. C.
Maj. W. D. McCaw, surgeon, United States Army, War Department, Washington, D. C.
Capt. C. R. Darnall, assistant surgeon, United States Army, War Department, Washington, D. C.
First Lieut. Jas. Carroll, assistant surgeon, United States Army, War Department, Washington, D. C.
F. S. Nash, M. D., Washington, D. C.

WALTER REED (SCHULER).

PART II.—THE PUBLICATIONS OF WALTER REED AND HIS ASSOCIATES ON THE COMMISSION IN REGARD TO YELLOW FEVER.

Chapter 1.

BACILLUS ICTEROIDES AND BACILLUS CHOLERÆ SUIS—A PRELIMINARY NOTE.

By Walter Reed, M. D., Surgeon, United States Army, and James Carroll, M. D., Acting Assistant Surgeon, United States Army.

[Reprinted from the Medical News, April 29, 1899.]

In the course of a comparative study of *Bacillus x* (Sternberg) and *Bacillus icteroides* (Sanarelli) which has engaged our attention as opportunity would permit during the past 18 months, we have had occasion to observe the effect produced by the intravenous injection in dogs of other micro-organisms, such as the *Bacillus coli communis* and the *Bacillus choleræ suis*. Without entering into details in this preliminary note we may state that the same clinical symptoms, viz, vomiting, increased action of the bowels, and profound prostration, which are produced in dogs by the intravenous injection of *B. icteroides*, are also brought about by a like inoculation of the hog-cholera bacillus. When death occurs, the stomach contains a considerable quantity of fluid blood and extensive hemorrhagic lesions are present in the small intestine. We have not found fatty degeneration of the liver, since our dogs, few in number, injected with the hog-cholera bacillus, have died too early for this change to occur. We have also failed to discover any fatty degeneration in the liver of dogs that have died within a few days after the intravenous injection of *B. icteroides*. This change has only been met with in two instances, when the animals had survived until the ninth day after inoculation with *B. icteroides*. In neither of these cases, however, was the degree of fatty degeneration at all comparable with that present in the human liver in yellow fever.

In addition to the experiments upon dogs, we have compared the course of the infection and the lesions produced in guinea pigs and rabbits inoculated with small quantities of *B. icteroides* and *B. choleræ suis*, and have been much impressed with the similarity of the results obtained. The same cyclical course of the infection described by Sanarelli for guinea pigs inoculated with *B. icteroides* is seen in these animals when injected with like quantities of *B. choleræ suis*. The greater susceptibility and shorter course of the infection in rabbits applies equally to both micro-organisms. Theobald Smith has called attention to the extreme susceptibility of these animals to inoculation with minute quantities of the hog-cholera bacillus.[1] We have suc-

[1] Bulletin No. 6, U. S. Department of Agriculture, 1894.

Chapter 2.

THE ETIOLOGY OF YELLOW FEVER—A PRELIMINARY NOTE.[1]

By Walter Reed, M. D., Surgeon, United States Army, James Carroll, M. D.; A. Agramonte, M. D., and Jesse W. Lazear, M. D.,[2] Acting Assistant Surgeon, United States Army.

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 25 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 Habana, 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 nonimmune 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 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 Drs. Nicola Silverio, Manuel Herera, Eduardo Angles, and Acting Asst. Surgs. Roger P. Ames and Jesse W. Lazear, United States Army.

Those studied in Habana 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.

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[1] Reprinted from the Proceedings of the Twenty-eighth Annual Meeting of the American Public Health Association, Indianapolis, Ind., Oct. 22, 23, 24, 25, and 26, 1900.

[2] Died of yellow fever at Columbia Barracks, Cuba, Sept. 25, 1900.

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 microorganism 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 a 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. c.) in quantities of 0.5 c. c. 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 11 were designated as "severe" cases of yellow fever, with 4 deaths; 3 as "well-marked" cases, with no deaths; and 4 as "mild" cases, with no deaths.

From these 18 cases blood cultures were made, as shown in the following table:

Table I.—*Blood cultures during life.*

Day of disease.	Character of attack.	Number of cultures.	Number of bouillon tubes inoculated.	B. icteroides.
First	Severe	3	[1] 4	Negative.
Do	Well marked	1	4	Do.
Do	Mild	1	3	Do.
Second	Severe	6	18	Do.
Do	Well marked	1	2	Do.
Do	Mild	1	[2] 3	Do.
Third	Severe	7	[2] 18	Do.
Do	Mild	2	4	Do.
Fourth	Severe	5	14	Do.
Do	Well marked	2	6	Do.
Do	Mild	1	1	Do.
Fifth	Severe	5	[1] 12	Do.
Do	Well marked	1	3	Do.
Do	Mild	1	1	Do.
Sixth	Severe	4	6	Do.
Do	Well marked	1	2	Do.
Seventh	Severe	1	2	Do.
Do	Well marked	1	2	Do.
Eighth	Severe	2	6	Do.
Do	Well marked	1	2	Do.
Ninth	Severe	1	2	Do.

[1] 3 agar plates. [2] 6 agar plates.

Number of cultures	48
Number of bouillon tubes inoculated	115
Number of 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 18[1] 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 13 of the 14 cases, with 1 negative" (92.85 per cent), we, by withdrawing blood from the veins of 18 patients, have to record 100 per cent of failures.

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 succeed in doing so. Tubes containing about 10 c. c. 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 gelatin 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 gelatin plates on the following days, the corresponding bouillon tubes were also plated on agar and gelatin. 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.	B. icteroides.
1	Seventh	2 hours after death	Blood, liver, spleen, kidney	Negative.
2	Sixth	13 hours after death	do	Do.
3	Fourth	8 hours after death	do	Do.
4	Eighth	4 hours after death	Abdominal cavity, blood, liver, spleen, kidney, bile, duodenum.	Do.
5	Fourth	do	Blood, liver, spleen, kidney, bile, duodenum.	Do.
6	Sixth	6½ hours after death	Abdominal cavity, blood, pericardial fluid, lung, spleen, kidney, liver, bile, duodenum.	Do.
7	do	50 minutes after death	Blood, lung, liver, spleen, kidney, bile, jejunum.	Do.
8	do	½ hour after death	Blood, lung, liver, spleen, kidney, urine, small intestine.	Do.
9	Fourth	2 hours after death	Liver, spleen, small intestine	Do.
10	Fifth	7 hours after death	Liver, kidney, spleen, small intestine	Do.
11	Third	½ hour after death	Liver, kidney, spleen	Do.

[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 can not be ascertained. These cultures were negative as regards the finding of Sanarelli's bacillus.

Our failure to isolate *B. icteroides* in these 11 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 Habana during the present year. In 2 of the 11 cases we had reason to believe that from the character of colonies seen in gelatin 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 gelatin plates without further study. We only mention this as a possible explanation of the large percentage of positive results recorded by some observers.

Pothier, of New Orleans, La., only succeeded, however, in isolating *B. icteroides* in 3 out of 51 autopsies. (Journal of American Medical Association, Apr. 16, 1898.)

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* can not 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 Habana, 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 Surg. Henry R. Carter, United States 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 Myers, to whom we had the pleasure of submitting Carter's observations, have been equally impressed by their importance. (British Medical Journal, Sept. 8, 1900, pp. 656–657.)

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 farmhouses 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 noninfected 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 9 to 16 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 19 years; and also for ova of the species of mosquito with which he had made his several inoculations. An important observation 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: Estadistica de las Inoculaciones con mosquitos contaminados, etc., reprint, Havana, 1891; Fiebre Amarilla, Estudio Clinico Patologico y Etiologico, reprint, Habana, 1895; and Yellow Fever Immunity—Modes of Propagation: Mosquito Theory, 8th Congress of International Hygienic 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 5 to 25 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 nonimmune 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 nonimmune individuals through the bite of mosquitoes (C. faciated.)*

Number of case.	Age.	Nativity.	Date of inoculation.	Character of attack.	Number of patients bitten.	Day of disease.	Time between infection of mosquito and inoculation.	Number of mosquitoes.	Result.	Remarks.
							Days.			
1		United States	Aug. 11	Mild	1	Seventh	5	1	Negative	
2		do	do	Very mild	1	Fifth	5	1	do	
3	24	do	Aug. 12	do	1	do	6	1	do	
4	20	do	do	do	1	do	6	1	do	
5	24	do	Aug. 14	do	1	do	8	1	do	
6	34	do	Aug. 16	do	1	do	10	1	do	
7	22	do	Aug. 18	Severe	1	Second	3	1	do	
8	20	do	Aug. 19	Very mild	1	Fifth	13	2	do	
				Severe	1	First	3			
9	28	do	Aug. 25	Fatal	1	Second	6			
				Mild	1	First	4	1	do	
				Severe	1	Second	2			
10	46	England	Aug. 27	do	1	do	12			
				Mild	1	First	6	1	Positive	Severe attack of yellow fever.
				Severe	1	Second	4			
				Mild	1	do	2			
11	24	United States	Aug. 31	Fatal	1	do	12			
				Mild	2	do	4 and 10	1		
				Severe	2	Second and ninth	2 and 8			
				do	3	First, second, and second	2, 8 and 16	1		
				Mild	2	First and second	6 and 10		do	Well-marked attack of yellow fever.
				Fatal	1	Second	12			
				Severe	1	First	2	1		
				Mild	3	First, second, and second	4, 6, and 10			
				Severe	3	All on first	2, 4, and 8	1		
				Mild	1	Second	6			

It will be seen that we record 9 negative and 2 positive results. It is, we think, important to observe that of the 9 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 9 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 3 days later.) To this fact may possibly be attributed the negative results. Of the remaining 3 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 2 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 9 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, United States 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), some time 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 30: During the afternoon, although not feeling well, Dr. Carroll visited La Playa, distant about 1½ miles from Columbia Barracks, and took a sea bath.

August 31, a. m.: Dr. Carroll realized that he was sick and that he had fever, although he refrained from taking his temperature, but did visit the laboratory, distant about 140 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 1, 7 a. m.: Temperature 102° F. Blood again carefully examined by Dr. Lazear with negative results.

11 a. m.: Temperature 102°.

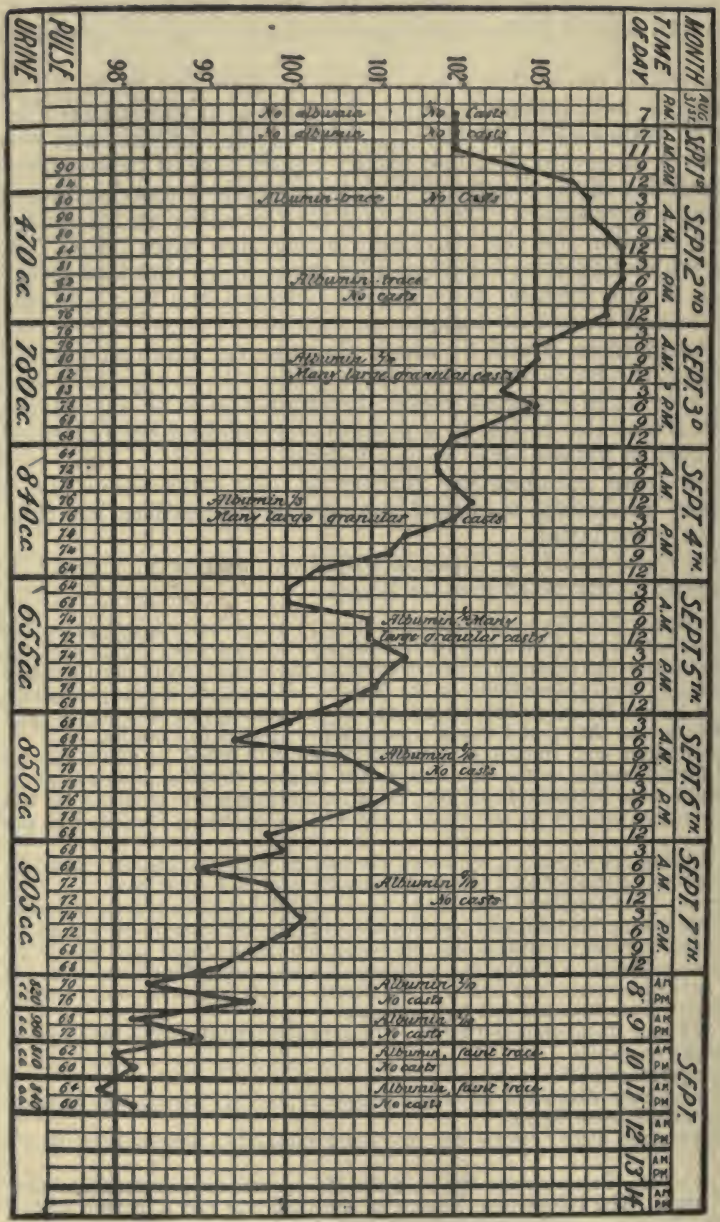
The case having been diagnosed as one of yellow fever, Dr. Carroll was at noon removed to the yellow fever wards.

9 p. m.: Temperature 102.8°, pulse 90; 12 o'clock midnight, temperature 103.4°, pulse 84.

September 2, 3 a. m.: Temperature 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 3.

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. Carroll's movements for a period of 10 days preceding the mosquito inoculation, and



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

during the period elapsing from the bite of the insect until the commencement of the attack.

On August 21, 22, and 23, Dr. Carroll was at Columbia Barracks, outside of the epidemic zone. On August 24 he visited the autopsy room of Military Hospital No. 1, which is situated on Principe Hill overlooking the city of Habana. He was present in this autopsy room while an autopsy was made by Dr. Agramonte on a case of pernicious malarial fever. Dr. Carroll 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. Carroll's visit to it.

According to Dr. Carroll, the room was by no means in a cleanly condition. As Dr. Carroll's visit to this room was made on August 24, and as he began to complain on August 29, 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, United States Army, who is detailed for that purpose, and whose duty it is to assist and to afterwards attend to the cleaning of the autopsy table. This soldier, a nonimmune 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. 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 nonimmune 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. Carroll 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 Habana, as here yellow-fever patients are admitted in large numbers. We have already pointed out that Dr. Carroll was complaining of lassitude at the hour of his visit, which was about 50 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. Carroll 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. Carroll's case after we have given the history of case No. 11, which we have designated as our second positive result. Wm H. Dean Troop B 7th Cav.

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. Carroll) 4 days before, and which in the meanwhile had bitten a mild case of yellow fever (first day) 2 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 2 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 3 mild cases (first, second, and third day) 4, 6, and 10 days before; finally, by a fourth mosquito that had bitten 3 severe cases of yellow fever (all on the first day) 2, 4, and 8 days previously, and 1 mild case (second day) 6 days before. (Vide Table III.)

It will thus be seen that X. Y. was bitten by 4 mosquitoes, 2 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 25.—X. Y. began to experience a sense of dizziness and disinclination to work. This was just 5 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., temperature 102.8° F., eyes slightly injected, face suffused. Patient removed to the yellow fever wards; 9 a. m., temperature 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, United States Army, 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. Ames 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 10 days preceding the bite of the mosquitoes and from this time until 5 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 Habana. Sixteen days before the inoculation, he rode on horseback with 6 other nonimmunes a distance of about 1½ miles toward 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 57 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

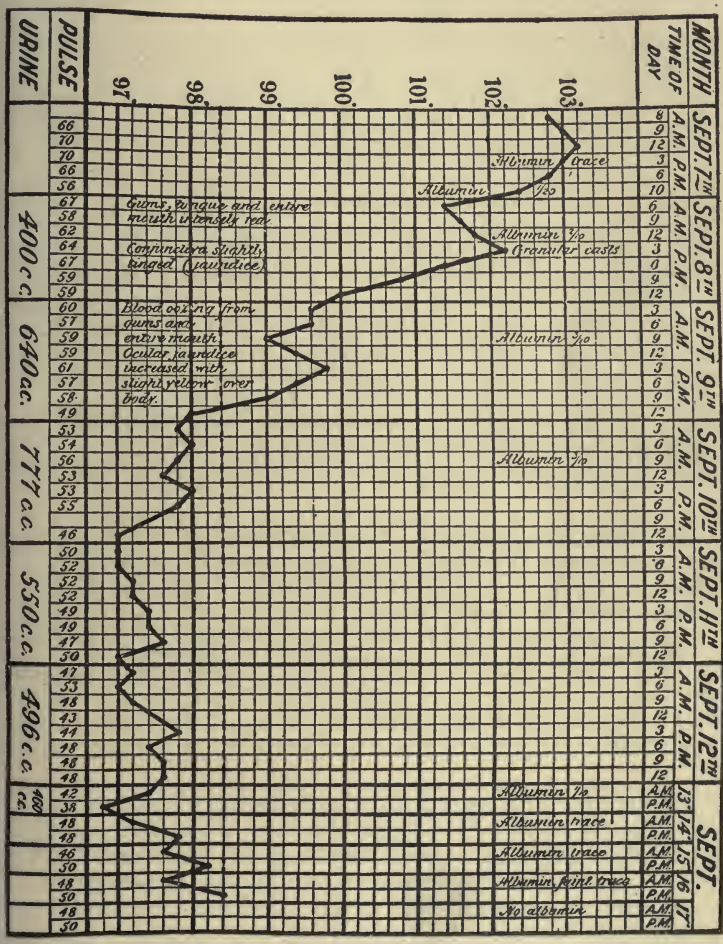


Chart II. Yellow fever following within the usual period of incubation, the bite of an infected mosquito, (Culex fasciatis)

we answer that since the commencement of the present epidemic of yellow fever in Habana, dating from May, 1900, the average monthly population of this station, including civilian employees, has been 1,400, nearly all of whom are young nonimmunes.

There have occurred amongst this nonimmune population from May 1 to October 13, 1900, 16 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 1

other case of which we shall presently speak. These cases have been distributed as follows:

	Cases.
May 24	1
June 10	1
June 17	1
June 19	2
June 21	1
June 29	1
July 9	1
July 26	1
July 29	1
Aug. 11	1
Aug. 12	1
Aug. 16	1
Aug. 31	1
Sept. 7	1
Sept. 19	1
Total	16

Ten of these cases have occurred amongst an average monthly military population of 1,295 men, and 6 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 Habana, 6 miles distant, or to some other nearer Cuban settlement.

We now invite attention to the fact that from August 17 to October 13, a period of 57 days, only 3 cases of yellow fever have occurred amongst this population of 1,400 nonimmune Americans, and we consider it very important to note that two of these had been bitten, within 5 days of the commencement of their attack, by contaminated mosquitoes.

Taken in connection with case 2, in which we have been unable to find any other source of infection than the bite of an infected mosquito, 5 days preceding the attack, the case of Dr. Carroll (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, United States Army, a member of this board, was bitten on August 16, 1900 (case 6, Table III), by a mosquito (*Culex fasciatus*) which 10 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 undertermined). As Dr. Lazear 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 18, 5 days after the bite, Dr. Lazear complained of feeling "out of sorts," and had a chill at 8 p. m.

September 19: Twelve o'clock noon, temperature 102.4°, pulse, 112. Eyes injected, face suffused; 3 p. m., temperature, 103.4°, pulse, 104; 6 p. m., temperature, 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. Lazear 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 can not 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.

Chapter 3.

THE ETIOLOGY OF YELLOW FEVER.—AN ADDITIONAL NOTE.[1]

Walter Reed, M. D., Surgeon, United States Army, Jas. Carroll, M. D., and Aristides Agramonte, M. D., Acting Assistant Surgeons, United States Army.

At the twenty-eighth annual meeting of the American Public Health Association,[2] held in Indianapolis, Ind., October 22–26, 1900, we presented, in the form of a preliminary note, the results of our bacteriologic study of yellow fever, based on cultures taken from the blood in 18 cases at various stages of the disease, as well as on those which we have made from the blood and organs of 11 yellow-fever cadavers. We also recorded the results obtained from the inoculation of 11 nonimmune individuals by means of the bite of mosquitoes (*Culex fasciatus*, Fabr.) that had previously fed on the blood of patients sick with yellow fever. We were able to report two positive results, in which the attack of yellow fever followed the bite of a mosquito within the usual period of incubation of this disease.

In one of these cases all other sources of infection could be positively excluded. From our several observations we drew 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. Since the publication of our preliminary note we have continued our investigations, especially as regards the means by which yellow fever is propagated from individual to individual, and as to the manner in which houses become infected with the contagium of this disease. The results already obtained are so positive and striking that, with the permission of Surg. Gen. Sternberg, we have concluded to present to this congress an additional note, in which we will record these later observations. We desire to here express our sincere thanks to the military governor of the island of Cuba, Maj. Gen. Leonard Wood, United States Volunteers, without whose approval and assistance these observations could not have been carried out.

In order to exercise perfect control over the movements of those individuals who were to be subjected to experimentation, and to avoid any other possible source of infection, a location was selected in an open and uncultivated field, about 1 mile from the town of Quemados, Cuba. Here an experimental sanitary station was established under the complete control of the senior member of this board. This station was named Camp Lazear, in honor of our late colleague, Dr. Jesse W. Lazear, acting assistant surgeon, United States Army, who died of yellow fever, while courageously investigating the causation of this disease. The site selected was very well drained, freely exposed to sunlight and winds, and, from every point of view, satisfactory for the purposes intended.

[1] Read at the Pan Am. Med. Cong., held in Habana, Cuba, Feb. 4–7, 1901.
[2] Phila. Med. Jour., Oct. 27, 1900.

The personnel of this camp consisted of two medical officers, Dr. Roger P. Ames, acting assistant surgeon, United States Army, an immune; in immediate charge; Dr. R. P. Cooke, acting assistant surgeon, United States Army, nonimmune; one acting hospital steward, an immune; nine privates of the hospital corps, one of whom was immune; and one immune ambulance driver.

For the quartering of this detachment, and of such nonimmune individuals as should be received for experimentation, hospital tents, properly floored, were provided. These were placed at a distance of about 20 feet from each other, and were numbered 1 to 7, respectively.

Camp Lazear was established November 20, 1900, and from this date was strictly quarantined, no one being permitted to leave or enter camp except the three immune members of the detachment and the members of the board. Supplies were drawn chiefly from Columbia Barracks, and for this purpose a conveyance under the control of an immune acting hospital steward, and having an immune driver, was used.

A few Spanish immigrants, recently arrived at the port of Habana, were received at Camp Lazear, from time to time, while these observations were being carried out. A nonimmune person, having once left this camp, was not permitted to return to it under any circumstances whatever.

The temperature and pulse of all nonimmune residents were carefully recorded three times a day. Under these circumstances any infected individual entering the camp could be promptly detected and removed. As a matter of fact only two persons, not the subject of experimentation, developed any rise of temperature; one, a Spanish immigrant, with probably commencing pulmonary tuberculosis, who was discharged at the end of three days; and the other, a Spanish immigrant, who developed a temperature of 102.6° F. on the afternoon of his fourth day in camp. He was at once removed with his entire bedding and baggage and placed in the receiving ward at Columbia Barracks. His fever, which was marked by daily intermissions for three days, subsided on the administration of cathartics and enemata. His first attack was considered to be due to intestinal irritation. He was not permitted, however, to return to the camp.

No nonimmune resident was subjected to inoculation who had not passed in this camp the full period of incubation of yellow fever, with one exception, to be hereinafter mentioned.

OBSERVATIONS.

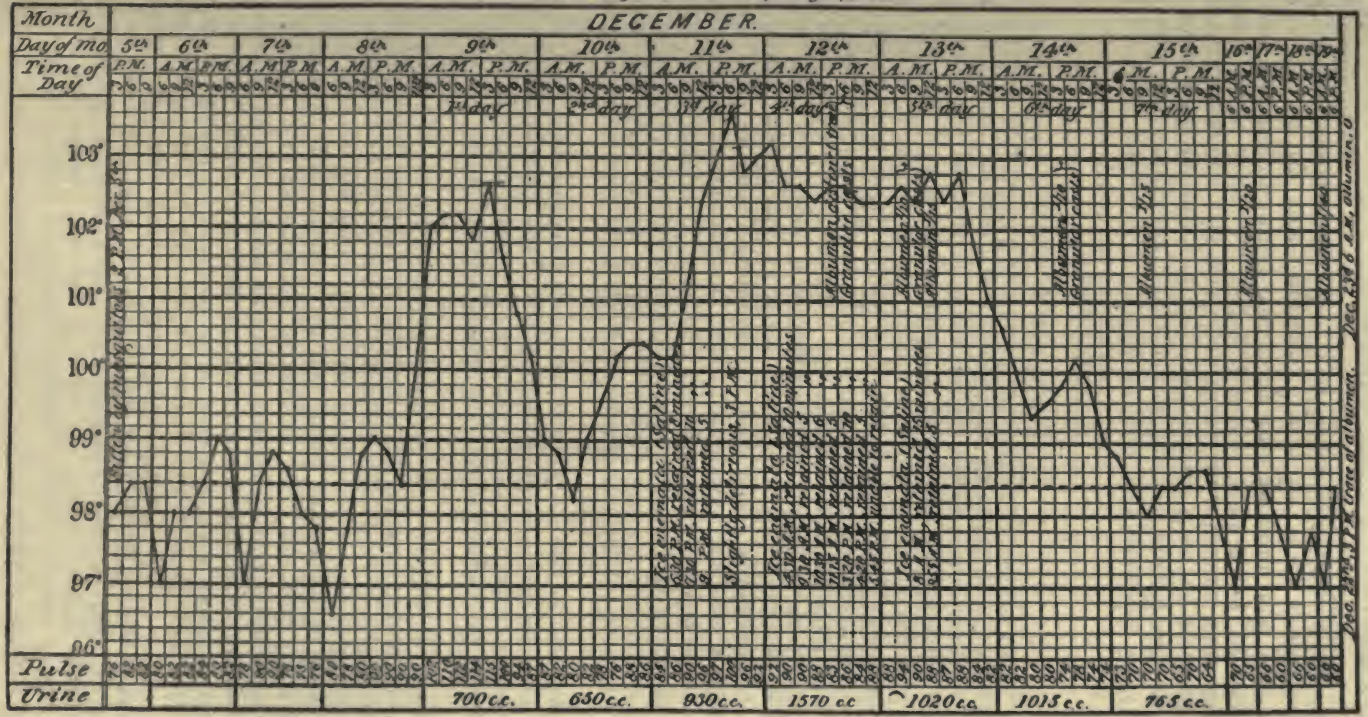
Having thus sufficiently indicated the environment of Camp Lazear and the conditions under which its residents lived, we will now proceed to a narration of the observations thus far made at this experimental station. At the time these inoculations were begun, the several tents were occupied as follows: Tent No. 1 by one immune and one nonimmune; No. 2 by one immune and two nonimmunes; No. 3 by two immunes; No. 4 by three nonimmunes; No. 5 by three nonimmunes; No. 6 by two nonimmunes; and No. 7 by one nonimmune.

For the purpose of experimentation, subjects were selected as follows: From tent No. 2, two nonimmunes, and from tent No. 5, three nonimmunes. Later, one nonimmune in tent No. 6 was also designated for inoculation.

Chart I

Yellow fever, produced by the bite of Culex fasciatus

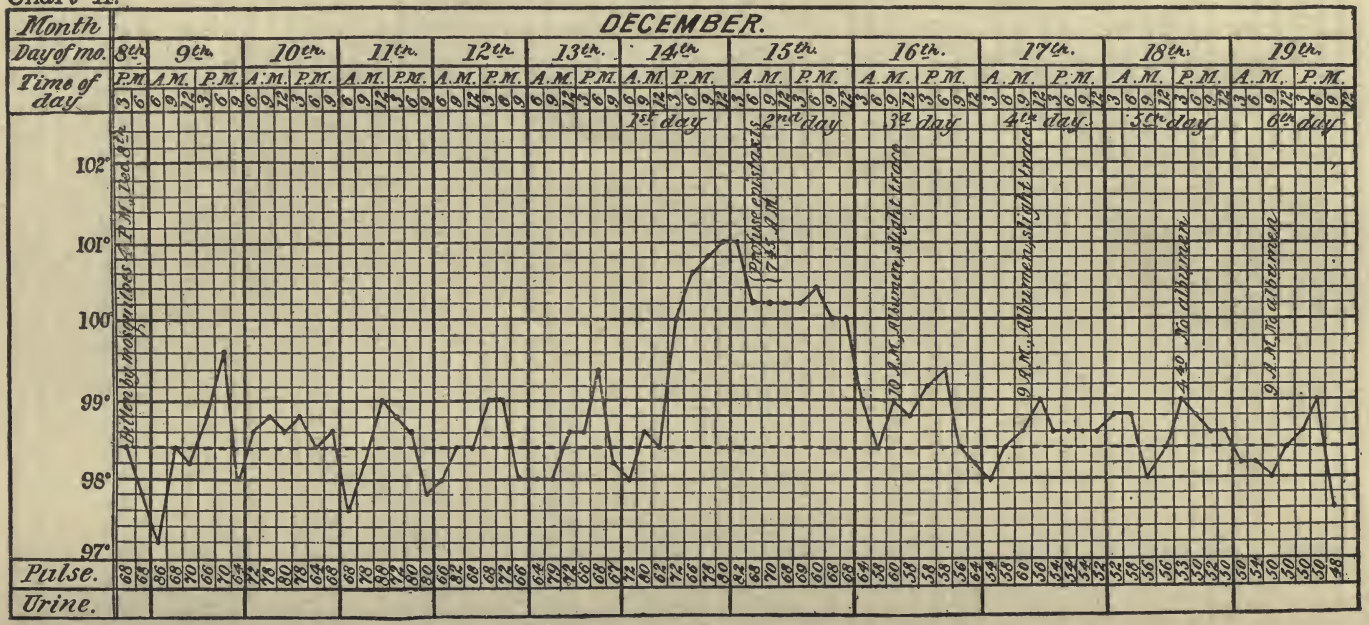
Period of incubation, 3 days 9½ hours.



Yellow fever, produced by the bite of Culex fasciatus.

Period of incubation, 4 days 20 hours.

Chart II.



Case 1.—Pvt. John R. Kissinger, Hospital Corps, United States Army, aged 23, a nonimmune, occupant of tent No. 2, with his full consent, was bitten at 10.30 a. m., November 20, 1900, by a mosquito (*C. fasciatus*) that had bitten a severe case of yellow fever on the fifth day, 11 days previously; another severe case, on the third day, 6 days before; and a third severe one on the third day, 3 days before. As Kissinger had not absented himself from Columbia Barracks for a period of more than 30 days, it was considered safe to inoculate him without waiting for his period of incubation to pass.

November 23, 1900, Kissinger was again bitten by the same mosquito. The result of both inoculations was negative. The mosquito, therefore, was incapable of conveying any infection on the eleventh or fourteenth day after it had bitten a severe case of yellow fever on the third day of the disease. This insect had been kept at ordinary room temperature and died November 26, 1900.

December 5, 1900, at 2 p. m., 12 days after the last inoculation, Kissinger was again bitten by 5 mosquitoes (*C. fasciatus*), 2 of which had bitten fatal cases of yellow fever, 1 the second day, 15 days before; 1 a severe case on the second day, 19 days previously, and 2 a mild case on the third day, 21 days before.

The record of temperature and pulse, taken every 3 hours following this inoculation, showed that the subject remained in his usual state of health during the following 3 days, except that on December 8, on the third day, Kissinger had slight vertigo upon rising, which soon passed away. At 4.30 p. m.—commencement of fourth day—he complained of frontal headache; otherwise he felt well and partook of supper with appetite; at 9 p. m., temperature was 98.4° F., pulse 90; at 11.30 p. m., he awoke with a chill, his temperature 100° F., pulse 90; he complained of severe frontal headache and backache; his eyes were injected and his face suffused. December 9 at 3 a. m., his temperature was 102° F., pulse 102; he had violent headache and backache, with nausea and vomiting. He was then removed to the yellow-fever wards. His subsequent history was that of a case of yellow fever at moderate severity. Albumin appeared in the urine on the fourth day, increased to one-fifth by volume on the sixth day, and disappeared on December 22. Granular casts were present in considerable numbers from the fourth to the eighth day. The conjunctivæ were jaundiced on the third day. The diagnosis of yellow fever in this case was made by Drs. Juan Guitéras, Carlos Finlay, W. C. Gorgas, and A. Diaz Albertini, the board of yellow-fever experts of the city of Habana, who saw the patient on several occasions during his illness. (See Chart I.) The period of incubation in this case was 3 days, 9½ hours.

Case 2.—John J. Moran, aged 24, an American, nonimmune, occupant of tent No. 2, with his full consent, was bitten at 10 a. m., November 26, 1900, by a mosquito (*C. fasciatus*) which 12 days before had bitten a case of yellow fever of moderate severity, on the third day of the disease. This insect had also bitten a well-marked case of yellow fever—second day—10 days previously.

November 29, at 2.20 p. m., Moran was again bitten by the same mosquito. The result of both of these inoculations was negative. This insect was therefore incapable of conveying the infection 15 days after having bitten a case of yellow fever of moderate severity on the third day, and 13 days after it had bitten a well-marked case of this disease on the second day. This mosquito had been kept at room temperature. Moran's case will be again referred to when we come to speak of the infection of a building by means of contaminated mosquitoes.

Case 3.—A Spanish immigrant, aged 26, a nonimmune occupant of tent No. 5, with his full consent, was bitten at 4 p. m., December 8, 1900, by 4 mosquitoes (*C. fasciatus*) which had been contaminated as follows: One by biting a fatal case of yellow fever, on the third day, 17 days before; 1 a severe case, on the third day, 18 days before; 1 a severe case, on the second day, 22 days before, and 1 a case of moderate severity, on the third day, 24 days previously.

The record of temperature and pulse, taken every 3 hours after the inoculation, shows no rise of temperature above 99° F. until 6 p. m., December 13, on the sixth day, when 99.4° F. is recorded; pulse, 68. The subject, who was of a very lively disposition, retained his usual spirits until noon of the 13th, although he complained of slight frontal headache on the 11th and 12th. He took to his bed at noon of the 13th, the fifth day, complaining of increased frontal headache and a sense of fatigue. At 9 p. m., his temperature was 98.2° F., pulse 62.

December 14, at 6 a. m., temperature was 98° F., pulse 72, and he still complained of frontal headache and general malaise. Profuse epistaxis occurred at 7.45 a. m.; at 9 a. m., temperature was 99.6° F., pulse 80; at 1.15 p. m., temperature was 100° F., pulse 80, and he complained of a sense of chillness, with frontal headache increased, and slight pain in the back, arms, and legs; at 3 p. m., temperature was 100 ° F., pulse 80; at 4.15 p. m., temperature 100.7° F., pulse 68; his face flushed and eyes congested. He was removed to the yellow-fever wards. A trace of albumin was found in the urine

passed at 3.30 p. m., December 15; a few hyaline cases were present. He was seen at this time by the Habana board of experts, and the diagnosis of mild yellow fever confirmed. (See Chart No. 2.)

The period of incubation in this case was 4 days and 24 hours, counting from the time of inoculation to the hour when the patient took to his bed; if reckoned to the onset of fever, it was 5 days and 17 hours.

Case 4.—A Spanish immigrant, aged 27, a nonimmune occupant of tent No. 5, with his full consent, was bitten at 10 a. m. November 26, 1900, by a mosquito (*C. fasciatus*) which had bitten a severe case of yellow fever on the second day 10 days before. Three days later, November 29, he was again bitten by the same insect. December 2, after an interval of 3 days, he was again bitten by the same insect, and also by a second mosquito (*C. fasciatus*) which 12 days before had been contaminated by biting a fatal case of yellow fever on the third day. No unfavorable effects followed any of these attempted inoculations. The first-mentioned mosquito, therefore, was incapable of conveying any infection on the seventeenth day after biting a severe case of yellow fever on the second day; the other also failed to infect on the twelfth day after biting a fatal case of yellow fever on the third day. Both of these mosquitoes had been kept at ordinary room temperature.

December 9, after an interval of 7 days, the subject was again bitten, at 10.30 a. m., by 1 mosquito (*C. fasciatus*) which had been infected 19 days before by biting a fatal case of yellow fever on the second day of the disease. He remained in his usual health until 9 a. m. December 12, the third day, when he complained of frontal headache; his temperature was 98.8° F., pulse 96. This headache continued during the entire day. At 6 p. m. temperature was 99° F., pulse 94; at 9 p. m. temperature 99° F., pulse 84; at 9.30 p. m. temperature 99.4° F., pulse 82. Severe headache and backache was complained of; his eyes were injected and his face suffused. The following morning he was sent to the yellow-fever wards. Urine passed at 4.20 p. m. December 15, the third day, gave a distinct trace of albumin. Many hyaline casts were present on the same date. The conjunctivæ were jaundiced on the third day.

The patient was seen by the board of experts on December 14 and the diagnosis of yellow fever made. (See Chart No. 3.)

The period of incubation in this case was 3 days 11½ hours.

Case 5.—A Spanish immigrant, aged 26, a nonimmune occupant of tent No. 5, with his full consent, was bitten at 10 a. m. November 26, 1900, by a mosquito (*C. fasciatus*) that had bitten a well-marked case of yellow fever on the third day 12 days before. November 29 he was again bitten by the same insect. December 2 he was for the third time bitten by 2 mosquitoes (*C. fasciatus*), both of which had bitten a well-marked case of yellow fever on the third day, 18 days before. As no bad results followed any of these inoculations, it follows that these mosquitoes were incapable of conveying any infection 18 days after they had bitten a well-marked case of yellow fever on the third day. Both of these insects had been kept at room temperature.

December 11, after an interval of 9 days, the subject was again, at 4.30 p. m., bitten by the same mosquitoes, 4 in number, that had been applied to case 3 three days prior to this time, with positive results.

The record of temperature and pulse, taken every 3 hours following the inoculation, showed no change till December 13, the second day, at 9 a. m., when the temperature was 99° F., and the pulse 78. From this hour till 6 p. m. the temperature varied from 99.2° to 99.6° F. The subject complained of frontal headache, slight in degree, during the entire day. At 9 p. m. his temperature was 98.4° F., pulse 62.

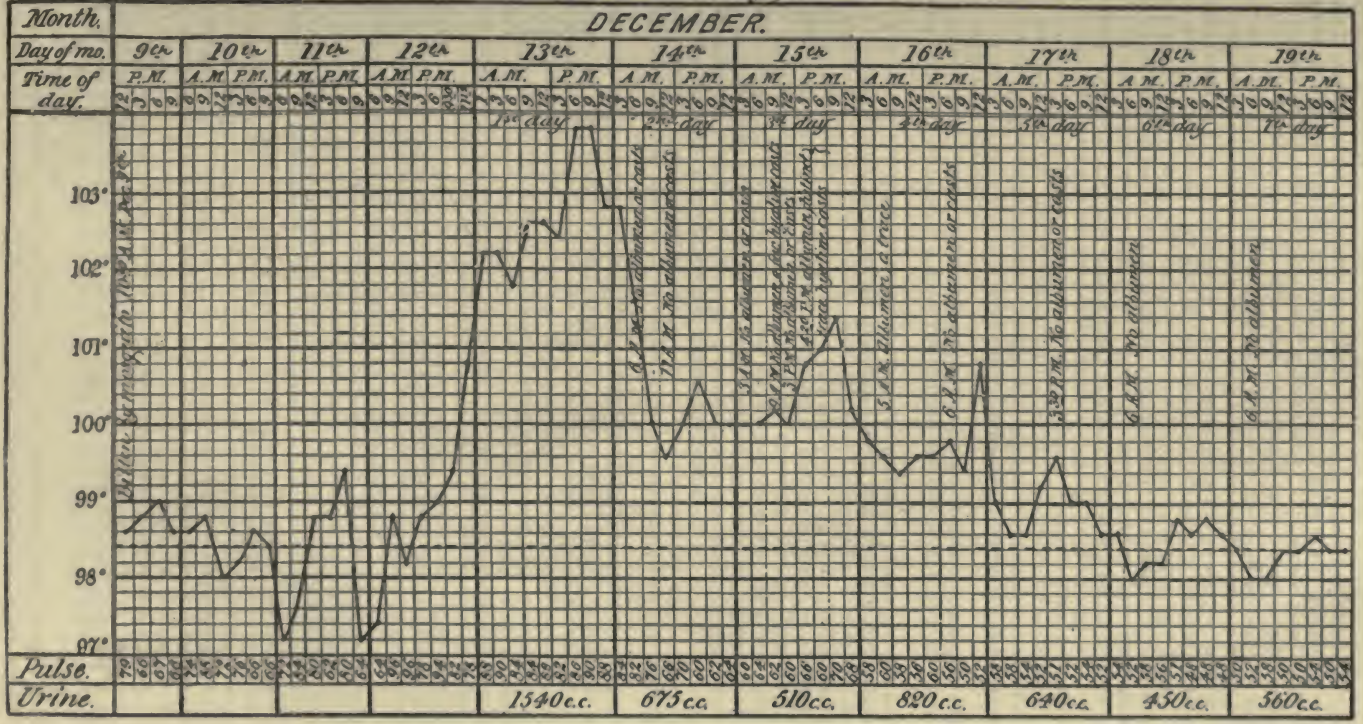
December 14, the third day, he complained of slight frontal headache during the entire day, and was indisposed to exertion. From 6 a. m. to 6 p. m. the temperature averaged 99.2° F., and the pulse varied from 64 to 90; at 9 p. m. it was 98.4° F., the pulse 78. December 15, the fourth day, at 6 a. m. temperature was 98.2° F., pulse 78. He still had frontal headache. At 9 a. m. temperature was 99.2° F., pulse 80; at 12, noon, the former was 99.2° F., the pulse 74. The subject now went to bed, complaining of headache and pains throughout the body. At 2 p. m. the temperature was 100° F., the pulse 80; eyes much congested; face flushed. At 6 p. m. his temperature had risen to 102° F., and the pulse to 90. He was then transferred to the yellow fever wards. Albumin appeared in the urine at 7.30 a. m., December 17. Bleeding from the gums and roof of the mouth occurred on the sixth and seventh days of his illness.

The case was examined by the board of experts on the 16th and 19th, and the diagnosis of yellow fever made.

Albumin disappeared on the sixth day, the temperature falling to normal on this date, and remaining near this point till December 23, the ninth day of sickness, when a relapse occurred, attended with bleeding from the gums on December 24

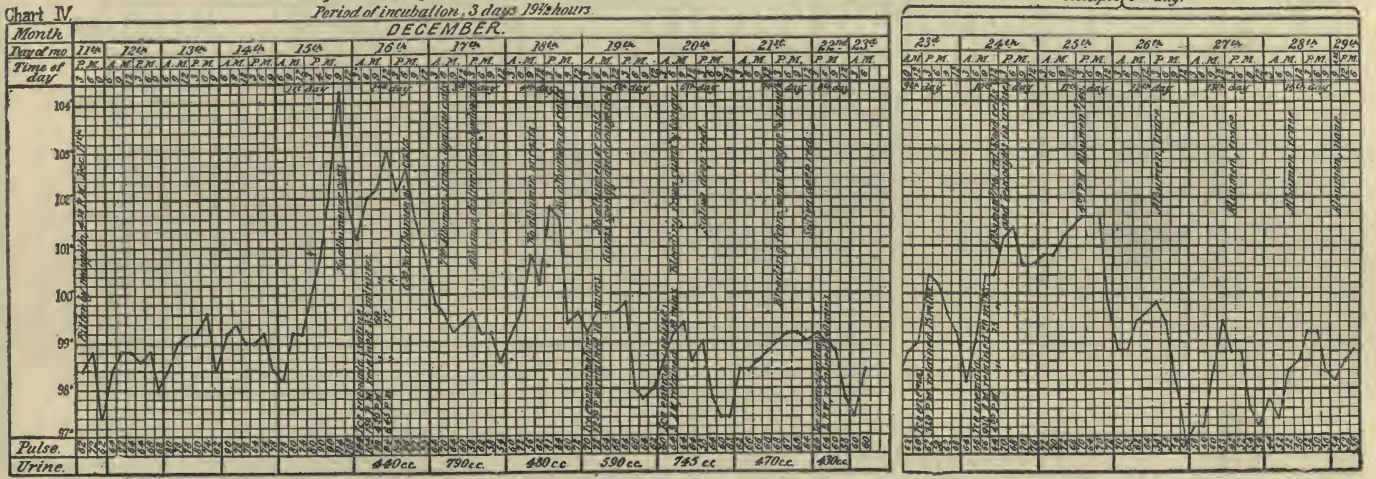
Yellow fever produced by the bite of Culex fasciatus.

Chart III. *Period of incubation 3 days, 11 hours.*



Yellow fever, produced by the bite of Culex fasciatus

Chart IV. *Period of incubation, 3 days 19½ hours.* *Relapse, 9th day.*



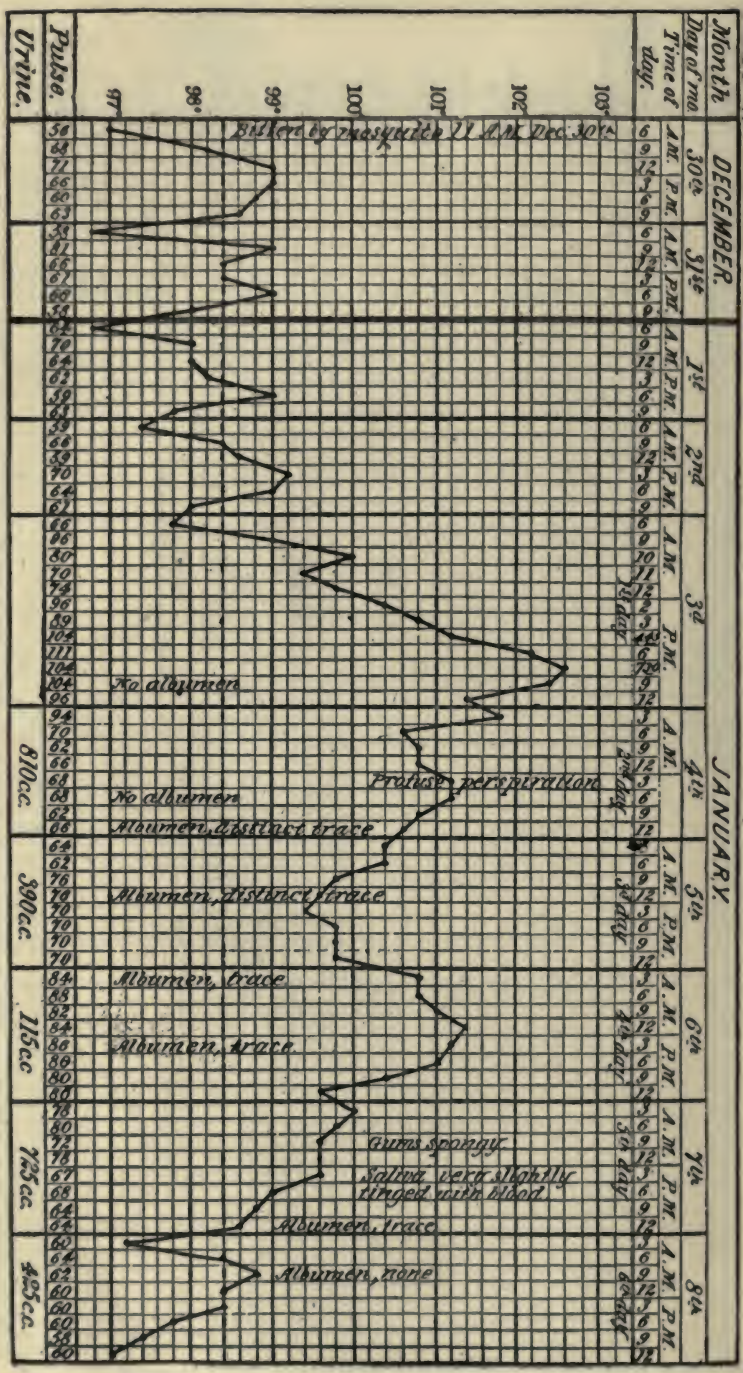
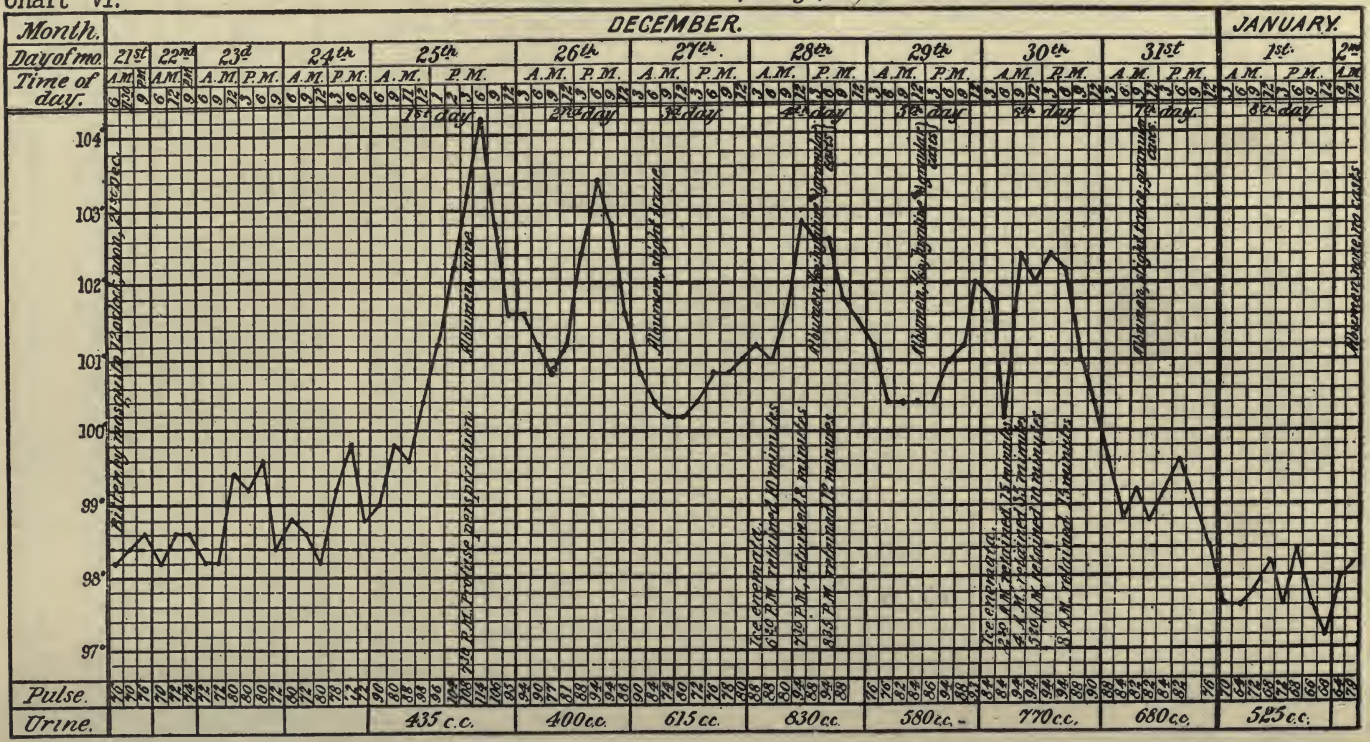


Chart V.
Yellow fever, produced by the bite of Culex fasciatus.
Period of incubation, 3 days, 22 hours.
Month
DECEMBER.
JANUARY.
Day of mo.
30th
31st
1st
2nd
3rd
4th
5th
6th
7th
8th
Time of day.
A.M.
P.M.
Pulse.
Urine.
97°
98°
99°
100°
101°
102°
103°
Bitten by mosquito 11 A.M. Dec. 30th
3 days
2nd day
3rd day
4th day
5th day
6th day
No albumen
Profuse perspiration
No albumen
Albumen, distinct trace
Albumen, distinct trace
Albumen, trace
Albumen, trace
Gums spongy
Saliva very slightly tinged with blood
Albumen, trace
Albumen, none
810cc.
390cc.
115cc.
735cc.
485cc.

Yellow fever, produced by the bite of Culex fasciatus.

Period of incubation, 3 days, 23 hours.

Chart VI.



and 25, with the appearance of red blood cells and pus cells in the urine in moderate numbers. Fever subsided on December 26, and the urine became normal on December 29. (See Chart 4.)

The period of incubation in this case, if reckoned from the time of inoculation to the hour when the patient took to his bed, was 3 days, 19½ hours.

The four patients whose histories we have given above were also examined by a number of physicians of Habana, among whom we may mention Dr. Bango, of "La Covadonga," Dr. Sanchez, of "La Benéfica," and Dr. Moas, of "La Purissima Concepcion," by all of whom the diagnosis of yellow fever was confirmed. Let us now rapidly review the circumstances attending these cases of experimental yellow fever, in order to emphasize certain points of interest and importance in connection with their occurrence. (We omit any reference to the clinical histories.)

It should be borne in mind that at the time when these inoculations were begun there were only 12 nonimmune residents at Camp Lazear, and that 5 of these were selected for experiment, viz, 2 in tent No. 2 and 3 in tent No. 5. Of these we succeeded in infecting 4, viz, 1 in tent No. 2 and 3 in tent No. 5, each of whom developed an attack of yellow fever within the period of incubation of this disease. The one negative result, therefore, was in case 2—Moran—inoculated with a mosquito on the fifteenth day after the insect had bitten a case of yellow fever on the third day. Since this mosquito failed to infect case 4, three days after it had bitten Moran, it follows that the result could not have been otherwise than negative in the latter case. We now know, as the result of our observations, that in the case of an insect kept at room temperature during the cool weather of November, 15 or even 18 days would, in all probability, be too short a time to render it capable of producing the disease.

As bearing on the source of infection, we invite attention to the period of time during which the subjects had been kept under rigid quarantine, prior to successful inoculation, which was as follows: Case 1, 15 days; case 3, 9 days; case 4, 19 days; case 5, 21 days. We further desire to emphasize the fact that this epidemic of yellow fever, which affected 33.33 per cent. of the nonimmune residents of Camp Lazear, did not concern the 7 nonimmunes occupying tents No. 1, 4, 6, and 7, but was strictly limited to those individuals who had been bitten by contaminated mosquitoes.

Nothing could point more forcibly to the source of this infection than the order of the occurrence of events at this camp. The precision with which the infection of the individual followed the bite of the mosquito left nothing to be desired in order to fulfill the requirements of a scientific experiment.

The epidemic having ceased on December 15, 1900, no other case of yellow fever occurred in this camp until we again began to expose individuals to inoculation. Thus 15 days later we made the following observation:

Case 6.—A Spanish immigrant, aged 27, a nonimmune occupant of tent No. 6, with his full consent, was bitten at 11 a. m., December 30, 1900, by 4 mosquitoes (*C fasciatus*) that had been contaminated 17 days previously by biting a mild case of yellow fever on the first day of the disease (case 4). These insects had been kept at a temperature of 82° F.

The subject remained in his normal condition until the evening of January 2, 1901, the third day, when he complained of frontal headache. At 6 p. m., his temperature was 99° F., pulse 64. He slept well, but still complained of headache on the following morning, January 3. He partook sparingly of breakfast, and afterwards lay on his bed,

being disinclined to exert himself. At 9 a. m., the temperature was 99° F., the pulse 96; at 10.30 a. m., temperature 100° F., pulse 80. A sense of chilliness and sharp frontal headache was complained of, and at 3 p. m. his temperature was 100.8° F., his pulse 89, and his eyes were congested and face flushed. He was removed to the yellow-fever wards. A specimen of urine passed at midnight, January 4, contained a distinct trace of albumin. Slight bleeding from the gums occurred on the fifth and sixth days. The patient was seen by the board of experts on the second and seventh days of his attack, and the diagnosis of yellow fever confirmed. (See Chart 5.)

The period of incubation in this case was 3 days. 22½ hours. The subject had remained in strict quarantine for 22 days preceding his inoculation.

In considering the character of the attacks and the course of the disease in these five cases of experimental yellow fever, it must be borne in mind that these infected individuals were all young men, in good general physical condition and placed amid excellent hygienic surroundings. Further, it must not be forgotten that, on the earliest manifestation of an approaching infection, they were each and all put to bed at once, and were even carried to the yellow-fever wards while occupying the same bed. In other words, these men were kept at absolute rest from the first inception of the disease. Just what bearing this may have had on the subsequent course of the fever, we can not say, but since so much stress is laid on absolute rest of the patient by those having most experience in the treatment of yellow fever, the influence of this enforced rest, in our case, upon the subsequent course of the attack, was doubtless of much importance. We reserve a consideration of the clinical side of these cases for a future report.

In our opinion, the experiments above described conclusively demonstrate that an attack of yellow fever may be readily induced in the healthy subject by the bite of mosquitoes (*C. fasciatus*) which have been previously contaminated by being fed with the blood of those sick with yellow fever, provided the insects are kept for a sufficient length of time after contamination before being applied to the person to be infected.

Our observations do not confirm Finlay's statement that the bite of the mosquito may confer an abortive attack of yellow fever when applied to the healthy subject 2 to 6 days after it has bitten a yellow fever patient. We have always failed to induce an attack even of the mildest description when we have used mosquitoes within less than 12 days from the time of contamination, although the insects were constantly kept at summer temperature. We could cite instances where we have applied mosquitoes at intervals of 2, 3, 4, 5, 6, 9, and 11 days following the contamination of the insect with the blood of well-marked cases of yellow fever early in the disease without any effect whatever being produced by the bite. Thus in 1 case no result followed the bite of 14 mosquitoes which 4 days previously had been contaminated by biting a case of yellow fever on the first day. Again, 7 days later, or 11 days after contamination, the surviving 7 of these insects failed to infect an individual. On the seventeenth day after contamination, however, the bite of 4 of these mosquitoes—all that remained of the original 14—was promptly followed by an attack of yellow fever in the same individual. These insects had been kept during the whole of this time at an average temperature of 82° F.

Our observations would seem to indicate that after the parasite has been taken into the mosquito's stomach, a certain number of days must elapse before the insect is capable of reconveying it to man.

This period doubtless represents the time required for the parasite to pass from the insect's stomach to its salivary glands, and would appear to be about 12 days in summer weather and most probably about 18 or more days during the cooler winter months. It follows also that our observations do not confirm Finlay's opinion that the bite of the contaminated mosquito may confer immunity against a subsequent attack of yellow fever. In our experience an individual may be bitten on three or more occasions by contaminated mosquitoes without manifesting any symptoms of disturbance to health, and yet promptly sicken with yellow fever within a few days after being bitten by an insect capable of conveying the infection.

ACQUIREMENT OF THE DISEASE.

Having shown that yellow fever can be conveyed by the bite of an infected mosquito, it remains to inquire whether this disease can be acquired in any other manner. It has seemed to us that yellow fever, like the several types of malarial fever, might be induced by the injection of blood taken from the general circulation of a patient suffering from this disease. Accordingly we have subjected four individuals to this method of infection, with one negative and three positive results. Reserving the detailed description of these cases to a subsequent occasion, we may state that in one of the positive cases an attack of pronounced yellow fever followed the subcutaneous injection of 2 c. c. of blood taken from a vein at the bend of the elbow on the first day of the disease, the period of incubation being 3 days and 22 hours; in the second case, 1.5 c. c. of blood, taken on the first day of the disease and injected in the same manner, brought about an attack within 2 days and 12 hours; while in our third case, the injection of 0.5 c. c. of blood, taken on the second day of the disease, produced an attack at the end of 41 hours.

In the case mentioned as negative to the blood injection, the subsequent inoculation of this individual with mosquitoes already proved to be capable of conveying the disease, also resulted negatively. We think, therefore, that this particular individual, a Spanish immigrant, may be considered as one who probably possesses a natural immunity to yellow fever.

It is important to note that in the three cases in which the injection of the blood brought about an attack of yellow fever, careful cultures from the same blood, taken immediately after injection, failed to show the presence of Sanarelli's bacillus.[1]

Our observations, therefore, show that the parasite of yellow fever is present in the general and capillary circulation, at least during the early stages of this disease, and that the latter may be conveyed, like the malarial parasite, either by means of the bite of the mosquito or by the injection of blood taken from the general circulation.

[1] A fourth case of yellow fever, severe in type, has been produced by the subcutaneous injection of 1 c. c. of blood taken from the general circulation on the second day of the disease, the period of incubation being 3 days and 1 hour. The patient from whom the blood was obtained was an experimental case which was in turn produced by the injection of blood—0.5 c. c.—derived from a nonexperimental case of fatal yellow fever. As "controls," cases 1, 4, 6, and 7 of this report were also injected subcutaneously with 1 c. c. of the same blood without manifesting any symptoms whatever. The blood which produced this fourth case of yellow fever, when transferred at the same time to bouillon tubes in considerable quantities, gave no growth whatever.

CAN YELLOW FEVER BE PROPAGATED IN ANY OTHER WAY?

We believe that the general consensus of opinion of both the medical profession and the laity is strongly in favor of the conveyance of yellow fever by fomites. The origin of epidemics, devastating in their course, has been frequently attributed to the unpacking of trunks and boxes that contained supposedly infected clothing; and hence the efforts of health authorities, both State and National, are being constantly directed to the thorough disinfection of all clothing and bedding shipped from ports where yellow fever prevails. To such extremes have efforts at disinfection been carried, in order to prevent the importation of this disease into the United States, that during the epidemic season all articles of personal apparel and bedding have been subjected to disinfection, sometimes both at the port of departure and at the port of arrival; and this has been done whether the articles have previously been contaminated by contact with yellow fever patients or not. The mere fact that the individual has resided, even for a day, in a city where yellow fever is present, has been sufficient cause to subject his baggage to rigid disinfection by the sanitary authorities.

To determine, therefore, whether clothing and bedding, which have been contaminated by contact with yellow fever patients and their discharges, can convey this disease is a matter of the utmost importance. Although the literature contains many references to the failure of such contaminated articles to cause the disease, we have considered it advisable to test, by actual experiment on nonimmune human beings, the theory of the conveyance of yellow fever by fomites, since we know of no other way in which this question can ever be finally determined.

For this purpose there was erected at Camp Lazear a small frame house consisting of one room 14 by 20 feet, and known as "Building No. 1," or the "Infected clothing and bedding building." The cubic capacity of this house was 2,800 feet. It was tightly ceiled within with "tongue and grooved" boards, and was well battened on the outside. It faced to the south and was provided with two small windows, each 26 by 34 inches in size. These windows were both placed on the south side of the building, the purpose being to prevent, as much as possible, any thorough circulation of the air within the house. They were closed by permanent wire screens of 0.5 mm. mesh. In addition sliding glass sash were provided within and heavy wooden shutters without; the latter intended to prevent the entrance of sunlight into the building, as it was deemed undesirable that the disinfecting qualities of sunlight, direct or diffused, should at any time be exerted on the articles of clothing contained within this room. Entrance was effected through a small vestibule, 3 by 5 feet, also placed on the southern side of the house. This vestibule was protected without by a solid door and was divided in its middle by a wire screen door, swung on spring hinges. The inner entrance was also closed by a second wire screen door. In this way the passage of mosquitoes into this room was effectually excluded. During the day, and until after sunset, the house was kept securely closed, while by means of a suitable heating apparatus the temperature was raised from 92° to 95° F. Precaution was taken at the same time to maintain a sufficient humidity of the atmosphere. The average

temperature of this house was thus kept at 76.2° F. for a period of 63 days.

November 30, 1900, the building now being ready for occupancy, three large boxes filled with sheets, pillow slips, blankets, etc., contaminated by contact with cases of yellow fever and their discharges were received and placed therein. The majority of the articles had been taken from the beds of patients sick with yellow fever at Las Animas Hospital, Habana, or at Columbia Barracks. Many of them had been purposely soiled with a liberal quantity of black vomit, urine, and fecal matter. A dirty "comfortable" and much-soiled pair of blankets, removed from the bed of a patient sick with yellow fever in the town of Quemados, were contained in one of these boxes. The same day, at 6 p. m., Dr. R. P. Cooke, acting assistant surgeon, United States Army, and two privates of the Hospital Corps, all nonimmune young Americans, entered this building and deliberately unpacked these boxes, which had been tightly closed and locked for a period of two weeks. They were careful at the same time to give each article a thorough handling and shaking in order to disseminate through the air of the room the specific agent of yellow fever, if contained in these fomites. These soiled sheets, pillow cases, and blankets were used in preparing the beds in which the members of the Hospital Corps slept. Various soiled articles were hung around the room and placed about the bed occupied by Dr. Cooke.

From this date until December 19, 1900, a series of 20 days, this room was occupied each night by these three nonimmunes. Each morning the various soiled articles were carefully packed in the aforesaid boxes, and at night again unpacked and distributed about the room. During the day the residents of this house were permitted to occupy a tent pitched in the immediate vicinity, but were kept in strict quarantine.

December 12, a fourth box of clothing and bedding was received from Las Animas Hospital. These articles had been used on the beds of yellow-fever patients, but in addition had been purposely soiled with the bloody stools of a fatal case of this disease. As this box had been packed for a number of days, when opened and unpacked by Dr. Cooke and his assistants, on December 12, the odor was so offensive as to compel them to retreat from the house. They pluckily returned, however, within a short time and spent the night as usual.

December 19, these three nonimmunes were placed in quarantine for 5 days and then given the liberty of the camp. All had remained in perfect health, notwithstanding their stay of 20 nights amid such unwholesome surroundings.

During the week, December 20–27, the following articles were also placed in this house, viz: Pajama suits, 1; undershirts, 2; nightshirts, 4; pillow slips, 4; sheets, 6; blankets, 5; pillows, 2; mattresses, 1. These articles had been removed from the persons and beds of four patients sick with yellow fever and were very much soiled, as any change of clothing or bed linen during their attacks had been purposely avoided, the object being to obtain articles as thoroughly contaminated as possible.

From December 21, 1900, till January 10, 1901, this building was again occupied by two nonimmune young Americans under the same conditions as the preceding occupants, except that these men slept

every night in the very garments worn by yellow-fever patients throughout their entire attacks, besides making use exclusively of their much-soiled pillow slips, sheets, and blankets. At the end of 21 nights of such intimate contact with these fomites, they also went into quarantine, from which they were released 5 days later in perfect health.

From January 11 till January 31, a period of 20 days, "Building No. 1" continued to be occupied by two other nonimmune Americans, who, like those who preceded them, have slept every night in the beds formerly occupied by yellow-fever patients and in the night-shirts used by these patients throughout the attack, without change. In addition, during the last 14 nights of their occupancy of this house, they have slept, each night, with their pillows covered with towels that had been thoroughly soiled with the blood drawn from both the general and capillary circulation, on the first day of the disease, in the case of a well-marked attack of yellow fever. Notwithstanding this trying ordeal, these men have continued to remain in perfect health.

The attempt which we have therefore made to infect "Building No. 1" and its 7 nonimmune occupants, during a period of 63 days, has proved an absolute failure. We think we can not do better here than to quote from the classic work of La Roche.[1] This author says:

> In relation to the yellow fever, we find so many instances establishing the fact of the nontransmissibliity of the disease through the agency of articles of the kind mentioned, and of merchandise generally, that we can not but discredit the accounts of a contrary character assigned in medical writings, and still more to those presented on the strength of popular report solely. For if in a large number of well authenticated cases such articles have been handled and used with perfect impunity—and that, too, often under circumstances best calculated to insure the effect in question—we have every reason to conclude that a contrary result will not be obtained in other instances of a similar kind, and that consequently the effect said to have been produced by exposure to those articles must—unless established beyond the possibility of doubt—be referred to some other agency.

The question here naturally arises: How does a house become infected with yellow fever? This we have attempted to solve by the erection at Camp Lazear of a second house, known as "Building No. 2," or the "Infected mosquito building." This was in all respects similar to "Building No. 1," except that the door and windows were placed on opposite sides of the building so as to give through-and-through ventilation. It was divided, also, by a wire-screen partition, extending from floor to ceiling, into two rooms, 12 by 14 feet and 8 by 14 feet, respectively. Whereas, all articles admitted to "Building No. 1" have been soiled by contact with yellow-fever patients, all articles admitted to "Building No. 2" were first carefully disinfected by steam before being placed therein.

On December 21, 1900, at 11.45 a. m., there were set free in the large room of this building 15 mosquitoes (*C. fasciatus*) which had previously been contaminated by biting yellow-fever patients, as follows: One, a severe case, on the second day, November 27, 1900, 24 days; 3, a well-marked case, on the first day, December 9, 1900, 12 days; 4, a mild case, on the first day, December 13, 1900, 8 days; 7, a well-marked case, on the first day, December 16, 1900, 5 days—total, 15.

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[1] R. La Roche: Yellow Fever, Vol. II, p. 516, Philadelphia.

Only one of these insects was considered capable of conveying the infection, viz, the mosquito that had bitten a severe case 24 days before, while 3 others—the 12-day insects—had possibly reached the dangerous stage, as they had been kept at an average temperature of 82° F.

At 12 M. of the same day, John J. Moran—already referred to as Case 2 in this report, a nonimmune American, entered the room where the mosquitoes had been freed and remained 30 minutes. During this time he was bitten about the face and hands by several insects. At 4.30 p. m., the same day, he again entered and remained 20 minutes, and was again bitten. The following day, at 4.30 p. m., he, for the third time, entered the room and was again bitten.

Case 7.—On December 25, 1900, at 6 a. m., the fourth day, Moran complained of slight dizziness and frontal headache. At 11 a. m. he went to bed, complaining of increased headache and malaise, with a temperature of 99.6° F., pulse 88; at noon the temperature was 100.4° F., the pulse 98; at 1 p. m., 101.2° F., the pulse 96, and his eyes were much injected and face suffused. He was removed to the yellow fever wards. He was seen on several occasions by the board of experts and the diagnosis of yellow fever confirmed. (See Chart 6.)

The period of incubation in this case, dating from the first visit to "Building No. 2," was 3 days and 23 hours. If reckoned from his last visit it was 2 days and 18 hours. There was no other possible source for his infection, as he had been strictly quarantined at Camp Lazear for a period of 32 days prior to his exposure in the mosquito building.

During each of Moran's visits, two nonimmunes remained in this same building, only protected from the mosquitoes by the wire-screen partition. From December 21, 1900, till January 8, 1901, inclusive—18 nights—these nonimmunes have slept in this house, only protected by the wire-screen partition. These men have remained in perfect health to the present time.

December 28, after an interval of 7 days, this house was again entered by a nonimmune American, who remained 25 minutes. The subject was bitten by only one insect. The following day he again entered and remained 15 minutes, and was again bitten by one mosquito. The result of these two visits was entirely negative. As the mortality among the insects in this room, from some unknown cause, had been surprisingly large, it is possible that the subject was bitten by insects not more than 13 days old, in which case they would probably not infect, since they had been kept for only 5 days at a temperature of 82° F., and for 8 days at the mean temperature of the room, 78° F.

Be this as it may, nothing can be more striking or instructive as bearing upon the cause of house infection in yellow fever than when we contrast the results obtained in our attempts to infect Buildings No. 1 and No. 2; for whereas in the former all of 7 nonimmunes escaped the infection, although exposed to the most intimate contact with the fomites for an average period of 21 nights each, in the latter an exposure, reckoned by as many minutes, was quite sufficient to give an attack of yellow fever to one out of two persons who entered the building—50 per cent.

Thus, at Camp Lazear, of 7 nonimmunes whom we attempted to infect by means of the bites of contaminated mosquitoes, we have succeeded in conveying the disease to 6, or 85.71 per cent. On the

other hand, 7 nonimmunes whom we tried to infect by means of fomites, under particularly favorable circumstances, we did not succeed in a single instance. Out of a total of 18 nonimmunes whom we have inoculated with contaminated mosquitoes since we began this line of investigation, 8, or 44.4 per cent, have contracted yellow fever. If we exclude those individuals bitten by mosquitoes that had been kept less than 12 days after contamination, and which were, therefore, probably incapable of conveying the disease, we have to record 8 positive and 2 negative results—80 per cent.

CONCLUSIONS.

1. The mosquito (*C. fasciatus*) serves as the intermediate host for the parasite of yellow fever.
2. Yellow fever is transmitted to the nonimmune individual by means of the bite of the mosquito that has previously fed on the blood of those sick with this disease.
3. An interval of about 12 days or more after contamination appears to be necessary before the mosquito is capable of conveying the infection.
4. The bite of the mosquito at an earlier period after contamination does not appear to confer any immunity against a subsequent attack.
5. Yellow fever can also be experimentally produced by the subcutaneous injection of blood taken from the general circulation during the first and second days of this disease.
6. An attack of yellow fever, produced by the bite of the mosquito, confers immunity against the subsequent injection of the blood of an individual suffering from the nonexperimental form of this disease.
7. The period of incubation in 13 cases of experimental yellow fever has varied from 41 hours to 5 days and 17 hours.
8. Yellow fever is not conveyed by fomites, and hence disinfection of articles of clothing, bedding, or merchandise, supposedly contaminated by contact with those sick with this disease, is unnecessary.
9. A house may be said to be infected with yellow fever only when there are present within its walls contaminated mosquitoes capable of conveying the parasite of this disease.
10. The spread of yellow fever can be most effectually controlled by measures directed to the destruction of mosquitoes and the protection of the sick against the bites of these insects.
11. While the mode of propagation of yellow fever has now been definitely determined, the specific cause of this disease remains to be discovered.

DISCUSSION.

Dr. Louis Perna, Cienfuegos, Cuba, in opening the discussion, said that it is sophism to believe that post hoc, ergo propter hoc; that is to say, that, as Carmona, Freire, Sanarelli, and others have fallen to this error, we must not be too precipitate in accepting the result of statistics. The studies made of mosquitoes are very old. A French physician, who died about 1850, expressed the opinion that malaria, yellow fever, and cholera were propagated by mosquitoes. Dr. Perna also criticized the methods employed by the commission

in making experiments on human beings and is entirely opposed to such experiments.

Dr. San Martin eloquently defended, and with strong arguments, the high scientific standard of the experiments as carried out by this commission, and also brought out the point that it was not statistics but facts that this commission presented.

Dr. H. B. Horlbeck, Charleston, S. C., expressed his opinion that the problem of 200 years was about to be solved, that the old quarantine regulations should be greatly modified. He also described the existence of a pine belt within a short distance of Charleston, S. C., in which yellow fever never developed as an epidemic, although the afflicted therewith would go there during the existence of the epidemic in Charleston, would die from the disease, and yet it would not spread. Mosquitoes are not known in that region, and probably this is the true explanation of the above fact. He concluded by emphasizing the inestimable value of these experiments if they prove to be true.

Dr. Emilio Martinez, Habana, laid emphasis on Dr. San Martin's views. He took up the moral question and claimed that without these no truth could have been found.

Dr. Manuel Gutierrez, Mexico, who up to within a short time had been adverse to the theory of the transmission of this disease by mosquitoes, now accepted as incontrovertible the results of the experiments of the commission. He followed with interest many of the experiments, and as a member of the commission saw most of these cases, which he had no hesitation in pronouncing typical cases of yellow fever. A fact which impressed him forcibly was the absolute control of the epidemic by Dr. Reed. The cases would develop or not, as he wished. He does not think that the mosquito should be called the *Culex fasciatus*. Giles's description of the *Culex tiniads* mosquito agrees more closely than with the *Culex fasciatus*. He describes the difference between them. He is inclined to consider them a genus apart because they lay different eggs.

Dr. C. Finlay, Habana, expressed his admiration for the work of the commission. He believes that this session of the congress will go down in history as of great importance and that the differences between his opinion and that held by the commission will disappear in the course of time. He states that they were based on the fact that he investigated with three varieties of mosquitoes, while the commission has been restricted to one variety; that the board was placed on better footing for obtaining satisfactory results; that the negative result obtained by the inoculation of mosquitoes of short infection should not induce the commission or the board to make such hard and biased rules as are evidenced in its conclusions.

Dr. Reed, in conclusion, said he was profoundly impressed with the interest and attention given to these experiments. In regard to the moral aspect of the case, he did not think that anyone appreciated the position in which he found himself—the difficulties that beset his path. The first experiment was made on a member of the board, Dr. Carroll. The senior member expected to take his bite in turn, but was unexpectedly called north. As no animal could be given the disease, and it was useless to follow the previous indefinite experiments, it was absolutely necessary to make these experiments on human subjects, or otherwise volumes could have been written and

discussed, and yet we would have been no nearer the truth than at first. No progress could have been made toward an exact knowledge of the disease unless human subjects had been used. All experiments were performed on persons who had given their free consent.

In reference to the remarks of Dr. Holbeck, of Charleston, the disinfection of vessels should by no means be dispensed with, but only of such articles as bedding and clothing, though it is necessary to get rid of the mosquitoes, and this simplified the process of disinfection.

In regard to the remarks of Dr. Gutierrez, in reference to the name of the mosquito, Dr. Howard, of Baltimore, told him that *Culex fasciatus* is identical with *Culex tiniads* as described by Giles. Theobolt separates *Culex tiniads* from the genus *Culex* and places it in a new genus, *Stegamina*. These lay their eggs in a peculiar way, and there is also a difference in the anterior claws of the male insect from those of the other *Culex*. There is also a difference in the larva of the *Culex fasciatus*. It is very interesting also to note the fact that this is the very mosquito that Dr. Finlay used in his experiments and that this particular mosquito does not belong to the genus *Culex;* therefore malaria has a genus of its own, *Anopheles*, and yellow fever the genus *Stegamina*.

Chapter 4.

THE PROPAGATION OF YELLOW FEVER—OBSERVATIONS BASED ON RECENT RESEARCHES.[1]

By Walter Reed, M. D., Surgeon, United States Army.

Mr. President and Gentlemen of the Faculty: If, upon receipt of your kind invitation to be present with you to-night my first impulse was to decline, I beg that you will not attribute this to any want of appreciation on my part of the honor conferred, but solely to my desire to avoid what I felt would be a very embarrassing position should I attempt to follow in the footsteps of the distinguished gentlemen whom you have invited to fill this position from year to year. Recognizing in them, as all willing leaders do, leaders in the profession, who, by their well-considered addresses, have been able to add so much to the scientific interest of your annual meetings, I could but feel that the burden which you proposed to put upon me was greater than I could bear. That, nevertheless, I am here in the capacity of your annual speaker is due to my unwillingness even to appear disobliging to this old and honorable association of physicians, among whose number I find included some of my most valued friends; friends who in years gone by have labored so faithfully to instill into my mind the value of the scientific method, but to whom I have been able to make such small return. If, therefore, I drew some encouragement from the feeling that I should not be wholly among strangers, I found yet more in the thought that such an eminent body of physicians as this faculty must ever be willing to welcome any contribution that promises to shed light upon a subject hitherto enshrouded in darkness, and which thereby holds out the prospect of an addition to our knowledge in the larger field of preventive medicine.

In the hope that what I have to say to-night may contribute to the solution of a somewhat obscure problem, and may assist us hereafter in the struggle with a grave epidemic disease, I have concluded to present for your consideration "The propagation of yellow fever, based on recent researches."

Before proceeding to the discussion of this subject, it is fitting that I should pay brief tribute to the memory of a former member of this faculty, the late Dr. Jesse W. Lazear, United States Army. I can hardly trust myself to speak of my late colleague, since the mention of his name brings back such scenes of anxiety and depression as one recalls only with pain. Along with these sad memories, however, come other recollections of a manly and fearless devotion to duty such as I have never seen equaled. In the discharge of the latter, Dr. Lazear seemed absolutely tireless and quite oblivious

[1] Address delivered at the One hundred and third annual meeting of the Medical and Chirurgical Faculty of the State of Maryland, held at Baltimore, April 24-27, 1901.

of self. Filled with an earnest enthusiasm for the advancement of his profession and for the cause of science, he let no opportunity pass unimproved. Although the evening might find him discouraged over the difficult problem at hand, with the morning's return he again took up the task full of eagerness and hope. During a service of less than one year in Cuba he won the good will and respect of his brother officers and the affection of his immediate associates. Almost at the beginning of what promised to be a life full of usefulness and good works he was suddenly stricken, and, dying, added one more name to that imperishable roll of honor to which none others belong than martyrs to the cause of humanity.

It is my own earnest wish that, whatever credit may be hereafter given to the work of the American commission in Cuba during the past year, the name of my late colleague, Dr. Lazear, may be always associated therewith.

I do not propose to set before you this evening so much the views of others in relation to the etiology of yellow fever, or to the conditions under which it originates and spreads, as to give you the results of my own experience with regard to the manner in which this disease propagates itself. In the ordinary course of Army administration, I found myself brought in contact with yellow fever during the summer of 1900, under such circumstances as permitted me to give my entire time to the study of its etiology and propagation. Permit me here to remark that so many claims have been made as to the specific cause of yellow fever—claims that could not be confirmed by other investigators—that one must needs feel considerable hesitancy in considering this remarkable disease from any aspect. I must confess that I have experienced, in the highest degree, this feeling of reluctance to write or speak about yellow fever, especially when I recall the frame of mind of myself and my colleagues—that of utter perplexity and wonder—as we stood by the bedside of patients, or at the autopsy table of those who had died of this mysterious malady. I trust, therefore, that whatever I may say here to-night will be considered as a modest expression of opinion growing out of an unprejudiced study of yellow fever, for the most part from the point of view of its propagation.

Although considerable attention had been given to the laboratory study of the microorganisms isolated by Sternberg and Sanarelli from the organs of yellow-fever cadavers, this did not enable one to form any opinion concerning the nature of the disease or the mode of its propagation.

At the time of our arrival in Cuba—June, 1900—the situation as regards the etiology of yellow fever may be briefly stated as follows: The claims of all investigators for the discovery of the specific agent of this disease had been disproved by the exhaustive work of Sternberg,[1] published in 1890, except that made by Dr. Sanarelli, in June, 1897, for his *bacillus icteroides*. I need not take up time here with mention of those who had investigated Sanarelli's claim, except to state that the confirmation of his discovery came chiefly from workers in the United States, of whom I may speak of Achinard and Woodson, of New Orleans, and especially of Wasdin and Geddings, of the

[1] Report on the Etiology and Prevention of Yellow Fever, 1890.

Marine-Hospital Service. The latter, in a report[1] submitted during the summer of 1899, accepted in the fullest Sanarelli's claim for the specific character of *bacillus icteroides*, basing their confirmation on the finding of this bacillus in 13 out of 14 cases of yellow fever studied by them in the city of Habana. Under these circumstances, it was of the first importance that we should give our entire time to the search for *bacillus icteroides* in the bodies of yellow-fever cases. The result of this study, embracing 21 cases during life and 11 autopsies, and which was entirely negative, has already been given in our Preliminary Note,[2] read at the last meeting of the American Public Health Association (1900).

Turning for a moment to our knowledge concerning the mode of propagation of yellow fever, the situation, when we began work, was about as follows: The battle for or against its importation having been already decided in favor of the former belief, its transmissibility from place to place was attributed to the individual affected by the disease, but especially to his clothing; with the proviso, however, that intimately connected with its spread was involved a proper constitution of the atmosphere of the place, this latter due chiefly to insanitary conditions of soil. That the excreta of the patient contained the specific agent of the disease was supported by many good authorities. That the disease could be propagated by fomites was not disputed by anyone. Against its spread by the sick and by fomites all quarantine measures were being then directed.

The theory of Finlay for the propagation of yellow fever by the mosquito, concerning which I shall presently have something to say, had either gained no credence or been rejected by reason of the absence of any results that had been presented by its author in support of it. In the meantime, and before we had completed our search for Sanarelli's bacillus, certain facts had been cropping out, as it were, which served to arrest the attention. Just here, while mentioning the first fact, let me say that one does not like to confess his ignorance of such a well-known disease as yellow fever, especially before an audience some of whose members may have already treated cases during the last epidemic in this city, in the year 1876; and yet candor compels me to record my very great surprise, when brought face to face with yellow fever, to learn that attendance on patients by non-immune nurses, in every stage of the malady, involved no danger. In other words, that yellow fever, both in the wards at Columbia Barracks, as well as in the wards of Las Animas Hospital, Habana, was not contracted by the attendants under circumstances such as those in which typhoid fever and Asiatic cholera are too often conveyed. Further inquiry along this line seemed to indicate that the disease had not been contracted in hospitals, even during the earlier epidemics, when disinfection of articles of clothing and bedding was unknown.

A second fact which appeared worthy of note, was the discharge of patients from the wards during early convalescence, and their return to the companionship of their comrades with apparently no danger of establishing fresh foci of the disease. This hardly seemed in keeping with the presence of a specific agent in the excreta of the sick.

A third fact which stood out prominently was that, in certain of our cases, no growth whatever was obtained on our present laboratory

[1] The Cause of Yellow Fever. Washington, 1899.
[2] The Etiology of Yellow Fever. A Preliminary Note. Phil. Med. Journal, Oct. 27, 1900.

media, either by frequent cultures taken from the blood during life or from the organs after death. In other words, no bacterium was obtainable by aerobic methods, in certain of our cases, either during life or after death. This result had considerable weight in controlling our future work.

During the time that these cases were being studied, opportunity was afforded to investigate an epidemic of fever which was prevailing in Pinar del Rio Barracks, near the town of this name, distant 110 miles from Habana, and of which fever several soldiers, in a garrison of about 900 men, had already died. A visit was made to this garrison with my colleague, Dr. Agramonte, on the 31st day of July, 1900, and a body sectioned the same afternoon. The lesions found were those of yellow fever. Inquiry showed that under the diagnosis of "remittent malarial fever" or "pernicious malarial fever," the disease had been prevailing for at least 37 days prior to our arrival—July 21—and that about 35 cases had been under treatment in the post hospital, of which number 11 had died. As the true nature of the disease had not been suspected, no precautionary measures had been taken as regards the disinfection of bedding and clothing used by the patients, except that in case of death the sheets and pillow slips were put in bichloride solution and the mattresses and pillow exposed to sunlight. An order required that the excreta of all patients under treatment in this hospital should be carefully disinfected, and this was probably carried out fairly well. The excreta for the garrison at large were incinerated in permanent crematories, fires being lighted in these twice a week.

Notwithstanding the omission to disinfect the bulk of the contaminated articles of bedding and clothing, the disease had not been contracted by the nurses, nor by the other patients in the several wards, nor by the three men who washed all of these articles. A little inquiry showed that contaminated clothing was in all of the eight barrack rooms without apparent detriment to the occupants. Further investigation showed that a death from yellow fever had occurred in this garrison as early as May 16, 1900, and that the source of infection for this case, as well as for the present outbreak, was in the immediately adjacent town of Pinar del Rio, to which the soldiers had free access.

An interesting observation was the sudden attack of yellow fever experienced on July 12, 1900, by a general prisoner who had been confined in a cell in the guardhouse since June 6, 1900. His death occurred at the post hospital on July 18, 1900. This cell was occupied at the time by eight other prisoners, none of whom contracted the disease, although one of them continued to occupy the bunk vacated by the sick man. As these nine prisoners had been kept under strict military guard, it was impossible that the individual attacked could have acquired his infection in the town of Pinar del Rio. He was, as far as could be ascertained, exposed to no source of infection to which his companions had not been equally exposed, and yet he alone acquired the disease. It was conjectured at the time that perhaps some insect capable of conveying the infection, such as the mosquito, had entered through the cell window, bitten this particular prisoner, and then passed out. This was, however, only a supposition.

Two instances of undoubted exposure to fomites, involving four individuals, came under my observation during this inspection. In

the one case a box of clothing, belonging to a soldier who had died of yellow fever on July 3, and which had been packed by an enlisted man on July 4, and placed in the company storeroom, was unpacked for the purpose of making an inventory of the articles, and carefully repacked on July 18 by two nonimmune soldiers, who did not contract the disease by this exposure. In the other case the very bed vacated on July 18 by the commissary sergeant, who was taken sick on July 17, and died on July 21, was occupied by a nonimmune soldier on the nights of the 19th and 20th of July. Although this individual was badly frightened when the true character of the sergeant's attack was announced, the combination of fright and exposure to fomites was not sufficient to produce an attack of yellow fever.

The data gathered, therefore, during the investigation of this small epidemic at Pinar del Rio did not tend to strengthen one's belief in the theory of the propagation of yellow fever by fomites. This belief had already been shaken by the manner in which the disease had spread in the town of Quemados, Cuba, from which we had obtained cases for bacteriologic study; for here we saw the disease pass from No. 102 Real Street around the corner to No. 20 General Lee Street, and thence to a house immediately across this latter street, without the passage of any persons between these three houses, and to the exclusion of any article of clothing, as the three families had no acquaintance whatever with each other. Here the infection was just as plainly carried through the air as it had been taken, through this medium, to the prisoner in the cell at Pinar del Rio. We also observed in this town that the contagion passed down General Lee Street with a bound to the distance of a square, passing in its journey a house containing two nonimmunes, only to return a few days later to this very house and seize upon both of its nonimmune inmates. This hardly seemed in keeping with the idea of a diffusible poison carried by the atmosphere. During our first week on the island, we noted in a house in Quemados, where the husband and wife were taken down with yellow fever a few days apart, that neither the young daughter, who was removed to a place of safety on the fourth day, nor an attendant who had remained in the sick room for the entire 24 hours of the seventh day, had acquired the disease; but that of the two remaining nurses who continued to perform their duties, one was seized on the fourteenth day and the other on the fifteenth day with an attack of yellow fever. This observation was recorded at the time for what it was worth. Later it was found to harmonize with the observations which had been made by Surg. Henry R. Carter, of the Marine-Hospital Service, in 1898. As I shall recur to these observations later in my remarks, it will suffice to here state that at this stage of our investigation it seemed to me, and I so expressed the opinion to my colleagues, that the time had arrived when the plan of our work should be radically changed; that the search for the specific agent of yellow fever, while not abandoned, should be given secondary consideration, until we had first definitely learned something about the way or ways in which the disease was propagated from the sick to the well. I felt well-nigh convinced that we could obtain no light whatever upon the task that had been set before us, unless we substituted this line of work for the one we had been pursuing, and that in view of the splendid work of Ross,

Bignami, and others with regard to the propagation of malarial fever, together with the well-known thermal influences intimately connected not only with the epidemiology of the disease in the United States, but also with its endemiology on the Island of Cuba, it was of the highest importance that the agency of an intermediate host, such as the mosquito, should either be proven or disproven.

Remember, if you please, that here we were dealing with an epidemic disease concerning which there was no evidence whatever to show that it had ever been spread by contamination of either water or food; that it had always demanded a certain elevated temperature before it would begin its progress, which latter, both in its manner and rate, was quite unlike that of other epidemic diseases, such as smallpox or typhoid fever or Asiatic cholera; that once having begun its march, no hygienic measures ever instituted had been able to arrest its course, except depopulation of the locality affected; that while, if introduced into certain localities, it would readily propagate itself, those sick with this disease could be carried in large numbers into other places without any danger of its spread—a fact which had been attested in hundreds of instances; that ships with nonimmune crews could remain at anchor with perfect safety at about 300 yards from an infected shore. Couple with this the natural law by which it was governed, viz, its prompt control by frost, and tell me what other epidemic disease could be associated in the mind with this except malarial fever.

The theory that the spread of yellow fever could not be explained by the assumption of a diffusible miasm in the atmosphere, but required the presence of an intermediate host, appears to have been first advanced by Dr. J. C. Nott, of Mobile, Ala., in March, 1848. His views were given in full in the New Orleans Medical Journal for that year. It was also in this paper that Nott suggested the mosquito as the possible agent in the dissemination of malarial fevers. He evidently did not have in mind the mosquito as the bearer of the yellow-fever poison, but rather that this important office was performed by some insect or insects that remained very close to the ground. Referring to the fact to which all writers were agreed, that a very imperfect barrier, such as a row of houses or of trees, would often protect dwellings from the access of malarial poison, he says:

> I have been able in my researches to discover no facts of this kind in connection with yellow fever, and my personal observation repudiates this in toto. We never find yellow fever, as the sportsman says, "up a tree," but on the contrary the materies morbi, whatever it may be, creeps along the ground, regardless of winds, passing under and through houses and trees, etc., and knowing no impediment but a sheet of water.

Again:

> It is a curious fact that from 1829 to 1837 there was no epidemic of yellow fever in Mobile, and during this time the streets were beautifully shelled; since 1837 we have had it five times and the shelling was not continued. If the insect theory be correct, could the lime be an impediment to their progress across the street?

To Dr. Carlos J. Finlay, of Habana, must be given, however, full credit for the theory of the propagation of yellow fever by means of the mosquito, which he proposed in a paper read before the Royal Academy in that city at its session on the 14th day of August, 1881. From that date to the present time Finlay has made a number of valuable contributions to the origin and mode of transmission and

the prevention of yellow fever. During this time his views have undergone some slight modification. Starting with the idea that the specific poison adhered to the mosquito's proboscis and was thus mechanically transferred to the individual next bitten (which specific agent was claimed by him in 1887, and even at the present time, to be his micrococcus tetragenus febris flavæ), he later—1899—modified his original theory, based upon the studies of Theobald Smith on Texas fever, "so as to include the important circumstances that the faculty of transmitting the yellow-fever germ need not be limited to the parent insect, directly contaminated by stinging a yellow-fever patient (or perhaps by contact with or feeding from his discharges), but may be likewise inherited by the next generation of mosquitoes issued from the contaminated parent" (New York Medical Record, May 27, 1900). Of the 100 individuals experimented upon from June, 1881, to May, 1895, Finlay claimed to have produced three cases of "mild albuminuric fever" after a period of incubation varying from 5 to 25 days; but as he exercised no control over these individuals, to the exclusion of other sources of infection, no value could be attached to his results. If, indeed, one were guided by the results obtained, the only logical conclusion to be drawn was that Finlay had disproved his own theory. His failure to produce positive results—which we now believe to be due to the fact that he did not keep his insects for a sufficient length of time after contamination before applying them to the individual to be infected—doubtless led Finlay to promulgate the later idea that the bite of the contaminated mosquito, while not producing the disease, conferred immunity upon the individual bitten. He has made use of the bite of the contaminated mosquito for this purpose in a considerable number of individuals. Notwithstanding the fact that Finlay had no results to show in support of his theory, and that the latter had been wholly rejected by other investigators, the argument in favor of an intermediate host seemed so strong, as I have already stated, that further investigation along this line was determined upon. The mosquito selected was the one that had been used by Finlay in his previous work, and which, with *Culex pungens*, is the most prevalent and annoying mosquito in the city of Habana, and for that matter in all the larger towns on the island. Originally designated by Fabricius as *Culex fasciatus*,[1] it had later been called by Desvoidy, *Culex mosquito*. Unlike *Culex pungens* this mosquito bites by day as well as during the nighttime. Judging from my own experience, I should say that its favorite hours for feeding were from 4 p. m. to 10 p. m.

In our preliminary note, above referred to, we recorded, among 11 individuals bitten by contaminated mosquitoes of this species, 9 negative and 2 positive results; the attack in both of the latter occurring within the period of incubation of yellow fever. As the circumstances surrounding the infection of one of these cases was such as to exclude any other source of infection, we announced the conclusion that "the mosquito served as the intermediate host for the parasite of yellow fever." Subsequent observations have pointed, in the most convincing manner, to the soundness of this conclusion. It is to these later observations that I now desire to invite your attention.

[1] It is interesting and important to observe that since the publication of our Preliminary Note, Theobold, the English entomologist, has taken *C. fasciatus* from the genus Culex and placed it in a new genus—Stegomyia.

Dismiss from your minds, if you please, the idea that yellow fever is so prevalent on the island of Cuba, and that the ways of acquiring the disease are so numerous, that experimental results obtained at any point in the so-called endemic zone of yellow fever must be thereby vitiated. Nothing to my mind could be more improbable than such an opinion; for, as a matter of fact, yellow fever has been confined, during the year 1900, to Habana and a few other towns, coast or inland, and has not been present elsewhere on the island. Hence any location selected, provided it should be 1 mile from such a center of infection and surrounded by proper safeguards, would be just as free from the occurrence of yellow fever as if it were located 10 miles from such a town. My own experience on the island of Cuba had already taught me that yellow fever could be easily kept out of a military garrison, although prevailing in epidemic form in a town less than 1 mile distant. For this reason it was not considered advisable to establish our experimental sanitary station at a greater distance than 1 mile from Quemados, Cuba. Thus Camp Lazear could be easily reached by the members of the board and was conveniently located as regards its base of supplies. The occurrences at this camp fully justified this decision. Placed in an open field, which was fairly swept at all times by the prevalent winds, and having a military garrison each of whose members had been personally selected by reason of former good conduct and interest in the work to be here undertaken, no difficulty whatever was experienced in maintaining the strictest quarantine against the outside.

Let us now present to you, as succinctly as possible, our observations at this camp, prefacing what I shall have to say with the remark that here we proposed to attempt the infection of nonimmune individuals in three ways, viz, first, by the bites of mosquitoes that had previously bitten cases of yellow fever; secondly, by the injection of blood taken during the early stages from the general circulation of those suffering with the disease; and, thirdly, by exposure to the most intimate contact with fomites. For this purpose, in addition to the seven tents provided for the quartering of the detachment, two frame buildings, each 14 by 20 feet in size, were constructed. These buildings, having a cubic capacity of 2,800 feet, were exactly similar, except that one of them, known as the "Infected mosquito building," was divided near its middle by a permanent wire-screen partition and had good ventilation; while the other, designated as the "Infected clothing building," was purposely so constructed as to exclude anything like efficient ventilation. These houses were placed on opposite sides of a small valley, about 80 yards apart, and each 75 yards distant from the camp proper. Both houses were provided with wire-screen windows and double wire-screen doors, so that mosquitoes could be kept without or within the buildings, as the experimenter might desire.

At first the results obtained at this station were not encouraging. From November 20, 1900, the date of the establishment of the station, until December 4—a period of 2 weeks—we had tried to infect 4 individuals, with entirely negative results. Two of these had been bitten twice, at intervals of 3 days, by contaminated mosquitoes which had been kept from 10 to 14 days after they had fed on yellow-fever cases; while the other 2 nonimmunes had been thrice bitten, at

the same intervals, by mosquitoes that had bitten cases of yellow fever 10 to 18 days before. As the weather during this time was cool and the insects had been kept at room temperature (and this is practically outdoor temperature in Cuba), we conjectured that the negative results might, perhaps, be thus explained. We remembered that Daniels [1] in repeating, during the winter season, Ross's observations with proteosoma infection of birds, had obtained a much smaller percentage of successes than had Ross, who worked during summer weather. We would have been glad to draw some encouragement from our negative experiments, also, with infected bedding, but, as at this date (Dec. 4) our 3 subjects had been sleeping with fomites only 4 nights (which is within the period of incubation of the disease), this comfort was debarred.

On the fifteenth day of our encampment therefore (Dec. 5, at 2 p. m.) we concentrated our insects, so to speak, on one of these non-immunes—Kissinger by name—selecting 5 of our most promising mosquitoes for the purpose. These had been contaminated as follfollows: Two, 15 days; 1, 19 days; and 2, 21 days previously. This inoculation was more successful, for, at the expiration of 3 days and 9½ hours the subject, who had been under strict quarantine during 15 days, was suddenly seized with a chill about midnight, December 8, which was the beginning of a well-marked attack of yellow fever.

I can not let this opportunity pass without expressing my admiration of the conduct of this young Ohio soldier, who volunteered for this experiment, as he expressed it, "solely in the interest of humanity and the cause of science," and with the only proviso that he should receive no pecuniary reward. In my opinion this exhibition of moral courage has never been surpassed in the annals of the Army of the United States.

The following morning (Sunday, Dec. 9, at 10.30 a. m.) we selected from those insects that had bitten Case I, one mosquito that seemed to us to possess the best record of contamination, as it had bitten a fatal case of yellow fever, on the second day of the disease, 19 days before. This insect was applied to a Spanish immigrant, who had been strictly quarantined at our station for 19 days. At the expiration of 3 days and 11 hours (Dec. 9, 9.30 p. m.) this individual was also seized with an attack of yellow fever.

In the meanwhile, on December 8, 1900, at 4 o'clock p. m., we had applied to a young Spaniard three of the mosquitoes that had, three days previously, bitten Case I, together with an additional mosquito contaminated 17 days before. At the end of 4 days and 20 hours (Dec. 13, noon) this Spaniard suddenly lost his vivacity and took to his bed. The following morning at 9 a. m. his febrile paroxysm began. His case, which was the mildest of our series, was also marked by a long period of incubation, viz, 5 days and 17 hours. He had been in quarantine 9 days.

December 11, at 4.30 p. m., the identical 4 insects which had bitten Case III were fed on a Spanish immigrant who had been in quarantine for the past 21 days. At the expiration of 3 days and 19½ hours (Dec. 15, noon) he was likewise seized with yellow fever.

Thus within the period of one week—December 9 to 15—we had succeeded in producing an attack of yellow fever in each of the 4

[1] On transmission of Proteosoma to Birds by the Mosquito—Royal Society, Reports of Malarial Committee. London, 1900.

individuals whom we had caused contaminated insects to bite, and in all save 1 of the 5 nonimmunes whom we had originally selected for experimentation.

It can readily be imagined that the concurrence of 4 cases of yellow fever in our small command of 12 nonimmunes within the space of 1 week, while giving rise to feelings of exultation in the hearts of the experimenters, in view of the vast importance attaching to these results, might inspire quite other sentiments in the bosoms of those who had previously consented to submit themselves to the mosquito's bite. In fact, several of our good-natured Spanish friends who had jokingly compared our mosquitoes to "the little flies that buzzed harmlessly about their tables," suddenly appeared to lose all interest in the progress of science, and, forgetting for the moment even their own personal aggrandizement, incontinently severed their connection with Camp Lazear. Personally, while lamenting to some extent their departure, I could not but feel that in placing themselves beyond our control they were exercising the soundest judgment. In striking contrast to the want of confidence shown by these Andalusians who had agreed to be bitten by mosquitoes was the conduct now displayed by the three young Americans, who had consented to jeopardize their lives by exposure to fomites and who, as a matter of fact, had already spent 15 nights in a small, illy ventilated building, breathing in an atmosphere dreadfully contaminated by the soiled garments of yellow-fever patients. With the occurrence of these cases of mosquito infection, the countenances of these men, which had before borne the serious aspect of those who were bravely facing an unseen foe, suddenly took on the glad expression of "schoolboys let out for a holiday," and from this time their contempt for "fomites" could not find sufficient expression. Thus illustrating once more, gentlemen, the old adage that familiarity, even with fomites, may breed contempt.

As the continued good health of those who were occupying the "infected clothing building" pointed strongly to the harmlessness of fomites, the next experiment at this station was undertaken for the purpose of demonstrating that the essential factor in the infection of a building with yellow fever is the presence therein of mosquitoes that have bitten cases of yellow fever.

Accordingly at 11.55 a. m., December 21, 1900, 15 mosquitoes were freed in the larger room of the "infected mosquito building," which, as I have said, was divided into two compartments by a wire-screen partition. The interval that had elapsed since the contamination of these insects was as follows: One, 24 days; three, 12 days; four, 8 days; and seven, 5 days. The only articles of furniture in this building consisted of three beds, one being placed in the mosquito room and two beyond the wire screen, these latter intended to be occupied by two "control" nonimmunes. The articles of bedding as well as the bedsteads had been carefully disinfected with steam. At noon on the same day, 5 minutes after the mosquitoes had been placed therein, a plucky Ohio boy, Moran by name, clad only in his nightshirt, and fresh from a bath, entered the room containing the mosquitoes, where he lay down for a period of 30 minutes. On the opposite of the screen were the two "controls" and one other nonimmune. Within 2 minutes from Moran's entrance he was being bitten about the face and hands by the insects that had promptly

settled down upon him. Seven in all bit him at this visit. At 4.30 p. m., the same day, he again entered and remained 20 minutes, during which time 5 others bit him. The following day at 4.30 p. m., he again entered and remained 15 minutes, during which time 3 insects bit him, making the number 15 that had fed at these three visits. The building was then closed, except that the two non-immune "controls" continued to occupy the beds on the noninfected side of the screen. On Christmas morning, at 11 a. m., this brave lad was stricken with yellow fever, and had a sharp attack, which he bore without a murmur. The period of incubation in this case was 3 days and 23 hours, counting from his first visit, or 2 days and 17½ hours if reckoned from his last visit. The two "controls" who had slept each night in this house, only protected by the wire screen, but breathing the common atmosphere of the building, had remained in good health. They continued to so remain, although required to sleep here for 13 additional nights. As Moran had remained in strict quarantine for the period of 32 days prior to his attack, the source of his infection must be found within this house.

In the order of succession, the next experiment undertaken at this camp was the injection of blood, taken from Case V (Moran), beneath the skin of a Spaniard, but I will defer further mention of this line of experimentation until I have completed the mosquito series, as these are by far the most important. I, therefore, invite your attention to Case VI, Martinez by name. His case is of interest as bearing upon the number of days which must elapse after the contamination of the mosquito before it can convey the disease to a second individual.

An additional point of some importance, I think, is that whereas prior to the time of Moran's infection (Case V) the contaminated mosquitoes had been taken to the men in their tents and there applied, from this date—December 17—the subjects were invited to visit a particular room attached to our "Mosquito building," but quite separate from it, where the contaminated insects were kept at summer temperature, and were there given the opportunity of exposing themselves to an attack of yellow fever by putting their hands inside of certain mosquito-inhabited jars. I may as well tell you now that of seven persons who availed themselves of this privilege five acquired yellow fever.

After a quarantine period, therefore, of 9 days, Martinez visited this room on December 17, 1900, and was bitten by 14 mosquitoes which 4 days before had fed upon Case I of this series. The result was quite negative. December 24, or on the eleventh day after contamination, the subject was again bitten by 7 of these insects—all that remained of the original 14. Again no infection took place. After 6 full days, or on December 30, at 11 a. m., Martinez was again bitten by the surviving 4 of these mosquitoes, i. e., on the seventeenth day after their contamination. On the fourth day thereafter, January 3, 1901, at 10.30 a. m., he was seized with yellow fever, which ran a typical course. The period of incubation was 3 days 22½ hours. Although we can not say on what particular day these insects became capable of conveying the disease, we are able to state that they were incapable of infecting on the fourth or eleventh day

after contamination. This experiment agrees with others that we have made during this investigation and in which we have failed to convey the disease by the bites of insects at intervals varying from 2 to 9 days after contamination. These observations seem to indicate that after the parasite has been taken into the mosquito's stomach a certain number of days must elapse before the insect is capable of reconveying it to a second individual. This period probably represents the time required for the parasite to undergo its cycle of development and reach the mosquito's salivary glands, and, as far as our experience goes, would appear to be about 12 days in summer weather and most probably about 18 or more days during the cooler winter months. Case VI, therefore, does not support the opinion of Finlay that the bite of the contaminated mosquito confers immunity against a subsequent attack of the disease, since we have seen that neither the bites of 14 insects on the fourth day nor the bites of 7 on the eleventh day after contamination prevented in the least the conveyance of the infection by the bites of 4 only of these mosquitoes on the seventeenth day.

I will now ask you to look at Case IX, as this case serves to illustrate some points of interest. In the first place, this subject, an American, was bitten by insects that had fed upon Case I of our series on the third day of his illness; that is, during the secondary fever which followed a complete intermission in this case. Secondly, these mosquitoes had been kept alive on sugar and water for a period of 39 days before being applied to Case IX. Of the original 5 insects that had bitten Case I on the third day, 4 were still alive on the thirty-ninth day thereafter and 3 showed every evidence of good appetite. Thirdly, this particular subject having passed 21 nights in the "Infected clothing building," during which time he was exposed to the most intimate contact with fomites, without apparent detriment to his health, had been kept in strict quarantine for yet 30 days longer at Camp Lazear. At the expiration of this time, or on January 19, 1901, at 4.30 p. m., he visited our mosquito room, where he was bitten by these 39-day-old insects, 3 in number. This inoculation was followed by an attack of yellow fever of moderate severity, which began at 4 p. m., January 23, the period of incubation being 3 days 23½ hours.

Case XII you will find of equal interest, as this individual was infected, in the same room, by the bites of two of these same mosquitoes on the fifty-first day after their contamination, the period of incubation being 3 days 2½ hours and the character of the attack mild, while Case XIII will conclusively demonstrate that these identical insects, on the fifty-seventh day after their contamination, were not only capable of conveying the infection, but of producing an attack of such severity that the subject's life hung in the balance for several days. I regret to have to state that the individual who had consented to be bitten by these insects on the sixty-fifth day after their contamination failed to fulfill his promise at the last moment; so that otherwise I can not say to what old age these mosquitoes might have attained. Deprived of further opportunity to feed on human blood, one died on the sixty-ninth day and the other on the seventy-first day after their original contamination. The duration of life in the case of these mosquitoes will readily explain how the poison of yellow fever can remain even in a depopulated area for a period of

2½ months; so that, as is well known, those who enter the infected area, even at the expiration of this period, are liable to acquire the disease.

Case XIV is that of our tenth and last successful mosquito infection at Camp Lazear. This individual after 25 days' quarantine, having been bitten on February 7, 1901, at 2 p. m., by two mosquitoes on the sixteenth day after their contamination, was seized with an attack of yellow fever at noon, February 10, after an incubation stage of 2 days 22 hours.

Thus you will observe that at this station, under strict quarantine precautions, we succeeded in conveying the disease to 10 nonimmunes by means of the bites of mosquitoes that had previously fed on cases of yellow fever at intervals varying from 16 to 57 days before being applied to the person to be infected; that the attack of yellow fever always followed the bite of the mosquito within the period of incubation of this disease, and that during the period which elapsed from December 5, 1900, the date of our first inoculation, till February 7, 1901, the date of our last inoculation (65 days), the order of occurrence of these cases corresponds with the order of inoculation, except that Case II, having a longer incubation period than Case III, the order of their relative occurrence became reversed.

Table I serves to illustrate this point.

By an examination of this table it will be seen that of 13 individuals whom we attempted to infect by bites of contaminated mosquitoes we succeeded in 10, or 76.92 per cent. Of the three negative cases, it will be observed that one (Case VI), who had reacted negatively to the subcutaneous injection of 1.5 c. c. of blood on December 26, 1900, also reacted negatively to the bites of mosquitoes on January 8, 1901, and this notwithstanding the fact that he was bitten by the very same insects which nine days before had infected Case VII. We have good ground for the opinion, therefore, that this Spaniard may be looked upon as one who possessed a natural immunity to yellow fever, especially as he was the only one of five persons who did not develop the disease after receiving an injection of blood taken from the general circulation, and was also the only one of five nonimmunes who did not contract yellow fever when bitten by insects which already had been proven capable of conveying the disease to other individuals. Case VIII, while negative to mosquito inoculation on December 28 and 29, 1900, reacted positively to a blood injection (2 c. c.) on January 8, 1901. This particular individual, Jernigan, entered our "infected mosquito building" on December 28 and 29, 1900, one week after Moran's visit, and was bitten on each occasion by one mosquito. As 66 per cent of the mosquitoes freed in the building on December 21, 1900, had already been destroyed—most probably by the small red ants that were present in considerable numbers—the subject may have been bitten by insects that were not more than 13 days old, in which case he would hardly have become infected. While considering the advisability of adding other contaminated insects to those in the house for the purpose of infecting Jernigan, opportunity presented for making a blood injection, and, as he was the only available subject in the camp at the time, it was determined to make use of him for this purpose.

Case XIII, our third negative case of mosquito inoculation, was bitten by 12 mosquitoes that had fed on Case VII within 8 hours of

the commencement of his attack. Although these insects were 22 days old when applied to Case XIII, on January 25, 1901, no result followed the bites. As the subcutaneous injection of 2 c. c. of blood taken from the general circulation of Case VII, at the end of 24 hours, produced an attack of yellow fever in Case VIII within the period of incubation, it would appear to indicate that the mosquito at certain periods of the disease may fail to obtain the parasite owing to its absence, at that particular time, from the capillary circulation. This is not unlike what we sometimes find as the result of an examination of the blood of malarial fever, especially in the æstivo-autumnal type of the disease. Table I also shows that, in addition to the positive case (VIII) to which I have already invited your attention, we obtained three other positive results by the subcutaneous injection of blood taken from the general circulation on the first and second days of the disease, viz, Cases VIII, XI, XII. The quantity of blood injected in these three cases was 1.5 c. c., 0.5 c. c., and 1 c. c., respectively. The production of yellow fever in this way is of much scientific interest—first, as serving to confirm what the mosquito inoculations had already shown, viz, that the parasite is present in the general circulation; second, that passage through the body of the mosquito, although this would seem to be nature's method, is not absolutely essential in the life history of this microorganism; and third, that the period of incubation of the disease, when thus produced, corresponds fairly closely to that occasioned by the mosquito's bite. A point of considerable importance brought out by the blood injection was the absence from this blood, on careful bacteriologic culture, of any bacterium which grows on our ordinary media by aerobic methods, thus excluding absolutely the *bacillus icteroides* of Sanarelli from further claim as the specific agent of yellow fever.

TABLE I.

Number of case.	Name.	Inoculation.		Method of inoculation.	Incubation.	Result.	Order of occurrence.	Date of occurrence.
		Hour.	Date.					
					Hours.			
I	Kissinger	2 p. m.	Dec. 5, 1900	Mosquito	81½	Positive	I	Dec. 8, 1900
II	Fernandez	4 p. m.	Dec. 8, 1900	do	137	do	III	Dec. 13, 1900
III	Beningo	10.30 a. m.	Dec. 9, 1900	do	83½	do	II	Dec. 12, 1900
IV	Presedo	4.30 p. m.	Dec. 11, 1900	do	91½	do	IV	Dec. 15, 1900
V	Moran	12 noon	Dec. 21, 1900	do	95	do	V	Dec. 24, 1900
VI	Alvarez	10 a. m.	Dec. 26, 1900	Blood injection		Negative		
	do	10 a. m.	Jan. 8, 1901	Mosquito		do		
VII	Martinez	11 a. m.	Dec. 30, 1900	do	94½	Positive	VI	Jan. 3, 1901
VIII	Jernigan	11 a. m.	Dec. 28, 29, 1900	do		Negative		
	do	11 a. m.	Jan. 4, 1901	Blood injection	94	Positive	VII	Jan. 8, 1901
IX	Olsen	9 p. m.	Jan. 8, 1901	do	60	do	VIII	Jan. 11, 1901
X	Folk	8.30 p. m.	Jan. 19, 1901	Mosquito	95½	do	IX	Jan. 23, 1901
XI	Forbes	1 p. m.	Jan. 22, 1901	Blood injection	43	do	X	Jan. 24, 1901
XII	Andrews	12.15 p. m.	Jan. 25, 1901	do	73	do	XI	Jan. 28, 1901
XIII	Weatherwalk	10.30 a. m.	do	Mosquito		Negative		
XIV	West	9.30 a. m.	Jan. 31, 1901	do	74½	Positive	XII	Feb. 8, 1901
XV	Hanberry	11 a. m.	Feb. 6, 1901	do	78	do	XIII	Feb. 9, 1901
XVI	Sontag	2 p. m.	Feb. 7, 1901	do	70	do	XIV	Feb. 10, 1901

You will recall that we undertook at Camp Lazear still a third method of propagating this disease, viz, by fomites. I must now tell you that during the whole time that we were producing cases of yellow fever by the bite of the mosquito and by blood injection, we were leaving no stone unturned in order to produce the disease by contact with fomites. Sleeping every night in the "Infected clothing building," to which no sunlight ever came, and in which the circulation of air was purposely made as defective as possible; engaged in the morning in packing boxes with garments much soiled by contact with the bodies and excreta of yellow-fever patients, and at night unpacking these same boxes in order to obtain articles for their beds and clothing for their bodies—in other words, sleeping in the very beds and garments just vacated by cases of yellow fever, seven nonimmune young Americans, averaging each 21 nights amid such uninviting surroundings, came out of this pesthouse, so to speak, at the expiration of their term none the worse for their experience. Not one had contracted the disease.

In the light of these results we can hardly be expected hereafter to lend much credence to such observations as that given by Harvey Brown, in 1872,[1] as narrated by Dr. A. A. Baldwin, of Jacksonville, Fla., presumbly from memory, some 13 years after the event. In this instance two children in Jacksonville, Fla., "contracted the disease by being present at the opening of a trunk belonging to their uncle who, a few days before leaving Habana, had visited the yellow-fever hospital, where he passed by the beds of those who were throwing up black vomit; and this, notwithstanding the fact that his coat, the only woolen clothing he had on at the time, had been sponged with alcohol after his return from the hospital!"

Or this, recorded by Rochester,[2] as an example "of the wonderful tenacity with which fomites hold the pestiferous material" and afterwards "convey it to mankind with intense effect." "In September, 1856, an infected ship from Cuba was detained at the quarantine anchorage off Staten Island, N. Y. Several passengers died, and some were ill on board. The garments and bedding were thrown overboard. Bay Ridge, a delightful suburban neighborhood of Brooklyn, lies directly across the bay, distant about 1 mile from the anchorage mentioned. The wind and tide deposited a number of garments that had been thrown away on the beach which terminated the lawn of Col. Charles Prince, an old and respected resident. In taking his usual morning walk he discovered the clothing and examined it with his cane, not otherwise handling it. He had no suspicion that it came from quarantine and never saw it again. In four days he was taken illl and died in a week of yellow fever." We lose our faith in this brine-soaked bedding when we find, according to Elisha Harris's report,[3] that on the Long Island shore, directly opposite the quarantine grounds (Bay Ridge) 6 cases of yellow fever and 3 deaths from black vomit had already occurred between the 13th and 21st of July, 1856, and that "from the latter date the malady extended fearfully until it had visited nearly every dwelling on the shore of that beautiful Bay Ridge, 30 cases and 15 deaths having occurred in that district previous to August 1."

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[1] Report on Quarantine, 1872, pp. 34 and 35.
[2] Transactions Am. Med. Association, vol. 30, 1899, pp. 128, 129.
[3] Annual Report of the Physicians of Marine Hospital, 1857.

I could quote many other instances contained in the literature, but as not one of them, as far as my search has gone, will bear the slightest intelligent criticism, I will not further trespass on your time except to say that, in my opinion, every epidemic of yellow fever that has occurred in the United States, both prior to and since the period when disinfectants were used, has pointed in the plainest manner to the innocence of fomites as a means of propagation of this disease; for with the onset of cold weather and under those conditions of lessened ventilation of dwellings and artificial heat that should have aided in the spread of the epidemic, just the contrary effect has always resulted. Under the circumstances one must either conclude that an external temperature of 32° F. is quite sufficient to bring about, and that speedily, the thorough disinfection of the many tons of infected clothing and bedding contained in the houses of a large city at the end of an epidemic of yellow fever or that fomites have no part in the propagation of the disease. The latter conclusion, it seems to me, is the only intelligible one, in view of our present knowledge of the disinfectant action of cold on bacteria.

Let us now see if there are any facts observed by others in connection with the ordinary propagation of yellow fever which support those recorded by us as the result of mosquito bites at Camp Lazear. Since in our limited experience, affecting 23 individuals, we have not observed the production of the disease by the bite of the mosquito within less than 12 days after contamination, we would expect that, when a case of yellow fever was imported into a town or house where the conditions were favorable for its propagation, a secondary case would not occur within a less period of time than about 14 or more days. I may say that various observers have noted that after the occurrence of the first case in a town, a considerable interval elapses (2 or 3 weeks) prior to the appearance of other cases. Although such general statements are of value, what we need are exact observations recorded under such conditions that the secondary cases can be positively referred to a certain limited source of infection. This, of course, can best be done where the disease has been imported into small settlements or into isolated houses, and it was under just such favorable circumstances that Carter, of the Marine Hospital Service, made his observations at Orwood and Taylor, Miss., in 1898, "on the interval between the infecting and secondary cases of yellow fever." Here, in a community of more than average intelligence, consisting "not of a town, or even a hamlet, but only of a neighborhood," as Carter puts it, it was possible to record with accuracy the date of introduction of the infecting cases and the date of occurrence of secondary cases.

Table II gives the results of this investigation.

This table shows that of 16 houses in which the interval between the infecting case and the first secondary case was recorded, 15, or 93.7 per cent, correspond with the mosquito interval; that is, the secondary cases occur at just the interval—13 to 23 days—when we would expect them to develop, provided the mosquito was concerned in the propagation of the disease. It will be observed that in only 1 of the 16 first secondary cases was the interval as short as 11 days and 15 hours. If the commencement of the attack in this case has been recorded correctly, it would indicate that the number of days

which we have given as "about 12" for the development of the parasite within the mosquito would have to be shortened somewhat—probably to 10 days. In our first successful experimental case, where the disease was produced by the bite of the mosquito on the twelfth day after the insect's contamination, we could not say, of course, that this particular mosquito would not have conveyed the infection had it been allowed to bite on the tenth or eleventh day after contamination.

On the other hand, if we take all the secondary cases that occurred in these 16 houses, we will find that of a total of 71 cases, only 1 developed the disease after so short an interval as 11 days and 15 hours; in other words, 70, or 98.5 per cent, of the secondary cases occurred after an interval of 13 days. As a matter of fact only 2 of these secondary cases occurred within a less period than 14 days, 1 developing on the twelfth and the other on the thirteenth day.

TABLE II.—*Interval between infecting and secondary cases of yellow fever.*

	House.	Year.	Date of infecting cases.	Date of first secondary case.	Interval in days.	Next secondary case.	Number of secondary cases.
Orwood, Miss	1	1898	Aug. 6	Aug. 23	16½	Aug. 24	6
Do	2	1898	Aug. 29	Sept. 13	15	Sept. 13	6
Do	3	1898	...do....	Sept. 18	20	Sept. 18	4
Do	5	1898	Aug. 31	Sept. 29	29	Oct. 2	3
Do	6	1898	...do....	Sept. 20	20½	Sept. 20	5
Do	7	1898	Sept. 3	Sept. 26	23	Sept. 30	6
Do	8	1898	Sept. 17	Oct. 8	21	Oct. 8	2
Do	9	1898	Aug. 31	Sept. 22	21½	Sept. 22	4
Do	10	1898	Sept. 4	Sept. 20	16	...do....	2
Do	11	1898	Sept. 25	Oct. 8	13	.....	1
Do	15	1898	Sept. 2	Sept. 22	20½	.....	1
Do	16	1898	Aug. 29	Sept. 9	[1] 11½	.....	.....
Taylor, Miss	1	1898	Aug. 7	Aug. 27	20	Sept. 3	13
Do	2	1898	Aug. 17	Sept. 2	16	Sept. 6	8
Do	3	1898	Aug. 10	Aug. 25	15	Aug. 28	2
Edwards, Miss	.....	1897	Aug. 8	Aug. 22	14	Aug. 26	10

[1] 11 days 15 hours.

I do not know what conclusion you may draw from the data contained in Table II, but to my mind they are strongly suggestive that the same mode of propagation which we were making use of at Camp Lazear during the past winter was at work in the epidemic of yellow fever at Orwood and Taylor, Miss., during the summer of 1898.

From my own personal experience, I can only add one observation to those given by Carter, viz, at Quemados, Cuba, where of two nurses who remained continuously in attendance upon a case of yellow fever, one contracted the disease on the fourteenth day and the other on the fifteenth day after the commencement of the primary case.

While the temptation is great to extract from the literature other observations confirmatory of those given (and they are numerous), I must refrain from doing this, since I promised to confine myself largely to my own experience in regard to the propagation of yellow fever. For this reason and because I feel that I have already trespassed on your patience longer than I had any right to do, I must omit any reference to the habits of *culex fasciatus*, or of the thermal influences concerned in the propagation of this mosquito, both of which are of much importance in connection with the subject under consideration.

I trust that I have said enough, however, to indicate to you that, in my opinion, the ideas which we have heretofore held concerning the propagation of yellow fever must undergo considerable recasting. I do not believe that we can longer ascribe with confidence any part of the spread of this disease to fomites, for under such conditions of intimate and long-continued exposure as could never occur in the natural course of every-day life we have looked in vain for its development.

While in matters pertaining to the public health, cleanliness should always stand next to godliness, I do not think that we will be justified in assigning so much importance hereafter to those insanitary conditions of soil which, being due especially to pollution with animal matter, were supposed, in some mysterious way, to aid in the spread of this disease. Strange as it may sound, I do not believe that the enforcement of the most rigid hygienic regulations, such as we have heretofore known them, will prevent the propagation of this grave epidemic disease, provided it should again be imported into this country. I seriously doubt if we can longer class yellow fever with the "filth diseases." The apparent results obtained by the improved sanitary arrangements instituted by Gen. Butler in the city of New Orleans, during the year 1862, and carried on by his military successors, probably served to strengthen, as much as anything else, the view held by the profession that filth was, if not essential, yet of extreme importance, in aiding the spread of yellow fever. I dare say that but few stopped to consider that Gen. Butler found the city of New Orleans already quite free of yellow fever, and that the same system of blockade which kept this disease out of the former city, under improved sanitary conditions, kept it out of other Southern seaports during the same period, although their sanitary conditions remained unchanged. If one is inclined to believe that improved hygienic conditions, as usually understood, will arrest the spread of yellow fever, let him turn to the city of Habana under American sanitary administration. Probably in no city in the world have such unremitting sanitary efforts been put forth as in the city of Habana since our occupation in January, 1899. We were told that the hard work of Gen. Ludlow and his assistants was responsible for the marked decrease of cases of yellow fever during the first seven months of 1899—and appearances seem to indicate as much—nevertheless, with the commencement of Spanish immigration, during August of that year, and the introduction of susceptible material, cases of yellow fever began to rapidly multiply, so that the city had a late summer and fall epidemic of this disease. Concerning the occurrence of yellow fever in that city during the past year, Maj. Harvard, chief surgeon, Department of Cuba, in a recent report, after describing the thorough work which had been done by the sanitary authorities and its marked effect upon the reduction in deaths, especially from tuberculosis, goes on to say:

> It is certain that in Habana, in 1900, no visible correlation could be seen between dirt and yellow fever; the district which became first strongly infected lies east and south of the Parque Central, and is one of the cleanest and best constructed, while the most insanitary wards became infected late in the season and only to a slight extent; the malodorous district reserved to houses of ill-fame hardly had a case. Yellow fever has not followed the poor and unclean, nor the mark of previous infection, but rather the movement of nonimmunes; wherever these located, there the infection searched and found them, regardless of the hygienic conditions of their premises.

What is the sanitary story, then, for the year 1900? Simply that with the return of summer weather and the continued influx of new material, and in spite of unremitting efforts to keep the city clean, Habana has experienced a more serious epidemic of yellow fever, affecting its civilian population, than it has had during the preceding 20 years. Need we now express surprise at such a result? Have we not seen at Camp Lazear, under the very best hygienic surroundings, six individuals attacked with yellow fever, after a few short visits to a new building whose foundation stood on the unbroken turf and whose rooms were filled with sunshine and with an atmosphere just swept in from the ocean, at the very moment of infection? Where then, gentlemen, shall we look for the agent that is vitally concerned in the propagation of yellow fever? In the light of these newer observations which I have had the pleasure of presenting to you, I believe that we may affirm, with some degree of confidence, that here, substituting *culex* for *anopheles*, we have to deal with the same source of infection to which we now trace the malarial fevers—the mosquito.

Chapter 5.

EXPERIMENTAL YELLOW FEVER.[1]

By Walter Reed, M. D., Surgeon, United States Army., James Carroll, M. D., and A. Agramonte, M. D., Contract Surgeons, United States Army.

Subsequent to the presentation of our paper to the Pan-American Congress [2] in Habana, we succeeded in producing some additional cases of yellow fever at our experimental sanitary station near Quemados, Cuba. We have thought that brief reports of these cases, to be followed by remarks on experimental yellow fever from the clinical point of view, would be of interest to the members of this association, and especially to those who reside in sections of the country where each year yellow fever is liable to appear in epidemic form.

Perhaps it might be well to recall the fact that the cases of yellow fever here to be recorded were produced like those heretofore reported by us, under strict quarantine regulations and at a special experimental sanitary station, near the town of Quemados, Cuba.

In a series of 12 experimental cases produced at this camp during the period from December 5, 1900, to February 7, 1901—an interval of 65 days—it should be borne in mind that the order of occurrence exactly correspond with the order of inoculation, except that Case II, inoculated at 4 p. m., December 8, 1900—having a longer period of incubation than Case III, inoculated at 10.30 a. m., December 9, 1900—the order of their relative occurrence became reversed [3]. Moreover the attack always followed within the period of incubation of the disease, and concerned only those nonimmune individuals who had consented to submit themselves for experimentation. Of a total of 16 individuals who thus consented, 14 contracted yellow fever; whereas of 5 nonimmunes, who did not consent and were therefore not subjected to experimentation, none acquired the disease, although otherwise placed under exactly similar surroundings. In its occurrence, therefore, at this station, yellow fever strictly obeyed the behests of the experimenters, both as to place and time of occurrence. Recovery took place in all cases.

(A) CASES PRODUCED BY THE INJECTION OF BLOOD.

Case I.—W. J., American, nonimmune, aged 27—in quarantine since December 20, 1900—with his full consent, at 11 a. m., January 4, 1901, was injected subcutaneously with 2 c. c. of blood taken from the general circulation of a case of mild yellow fever at the beginning of the second day of the disease and having a temperature of 100.8° F. The subject, who had been in strict quarantine at the station for the period of 45 days, remained in his usual health until the early morning of January 8, when he complained of slight frontal headaches. At 6 a. m. his temperature was 98.2° F., and pulse 70; 9 a. m., temperature 99.8° F., pulse 95; frontal headache increased, with

[1] Read before the Sixteenth Annual Meeting of the Association of American Physicians, held at Washington, April 30, May 1 and 2, 1901.

[2] The Etiology of Yellow Fever. An Additional Note. Read at the Pan-American Congress, Habana, February 4-7, 1901.

[3] These cases were reported in our Additional Note.

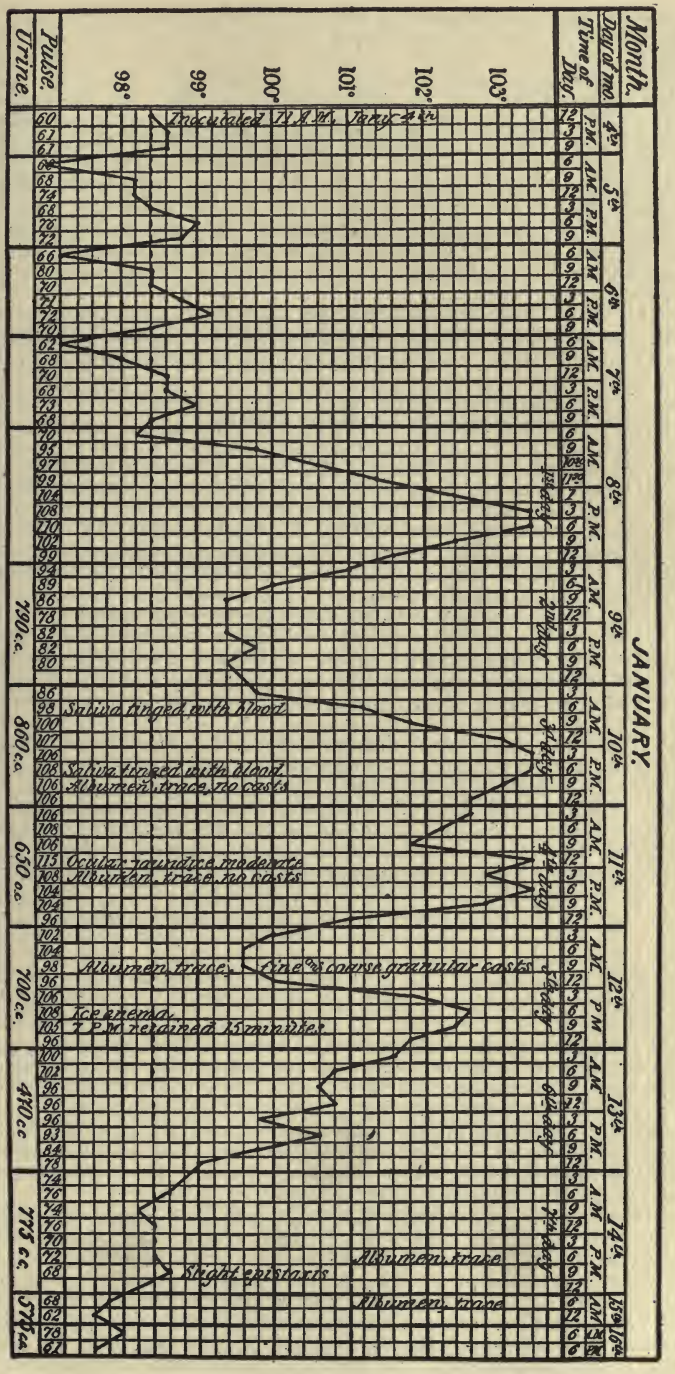

CHART I.—Yellow fever produced by injection of 2 cc. of blood. Period of incubation, 3 days, 22 hours.

slight chilly sensations in the feet and lower extremities. There were some congestion of the eyes and his usual florid complexion was heightened in color. At 10.15 a. m., temperature 100.6° F., pulse 97. Complains of some pain in the lumbar region. At 11.20 a. m., temperature 101.4° F., pulse 99. The height of the febrile paroxysm was reached at 3 p. m. the same day, when the temperature was 103.4° F. and pulse 108. The facial expression was now characteristic of yellow fever. The eyes were deeply injected and watery and the face much suffused. Photophobia moderate—frontal headache and backache severe. The skin was moist. The remission occurred at the end of 24 hours—9 a. m. January 9—when the temperature had fallen to 99.4° F. and the pulse to 86. The subsequent history was that of a case of yellow fever of moderate severity. Albumin was found in the urine at the end of the sixty-first hour. There was some bleeding from the gums on the third day and moderate ocular jaundice on the fourth day. Fever disappeared on the morning of the seventh day. (Chart I.)

Case II.—W. O., American, nonimmune, aged 28, in quarantine since December 20, 1900. On January 8, 1901, at 9 p. m., with his full consent, he was given by subcutaneous injection 1.5 c. c. of blood taken from the mediancephalic vein of Case I, just 12 hours after the beginning of the attack and when the temperature was 102.4° F., that is, just after the first febrile paroxysm began to decline. The subject remained in his usual condition during the following two days.

January 11, 1901, at 6 a. m. his temperature was 98.9° F. and pulse 70. He complained of being disturbed by dreams during the night and had some frontal headache. At 9 a. m. temperature 100° F., pulse 77. At 10.15 a. m. temperature 101.4° F., pulse 76. Eyes decidedly congested and face moderately suffused. At 12 o'clock noon, when the temperature had risen to 103.2° F. and the pulse to 102, the height of the primary paroxysm had been reached. Headache and backache were now much complained of. The facial expression was characteristic. The remission occurred at the end of 24 hours, lasted one day, and was followed by a very moderate secondary fever. A distinct trace of albumin was found in the urine passed at 2 a. m. January 12, 17 hours after the attack began. A few hyaline casts were also present. Slight bleeding from the gums occurred on the second and third days of sickness. The character of the attack in this case was vey mild. The albumin, which at no time amounted to more than a distinct trace, did not disappear, however, until January 24. (Chart II.)

Case III.—W. F., American, nonimmune, aged 23, was, with his full consent, at 1 p. m. o'clock January 22, 1901, injected subcutaneously with 0.5 c. c. of blood taken on the second day from the general circulation of a severe case of yellow fever, which was fatal on the seventh day of the disease. The patient's temperature, when the blood was withdrawn, was 103° F. and pulse 90. The subject remained well during the following day. January 24, at 6 a. m., his temperature was 98.4° F., and pulse 78. He partook of a hearty breakfast at 6.30 a. m., which he vomited soon afterwards. At 7 a. m. he complained of dizziness and general lassitude. Temperature, 98.4°, pulse 78. At 9 a. m., chilliness complained of, but there is no record of temperature or pulse. At 9.30 a. m., temperature 100.6° F., pulse 82. Frontal headache well marked. Eyes already injected and face slightly suffused. At 10.30 a. m., temperature 101.2° F. and pulse 86. An hour later his temperature was 102.6° F. and pulse 82. The height of the primary paroxysm was reached at 1 p. m. when the temperature was 102.8° F. and pulse 98. At this hour photophobia was well marked and constant complaint made of severe frontal headache and backache, together with pains in the lower extremities. The skin was moist. The remission occurred at the end of 36 hours. The subsequent course was that of a case of yellow fever of moderate severity. With the return of the secondary fever there were present sharp backache and headache. Albumin appeared in the urine at the end of 57½ hours. Ocular jaundice was present on the third day and thereafter until convalescence. The gums did not bleed, although they were swollen and injected. Fever subsided on the sixth day, and albumin disappeared on the eighth day. (Chart III.)

Case IV.—J. H. A., American, nonimmune, aged 22, with his full consent, received subcutaneously, at 12.15 p. m., January 25, 1901, 1 cc. of blood taken from the mediancephalic vein of Case III, just 27½ hours after the commencement of the latter's attack of yellow fever (T. 100.6° F.). The subject remained in his usual condition during January 26 and 27, except that on the afternoon of the last-mentioned date he complained of occipital headache. This was present on the following morning, January 28; otherwise he felt well. His temperature at noon was 98.6° F., and pulse 68. Occipital headache continued. He partook of dinner with fair appetite. He was not seen again until 3 p. m. In the meanwhile, at 1.15 p. m., the subject states that, while sitting alone in his tent, he began to feel cold, and that this was quickly followed by a decided chill with increase of headache. He noted the hour in writing at

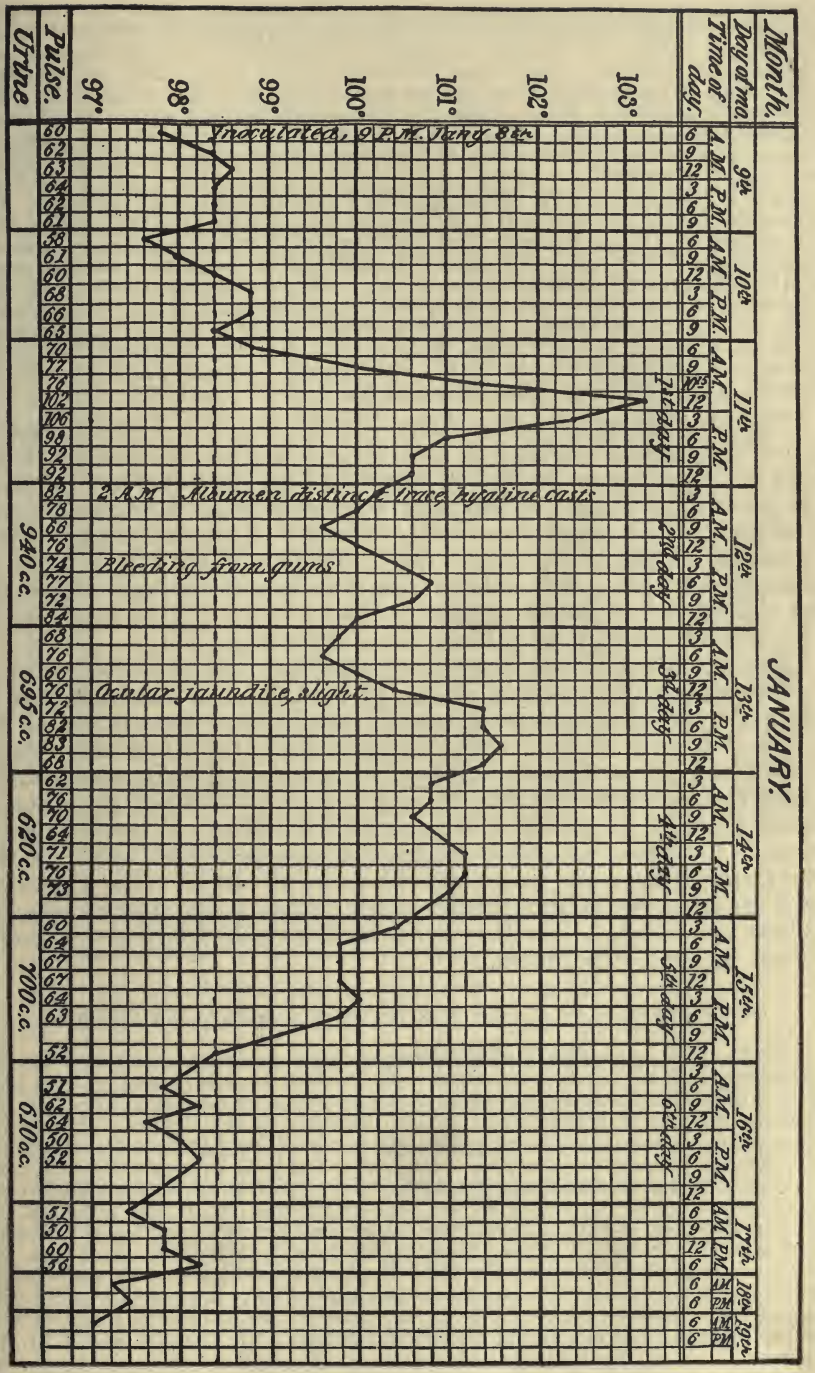

CHART II.—Yellow fever produced by injection of 1.5 cc. of blood. Period of incubation, 2 days, 12 hours.

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the time. At 3 p. m. his temperature was 103.6° and pulse 120. The eyes were intensely congested and the face deeply suffused. The patient was very restless, and complained bitterly of occipital headache and backache. Photophobia was very marked. He vomited several times within the next 2 hours. Skin hot and dry. The height of the primary paroxysm was reached at 3.30 p. m., at which hour the temperature was 104.2° F., and pulse 120. The subsequent history was one of severe yellow fever. There was no remission in the fever until the fourth day, when the temperature fell to 101.2° F. Now, for the first time, the patient ceased to complain of occipital headache and backache. Albumin appeared at the end of 18½ hours (7.30 a. m., January 29). A few hyaline casts were also present at this time. The specimen of urine passed at 6.40 a. m., January 30, contained albumin one-twentieth by volume, and many fine and coarse, granular, bile-tinted casts. Ocular jaundice appeared on the third day. The skin of the face and of the anterior part of the neck and thorax was tinted on the fourth day. This rapidly became intensified and general. The secondary fever lasted about 30 hours, the temperature falling to 97.2° F. at 12 o'clock (midnight) of the fifth day. Marked fluctuations of temperature continued until the eleventh day of illness. Recovery was slow and much delayed by the development of a carbuncle in the left sacral region. A trace of albumin was still present on March 1, 32 days after the attack had begun. (Chart IV.)

The production of yellow fever by the injection of blood taken from the general circulation is of much interest as showing, first, that the parasite is present in the blood, at least during the early stages of the disease, and secondly, that its passage through an intermediate host, although this would seem to be nature's method, is not essential in the life cycle of this parasite. Thus yellow fever is analogous to the malarial fevers, in that it may be produced either by the bite of a certain species of mosquito, or by the injection of blood taken directly from the general circulation.

Another point to which we have elsewhere referred, but which is considered of sufficient importance to bear repetition here, is that in each of the foregoing cases of experimental yellow fever produced by the injection of blood, careful cultures made from the same blood drawn from the vein immediately after injection or, as in one instance, made from the same syringeful of blood that conveyed the disease, failed to show the presence of Sanarelli's bacillus. In one case colonies of *Staphylococcus pyogenes citreus* were obtained, while in the remaining three cases no growth whatever occurred. The exclusion of *Bacillus icteroides* from further consideration as the specific agent of yellow fever would, therefore, seem to have been conclusively determined by these experiments.

(B) CASES PRODUCED BY THE BITE OF THE MOSQUITO, CULEX FASCIATUS.

Case V.—L. F., American, nonimmune, aged 28—in quarantine since December 20, 1900—was, with his full consent, at 3.30 p. m., January 19, 1901, bitten by three mosquitoes that had been contaminated 39 days previously, by feeding on the blood of a well-marked case of yellow fever, on the third day of the disease. The subject remained in his usual condition of health until the afternoon of January 23. At noon of this date his temperature was 97.8°. Soon after this hour he took to his bed, complaining of frontal headache and general lassitude. At 3 p. m. his temperature was 99.2° and pulse 78. At 4.10 p. m. the temperature was 100° F. and pulse 104. A sense of chilliness, especially of the lower extremities, and increased frontal headache, were now complained of. Eyes already injected and face flushed. At 5 p. m. the temperature was 101.2° F. and pulse 104. The height of the paroxysm was reached at 8.20 p. m., at which hour the temperature was 103.6° F. and the pulse 110. The eyes were deeply congested and photophobia very marked. Headache and backache were so intense as to cause the patient to complain bitterly. He vomited once at 9 p. m. January 24, 3 a. m., the temperature had fallen to 100.2° and the pulse to 104, but with only slight amelioration to the patient's discomforts. At noon the thermometer marked 102°. Remission occurred at the end of 33 hours, with marked diminution of all disagreeable symptoms. The secondary fever, attended by increased headache and

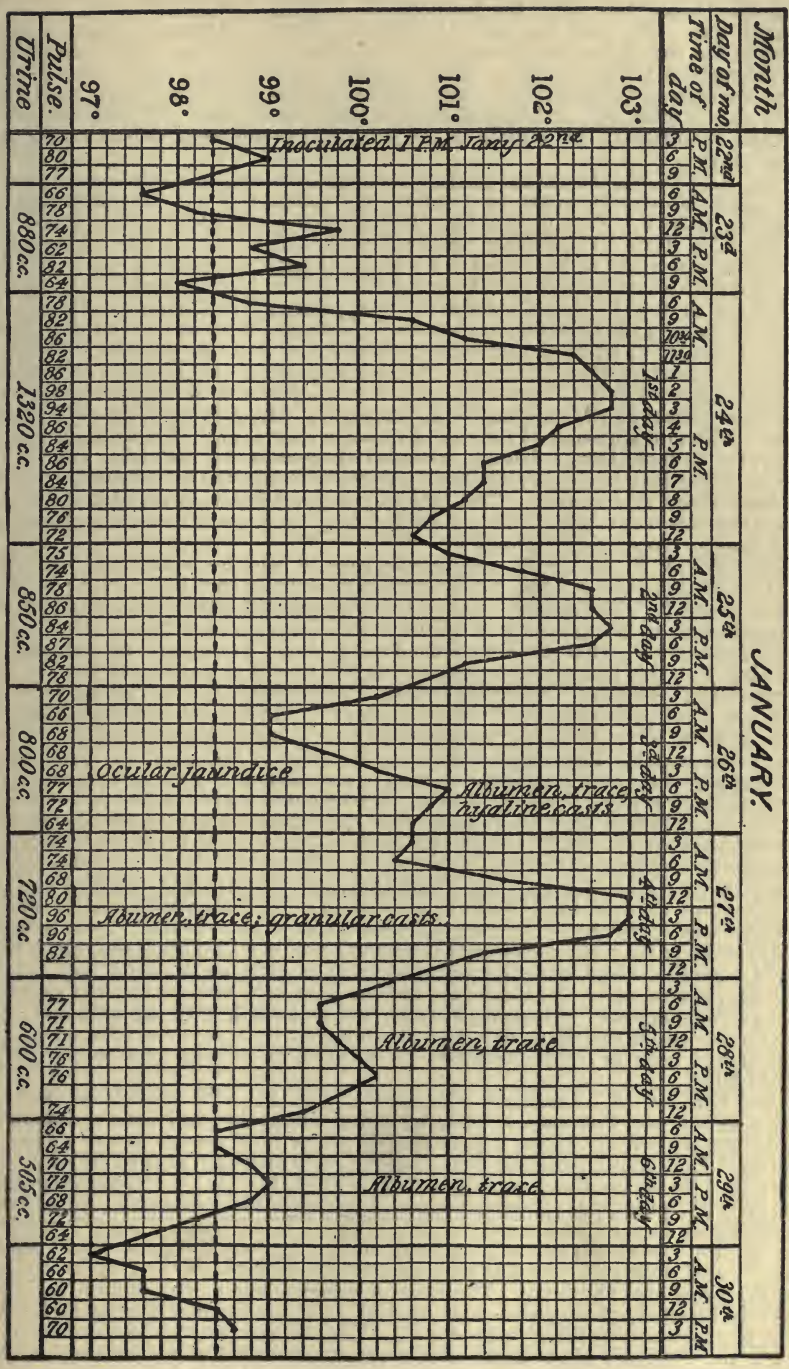

CHART III.—Yellow fever produced by injection of 5 cc. of blood. Period of incubation, 3 days, hour.

backache, lasted four days, the temperature dropping to normal at 6 p. m. of the seventh day. The case was one of moderate severity. Albumin appeared in the urine at the end of the forty-second hour. 'Ocular jaundice was quite noticeable on the afternoon of the second day. Some jaundice of the face and anterior region of the chest was seen on the fourth day. Many bile-tinted granular casts were present in the urine on the third day, and thereafter until the eleventh day. The albumin which reached one-fifteenth by volume on the sixth day disappeared on the twelfth day. (Chart V.)

Case VI.—C. W., American, nonimmune, aged 27, with his full consent, was at 9.30 a. m., January 31, bitten by 2 of the 3 mosquitoes that had been applied to the foregoing Case V. The interval that had elapsed since their contamination was, therefore, 51 days. The subject remained well until 12 o'clock noon, February 3, when he complained of heaviness in his legs and some supraorbital pain. His temperature at this hour was 99° F. and pulse 70. At 1.30 p. m. it had risen to 100° F., and at 5 p. m. to 100.° F. and pulse to 84. The primary rise of fever, which was somewhat fluctuating in character, did not reach its height until at the end of 24 hours, noon, February 1, when the temperature was 102.4° and the pulse 92. The facies was now suggestive of yellow fever. Remission occurred at the end of 45 hours and lasted for about 1 day. The secondary rise was slight in character, the temperature falling to normal on the morning of the sixth day. The case was very mild in character. Albumin appeared at the end of 75 hours (beginning of fourth day); it never amounted to more than a distinct trace and disappeared on the eighth day. There was no ocular jaundice, and although the gums were injected and swollen, there was no hemorrhage at any time. The patient perspired freely throughout the attack. Convalescence was rapid. The subject had been in quarantine for the period of 6 days prior to inoculation. (Chart VI.)

Case VII.—J. H., American, nonimmune, aged 26, with his full consent, was bitten at 11 a. m., February 6, 1901, by the same 2 mosquitoes that had 6 days previously bitten Case VI. Fifty-seven days had therefore elapsed since the insects had been contaminated by biting a case of yellow fever. He remained well until 12 o'clock noon, February 9, when he experienced slight chilly sensations, accompanied by yawning. At this hour his temperature was 99° F. and pulse 72. At 3 p. m., temperature 98.8°, pulse 72. Says that he feels "out of sorts," but has no headache. At 5.30 p. m. his temperature was 100.6° F., pulse 78. He was not seen until 7.30 p. m., when he complained of backache and severe general headache, more intense through the frontal region. Eyes much injected, photophobia very marked, face flushed. He was stretching and yawning constantly, complained of nausea, and vomited a small quantity of partially digested food. The height of the primary fever was reached at 3 p. m., February 10, i. e., 22 hours after the commencement of the attack, when the temperature was 102.8° and the pulse 98. Remission of the fever to 99.4° and pulse to 74 occurred at 6 a. m., February 11, making the duration of the primary paroxysm 36 hours. Twenty-four hours after the remission had occurred the temperature had risen to 102.4° with a pulse of 70. The fever continued to steadily increase until midnight of February 12, when a temperature of 105° F. was recorded, with a pulse of 90. The subsequent course was that of a case of severe yellow fever. Slight oozing of blood from the gums occurred as early as the third day. Ocular jaundice, beginning on the third day, became later very distinct and was associated with general jaundice. Albumin, however, did not appear until the sixth day. The fever subsided on the ninth day, and was followed by a slow convalescence. The subject had been in strict quarantine for a period of 78 days prior to inoculation. (Chart VII.)

Case VIII.—C. S., American, nonimmune, aged 28, with his full consent, was bitten at 2 p. m., February 7, 1901, by 3 mosquitoes that had been contaminated 16 days previously by biting a fatal case of yellow fever on the second day of the disease. The subject remained well until the early afternoon of the third day, February 10. He ate his dinner at noon with good appetite. At 1 p. m., his temperature was 100° F., pulse, 90. Frontal headache was now complained of. This became rapidly more marked, and pains in the limbs were also present. Three hours later, 4 p. m., the fever had risen only one-fifth of a degree, but at 6 p. m. it had reached 103° F. and pulse, 96. At this hour he had severe headache and backache, with general pains over the body. The facial expression was now characteristic. Eyes brightly injected, photophobia well marked, and face decidedly congested. At 9 p. m. temperature was 103.2° and pulse 112. The skin was moist. Remission occurred at 6 a. m., February 12, 41 hours after the commencement of the febrile paroxysm. The secondary fever, which was moderate in character, lasted 4 days, the fever subsiding on the seventh day. Ocular jaundice was slight. A few hyaline casts were present on the third and subsequent days, but no albumin was found until 1 p. m.,

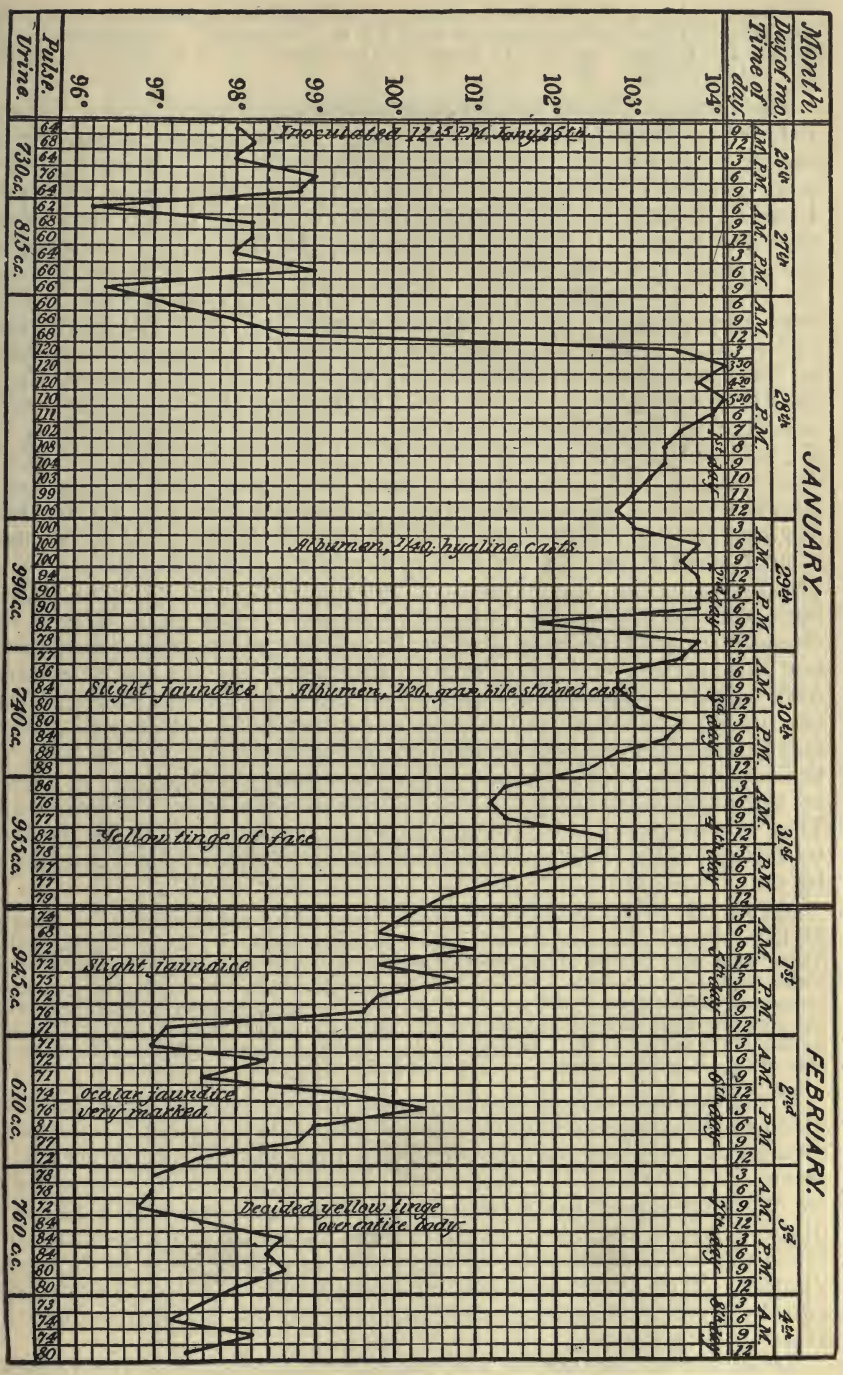

CHART IV.—Yellow fever produced by injection of 1 cc. of blood. Period of incubation, 1 day, 19 hrs.

February 18, that is, 36 hours after the fever had subsided. It was present at a distinct trace in all specimens examined until 3 p. m., February 23. Convalescence was rapid. The subject had been in quarantine for a period of 25 days prior to inoculation. (Chart VIII.)

The foregoing cases of experimental yellow fever (Cases V, VI, and VII) are, we think, of especial importance as showing the length of time during which the mosquito may remain capable of conveying the infection. In previous papers we have reported 6 cases of yellow fever produced by the bites of mosquitos at intervals varying from 12 to 24 days after the contamination of the insects. In the cases here reported the periods intervening between the contamination of the insect and the production of the disease were much longer, viz, 39, 51, and 57 days, respectively. As one of these insects lived until the sixty-ninth and another until the seventy-first day after contamination, we have for the first time an explanation of the fact, several times noted in the literature, that the contagion of yellow fever may cling for several months to a building that has been vacated by its occupants, or to the infected area of a town, even though this latter has been entirely depopulated. These particular insects also were contaminated at a later stage of the disease than in any of our other cases, i. e., on the third day and during the secondary rise of the fever, following a complete intermission in the temperature. We have, therefore, been able to demonstrate that the parasite is present in the general circulation both after and before the stage of remission. How much later in the disease the parasite may still be found—a matter of much interest and importance—the observations thus far made do not determine. Although the 3 mosquitoes applied on the third day, as above stated, acquired the parasites and were able to affect 3 individuals with yellow fever, a single mosquito applied to the same case of yellow fever on the fourth day of the disease failed to obtain the parasite, as shown by the negative result following its bite 40 days after contamination. That not all mosquitoes become infected, however, with the parasite by biting yellow fever patients is shown by several observations made by us. We submit only one.

Case IX.—J. W., American, nonimmune, was, with his full consent, on January 25, 1901, bitten by 12 mosquitoes (*C. fasciatus*) that had fed on a case of mild yellow fever—in a man named Martinez—on January 3, 1901, within 8 hours of the commencement of the attack. Although these mosquitoes had been kept at a summer temperature for 22 days, the result of the experiment was entirely negative. That the parasites were present in Martinez's blood at the end of 24 hours was fully shown by the effect produced by injecting 2 c. c. of his blood drawn at this time beneath the skin of Case I of this report.

Observations such as the foregoing would indicate that the mosquito at certain periods of the disease may fail to obtain the parasite, owing to its absence at that particular time from the capillary circulation. Concerning the matter of the propagation of yellow fever by other species of culex than *C. fasciatus*, we have only 1 negative observation to record of an individual bitten by 5 *C. pungens* that had been contaminated by biting a case of yellow fever 19 days previously. To a single negative experiment such as this no importance can be given, so that this question must be left for future observations to determine.

Touching the subject of the possible transmission of the parasite to the daughter insect by means of infection of the ovum, we have also but a single observation to record. In this case the bites of 14

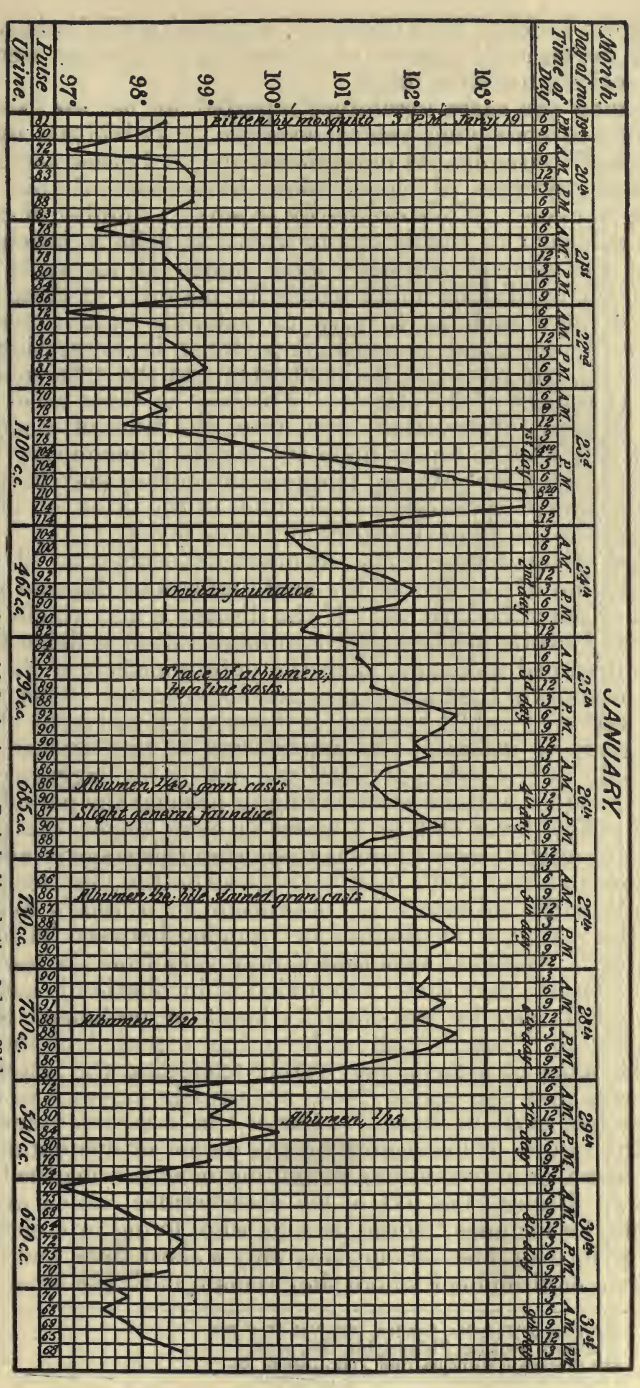

CHART V.—Yellow fever produced by the bite of *Culex fasciatus*. Period of incubation, 3 days, 23½ hours.

mosquitoes, hatched from the ova of a mosquito (*C. fasciatus*) that had already shown itself capable of conveying the disease, were followed by an entirely negative result.

Including the cases heretofore reported by us, we have thus far succeeded in conveying yellow fever to 12 individuals by means of the bites of contaminated mosquitoes, and to 4 other persons by subcutaneous injection of blood taken from cases of this disease—a total of 16 cases. While ordinarily so small a number of cases would not be sufficient to enable one to arrive at definite conclusions concerning the general character and course of an acute infectious disease, the conditions under which the majority of these cases were observed were such as to give us valuable data concerning two matters of very great practical importance in connection with this disease, viz, the period of its incubation and the difference in degree in the character of its attacks. Further, as these cases were kept under constant observation, even from the time of inoculation, we are not only able to report upon the earliest premonitory symptoms, but also to give the primary temperature curve; and, in addition, to note the time of appearance of albumin in the urine, all of which are of interest in the clinical history of yellow fever.

Period of incubation.—The accurate determination of the period of incubation of any one of the acute infectious diseases is always a matter of scientific interest. If the disease is one which, like yellow fever, is of exotic origin and whose importation is liable to give rise to a widespread epidemic, then the determination of its incubative stages becomes of the highest practical importance. This importance, as a question of public hygiene, is increased, if as recent observations would seem to indicate, the importation of this disease is brought about only by the sick individual and not by his baggage or clothing. While the older authors were willing to prolong the period of incubation of yellow fever to 2 or 3 weeks or even longer, the tendency of physicians at the present time is to shorten this stage to about 5 days. Reference to a few of the later text-books on the Practice of Medicine will sufficiently indicate this. Davidson, in Allbutt's System,[1] puts down the period of incubation as "ranging between 24 hours and 4 or 5 days." Stevens[2] says that it may vary from "a few hours to a week." Osler[3] says that "the period of incubation is usually 3 or 4 days, but it may be less than 24 hours or prolonged to 7 days." According to Tyson,[4] "yellow fever has a period of incubation of from 24 hours to 5 days, very rarely exceeding the latter." Sternberg[5] says that this period "does not usually exceed 4 or 5 days and may be less than 24 hours." Carter,[6] in a recent valuable paper, gives the results of his studies on the period of incubation of yellow fever, based on observations extending over a considerable number of years. Under Class III of his observations, which are the most valuable, he includes "those persons who, living in a clean environment, go into an infected one, stay only a short time, and then return to a clean environment where they remain until the fever develops."

[1] A System of Medicine, London, 1897, Vol. II, p. 394.
[2] Practice of Medicine, Philadelphia, 1898, p. 280.
[3] The Practice of Medicine, New York, 1899, p. 185.
[4] Practice of Medicine, Philadelphia, 1900, p. 85.
[5] Buck's Reference Handbook of the Medical Sciences, 1889, Vol. III, p. 58.
[6] The Period of Incubation of Yellow Fever, New York Medical Record, March 9, 1901.

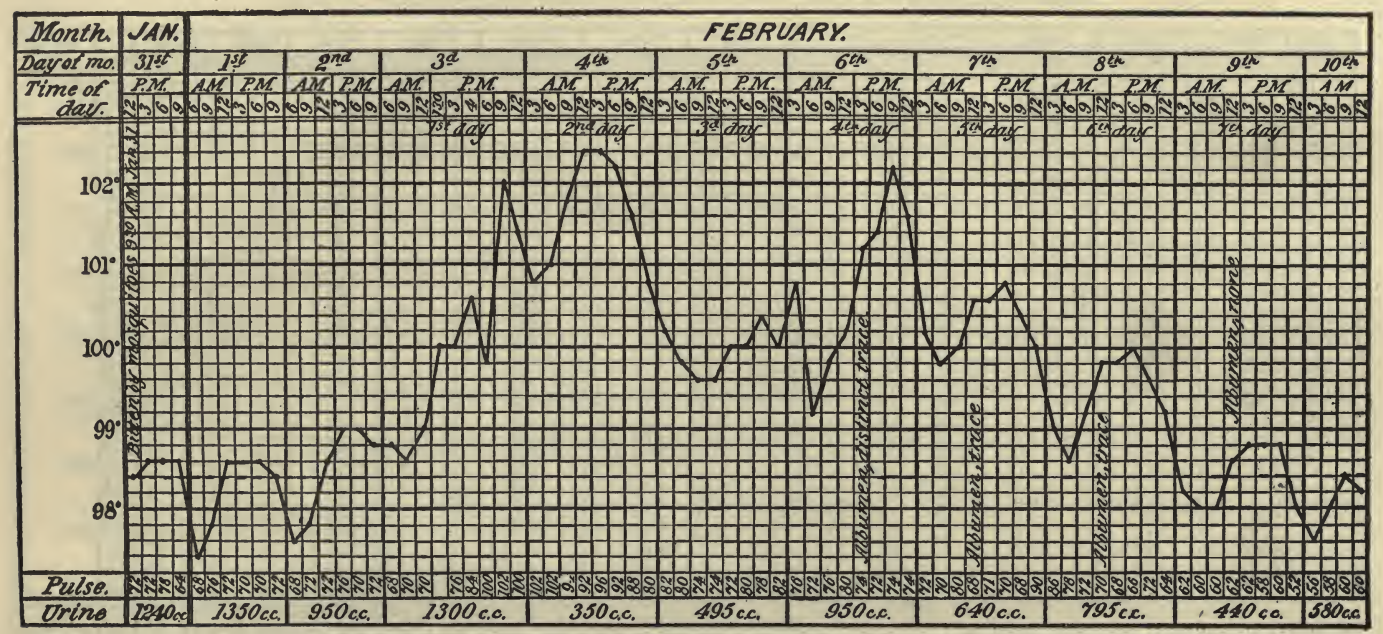

CHART VI.—Yellow fever produced by bite of *Culex fasciatus*. Period of incubation, 3 days, 2½ hours.

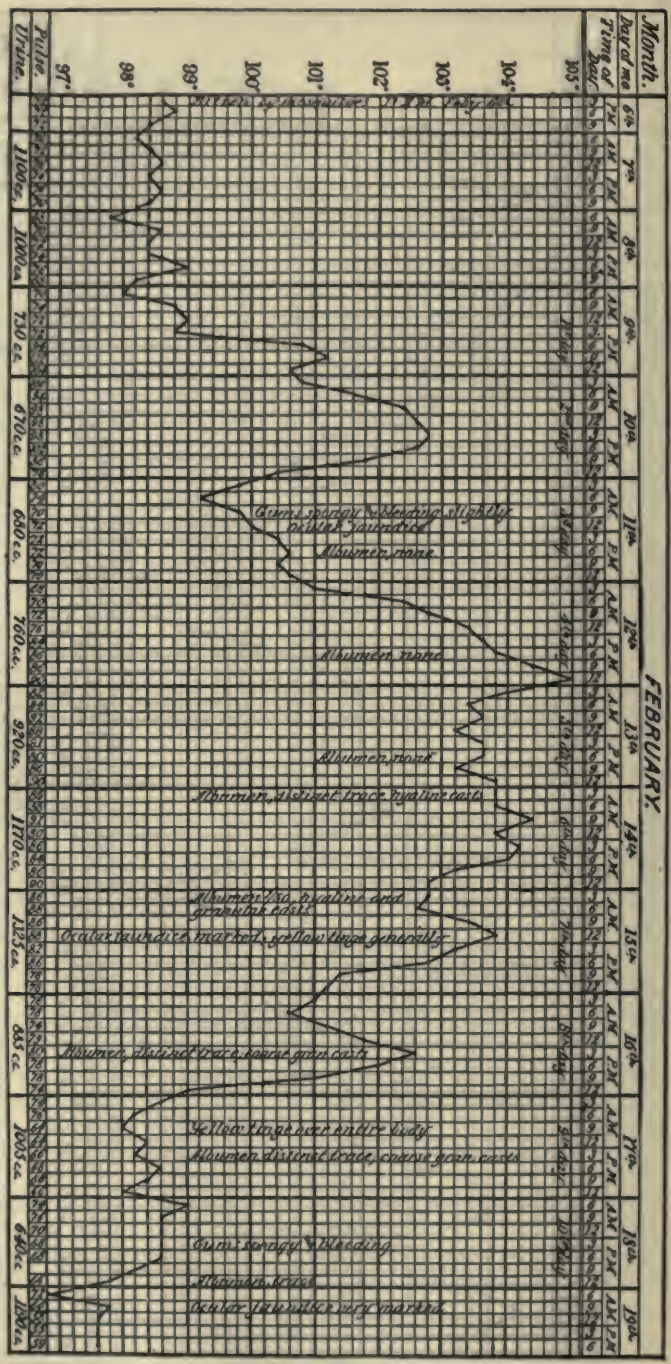

CHART VII.—Yellow fever produced by the bite of *Culex fasciatus*. Period of incubation, 3 days, 6 hours.

Of 12 cases thus accurately observed by himself the incubative stage was as follows:

Cases.	Days' incubation.
2	3
6	3+
2	4
1	4½
1	5¾
12	

The following table gives the result of our observations in 16 cases of experimental yellow fever.

TABLE I.—*Period of incubation of experimental yellow fever.*

No. of case.	Date of inoculation.	Method of inoculation.	Date of commencement of attack.	Incubation
				Dys. hrs.
1	Aug. 27, 1900, 2 p. m.	Mosquito	Aug. 31, 1900, 9 a. m.	3 7
2	Aug. 31, 1900, 11 a. m.	do	Sept. 6, 1900, 1 p. m.	6 2
3	Dec. 5, 1900, 2 p. m.	do	Dec. 8, 1900, 11.30 p. m.	3 9½
4	Dec. 8, 1900, 4 p. m.	do	Dec. 14, 1900, 9 a. m.	5 17
5	Dec. 9, 1900, 10.30 a. m.	do	Dec. 12, 1900, 9.30 p. m.	3 11½
6	Dec. 11, 1900, 4.30 p. m.	do	Dec. 15, 1900, 12 noon	3 19½
7	Dec. 21, 1900, 12 noon	do	Dec. 25, 1900, 11 a. m.	3 23
8	Dec. 30, 1900, 11 a. m.	do	Jan. 3, 1901, 10.30 a. m.	3 22½
9	Jan. 4, 1901, 11 a. m.	Blood injection	Jan. 8, 1901, 9 a. m.	3 22
10	Jan. 8, 1901, 9 p. m.	do	Jan. 11, 1901, 9 a. m.	2 12
11	Jan. 19, 1901, 3.30 p. m.	Mosquito	Jan. 23, 1901, 3 p. m.	3 23½
12	Jan. 22, 1901, 1 p. m.	Blood injection	Jan. 24, 1901, 9 a. m.	1 19
13	Jan. 25, 1901, 12.15 p. m.	do	Jan. 28, 1901, 1.15 p. m.	3 1
14	Jan. 31, 1901, 9.30 a. m.	Mosquito	Feb. 3, 1901, 12 noon	3 2½
15	Feb. 6, 1901, 11 a. m.	do	Feb. 9, 1901, 5 p. m.	3 6
16	Feb. 7, 1901, 2 p. m.	do	Feb. 10, 1901, 12 noon	2 22

The average period of incubation of the 16 cases embraced in Table I will be found to be 87¼ hours, or 3 days 15¼ hours. If we separate the 12 mosquito infections from the 4 cases produced by the injection of blood, we have for the former a period of incubation of 94 hours or 3 days and 22 hours, and for the latter an incubative stage of 67½ hours, or 2 days 19½ hours. The average period of incubation, therefore, in the cases brought about by subcutaneous injection of blood was shorter by 26½ hours than those occasioned by the mosquito's bite. By the former method, this stage varied from 43 hours to 94 hours, while in the mosquito infections the shortest incubative period was 70 and the longest 146 hours. If we accept those cases produced by the mosquito's bite as the usual method of propagation of this disease, it will be observed that of the 12 cases 1 occurred on the third day, 9 on the fourth day, 1 on the sixth day, and 1 at the beginning of the seventh day after incubation.

While our results, therefore, confirm the statement of later writers that the period of incubation of yellow fever does not usually exceed 4 or 5 days, they also seem to indicate very plainly that this stage may be prolonged more frequently, perhaps, than had been supposed.

In 16.6 per cent of our cases the period of incubation exceeded the usual quarantine period of 5 days. If we add Carter's cases to those observed by us, we find that of 24 cases the period of incubation

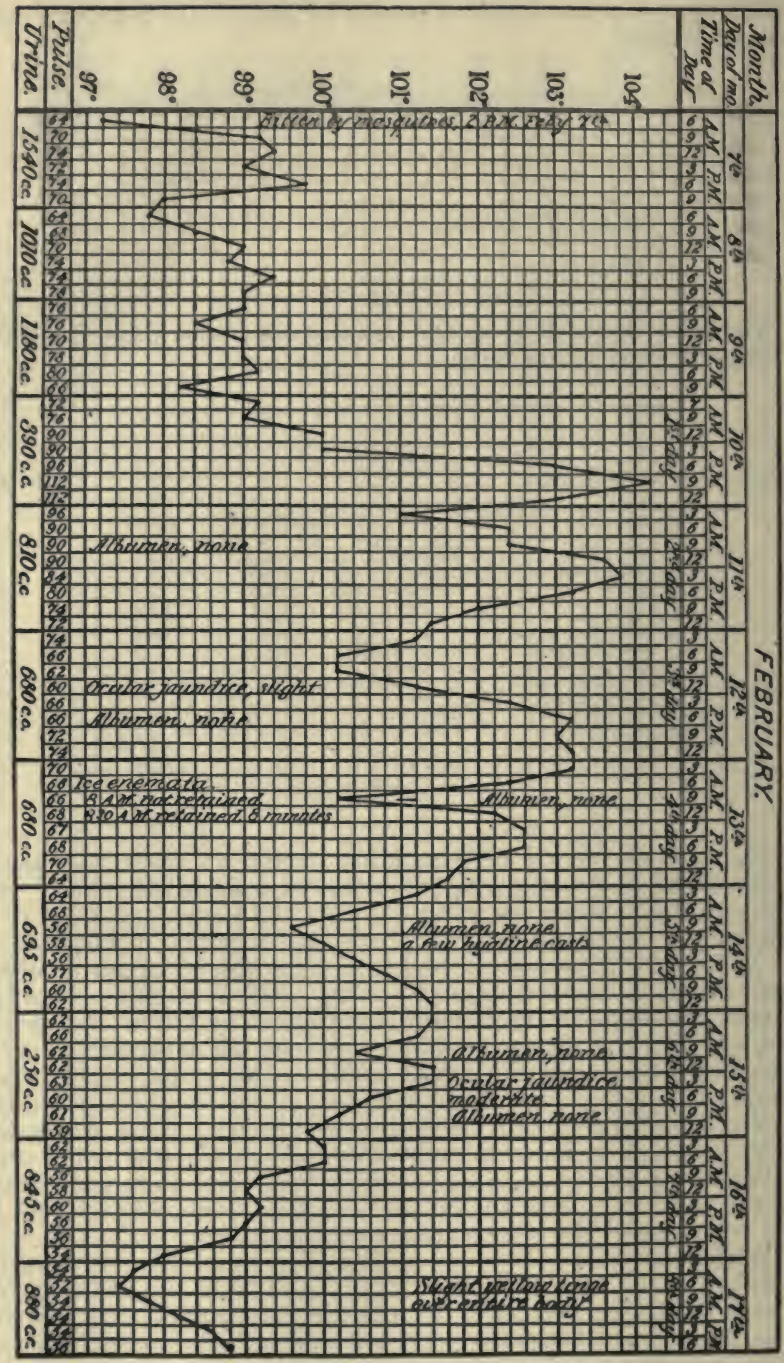

CHART VIII.—Yellow fever produced by bite of *Culex fasciatus*. Period of incubation, 2 days, 22 hours.

exceeded 5 days in 3, or 12.5 per cent. We will not further dwell on this subject than to remark that cases No. 2 and No. 4 of our series could have passed quarantine on the morning of the sixth day after inoculation, with a clinical thermometer under the tongue, without exciting any suspicion by reason of the presence of fever.

Character of the attack.—We desire to call attention particularly to the difference in the degree of severity of the attack as shown by our experimental cases. Like all of the other acute infectious diseases, we have reason to expect that yellow fever will affect different individuals according to their individual susceptibilities, and hence that we will encounter mild as well as severe cases. The results which we have obtained confirm this expectation. Based upon the character of the attack, the 12 cases due to mosquito inoculation may be divided as follows:

Severe	2
Moderately severe	6
Mild	3
Very mild	1
	12

The 4 cases produced by the injection of blood gave the following result:

Severe	1
Moderately severe	2
Mild	1
	4

Thus the cases which were mild or very mild in character constituted 33 per cent of those infected by the mosquito's bite and 25 of those produced by blood injection. It is to the diagnosis of the former cases that we desire to direct special attention. To one familiar with yellow fever, or even to one unfamiliar with its clinical features, the diagnosis of our severe and moderately severe cases should have presented no difficulty. The sharp headache and backache, the characteristic facies, the ocular jaundice, together with the presence of albumin in the urine, except in 1 case to be hereafter referred to, with the negative result of a blood examination, would have been a sufficient complex of symptoms to have rendered the diagnosis tolerably certain. Even in our 3 "mild" cases, were the physician on his guard and acquainted with the temperature curve and pulse from the very onset of the attack and, besides, careful in the testing of each specimen of urine passed, a diagnosis of yellow fever could have been made with reasonable probability. We believe, however, that, in the ordinary course of events, where there was no reason to suspect the presence of yellow fever the average practitioner would have probably failed to appreciate the true nature of these attacks. Such was the admission which we ourselves were compelled to make, although in constant attendance and thoroughly acquainted with these cases from their very beginning. The short duration of the primary fever in one instance; the rapid amelioration of the earlier symptoms in all; the absence of albumen during the first 3 days, or its presence, as a mere trace, in certain specimens, followed by its absence in succeeding specimens; the slight icteroid hue of the conjunctiva—to be obtained only in a certain light and then doubtfully—all served to render a

positive diagnosis exceedingly difficult. Several physicians, who saw these milder cases at our request, readily acknowledged the improbability of a correct diagnosis being made in the absence of the complete data which we were able to furnish concerning them. In the one case which we have classed as "very mild" yellow fever we believe that the matter of a correct diagnosis would have been in the highest degree improbable. The attack consisted of a single paroxysm of 33 hours' duration, during which the temperature only reached 101° for a period of 6 hours. It is true that albumin was found in the urine at the end of 37 hours, but the quantity was exceedingly small and only to be detected by the most delicate testing. It was only present in 1 or 2 specimens passed on the third day. A slight trace was present in a specimen passed at 9 a. m. of the fourth day and in that passed at 4.40 p. m. of the fifth day. Intervening specimens of urine, several in number, contained no albumin. A well-marked papular eruption which appeared on the fourth day of the disease, and which was confined to the trunk and arms, would hardly have rendered the diagnosis easier. We suppose that during the prevalance of an epidemic of yellow fever a physician who was thoroughly acquainted with the several types of this disease would probably class this case as one of extremely mild yellow fever, with a wide margin for doubt. Under all other circumstances we feel confident that cases of this character would escape diagnosis. That cases of mild yellow fever may and do serve as foci for the development of other cases our own observations demonstrate, since we have been able to propagate the disease from one such mild case by means of the bites of contaminated mosquitoes, and from another case of like character by the subcutaneous injection of 2 c. c. of blood.

THE ONSET AND PREMONITORY SYMPTOMS.

Of the 12 cases produced by mosquito inoculation, the onset was sudden in 2 and gradual in 10. In both of the former the attack occurred during the night, the patient, also, in both instances, being awakened by the occurrence of a decided chill. In 1 of the 2 cases of sudden onset, the subject complained of slight supraorbital headache during the afternoon preceding the attack. Of 4 cases produced by the injection of blood, the onset was sudden in 1—the only case marked by a chill—and gradual in 3. The attack in all of these blood cases began during the daytime. As writers generally state that in yellow fever the chances of infection are greater during the night, we have thought that, perhaps, the time of inoculation of our experimental cases (which was during the day except in 1 instance), might have had some influence upon their occurrence, as a rule, during the daytime. If the hour of inoculation in all of our cases should have taken place at about sunset, then, with the same period of incubation, 7, or 43 per cent would have experienced their attacks at night.

Of the 13 cases in which the onset was gradual—by mosquito inoculation, 10; by blood injection, 3—frontal headache, the pain being referred to the supraorbital region and extending into the temporal region, was the most frequent premonitory symptom. It was present in 10 and absent in 3 cases. This symptom preceded the attack in these cases at intervals varying from 2 to 48 hours.

In 2 cases no premonitory headache was complained of, while in 1 case occipital headache preceded the onset by 24 hours, and continued to be of this character throughout the attack. Dizziness was complained of by 3 of the gradually developing mosquito cases, and a sense of weight in the lower extremities by the 2 others belonging to this group. All of the cases of gradual onset (13 in number) complained of lassitude and want of appetite, on which account all took to their beds prior to the onset of fever. Ten of these individuals complained of slight sensations of chilliness—generally confined to the lower extremities—at the beginning of the attack, while in 3 this symptom was entirely absent. In our experimental cases, therefore, frontal headache and muscular debility were the most frequent and prominent premonitory symptoms. After the attack had developed, the symptoms correspond to those described at length by various writers and with which all are familiar, except that black vomit did not occur in any of our cases.

THE FEVER.

As we have had prepared charts of our several cases of experimental yellow fever, from which all the data concerning temperature and pulse can be obtained, it will not be necessary for us to make extended remarks under this heading. Medication being practically nil in our cases, both temperature-curve and pulse can be accepted as faithfully representing what normally takes place in an attack of this disease. When ice water enemas or cold sponge baths were used by the attending physician, this is noted on the chart. It should also be remembered that our patients were put to bed at the very first manifestation of the disease, and carefully transported to the yellow-fever wards on the very same beds which they had occupied in camp. This probably had some effect upon the subsequent course of the fever. The record of temperature being taken every 3 hours from the time of inoculation enables us to give the complete curves of both the primary and secondary febrile paroxysm. Our charts therefore differ considerably from those given by the various writers on yellow fever in that they round out, as it were, the primary stage more fully. An examination of these charts will show that although the primary rise of temperature is tolerably abrupt and reaches its height within a comparatively short time, it does not reach its maximum so quickly as the description of writers would seem to indicate. The trihourly record in 10 of our mosquito inoculations shows that this period of primary rise varies from 12 to 24 hours. In 3 cases it was 12 hours; in 2, 15 hours; in 1, 15½ hours; in 1, 20½ hours; in 1, 22½ hours; and in 2, 24 hours. The average period of the 10 cases was therefore a fraction over 16 hours.

In striking contrast to these was the short period of the primary rise of temperature in the 4 cases produced by blood injection. In these it varied from 2¼ to 9 hours, the remaining 2 cases giving 6 and 7 hours respectively, the average for the 4 cases being only 6 hours. In all of the 12 cases due to mosquito inoculation, the primary rise of temperature was followed by a distinct remission or intermission, which was generally reached within 48 hours. The same remission was present in 3 of the 4 cases produced by blood injection. We are

able to give the duration of the primary paroxysm accurately in the 10 cases produced at Camp Lazear by the bites of mosquitos, viz.:

Case.	Hours.
1	33
1	33½
1	36
1	39
1	41
3	45
1	52
1	60
10	

The average duration of these 10 cases was 43 hours. In the 3 cases caused by the injection of blood the length of the primary paroxysm was 24 hours in 2 cases and 36 hours in 1 case—the average being 28 hours. We may therefore say that not only the average period of incubation, but also the primary rise of temperature, as well as the length of the first febrile stage were all shorter in the cases produced by blood injection than in those due to the mosquito's bite. Of the 12 cases due to the latter mode of inoculation the first febrile stage was followed by an intermission in 2, and a remission in 10 cases. Of those produced by the injection of blood, 3 showed a distinct remission and 1 no intervening fall of temperature. The duration of this intermission varied from 3 to 27 hours. This was followed by a second febrile stage or paroxysm in 11 of the 12 mosquito inoculations, and in 3 of the 4 cases due to the injection of blood. The duration of this second febrile paroxysm was from 2 to 5 days.

Experimental yellow fever then, as we saw it at Camp Lazear, consisted of a primary and secondary febrile paroxysm, with an intervening remission or intermission—more frequently the former. The secondary was much longer than the primary febrile stage.

In 1 of our mosquito inoculations a relapse occurred on the ninth day of the disease, and was characterized also by 2 febrile stages with an intervening remission. There were present headache and backache, with injection of the eyes and face, together with hemorrhage from the gums, as had been observed in the primary attack.

The want of correlation between temperature and pulse (Faget's law), upon which clinicians rely as an important diagnostic sign, was seen as a rule in our experimental cases, i. e., after the passage of the first febrile stage. In 1 case produced by the injection of blood, Faget's law was not complied with.

The urine.—We have confined our examination of the urine largely to testing for the presence of albumin and to the ordinary microscopic examination of this fluid. Heat and nitric acid was the method used in all cases for the detection of albumin, the specimen having first been carefully filtered.

Under this heading we desire to speak only concerning the presence of albumin. All writers dwell on the importance of a careful examination of the urine in suspicious cases of fever, since the presence of albumin in the urine is such a constant sign in yellow fever. Guiteras, who has had a large experience with this disease, says:

"The albumin appears in the urine usually on the third or fourth day of the disease. It may be very transient. In many mild cases the albumin is present only in the urine passed in the evening of the third or fourth day. In many cases it is only a trace." We may say that the results obtained from examination of the urine of experimental yellow fever accords for the most part with the statements above quoted.

TABLE II.

Case.	Albumin during period of incubation.	Time of appearance of albumin during the attack.	Time of disappearance of albumin dating from appearance.	Maximum quantity.
	Mosquito inoculation:	*Hours.*		
1	None	42	Tenth day	Eight-tenths by volume.
2	None	25	Eleventh day	Three-tenths by volume.
3	None	82½	Fifteenth day	Two-tenths by volume.
4	None	48	Fifth day	Distinct trace.
5	None	64½	Fourth day	Light trace.
6	None	43½	Third day	Distinct trace.
7	None	37½	Eighth day	Do.
8	None	43	Ninth day	One-fortieth by volume.
9	None	42	Twelfth day	One-twentieth by volume.
10	None	75	Eighth day	Distinct trace.
11	None	106	Fifteenth day	One-fortieth by volume.
12	None	None.	(1)	One-twentieth by volume.
	Blood inoculation:			
13	None	61	Thirteenth day	Distinct trace.
14	None	17	Twelfth day	Do.
15	None	57	Ninth day	Do.
16	None	18½	Fifteenth day	One-tenth by volume.

[1] Albumin did not appear till 36 hours after fever had subsided and persisted for five days.

In our earlier cases we did not examine for albumin until the onset of the attack. In our last 8 cases (those embraced in this report) we examined daily specimens from the time of inoculation until the attack began, and thereafter we endeavored to examine every specimen passed by the patient. Table II gives the results obtained.

An examination of the cases presented in this table will show that of the 12 mosquito inoculations the earliest appearance of albumin was at the beginning of the second day in 1 case; during the second day in 5; at the end of the second day in 1; during the third day in 1; during the fourth day in 2; during the fifth day in 1; while in 1—a well-marked case—no albumin could be detected till 36 hours after the temperature had reached the normal, i. e., till the second day of convalescence; it then persisted during 5 days. In all 23 specimens of urine were examined in this case during the 6 days of fever, but with an entirely negative result as regards the presence of albumin. An occasional hyaline or fine granular cast could be found in the majority of these specimens. We submit this case of experimental yellow fever as one of especial importance from the clinical standpoint, since the absence of albumin during the attack would have probably led to an error in diagnosis. How very exceptional such cases may be we have no means of knowing.[1]

It will be observed that the quantity of albumin present in this series of cases was very moderate, except in Cases I and II of Table II. These cases were the only 2 of the 16 that were not placed in bed from

[1] It is of interest to note that this particular individual, 2 weeks prior to successful inoculation and while in quarantine, had an intermittent albuminuria which lasted 3 days.

the very beginning of the attack. In the remaining 14, all of whom were kept at absolute rest during the whole period of the fever, the amount of albumin was small in 6 and insignificant in 8. We are inclined to believe, therefore, that both the course of the fever, as well as the quantity of albumin, were favorably affected by the early enforced rest of our patients.

In conclusion we desire to invite attention to 2 matters which we consider of considerable importance in connection with the possible importation and propagation of yellow fever. First, we believe that the facts herewith presented indicate that the period of incubation of yellow fever occasionally exceeds the quarantine period of 5 days, and that although exceptional this must not be left out of consideration. Secondly, that our observations emphasize anew the importance of the recognition by the profession of mild and very mild cases of yellow fever. Guiteras [1] says: "I can not insist too much upon the importance of the diagnosis of the first case of yellow fever in a locality." He adds: "Undoubtedly the cause of the epidemic of yellow fever is to be found in the introduction into a community of cases that are not suspected to be yellow fever." In the light of our investigations, we feel constrained to remark that the failure to detect cases of mild yellow fever has been, we believe, the most important factor in the development of the theory of the propagation of this disease by fomites.

[1] Report of United States Marine-Hospital Service, Vol. XXVII, 1897–1898, p. 300.

DR. JESSE W. LAZEAR.

Chapter 6.

THE PREVENTION OF YELLOW FEVER.[1]

By Walter Reed, M. D., Surgeon, United States Army, and James Carroll, M. D., Contract Surgeon, United States Army.

The prevention of yellow fever since its first importation into the United States in 1693, and especially during the latter half of the past century, has commanded, perhaps, more attention on the part of those who were concerned with matters pertaining to the public health than the prevention of any of the other acute infections. This has not been occasioned by the fact that its total sickness and mortality have exceeded that of other acute infectious diseases, such as typhoid fever or croupous pneumonia, but because rather of the proximity of its source to our shores; the lack of knowledge of its specific agent; the consequent mystery surrounding its origin and propagation; the alarmingly rapid spread and course of this disease, when once it had obtained a foothold, and the high mortality with which its epidemics have generally been attended. Although the duration of its presence in our seaports was plainly limited by certain seasonal conditions, yet during its brief reign—July to October—its ravages were such as to completely paralyze both the social and commercial interests of a given city, and even of an entire section of our country.

The interval between 1793 and 1888 is almost 100 years, but upon the appearance of yellow fever we observe no difference of behavior on the part of the inhabitants of Jackson, Miss., in 1888, from that shown by the citizens of Philadelphia in 1793, except that the terror of the former was greater and their flight from their homes more precipitate than in the case of the latter.

The recurrence of succeeding epidemics has, therefore, served to increase rather than to lessen the public alarm.

It would be difficult to determine with accuracy the loss of life occasioned by the 95 invasions of our territory by yellow fever during the past 208 years. We have endeavored to collect from the most available sources the mortality caused by this disease, but have been unable to obtain any reliable data for the earlier epidemics. If we confine ourselves to the epidemics which have occurred since 1793, we find that there have not been less than 100,000 deaths from this cause. The greatest sufferer has been the city of New Orleans, with 41,348 deaths, followed by the city of Philadelphia, with 10,038 deaths. The epidemics of 1855, 1873, 1878, and 1879 claimed 7,759 victims in the city of Memphis, Tenn. From 1800 to 1876, Charleston lost 4,565 of its citizens by attacks of yellow fever. New York, during the earlier and later invasions of this disease, has had 3,454 deaths, while the epidemic of 1855 in Norfolk, Va., caused over 2,000

[1] Read at the 29th annual meeting of the American Public Health Association, held in Buffalo, N. Y., Sept. 16-21, 1901.

deaths. During our brief occupation of the island of Cuba (July, 1898–December, 1900), with every precaution brought into exercise to ward off the disease, there have occurred among the officers and men of our Army 1,575 cases of yellow fever, with 231 deaths.

If we reckon the average mortality at 20 per cent, there have not been less than 500,000 cases of yellow fever in the United States during the period from 1793 to 1900.

Turning for a moment to other countries, we find that the great epidemic of 1800, in the province of Andalusia, Spain, caused 60,000 deaths, and that 20,000 more deaths attended the invasion of the city of Barcelona by this disease in 1821. From 1851 to 1883, the deaths from this cause in the city of Rio de Janeiro were 23,338, while in the city of Habana, between the years 1853 and 1900, 35,952 deaths have been recorded from yellow fever.

We have no means of computing the damage done to the commercial interests of the United States by epidemics of yellow fever. At the sixth annual meeting of this association, held in Richmond, Va., in 1878, Dr. Samuel Choppin, president of the State board of health of Louisiana, estimated the actual cost of the epidemic of that year to the material resources of the city of New Orleans as $10,752,500. Dr. Benjamin Lee, the present distinguished occupant of the presidential chair, at the seventeenth annual meeting of this association, held in Brooklyn, N. Y., in 1889, contributed a paper having the title, "Do the Sanitary Interests of the United States Demand the Annexation of Cuba?" From this we quote the following sentence: "A single widespread epidemic of yellow fever would cost the United States more in money, to say nothing of the grief and misery which it would entail, than the purchase money of Cuba." That this was no exaggeration, witness the language of the petition which the chairman of the committee on the etiology of yellow fever, in conjunction with other prominent members of this association, presented to the President of the United States on November 15, 1897, and again, on November 21, 1898, in accordance with a resolution adopted at the meeting of this association, held at Ottawa, Canada, in 1897. In addressing President McKinley, Dr. Horlbeck said: "It is hardly necessary to call your attention to the serious results of the recent epidemic of yellow fever in the States of Louisiana, Mississippi, and Alabama, but we may be permitted to mention the fact that the great epidemic of 1878 resulted in the loss of nearly 16,000 lives, and that it has been estimated that the total loss to the country resulting from this epidemic was not less than $100,000,000."

The importance of the study of the causative factors entering into the propagation of a disease so capable of quickly destroying the lives of the citizens and wrecking the commercial interests of the cities of the United States could hardly be overestimated. Did time permit, we would be glad to refer to the numerous and valuable contributions made to this subject by the members of the American Health Association. We can only mention the establishment of the National Board of Health and the appointment of the Habana Yellow Fever Commission of 1879 as two of the most important outcomes of the persistent efforts of this association, following "the deeply tragical events of the summer of 1878." The exhaustive reports made by Chaillé in 1880, and by Sternberg in 1890, must always stand as monuments to the earnest spirit of investigation with which the work was pursued.

Notwithstanding the importance of the work and the efforts put forth by students in this and other countries, we believe that we are safe in saying that no results had been obtained which would enable us to combat successfully this disease when once imported into our larger centers of population, and no means found to keep it out of our ports except such as would place very heavy burdens upon commerce. This inability to control the disease grew not only out of our ignorance as to the way or ways in which yellow fever was propagated, but also out of certain false opinions which we had formed as to the mode of its spread. The doctrine of the spread of yellow fever by fomites and by filth had taken such hold on the professional mind as completely to overshadow all other views, and to direct into false channels the work of those who were engaged in the investigation of this disease. The efforts to isolate or to discover the specific agent of yellow fever, if successful, would possibly have greatly simplified the problem; in the absence of such discovery, the first step in our knowledge of how to prevent this disease could only be found, we think, along another line, viz, that of its propagation from the sick to the well. This step we endeavored to take in connection with our colleagues, Dr. Agramonte and the late Dr. J. W. Lazear of the United States Army, during our recent investigations into the causation and spread of yellow fever at Quemados, Cuba.

The results of our earlier work relative to the etiology and propagation of this disease we had the pleasure of presenting to this association at its last meeting, held in Indianapolis, Ind.[1] You will recall that one of the conclusions which we then submitted was as follows: "The mosquito serves as the intermediate host for the parasite of yellow fever." In the same article, we briefly indicated the reasons which influenced us in pursuing this line of investigation, and it is, therefore, unnecessary here to repeat them.

Continuing our studies, especially as regards the means by which yellow fever is spread from individual to individual, and as to the manner in which houses become infected, we were able, under strict rules of isolation and quarantine, to bring about an attack of yellow fever in 10 nonimmune individuals (and always within the period of incubation of this disease) out of a total of 13 (76.84 per cent) whom we attempted to infect by means of the bites of mosquitoes—*Stegomyia fasciata*—that had previously been fed with the blood of yellow-fever patients during the first, second, and third days of their attacks. These results were reported in part to the Pan-American Congress held in Habana during February of this year,[2] and in part to the Association of American Physicians at its last meeting, held in the city of Washington.[3]

It will be seen that we were able to establish in the most conclusive manner that the mosquito does serve as the intermediate host for the parasite of yellow fever. At this same experimental sanitary station we were also able to demonstrate that an attack of yellow fever can not be induced by the most intimate and prolonged contact with the clothing and bedding of yellow-fever patients, even though these articles had been previously thoroughly and purposely soiled with the excreta of such patients. In other words, we were able to

[1] "The Etiology of Yellow Fever—A Preliminary Note." Philadelphia Medical Journal, Oct. 27, 1900.
[2] "The Etiology of Yellow Fever—An Additional Note." Journal American Medical Association, Feb. 16, 1901.
[3] "Experimental Yellow Fever." American Medicine, July, 1901.

prove that the garments worn, and the bedding used, by yellow-fever patients were no more concerned in propagating this disease than the clothing and bedding of patients suffering from malarial fever are concerned in the spread of the latter malady. The doctrine of the spread of yellow fever by fomites having, at the first touch of actual experiment on human beings, burst like a bubble, we may hereafter cast it aside, with other exploded beliefs, to the very great simplification of the problem how to prevent yellow fever. Indeed, in our opinion, the time has now arrived when the latter problem may be reduced to measures which shall prevent the propagation of this disease by mosquitoes. Although this specific agent of yellow fever has not, as yet, been discovered, this must remain largely a matter of scientific interest, and does not in the least lessen the efforts which we, as sanitarians, are now able for the first time to bring into action for the prevention of the spread of this disease, since in dealing with the mosquito we are dealing with the intermediate host which carries the specific agent from the sick to the well.

In considering, then, in a broad way, the prevention of yellow fever, the natural order would be to give our attention, first, to measures which will prevent the importation of this disease from infected places into the seaports of the United States; and secondly, to measures which will most effectually prevent the spread of this disease, provided it should gain a lodgment in one of the cities of this country.

With your permission, however, we will reverse the order of consideration above suggested, and will later refer in the briefest manner to the prevention of the importation of yellow fever into the United States from foreign ports, as this part of the subject will be presented by the health officer of the port of New York, who, from long experience, will be able to deal more intelligently than we with this part of the problem.

Since the mosquito, especially that species of stegomyia which has recently been designated by Theobald as *Stegomyia fasciata* (formerly known to entomologists as *Culex fasciatus* Fab.), has become so prominent a factor in the spread of yellow fever, it becomes necessary to consider this insect from the point of view of its identification; its habitat; its breeding places; the length of its generation; its hours of feeding; the influence of temperature upon both its propagation and stinging; the interval after contamination before the insect becomes capable of propagating the disease; the length of time during which it remains dangerous; the measures that should be used not only to protect the sick against the bites of these insects, but also to prevent the latter from infecting the healthy individual; and, finally, a consideration of the several agents which may be successfully employed both to prevent the breeding of mosquitoes as well as directed toward their destruction in the adult stage.

Aside from the standpoint of scientific interest, it is certainly a matter of hygienic importance, in taking up the question of how to prevent the spread of yellow fever, when imported into the United States, that the health authorities of our several coast cities, and, indeed, of some of our inland towns, should be able to determine whether the only species of mosquito, which, up to the present time, has been shown capable of conveying yellow fever, is or is not present in these cities. If it should hereafter be proven that only species of the genus *stegomyia* are capable of acting as intermediate hosts for

the specific agent of yellow fever, as appears to have been demonstrated for the genus *anopheles* in the spread of malaria, the presence or absence of the former genus will definitely determine whether yellow fever will or will not spread in a given locality. The presence or absence of mosquitoes that can propagate the disease is the only intelligible explanation of what has heretofore been considered an inexplicable problem, viz, the capability of this disease to propagate itself in certain localities, while in other places it could be introduced with perfect impunity to the public health. In other words, our present knowledge of this question solves, at last, the problem of the portability or nonportability of yellow fever.

Description of mosquito.—The identification of *stegomyia fasciata*, Theobald, should not be difficult. This mosquito, when examined closely with the naked eye and especially with a pocket lens, is a rather striking-looking and handsome insect. (Fig. 1.) Its most conspicuous markings are the broad semilunar silvery stripe, which is seen on the lateral surface of the thorax, and the white stripes at the bases of the tarsal joints. These may be readily distinguished with the naked eye. The bands on the hind legs are especially well marked, and occasionally the entire fifth hind tarsal joint is seen to be of a pure silvery white. The four stripes of silvery scales which are seen on the posterior surface of the thorax serve to distinguish this species from all other mosquitoes, except *stegomyia signifer*, Coquillet, in which, however, as we have been informed by Mr. L. O. Howard, the curved thoracic band is very narrow and of a somewhat different shape. Examined with a hand lens, the four stripes are seen to consist of two lateral, distinct silver lines—the continuation of the semilunar, broad stripes—and two fine, white lines situated between these, and which require that the insect shall be held in the proper light, in order that these delicate threads may be distinctly seen. The lateral surface of the thorax is also marked by several silvery dots and the abdomen by distinct white stripes. This description applies to both sexes. In the female, the palpi are short, as in the genus culex. The proboscis is of a dark blackish-brown color and is destitute of a whitish band near the middle. In the male (fig. 2), one of the front tarsal claws bears a tooth on the under side, while the other claw is destitute of such marking. In the female, both front tarsal claws bear a distinct tooth near the base of the under side of each.

Habitat.—We have found this mosquito in all of the principal cities of Cuba, and have received specimens from a number of the smaller towns on this island. According to Howard [1] it has been found at Kingston, Jamaica, on the Isle of Pines, and at Bluefields, Nicaragua. He also reports that Theobald has received specimens of this insect from Italy, Greece, Spain, Portugal, Gibraltar, and Malta. In the United States, Howard reports its presence at New Orleans, Natchitochez, and Napoleonville, La.,; in eastern Texas; Hot Springs, Ark.; Pelham, Ga.; and from Virginia Beach, near Norfolk, Va. To this we can add Augusta, Ga., from which city we have recently received specimens of *stegomyia fasciata* through the courtesy of Dr. T. O. Oertel of that city. Dr. Durham, of the English commission for the study of yellow fever, kindly showed us specimens of this insect which

[1] "Mosquitoes," etc., by L. O. Howard, New York, 1901.

he had collected at Para, Brazil, and at various places along the Amazon River. It will be seen, therefore, that *stegomyia fasciata* has a wide distribution in the warmer countries of the globe, and especially at low altitudes. A more exact knowledge of the distribution of this mosquito in the United States is, we think, a matter of considerable practical importance.

Breeding places.—In our search for the larvæ of this insect we have found them in the following places: (1) In rain-water barrels; (2) in sagging gutters containing rain water; (3) in tin cans that had been used for removing excreta and which still contained a small amount of fecal matter; (4) in cesspools; (5) in tin cans placed about table legs to prevent the inroads of red ants; (6) in the collection of water at the base of the leaves of the *agave americana;* (7) in one end of a

FIG. 1.—Stegomyia fasciata; female. *a*, Front tarsal claw.

horse trough that was in daily use. It follows that stegomyia, like culex, will breed in any collection of still water, rain or hydrant, and that the presence of fecal matter does not seem objectionable. Indeed, we have been in the habit of adding a very small quantity of the latter to our breeding jars, as it has seemed to hasten the development of the larvæ. In water, however, which contains much suspended soil—muddy water—the larvæ, in our experience, do not flourish, but die off rather rapidly.

Deposition of eggs.—The insect lays her eggs during the night, and, unlike culex, which deposits its eggs in boatlike masses, stegomyia extrudes her eggs on the surface of the water in pairs, in groups of three or more, or singly; in this respect resembling anopheles. (Fig. 3.) Exceptionally, the eggs are deposited in a rather close-

lying mass. (Fig. 4.) The whole batch is laid in one night, or extending over two or three nights. The number of eggs deposited varies from about 20 to about 75—rarely a larger number. Sixteen careful counts gave an average of 47 eggs. At the same time that the female deposits her eggs, she frequently, but not always, discharges a fluid which forms a very thin film over the surface of the water, which possibly assists in floating the eggs. The latter are of a jet-black color and, to the naked eye, cylindrical in shape, one end of the egg being rounded and blunt, while the other is slightly pointed, the whole resembling closely a Conchita cigar. They measure about 0.65 mm. in length by 0.17 mm. in width at the broadest part. Under a low power, the surface of the eggs is seen to be marked by tolerably regular six-sided plates, each of which is further marked in the center

FIG. 2.—Stegomyia fasciata; male. *a*, Front tarsal claw.

by a little round elevation, which gives to the surface of the egg a decidedly roughened appearance. (Fig. 5.) Under this low amplification it is also seen that, while one side of the egg is somewhat convex, the other is flat or slightly concave and that a cross section of the egg would present the appearance of a triangle instead of that of a cylinder. This flattening of the surface of the egg does not appear to extend quite to the ends, which are round in shape. Although floating perfectly if left undisturbed, any agitation of the water, especially of a rough character, is apt to cause some or a majority of the eggs to sink. If by slight pressure the egg is pushed beneath the surface of the water it at once sinks and does not rise again. This sinking of the eggs does not interfere with their subsequent hatching, as in our experience submerged eggs furnish about as many larvæ as those which are left floating on the surface.

The resistance of stegomyia's eggs to external influences is worthy of note. Drying seems to be but little injurious to their subsequent fertility. We have found that eggs dried on filter paper, and kept for periods of from 10 to 90 days, will promptly hatch when again submerged in water. Dried eggs brought with us from Habana, in February, were easily hatched during the month of May in Washington, furnishing about 60 per cent of the usual number of larvæ hatched from fresh eggs. Freezing does not destroy the fertility of the eggs; although freezing with a mixture of salt and ice for 30 minutes has several times seemed to prevent subsequent hatching; on one occasion a batch of 155 eggs, freshly deposited, which were frozen at a temperature of −17° C., for one hour, then thawed out at room temperature and placed in the incubator at 35° C., began to hatch on the sixth day, the majority furnishing active larvæ on the eighth day. In another observation, freshly deposited eggs, frozen at −17° C. for half an hour on two successive days, began to hatch on the third day as usual at incubator temperature. The resistance of stegomyia's eggs to drying for a period of three months would appear to demonstrate that this genus of mosquito could survive the winter in Habana without the presence of hibernating females. Doubtless the genus is preserved in both ways. It is probable that the same could occur in our extreme southern latitudes.

FIG. 3.—Stegomyia fasciata. Batch of fifty-two eggs as deposited by a single female. Slightly enlarged.

FIG. 4.—Stegomyia fasciata. Forty-eight eggs deposited in a close-lying mass. Enlarged.

Length of generation.—The impregnated female, having obtained a meal of blood, proceeds to deposit her eggs, in captivity, after an interval varying in our experience from 2 to 30 days—as a rule, the eggs are laid within 7 days; sometimes a second or third meal of blood is taken before any eggs are laid. Eggs placed under favorable conditions of warmth—i. e., summer or incubator temperature—begin to hatch, as a rule, on the third day, the period extending to about 1 week. The larval stage requires 7 or 8 days, and the pupal stage about 2 days. The period for the generation may be stated, therefore, as follows: Incubation, 3 days; larval stage, 7 days; pupal, 2 days; total, 12 days. As the eggs begin to hatch before the expiration of the third day, we generally obtain a few mosquitoes on the eleventh day. The shortest period of development observed by us during summer weather in Cuba was incubation, 2 days; larval stage, 6 days; pupal, 36 hours; making the total length of this generation 9½ days. This short period we believe to be quite exceptional. The

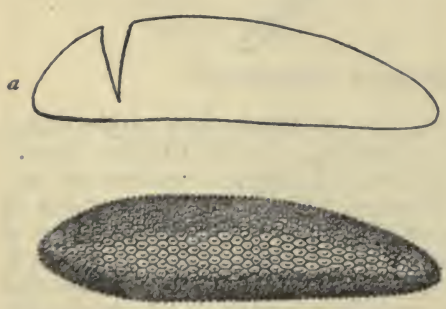

FIG. 5.—Stegomyia fasciata. Newly deposited egg. × 50. *a*, Empty shell from which larva has escaped.

first fully developed insects begin to emerge on the eleventh or twelfth day, and the whole number have reached maturity by the fifteenth or eighteenth day after deposition of the eggs. The young larvæ, in emerging, rupture the shell at a point about one-fifth the length of the egg from the larger end. This cap-like end can be frequently seen turned back and still adhering to the rest of the shell. (Fig. 5.)

The larva and pupa of stegomyia (figs. 6 and 7) resemble fairly closely those of culex, and the larvæ maintain the same relative position to the surface of the water; i. e., while in the act of breathing they assume a vertical position, with the head directed downward.

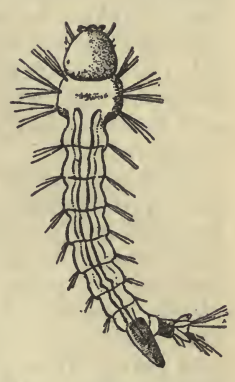

FIG. 6.—Stegomyia fasciata. Full-grown larva enlarged.

Influence of temperature on propagation.—We have just seen that at summer temperatures the time required for a complete generation of this insect is from 11 to 18 days. We may say that at an average temperature of 75° F., or over, stegomyia multiplies abundantly. Exposure to a cooler temperature, even for a short time daily, much retards the development of this mosquito. Thus, a batch of 51 eggs kept at 35° C., but which were placed in a cool chamber at 20° C. for two hours daily during the whole process of development, although furnishing a few larvæ at the end of the third day, were not all hatched until the eleventh day. The first pupæ appeared on the fourteenth day and the first mosquito on the nineteenth day; the whole process being completed in 27 days, instead of the usual 15 to 18 days. The loss of insects was about 50 per cent. Eggs kept at a temperature of 20° C. (68° F.) do not hatch, in our experience. Newly hatched larvæ kept at this temperature develop very slowly and require about 20 days to reach the pupal stage. Mosquitoes developed under such conditions are feeble, and but few arrive at maturity. Young larvæ kept at 10° C. (50° F.) have failed to reach the pupal stage, although some growth takes place. In one experiment more than 50 per cent were dead at the end of two weeks, and none survived the thirty-second day. Half-grown larvæ and pupæ exposed to a temperature of 20° C., and even as low as 10° C., continue to develop slowly, but the few insects which escape drowning have, as a rule, been of feeble strength and have refused to bite. Although the reduction of the temperature to the freezing point, or below, would not necessarily destroy the vitality of the eggs of this genus of mosquito, it should be remembered that a reduction of temperature to 68° F., or below, for even a few hours of the 24 will much retard the development of the generation. At a temperature less than 68° F. the eggs of this insect have ceased to hatch.

FIG. 7.—Stegomyia fasciata. Pupa, enlarged.

Influence of temperature on biting.—While the nonimpregnated female does not appear to bite, the impregnated female is generally ready to bite on the second or third day of her existence; they very rarely suck blood on the first day. This species of mosquito, when not deprived of its liberty, although occasionally biting during the morning hours, has, in our experience, been especially active from the hour of 4 p. m. till midnight. In captivity, the hungry impreg-

nated female will bite at any hour of the day or night. The meal of blood appears to have been thoroughly digested on the third day, when the insects, if applied to the surface of the skin, can be again readily induced to feed. When freed in a room, the female does not appear to bite a second time till about five, or even seven, days have elapsed.

As regards the effect of temperature in the stinging of *Stegomyia fasciata*, the results of a number of observations made by us show that this mosquito will bite at temperatures of 62° F. and above. At temperatures below this point, we have not, as yet, succeeded in inducing even very hungry females to suck blood. We may, therefore, say that observations thus far made appear to show that *Stegomyia fasciata*, while not breeding at temperatures below 68° F., will still bite at a temperature as low as 62° F., but probably not at lower temperatures.

If this insect is concerned in the propagation of yellow fever, it is now quite apparent why an epidemic of this disease should fall to a low ebb in the city of New Orleans during the month of November, with a mean temperature of 61.8° F., and practically cease in December, with a mean temperature of 55.3° F. A careful study of the charts herewith submitted (figs. 8 and 9), showing the monthly mean temperatures of the cities of Habana and New Orleans and Habana and Rio de Janeiro together with the relative monthly mortality from yellow fever in these cities, will prove of interest, we think, as showing better than laboratory observations the general effect of temperature upon the breeding and biting of *Stegomyia fasciata*. In the light of recent researches, we can now understand that while yellow fever can, and does, prevail during the entire year in Habana and Rio de Janeiro—although at a comparatively low ebb during the winter months—it can not propagate itself in New Orleans from December to May.

Interval after contamination before the mosquito becomes dangerous.—In our experimental work on human beings, we have not succeeded in inducing an attack of yellow fever by the bites of mosquitoes which had been kept less than 12 days after contamination. The same insects which failed to convey the disease on the eleventh day were capable of so doing on the seventeenth day after infection. This interval of about 12 days, which appears necessary for the development of the parasite within the mosquito, plus the period of incubation, agrees with the time that has been observed to elapse between the introduction of an infecting case into a locality and the occurrence of the first secondary case, viz, two to three weeks.

After the mosquito has once become dangerous, how long it remains capable of conveying the disease, although important, has not been determined. We have reported cases of yellow fever caused by the bites of stegomyia at intervals varying from 12 to 57 days after contamination. Here the dangerous interval was 45 days, but as one of these insects lived until the seventy-first day after biting a yellow-fever patient, the dangerous interval would here be prolonged to 59 days, or a little over 8 weeks. In our experience, the infected insect appears to live about as long as the noninfected mosquito, so that the answer to this question would depend upon the length of life of the mosquito. This we do not know. While in captivity, the majority of mosquitoes do

not survive, with the best of care, more than about five weeks, and many die within half of this time; we are ignorant as to the length of time during which they may live when under natural conditions. Certainly, during summer weather this will depend largely on the opportunity which the mosquito has of obtaining access to water.

Measures to prevent the spread of the disease when imported.—A case of yellow fever having been imported into one of our seaport cities, we are now prepared to discuss the measures that should be taken to prevent its spread. The problem resolves itself into the simple one of excluding mosquitoes from access to the sick individual and of destroying those insects that have already become infected. We can leave out of consideration any danger from wearing apparel or baggage, which, in our opinion, may be dismissed as harmless.

The fear that has been entertained that infected insects may be imported in boxes or trunks we believe to be absolutely groundless, and this for the simple reason, as shown by numerous observations made by us, that mosquitoes, when deprived of water, die within a few days. Even if allowed to fill themselves with blood immediately before the experiment is begun, and then deprived of water, practically all are dead by the expiration of the fifth or commencement of the sixth day. We may say that of a large number of insects tried in this way only one female has survived until the sixth day, and then in a feeble condition. Males and females which have been living on sugar and water, or fed two days before on blood, if deprived of water and food, begin to die after 24 hours, and all are dead on the fourth morning. Free access to water, therefore, is necessary for the existence of this mosquito.

Add to the deprivation of water the chances of injury to so frail an insect packed in with articles of clothing, etc., and we see that infected mosquitoes can not be imported alive in baggage that has been five days en route.

As the first special measure of prevention, then, we should give our prompt attention to the protection of the sick individual against the bites of mosquitoes. This can best be accomplished by thorough screening, without delay, of the windows and doors of the room occupied by the patient and with as little disturbance as possible, so that any insects already present in the room may be prevented from escaping. As it will not be feasible to make use of any of the destructive agents against mosquitoes already within the patient's room until recovery, every precaution should be used to see that the insects do not escape in opening and closing the door. Screens at windows should not, for this reason, be movable. As it is possible that mosquitoes that have already bitten the sick individual may have escaped into other apartments of the house, these should be closed tightly and subjected either to sulphur or to formaldehyde disinfection or to the fumes of burning pyrethrum. According to Dr. Gorgas, the efficient health officer of Habana, preference is given to pyrethrum powder, burned in the proportion of 1 pound to 1,000 cubic feet of air space.[1] He, however, adds:

> As the pyrethrum powder, even in this large quantity, does not certainly kill all mosquitoes, the room is opened at the end of three hours and the mosquitoes on the floor swept up and burned.

[1] Medical Record, New York, vol. 60, No. 10, Sept. 7, 1901.

We have mentioned above, in the order of their efficiency, the agents which are most destructive to stegomyia. According to our

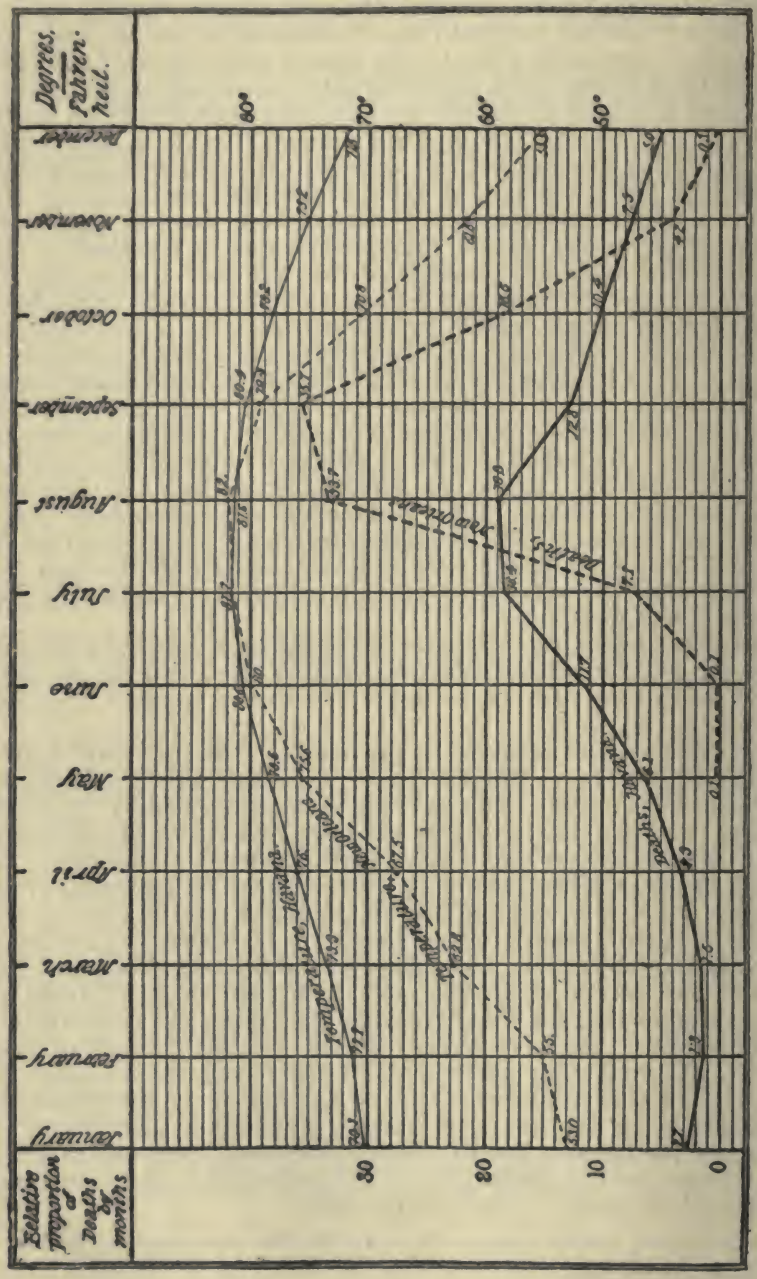

FIG. 8.—Chart showing the mean monthly temperature of New Orleans and Havana for ten years; and the relative monthly mortality from yellow fever in Havana from 1880 to 1899, and in New Orleans from 1847 to 1897.

observations, an exposure for one and a half hours to sulphur fumigation, in a well-closed room, in the proportion of 1 pound to 1,000

cubic feet of air space, will suffice effectually to destroy all mosquitoes. Formaldehyde gas is not quite so efficient. With Trenner's formaldehyde generator, charged with formalin, 900 c. c.; glycerin, 9 c. c.; methyl alcohol, 360 c. c., which we have found quite reliable for the destruction of bacteria, an exposure of not less than three and preferably four hours is required in order to kill these insects in a tight room having 2,800 cubic feet capacity. Pyrethrum powder, if burned in the proportion of 4 ounces to 1,000 cubic feet of air space, will stupefy all mosquitoes at the expiration of one hour, so that they will fall to the floor in a helpless condition. If used, however, the precaution above recommended by Dr. Gorgas should be strictly followed—that is, the room should be opened at the end of three hours and all insects carefully swept up and burned. The practice of destroying all mosquitoes in adjoining houses, as carried out in the city of Habana with such excellent results, we consider of the greatest importance, since only in this way can we hope to destroy infected mosquitoes, and thus prevent the occurrence of secondary cases. In other words, relying upon the well-known slow progress of the spread of yellow fever, we seek to catch and destroy all mosquitoes within a given radius of the first case. If secondary cases should occur, the same hygienic measures should be rigorously enforced along the lines above indicated. Upon the completion of the case, the room occupied by the patient should be disinfected, and in a matter where so much is at stake we believe that sulphur should be given the preference as a disinfectant. In case of death, the body should be carefully screened against mosquitoes, as stegomyia will bite the dead body and might in this way acquire the parasite.

We have said nothing about the protection of nonimmune individuals who enter the patient's room or house, since, if the case under consideration is the infecting case, no danger is incurred. As the duration of the attack is short, generally less than 10 days, the patient's room will have been disinfected and the infected mosquitoes destroyed before they have become susceptible of conveying the disease to others. We desire to emphasize the fact that the interval elapsing between the infection of this mosquito by biting a case of yellow fever and the time when it has become capable of conveying the disease, viz, about 12 days, is of the utmost importance in our efforts toward stamping out yellow fever at its very commencement, since it furnishes a nondangerous interval during which all infected insects should be easily destroyed. It thus makes the control of yellow fever hereafter a simpler and more certain matter than the suppression of an outbreak of any of the other acute infectious diseases. If nonimmunes entering an infected house desire protection against the bites of stegomyia, this may be obtained by rubbing all exposed surfaces of the body, including the ankle surfaces, with spirits of camphor, oil of pennyroyal, or a 5 per cent menthol ointment. The protective effect of these substances is, however, only temporary.

What we have already said concerning the breeding places of *Stegomyia fasciata* should sufficiently indicate the general hygienic measures that should be taken in order to prevent the spread of yellow fever. These should consist in enforcing such measures as will effectually destroy the breeding places of this very domestic mosquito.

The methods adopted by the chief sanitary officer of Habana, during the present year, may be taken as a model by our sanitary officials.[1] It should not be forgotten that a well-drained and well-sewered city, with a pure water supply and clean streets, has no protection against the spread of yellow fever, provided rain-water barrels and other collections of water are present, in which stegomyia may breed. In one of the forts, on the outskirts of Habana, which was otherwise in an excellent sanitary condition, we found thousands of *Stegomyia fasciata* breeding in tin cans placed about the legs of a table in an officer's kitchen. Our conception of yellow fever, therefore, as a "filth" disease must be abandoned, and our attention turned to yellow fever as a mosquito-borne disease. In illustration of what may be accomplished by sanitation based on the latter method of propagation, we present herewith a chart (fig. 10) showing the actual monthly mortality from yellow fever in Habana, for the period from 1880 to 1899, and also for the years 1900 and 1901. Comparing the mortality from this disease for 1899, which was the most favorable year for yellow fever that Habana had experienced in 20 years, with 1901, during which sanitation, based on the demonstration that yellow fever is propagated by the mosquito, has been enforced, we find a reduction in mortality of 83.3 per cent in favor of the present epidemic year (Apr. 1 to Aug. 31); or if we compare the mortality for the epidemic year 1900 with the present year we observe a still greater reduction in favor of the latter, viz, 411 per cent.

The sanitary regulations put into force February 15, 1901, by Dr. Gorgas, resulted in freeing Habana from yellow fever within 3 months, so that for a period of 54 days—May 7 to July 1—no case occurred. On the latter date, the disease was brought into Habana from Santiago de las Vegas, and, according to Gorgas, has been introduced into the city at least a dozen times from this and other sources. In spite of these new sources of infection, July has only furnished four cases, with one death, and August eight cases, with two deaths. If such admirable results, under new methods of sanitation, have been obtained in this hotbed of yellow fever, we can not believe that the intelligent and efficient boards of health of our cities will again permit this disease to assume an epidemic form in any city of the United States.

Measures directed against the importation of yellow fever into the United States.—Under the admirable system of inspection and reports, as carried out by the Marine Hospital Service, the appearance of yellow fever at any foreign port is promptly reported for the information of the health authorities of our several Atlantic ports. We may, therefore, divide foreign ports within the so-called epidemic zone into (*a*) infected, and (*b*) noninfected ports. Heretofore, no distinction has been made by the health officers of our southern ports as regards quarantine regulations from April 1 to November 1, between infected and noninfected places. All ports within the epidemic zone of yellow fever were considered as being infected places, and hence passengers and vessels were subjected to quarantine and to disinfection of both baggage and cargoes.

With our present knowledge of the way in which yellow fever is propagated, we believe that in the treatment of passengers, as well

[1] Medical Record, New York, vol. 60, Sept. 7, 1901.

as of cargoes, a sharp distinction should be made, first, between infected and noninfected ports; and, secondly, in the case of vessels sailing from infected ports, between those that have received their cargoes and passengers in midstream and those that have loaded at the wharf.

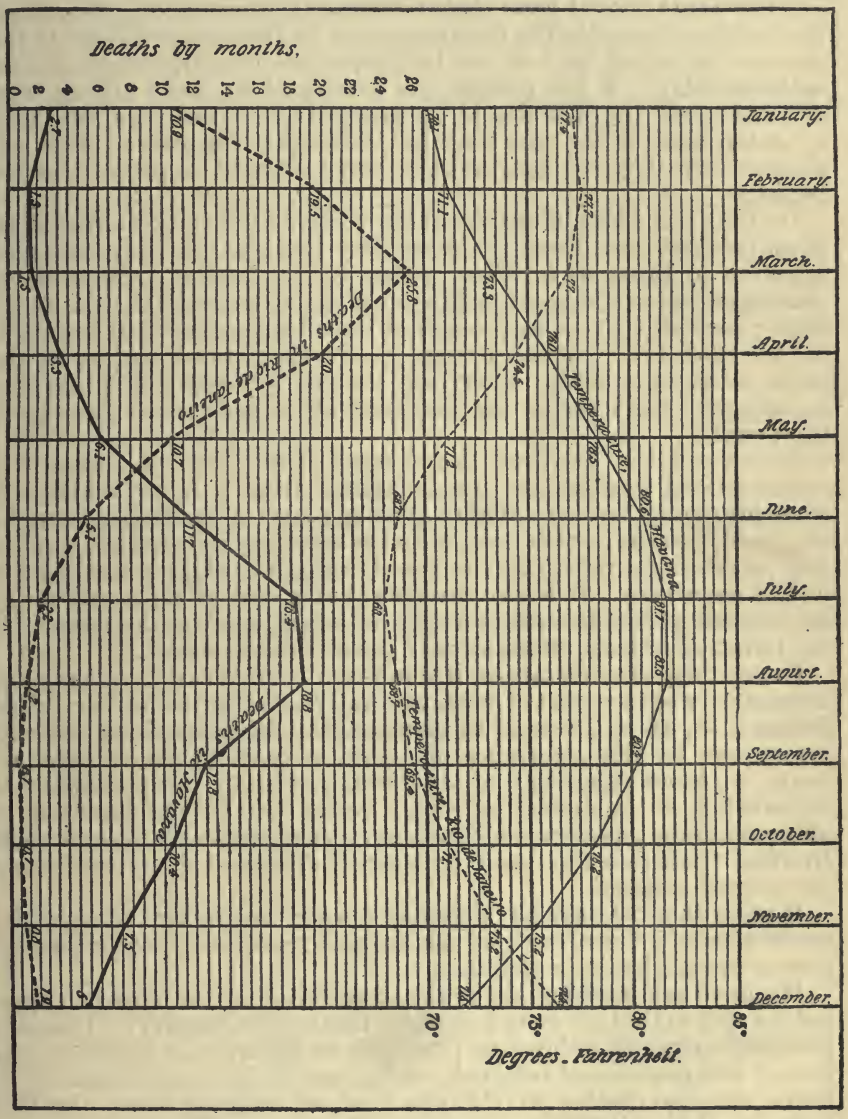

Fig. 9.—Chart Showing Mean Monthly Temperature of Havana and Rio de Janeiro for Ten Years; and the Relative Monthly Mortality from Yellow Fever in Havana from 1880 to 1889 and in Rio de Janeiro from 1851 to 1883.

We believe that no quarantine restrictions should be placed upon either passengers or cargo from noninfected ports. In the case of a vessel loading in midstream at an infected port by means of lighters, we believe that she can only receive infection in one way, i. e., by

passengers who have been exposed to yellow fever on shore, and who, coming aboard, may thereafter be seized with the disease. The possibility of infected mosquitoes reaching the vessel, either by flight or by means of lighters, may be considered as highly improbable.

Vessels, loaded under the foregoing circumstances (i. e., by lighters in midstream), and arriving at our ports without yellow fever developed en route should have their nonimmune passengers quarantined for five days, counting the time consumed by the voyage as part of the quarantine period, and should be allowed to discharge their cargoes without delay. If the disease has developed en route among crew or passengers, the sick should be promptly removed; the forecastle or staterooms, as the case may be, thoroughly disinfected with sulphur or formaldehyde gas, and the vessel allowed to proceed to her wharf.

On the other hand, if the vessel has received her cargo at the wharf of an infected port, there is a possibility that she may have received infection in three ways: First, either by contaminated mosquitoes that have bitten a case of yellow fever in the immediate vicinity on shore; secondly, by mosquitoes that have become infected from biting a yellow-fever patient present on another vessel loading at the same, or at an adjacent, wharf; or, thirdly, by some individual who has acquired the infection on shore and afterwards taken passage on the vessel.

In our opinion, however, the chances of infection of a vessel by contaminated mosquitoes coming aboard from a house or ship in close proximity are very slight; although such a possibility must be admitted, and the further possibility that recently infected mosquitoes may have sought refuge on the vessel during the night preceding her day of departure. It is also possible that a case of mild and hence undetected yellow fever may occur on board, and be the source for the infection of mosquitoes already present in the vessel.

Under these circumstances, if a sufficient number of days have not elapsed between her port of departure and port of arrival in the United States, i. e., 16 to 21 days, to demonstrate the presence of infected mosquitoes by the occurrence of a case or cases of yellow fever en route, we know of no way of absolutely excluding the possibility of importation of the disease by such a vessel than by the detention of all nonimmune passengers for such number of days as will show their freedom from infection, and by careful disinfection of crew's and passengers' quarters.

If more than 20 days have elapsed during the voyage, without the occurrence of yellow fever, we see no good reason why either passengers or vessel should be detained.

We have said nothing about the disinfection of the vessel's cargo, for the reason that we do not consider this to be necessary. The only possible excuse for subjecting the cargo to disinfection would be the fear of the presence of infected mosquitoes in the vessel's hold, provided she had loaded at the wharf of an infected port. In this instance, if the voyage has consumed five or more days, all mosquitoes contained in the hold will have died; for, as we have already pointed out, *Stegomyia fasciata* lives only a few days if deprived of water. We can not too strongly insist that the danger of importation of yellow fever into the United States lies, not in cargo or personal

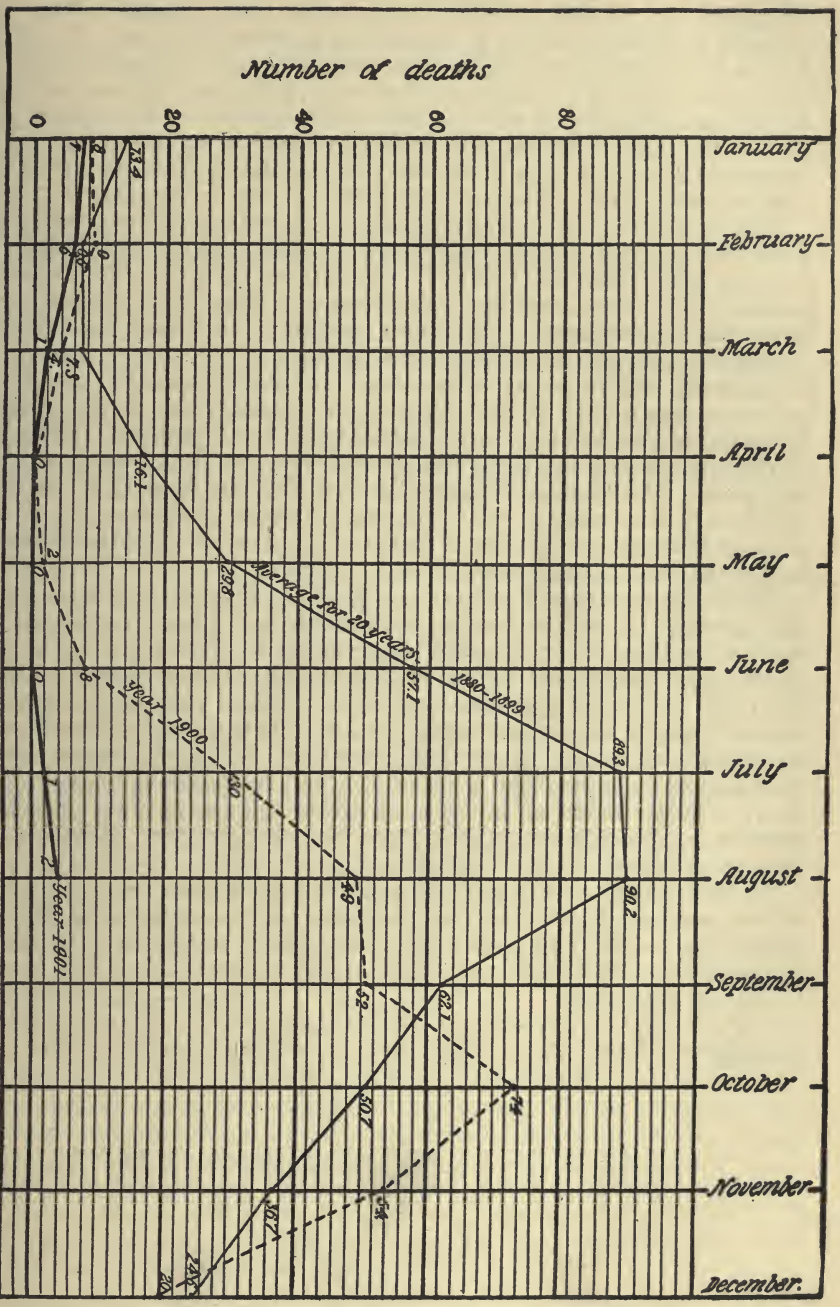

FIG. 10.—Chart Showing Monthly Mortality from Yellow Fever in the City of Havana for the Twenty Years, 1880 to 1899; for the year 1900, and from January 1 to August 31, 1901.

baggage, but in the individual sick with that disease. With our present knowledge of its propagation, personal baggage should no longer be subjected to disinfection, and, with our increased ability to prevent its spread by measures easy of application, instances should be few and exceptional when a vessel coming from a yellow-fever port should be delayed longer than will be necessary to remove her non-immune passengers who have not yet completed their period of five days since leaving the port of departure.

The chief duty of quarantine officers hereafter will consist in the detection of mild or very mild cases of yellow fever. In a series of 12 cases of experimental yellow fever produced by the bite of *Stegomyia fasciata*, we have, elsewhere,[1] pointed out that 4, or 33 per cent, were mild or very mild in character, and have indicated the difficulty of making a positive diagnosis in such cases.

In discussing the period of incubation of experimental yellow fever, we have shown that in 16.6 per cent of our cases the period of incubation exceeded the usual quarantine period of five days. If we add Carter's cases to those observed by ourselves, we find that of 24 cases the period of incubation exceeded five days in 3, or 12.5 per cent. We can thus readily see what great danger heretofore lay in the passage through quarantine of just such mild cases, or of those having an incubation stage of more than five days.

While the exclusion of such cases is of the greatest importance, we doubt whether, with our improved knowledge of how to prevent the spread of yellow fever, it would be advisable to place a greater burden upon ships' passengers by extending the quarantine period to more than five days. It appears to us rather that in view of the troublesome delays to which passengers and vessels from yellow-fever ports have been subjected in the past, the time has now arrived when, standing upon more solid ground, we will be justified in seeking in every way to lessen as much as possible the restrictions placed by present quarantine regulations upon the ship's cargo, while we add nothing to those of the passenger.

To this end a most important part will have been accomplished if we can persuade the sanitary authorities of our sister republic, Mexico, and of the Central and South American States, to join us in the adoption of more enlightened methods for the suppression of this widely prevalent epidemic.

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[1] "Experimental Yellow Fever." Transactions of the Association of American Physicians, Vol. XVI, 1901.

Chapter 7.

THE ETIOLOGY OF YELLOW FEVER—A SUPPLEMENTAL NOTE.[1]

By Walter Reed, M. D., Surgeon, United States Army, and James Carroll, M. D., Contract Surgeon, United States Army, of Washington, D. C.

In former contributions to this subject, we have shown by observations made on human beings that yellow fever may be produced in the nonimmune individual either by the bite of the mosquito (1) (genus *Stegomyia*) that has previously been permitted to fill itself with the blood of a patient suffering with yellow fever, during the first three days of the attack, or by the subcutaneous injection of a small quantity of blood (2) (0.5 to 2 c. c.) drawn from the general circulation of such a patient during the active stage of this disease. For further particulars regarding these observations the reader is referred to the original papers.

Although these experiments have demonstrated that the specific agent of yellow fever is present in the blood, we may say that the prolonged microscopic search which has been made by other investigators, as well as by ourselves, both with fresh and stained preparations of blood, taken at various stages of this disease and during early convalescence, has proved thus far entirely negative. We may add that the efforts which we have made with reasonable hope of reward, both in the bodies of infected mosquitoes, dissected in the fresh state, as well as by serial sections of the hardened insect, have likewise given no results which we consider worthy of record at the present time. Leaving out of consideration, therefore, for the time being, the further microscopic search for the specific agent in the blood of the sick and in the bodies of infected mosquitoes, we desire to call attention to some additional observations bearing on the etiology of the disease, which one of us (Carroll) has recently made at Las Animas Hospital, Habana, Cuba, and at Columbia Barracks, near Quemados, Cuba.

We here desire to express our sincere thanks to Dr. William H. Welch, of the Johns Hopkins University, who, during the past summer, kindly called our attention to the important observations which have been carried out in late years by Loeffler and Frosch relative to the etiology and prevention of foot-and-mouth disease in cattle. In the course of their investigations concerning a reliable method of immunization in this disease, the authors had occasion to dilute and afterwards to pass several times through a porcelain filter, lymph which had been collected from the blebs present in the mouth and on the feet of cattle sick with foot-and-mouth disease (4).

These observers, having already ascertained that immunity could be conferred upon cattle by the subcutaneous or intravenous injection of one-fortieth to one-fiftieth c. c. of pure lymph previously

[1] Read before the third annual meeting of the Society of American Bacteriologists, Chicago, Ill., Dec. 31, 1901, and Jan. 1, 1902.

mixed with 1 c. c. of the defibrinated blood of an animal that had recently recovered from the disease, desired to find out whether the injection into calves of given quantities of this filtered and bacteria-free lymph would not, also, enable them to confer immunity of, perhaps, a higher degree upon cattle.

The results were quite surprising, since it was shown that calves which had received one-tenth to one-fortieth c. c. of the diluted and filtered lymph developed foot-and-mouth disease just as promptly as calves that had been injected with corresponding quantities of the unfiltered lymph.

According to Loeffler and Frosch, there were two possible explanations of this remarkable result; either that the filtered lymph held in solution an extraordinary active toxin, or that the specific agent of the disease was so minute as to pass through the pores of a filter which prevents the passage of the smallest known bacteria.

The authors accept the latter explanation, since they were able, in later experiments (4), by means of the filtered lymph, to convey the disease through a series of six animals, the last of which sickened just as promptly after the injection of the filtered lymph as the first of the series.

Having, therefore, conclusively determined that the microorganism of foot-and-mouth disease of cattle is so extremely minute as to pass readily through a porcelain filter, it was natural that Loeffler and Frosch should have put forward the suggestion that, perhaps, the specific agent of some of the acute infectious diseases of man and animals, such as smallpox, scarlet fever, measles, rinderpest, etc., might also belong to this group of ultramicroscopic organisms.

It was for the purpose of ascertaining whether observations conducted along the same lines as those above mentioned might throw additional light upon the etiology of yellow fever that the following experiments were undertaken.

Of course it will be thoroughly appreciated that in experimentation on human beings, aside from the grave sense of responsibility, at times well-nigh insupportable, which the conscientious observer must always feel, even with the full consent of the subjects to be experimented upon, there must be added another factor, viz, the difficulty of finding willing and suitable nonimmune individuals for experimentation just at the proper and urgent moment. It so happened that on the day of Dr. Carroll's arrival at Habana, August 11, 1901, the first patient of the series of seven cases of yellow fever which Dr. Guitéras (5) had produced by bites of infected mosquitoes, was taken sick. The fatal termination of three of these cases produced a somewhat panicky feeling toward experimental yellow fever among the nonimmunes at Habana, which feeling was intensified by the sensational and distorted statements in one of the local Spanish papers. It was, therefore, extremely difficult—in fact, practically impossible—to obtain for inoculation purposes persons who could with reasonable certainty be regarded as nonimmunes.

Further, as it was not practicable to withdraw blood from any case of yellow fever under treatment in the city of Habana, it became necessary to produce cases by means of the bites of infected mosquitoes—*Stegomyia fasciata*—accepting such subjects as were willing to submit to this mode of inoculation. In all six individuals, supposedly nonimmunes, were bitten by mosquitoes, of whom four gave a negative and two a positive result.

The following are the negative cases:

August 14, 1901.—S. V., Spaniard, resident of Habana for a few months, was bitten by two insects that had been applied to a yellow fever patient 34 days previously. Result negative, although the bites of two mosquitoes from this same lot had already infected an individual, who later died of yellow fever.

September 5, 1901.—J. T., American, was bitten by nine insects that had been applied to a mild case of yellow fever on the second day of the attack, 23 days before. He was again bitten 30 days later by four mosquitoes that had been applied to a moderately severe case of experimental yellow fever 11 days before. The result of both inoculations were negative. This man had resided one year in Central America, and we were afterwards informed that he had confessed to a previous attack of the disease.

September 11, 1901.—A. P., Spaniard, was bitten by three insects which 53 days previously had bitten patient with a typical case, on the third day of the attack. These were among a lot of mosquitoes that had already infected three individuals, two of whom died of yellow fever. The result was negative. Five weeks later he received a subcutaneous injection of about one-fourth c. c. of blood drawn from a patient with a mild case of yellow fever, on the second day of illness. Result negative. The previous history of this man was not satisfactory, as he had recently returned from a residence in Mexico.

September 9, 1901.—A. V., Spaniard, was bitten by three mosquitoes that had been applied to a mild case of yellow fever on the second day of the attack, 27 days before. Three weeks later he was again bitten by one mosquito 49 days after it had been applied to a fatal case of yellow fever, on the third day of the attack. The result of both inoculations was negative.

We give brief sketches of the two positive cases:

Case I.—P. R. C., a Spaniard, had served in the Spanish army in the Philippines. He arrived in Habana from Spain about August 30.

On September 16, 1901, he was bitten at 4 p. m. by 4 mosquitoes that had previously fed upon cases of yellow fever as follows: One had bitten a patient having a fatal case, on the third day of the disease, 53 days before, and 3 had bitten a patient having a fatal case, on the second day of illness, 34 days previously. His attack began at 4.30 p. m., September 19, after an incubation period of 72½ hours. At the onset he experienced a slight chill with rigors and loss of appetite. Later in the evening he complained of slight frontal headache and pains in the lumbar region. On the following day the headache and backache were more severe. At 10 a. m. he vomited about 6 drams of slightly greenish fluid containing mucus. On the second day of the attack the gums were swollen, pale, and spongy, and there was soreness upon deep pressure over the epigastric and hypogastric regions; the face was flushed and the eyeballs were slightly yellow. September 24, fifth day, he was well jaundiced, epigastric and abdominal soreness were pronounced, and there was nausea with eructations. At this time an unfavorable prognosis was given by two physicians of large experience in yellow fever. Happily, with the decline of temperature on the sixth day, the symptoms were much ameliorated and the patient made an uninterrupted recovery. Albumin appeared in the urine on the third day and persisted for 17 days. The microscope showed the presence of bile-stained epithelial and granular casts on the third and subsequent days.

Early on the second day blood was drawn from the median-basilic vein with all precaution and 10 drops were immediately added to each of four flasks containing 200 c. c. of sterile nutritive bouillon. The flasks were kept under observation in the incubator and at room temperature for 14 days without the development of any growth. At the end of that time each flask was agitated and an agar slant was freely inoculated with fibrin and fluid from its contents. These cultures remained sterile 16 days later after being kept four days in the incubator and 12 at room temperature.

On the second day, blood was drawn for the purpose of obtaining serum for filtration, but owing to an accident to the vacuum pump the experiment had to be abandoned.

Specimens of the fresh blood were examined for malarial parasites, with negative results, on the second and fourth days of the attack. (Chart I.)

Case II.—J. M. A., Spaniard, recently landed at Havana, was bitten at 4 p. m. October 9, by 8 mosquitoes that had been applied to a severe case of yellow fever (Case I) on the second day of the disease, 18 days previously. The attack which followed was mild. According to his own account, he went to bed on the evening of the 12th feeling in perfect health. He awakened about midnight with frontal headache, but had no chill. October 13, 7 a. m., temperature was 102.2° F., pulse 92; complained of pain in the head and back; later in the day there was marked photophobia, pain in the region of the kidneys, and slight pains in the lower extremi-

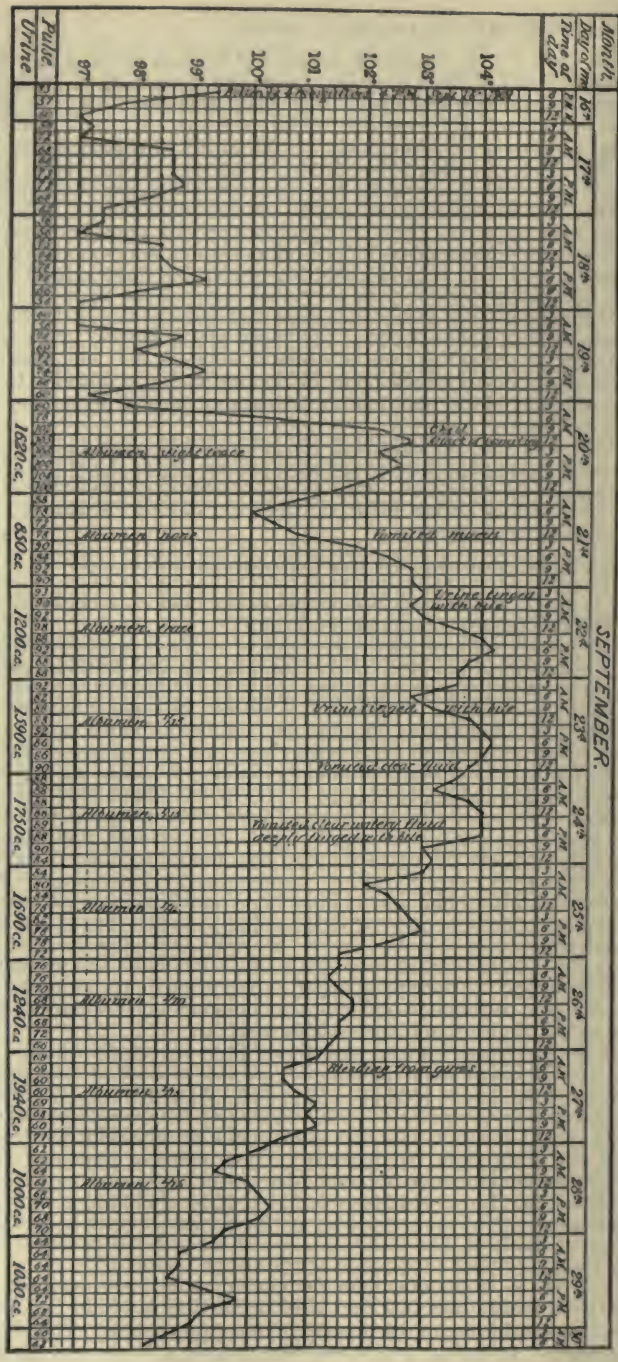

CHART I.—Yellow fever, produced by the bite of *Stegomyia fasciata*. Incubation, 72½ hours.

ties. The eyes were injected moderately and the gums slightly so. On the following day, October 14, the frontal headache was more severe, there was considerable soreness on pressure over the stomach and abdomen, and he complained of sharp lumbar pain. An examination of the fresh blood proved negative for malarial parasites. At 4 p. m. blood was drawn from a vein at the bend of the elbow and 10 drops were inoculated into each of 2 flasks containing 200 c. c. of sterile bouillon. One flask remained sterile, the other developed a growth which proved to be a white staphylococcus.

October 15 the gums were pale, swollen and spongy, their margins distinctly reddened, and blood could be easily pressed out from beneath the lower gums.

October 16 there was free oozing of blood from the gums and margin of the tongue. The case pursued a mild course, the temperature falling to normal at 9 p. m. of the fourth day. A trace of albumin was present in the urine passed on the morning of that day, and for a few days following hyalin and granular casts were found. The patient made a speedy recovery. (Chart II.)

On October 15, 11.30 a. m., at the beginning of the third day of illness, the temperature was 101° F.; 65 c. c. of blood were drawn, with antiseptic precautions, from a vein at the bend of the elbow. This was placed in a sterile test tube and set aside in the refrigerator. At 6 a. m., 5½ hours later, 19 c. c. of a slightly bloodstained serum were pipetted off into another sterile tube. After the addition of an equal quantity of sterilized distilled water the diluted serum was slowly filtered through a new Berkefeld laboratory filter that had been subjected to previous sterilization in an Arnold's sterilizer. In this way 35 c. c. of a slightly bloodstained filtrate were obtained, a part of which was subsequently used for the inoculation of Cases VII, VII, and IX of this report.

The original level of the blood having been marked upon the tube into which it was drawn, a sufficient quantity of sterilized distilled water was then added to replace the 19 c. c. of serum that had been pipetted off and to make up the original volume of blood. The whole, consisting of clot, remaining serum, and distilled water, was poured into a sterile vessel and whipped up with a sterilized egg beater. The mixture, which approximately represented the partially defibrinated blood, was then divided into two parts, one of which was reserved for the inoculation of a control subject (Case III), while the other part was placed in a double water bath previously heated, and exposed to a temperature of 55° C. for 10 minutes. It was then remo ved and immediately cooled in ice water. This cooled material was subsequently used for the injection of Cases IV, V, and VI.

It will thus be seen that we have at our disposal, for purposes of inoculation, three kinds of materials, derived from the blood in Case II, viz: (*a*) The unheated and partially defibrinated blood; (*b*) the partially defibrinated blood which had been heated to a temperature of 55° C. for 10 minutes, and (*c*) the diluted blood serum which had been filtered through a Berkefeld filter. Each of these materials was used for the inoculation of one or more nonimmune individuals with the results that follow herewith.

(*a*) THE UNHEATED AND PARTIALLY DEFIBRINATED BLOOD.

Case III.—M. G. M., Spaniard, arrived at Habana October 4, 1901. At 4 p. m. October 15 he was given a subcutaneous injection of 0.75 c. c. of the unheated and partially defibrinated blood obtained from Case II, 15½ hours previously, which had been kept 5½ hours in the refrigerator and 10 hours at room temperature. The earliest symptom, frontal headache, was complained of at 6 p. m., October 20, or at the expiration of 5 days and 2 hours after inoculation. Temperature 100.6° F., pulse 80. At 3 p. m. of the same day the temperature was 98.4° F., pulse 80. At that time the patient did not complain of any discomfort and there was nothing to indicate that he was about to be taken sick. October 21, 5 p. m., nearly 24 hours from the onset, there was flushing of the face, injection of the eyes and gums, and moderately severe headache; pain in the back, and tenderness on pressure in the epigastric region made the picture complete. On the third day the face was deeply flushed, eyes congested and distinctly yellow. There was slight oozing of blood from the gums. The urine passed at 7.30 p. m. contained a distinct trace of albumin. The case was seen by the Habana Board of Yellow Fever Experts and the diagnosis confirmed. The patient passed through a mild but typical attack, the temperature touching normal on the fifth day. (Chart III.)

This case, therefore, serves as a "control" for the observations which are to follow, since it demonstrates that the blood drawn from the general circulation of case II, at the beginning of the third day, contained the specific agent of yellow fever, and, in this respect, confirms the observations which have heretofore been reported by us (6).

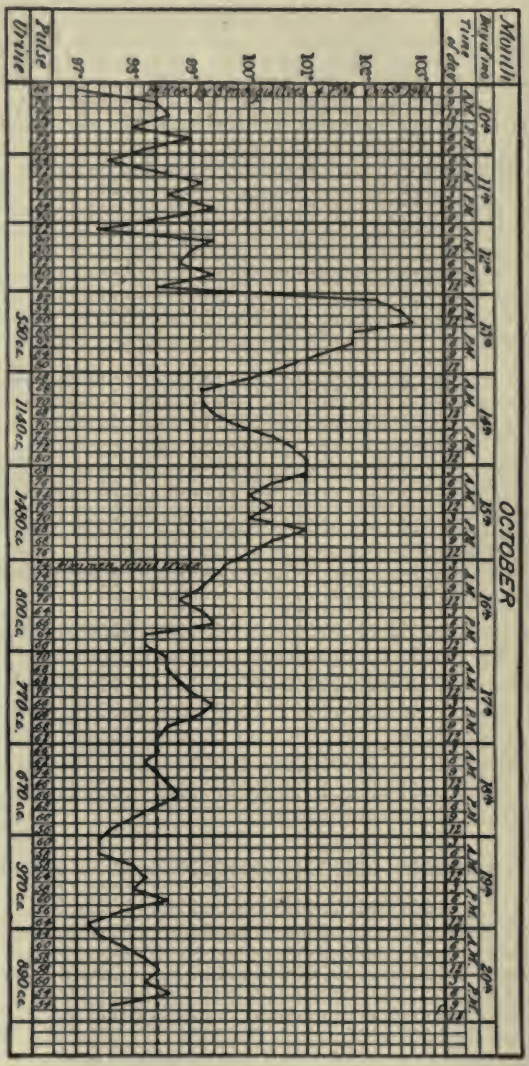

CHART II.—Yellow fever, produced by the bite of *Stegomyia fasciata*. Incubation, 80 hours.

(*b*) THE PARTIALLY DEFIBRINATED BLOOD HEATED FOR 10 MINUTES AT 55° C.

Case IV.—A. C., Spaniard, nonimmune, arrived at Habana, October 6, 1901. At 4.35 p. m., October 15, he was given subcutaneously 1.5 c. c. of the partially defibrinated blood which had been subjected to a temperature of 55° C. during 10 minutes. The specimen had been drawn from case II, 16 hours before. The result of this injection was entirely negative, as the subject remained in perfect health during the 10 days following.

Case V.—B. F. M., Spaniard, nonimmune, arrived at Habana, October 6, 1901. At 4.45 p. m., October 15, he received a subcutaneous injection of 1.5 c. c. of the same material that was used in case IV. Result negative.

Case VI.—S. O., Spaniard, nonimmune, arrived at Habana, October 7, 1901. At 4.50 p. m., October 15, he was given a subcutaneous injection of 1.5 c. c. of the same material that was used in cases IV and V. No rise of temperature or other symptoms of ill health followed this injection.

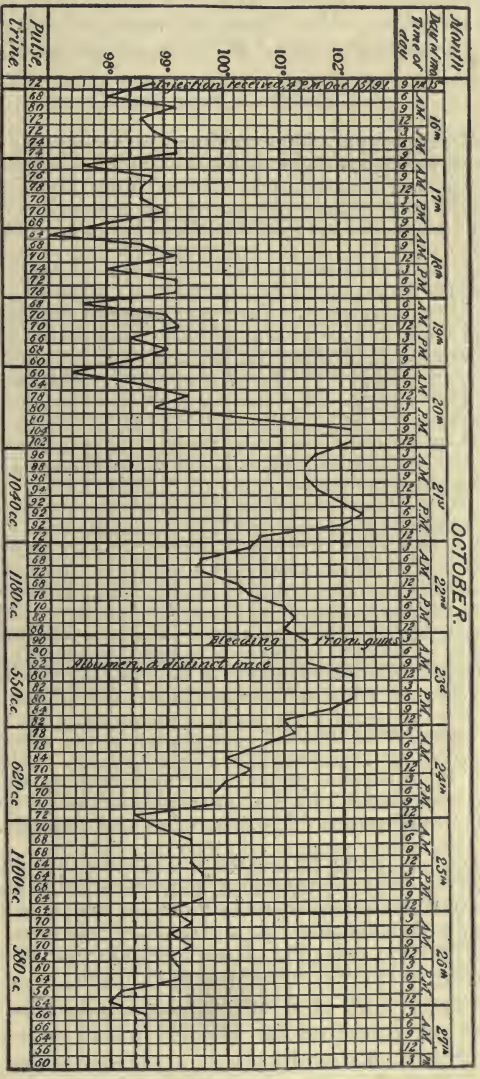

CHART III.—Yellow fever, produced by injection of 0.75 cc. of blood. Incubation, 5 days, 2 hours.

We desire to invite attention to the fact that the four subjects whose protocols have been given above were young Spaniards who arrived at Habana at a time when yellow fever was not present in the city; that they were carried from the quarantine camp, at Triscornia, across the bay, direct to Columbia Barracks, near Quemados, Cuba, where they were kept for seven full days prior to inoculation; and that after

inoculation they were kept under close daily observation for the further period of 10 days, during which time both temperature and pulse were recorded every third hour. Since under these circumstances each of the three nonimmunes (cases IV, V, and VI) received, without any disturbance to health, double the quantity of heated and partially defibrinated blood that sufficed when unheated to cause an attack of yellow fever in case III, it follows that the specific agent present in the blood in yellow fever is destroyed, or, at least markedly attenuated, by a temperature of 55° C. maintained for 10 minutes.

(c) THE DILUTED AND FILTERED SERUM.

Case VII.—P. H., American soldier, nonimmune, received at 11 a. m. October 15, 1901, a subcutaneous injection of 3 c. c. of the serum filtrate, representing 1.5 c. c. of the undiluted serum 10½ hours after the blood had been drawn from Case II. He remained in good health until 3 p. m. October 19, an interval of four days and four hours, when his face appeared flushed and his eyes somewhat injected. His temperature at this time was 101° F., his pulse 80. He did not complain of headache or other pain. From this hour his temperature declined, until at 12 o'clock midnight it registered 98° F., pulse 72. October 20, 9 a. m., temperature 100.8° F., pulse 78. Face more suffused and slight headache complained of. Fever continued on the 21st, with more marked flushing of the face and injection of the eyes. The height of the primary febrile paroxysm was reached at 6 p. m. October 21. Remission occurred at 9 a. m. October 22, when the temperature dropped to 98.8° F., pulse 64. This lasted for 24 hours and was followed by a secondary febrile paroxysm of 42 hours' duration. On the 23d blood was oozing from the lower gums and the eyeballs were tinged with yellow. Albumin appeared in the urine on the fourth day. The patient was visited by the board of experts and the diagnosis of yellow fever confirmed. Examination of the dried blood for malarial parasites was negative. The patient recovered. (Chart IV.)

Case VIII.—A. W. C., American soldier, nonimmune, was also given at 11.05 a. m. October 15, 1901, a subcutaneous injection of 3 c. c. of the diluted and filtered serum, being the equivalent of 1.5 c. c. of the undiluted serum, 10½ hours after the blood had been drawn. He remained in his usual health until about noon, October 19, at which time he felt "out of sorts" and ate but little dinner. This was 4 days and 1 hour after the injection. During the afternoon he lay down and slept until 3 p. m., when he awoke with a severe headache and backache. His face was flushed. Temperature 103.6° F., pulse 102. At this hour his face and eyes were deeply congested, and from this time his symptoms were characteristic of the disease. On the 23d his eyes were quite yellow and general jaundice followed later. No albumin was found in this patient's urine. He was seen by the board of experts and his illness pronounced a typical case of yellow fever. Careful examination of the dried blood for malarial parasites was negative. The patient made a good recovery. (Chart V.)

Case IX.—J. R. B., American, nonimmune, at 2.30 p. m. October 15, 1901, was given a subcutaneous injection of 3 c. c. of the diluted and filtered serum, equal to 1.5 c. c. of the undiluted serum. Fourteen hours had elapsed since the blood had been drawn from Case II.

This injection was followed by no symptoms of physical disturbance, until 3 p. m. October 19, an interval of four days and a half hour, when his temperature was 99.4° F., pulse 92. He complained of headache and flashes of heat, with slight pain between the shoulders, symptoms which, the subject stated, were quite unusual to him. At 9 p. m. temperature 98.4° F., pulse 84. There was no further febrile disturbance and the day following the subject was in his usual good health.

We thus observe that of 3 nonimmune individuals who received subcutaneously an injection of filtered blood serum derived from case II of this report, 2 developed an unmistakable attack of yellow fever, after a period of incubation of 98½ hours and 100 hours respectively, while in 1 case the result must be regarded as negative.

As already stated, the serum used for these inoculations had been slowly filtered through a new Berkefeld laboratory filter. As soon as possible thereafter the filter was resterilized by steam and thoroughly tested as to its effectiveness in preventing the passage of bacteria. For this purpose a recent bouillon culture of *Staphylococcus*

pyogenes aureus was used, of which 50 c. c. were passed through the filter. The filtrate thus obtained was transferred in quantities of 10 c. c. to each of two flasks containing 200 c. c. of sterile bouillon, which were incubated at 37° C. for 4 days and thereafter kept at room temperature for 10 days longer, at the end of which time no growth had occurred. It appears, therefore, that the filter used for the filtration of the blood serum in case II was to be relied upon for the delivery of a bacteria-free filtrate.

The production of yellow fever by the injection of blood serum that had previously been passed through a filter capable of removing all test of bacteria, is, we think, a matter of extreme interest and importance. The occurrence of the disease under such circumstances, and within the usual period of incubation, might be explained in one of two ways, viz, first, upon the supposition that the serum filtrate contains a toxin of considerable potency; or, secondly, that

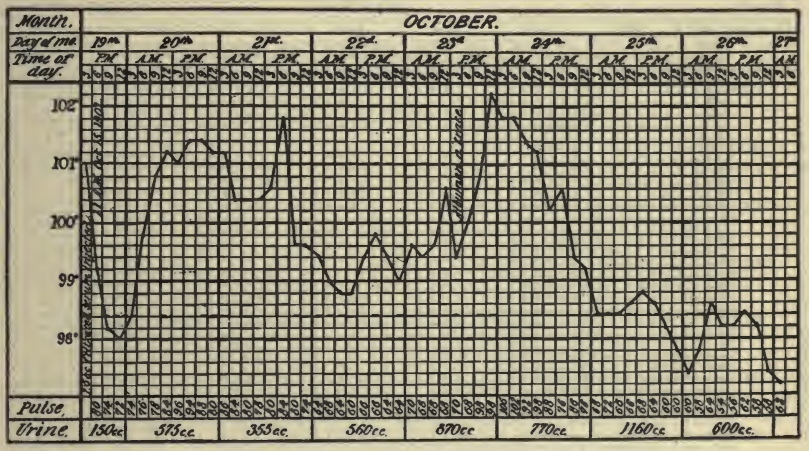

CHART IV.—Yellow fever, produced by injection of 1.5 cc. of filtered blood-serum. Incubation, 4 days, 4 hours.

the specific agent of yellow fever is of such minute size as to pass readily through the pores of a Berkefeld filter.

In favor of the supposition that in yellow fever an active toxin is present in the blood may be cited the early and well-marked jaundice; the free hemorrhage from the mucous membranes of the mouth and stomach, doubtless due to profound changes in capillary vessel walls; the rapid progress of the disease to a fatal termination, the advanced fatty degeneration of the hepatic cells, as well as the marked parenchymatous changes found in the kidneys. If present in the blood this toxin would in all likelihood be found in the serum filtrate obtained from the blood, and if injected in sufficient quantity might induce an attack of yellow fever in a susceptible individual after the usual period of incubation. In this respect it would bear analogy to the production of tetanus in the human being, after the usual period of incubation of this disease by the subcutaneous injection of a very small quantity of tetanus toxin, as reported by Nicolas (7) in 1893, and more recently by Bolton, Fisch, and Walden (8).

Against the view that a toxin is present in the serum filtrate, we invite attention to the innocuousness of the partially defibrinated blood when heated to 55° C. for 10 minutes, as shown by the negative results in cases IV, V, and VI. Here the toxin, which must have been present in just the same quantity as in the serum filtrate obtained from this blood, appears to have been completely destroyed by the temperature above mentioned. Now, although certain bacteria are destroyed by this temperature, as yet we know of no bacterial toxin that is rendered inert by such a low degree of heat continued for so short a time. The tetanus toxin, which has been found to be the most sensitive thus far requires, according to Kitasato, a temperature of 60° C. for 20 minutes, or 55° C. for 1½ hours, in order to destroy its activity. (9)

As a further test and in order to determine whether the serum filtrate contained something more particulate than a soluble toxin,

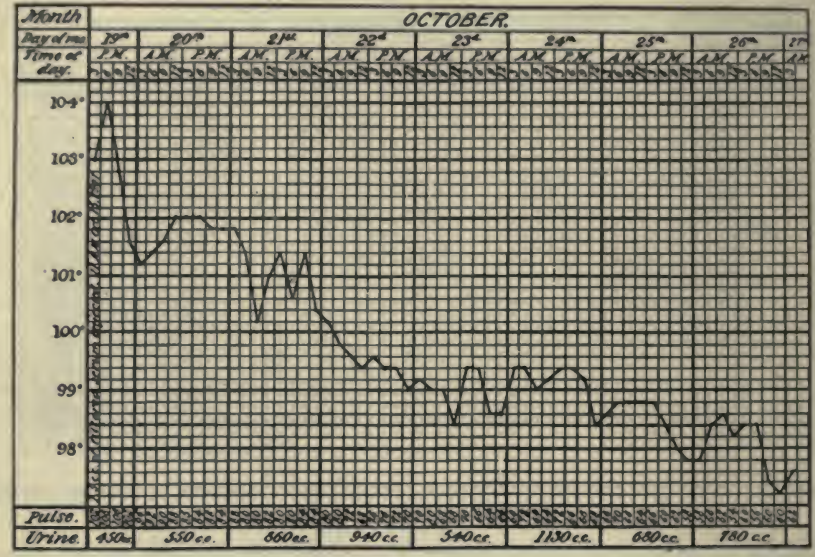

CHART V.—Yellow fever, produced by injection of 1.5 cc. of filtered blood serum. Incubation, 4 days, 1 hour.

we availed ourselves of the opportunity of observing the effect that would follow the transference to a third individual of blood drawn from one of the patients whose attack had been occasioned by the injection of 1.5 c. c. of serum filtrate (case VII). If under these circumstances it would be found that the injection of a small quantity of blood was followed by an attack of yellow fever in a third individual, the evidence would point in the strongest manner to the presence of the specific agent of the disease in such blood, since we can hardly believe that a toxin which had undergone so great a dilution in the body of the second individual would still be capable of producing the disease.

Case X.—October 22, 1901, 3 p. m., J. M. B., American, nonimmune, who on October 15, 1901, at 2.30 p. m., had been injected with 1.5 c. c. of serum filtrate with negative result (vide case IX), and who still desired to have his immunity further tested, was, at the beginning of this, the eighth day after his former inoculation, given

a subcutaneous injection of 1.5 c. c. of blood drawn from the venous circulation of case VII early in the fourth day of the disease. At the time of inoculation the subjects' condition was quite normal. October 23, 3 p. m., after an incubation period of just 24 hours, he complained of frontal and slight basal headache and some pain between the shoulders. His temperature was 99.6° F. and pulse 100. At 6 p. m., temperature 100.4°, pulse 100. Pain in the back quite severe. At 10.15 p. m., he suffered a slight chill. On the following morning the face was flushed and the eyes and gums injected; there was sharp frontal headache and some photophobia. The height of the primary paroxysm was reached at the end of 23 hours. Remission occurred at 9 a. m., October 25, and was followed by a second febrile paroxysm of 45 hours' duration. On the third day, during the secondary fever, the patient presented the typical picture of a mild case of yellow fever; the face was deeply flushed, eyes well injected and slightly yellow; there was sharp headache, and epigastric tenderness and pain in the lower extremities. Heller's test showed albumin in the urine drawn on the fourth day. His fever subsided on the later day and he made a prompt recovery. The case was seen by the board of experts and the diagnosis confirmed. (Chart VI.)

In considering this individual's attack, his infection must be attributed either to the injection of the serum filtrate derived from case II, in which event the onset of his disease was postponed until the commencement of the ninth day after inoculation, or to the injection

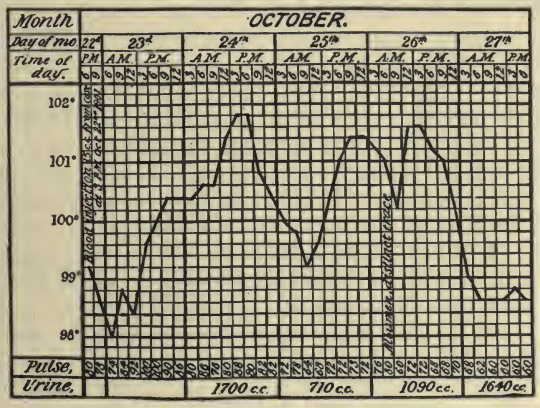

CHART IV.—Yellow fever, produced by injection of 1.5 cc. of blood. Incubation, 24 hours.

of blood obtained from case VII, after a period of incubation of 24 hours.

In our own experience (10) and that of Guitéras (11) of 22 cases of experimental yellow fever, following the bite of the mosquito, in which the period of incubation was definitely and accurately ascertained, the longest period was 6 days and 1 hour, and the shortest period 2 days and 13 hours. If we take the cases produced by the injection of blood, 7 in number, exclusive of the case under consideration, the longest period was 5 days and 2 hours (case III of this report) and the shortest 41 hours.

In view of these data, we believe we are justified in expressing the opinion that the source of infection in case X must be attributed to the injection of blood drawn from case VII, rather than to the injection of the filtered serum derived from the blood in case II; and further, that the blood in case VII contained the specific agent of yellow fever, which had, therefore, passed through the filter along with the filtrate with which this latter individual had been inoculated.

The important questions which naturally arise from the foregoing experiments must be left for the future observations to determine.

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Chapter 8.

RECENT RESEARCHES CONCERNING THE ETIOLOGY, PROPAGATION, AND PREVENTION OF YELLOW FEVER, BY THE UNITED STATES ARMY COMMISSION (THREE CHARTS).

By Walter Reed, M. D., Surgeon, United States Army, President of the Commission.

[From The Journal of Hygiene, Vol. II, No. 2, April, 1902.]

The efficient control of the spread of yellow fever is a matter of such vast practical importance, both from the hygienic and commercial point of view—not only for the countries where this disease prevails as an epidemic, but also for those in which, after importation, it may assume epidemic proportions—that it has seemed appropriate to bring together in this paper a summary of the work thus far accomplished by the United States Army Commission[1] on the island of Cuba, during the years 1900 and 1901, in order that English and Colonial readers who have not, perhaps, had access to the original contributions published in different American journals, may be able to form an intelligent opinion concerning the permanent value of this work. It will also afford opportunity for recording the more recent confirmatory observations made by others concerning the mode of transmission of yellow fever discovered by the commission, and for calling attention to the results already obtained by the United States Army Medical Department in the suppression of this disease, especially in the city of Habana, through the enforcement of sanitary measures based on these later researches.

The American commission was organized in May, 1900, and began its investigations during the following month (June), being equipped with suitable laboratory facilities for practical work, both at the military garrison of Columbia Barracks, near Quemados, Cuba, and also in the city of Habana. As yellow fever was already prevailing at the time of our arrival in Cuba suitable material for the scientific study of this disease was immediately available.

THE ETIOLOGY OF YELLOW FEVER.

Before giving the results of our investigations it may be well to recall the situation as regards the etiology of yellow fever at that time. Briefly it may be said that the claims of all investigators for the discovery of the specific agent of yellow fever—since modern bacteriological methods had come into use—had been disproved by the exhaustive observations of Sternberg (1), published in 1890, except that made by Sanarelli (2) for a small, motile bacillus isolated by him from the blood drawn during life in 2 of 6 cases of yellow fever, and from the blood and organs after death in 7 of 12 cases of this disease (58 per cent), studied at Montevideo and Rio de

[1] The members of this commission were Maj. Walter Reed, Surgeon, United States Army, and Drs. James Carroll, A. Agramonte, and the late Dr. Jesse W. Lazear, Contract Surgeons, United States Army.

Janeiro, Brazil. The results obtained, however, by those who had promptly undertaken to investigate Sanarelli's claim for the specific character of *Bacillus icteroides*, seemed to show a lack of agreement such as has never been reported, as far as the writer can recall, in connection with the supposed specific cause of any of the other acute infections. Thus while Achinard and Woodson (3) had, during the epidemic of 1897 in New Orleans, La., isolated a bacillus, claimed by them to be identical with *B. icteroides*, from the venous blood in 4 out of 5 cases, and from yellow fever cadavers in 32 out of 39 cases (82 per cent), Portier (4), working in the same city and during the same epidemic, could only obtain this bacillus 3 times in 51 autopsies, and failed to obtain it at all in cultures made from the venous blood during life in 10 cases. Again, while Wasdin and Geddings (5), in the city of Habana, were able to cultivate *B. icteroides* from blood withdrawn from the lobe of the ear, "not earlier than the third day of the disease" in 13 of 14 cases (92.8 per cent), and to find it in 85.7 per cent of their necropsies, Agramonte (6), studying the disease on the island of Cuba, failed to isolate *B. icteroides* in a single instance from blood drawn from the lobe of the ear in 37 cases or from the blood drawn from a vein at the bend of the elbow in 31 cases at various stages of the disease. The latter observer, however, reported finding this bacillus at autopsy in 11 of 35 cases (31.4 per cent). Without going further into detail, we may say that the results obtained by Lutz (7) and de Lacerda and Ramos (8) in Brazil, and by Matienzo (9) in Mexico, were equally conflicting and unsatisfactory.

Under these circumstances it seemed to the members of the commission of the first importance to give their entire attention to the bacteriological study of the blood of those sick with yellow fever and of the blood and organs of yellow-fever cadavers, having especially in view the isolation of *B. icteroides*. We were thus able during June, July, and August to take repeated cultures from the blood during life in 18 cases of yellow fever, adopting the usual method employed in withdrawing blood from a vein at the bend of the elbow, and transferring the blood at once, in quantities of 0.5 c. c., to each of several tubes containing 10 c. c. of nutritive bouillon which were afterwards incubated at 37° C. for a period of one week. In 7 cases, 4 of which were designated as "mild" yellow fever and 3 as "well-marked" yellow fever, only 1 culture was made from the blood in each case, viz, in 2 cases on the first day; in 1 case on the second day; in 3 cases on the third day; and in 1 case on the fourth day. In the remaining 11 cases, diagnosed as "severe" yellow fever, of whom 4 died, more frequent cultures were taken from the blood, these varying from 2 to 6 cultures on as many different days of the disease. In 2 of the fatal cases cultures were made each day from the commencement of the attack and including the day on which death occurred.

The negative result of these numerous cultures taken from the blood of cases of yellow fever, as regards the presence of *B. icteroides*, was reported in a "Preliminary note" presented at the meeting of the American Public Health Association (10), held in Indianapolis, Ind., October 22–26, 1900. To these 18 cases we can now add 6 other cases, or a total of 24, from which blood cultures have been made during life with negative results.

The importance of this negative finding as regards the growth of any specific bacterium will be better appreciated when it is seen, as I shall soon have occasion to point out, that yellow fever may be produced in nonimmune human beings by the subcutaneous injection of a small quantity (0.5–2 c. c.) of blood withdrawn from the venous circulation of a patient suffering with this disease.

In addition to the results above recorded, the careful study of 11 autopsies was equally barren as to the presence of any particular micro-organism, although the quantity of material with which our tubes were inoculated was greater than is usually made use of at autopsies.

In a word, then, the careful bacteriological study which the commission had made in cases of yellow fever had given no indications as to the presence of the specific agent of this disease. The same may be said concerning the result of numerous microscopic examinations of fresh and stained specimens of blood which we had in the meanwhile studied with a view of finding possibly some intracellular or extracellular body. Apparently no body, bacterial or protozoan, which could be brought into view with a one-twelfth Zeiss immersion objective, was present in the blood of these cases.

Although displaced from the order in which the following observations were made, it will be best to present, at this time, the results of the experiments which were later carried out by the commission on nonimmune human beings by means of the subcutaneous injection of blood, withdrawn during the active stage of the disease, as these results bear so directly upon the subject which we are now considering, viz, the etiology of yellow fever.

The only reference that I can find in the literature relative to an attempt to convey yellow fever in this way is cited by Sternberg (11), who states that at Veracruz, Mexico, in 1887, he saw Dr. Ruis inject into a nonimmune individual a hypodermic syringeful of blood drawn from a case of yellow fever on the eighth day of the disease. The result was negative, as was also the result of two other attempts related to him by Ruis.

Our own observations, undertaken for the purpose of ascertaining whether an attack of yellow fever could be induced in a second individual by the injection of a small quantity of blood, embrace experiments made on 12 American soldiers and Spanish immigrants, all nonimmune individuals.

These observations may be divided into the following classes:

(1) Injection of the fresh blood taken from a vein at the bend of the elbow. (2) Injection of partially defibrinated blood. (3) Injection of partially defibrinated blood heated for 10 minutes at 55° C. (4) Injection of blood serum previously diluted with sterilized water and filtered slowly through a Berkefeld laboratory filter.

The table following (I) gives the results of these several inoculations.

TABLE I.

No. of case.	Quantity and material used.	Day of disease.	Date of inoculation.	Result.	Date of attack.
I	2 c. c. fresh blood	Second	Dec. 26, 1900	Negative	
II	do	do	Jan. 4, 1901	Positive	Jan. 8, 1901
III	1.5 c. c. fresh blood	First	Jan. 8, 1901	do	Jan. 11, 1901
IV	0.5 c. c. fresh blood	Second	Jan. 22, 1901	do	Jan. 24, 1901
V	1 c. c. fresh blood	do	Jan. 25, 1901	do	Jan. 28, 1901
VI	0.75 c. c. partially defibrinated blood	Third	Oct. 15, 1901	do	Oct. 20, 1901
VII	1.5 c. c. partially defibrinated blood heated for 10 minutes at 55° C.	do	do	Negative	
VIII	Same as No. VII	do	do	do	
IX	do	do	do	do	
X	1.5 c. c. of filtered blood serum	do	do	Positive	Oct. 19, 1901
XI	Same as No. X	do	do	do	Do.
XII	Same as No. X	do	do	Negative	Oct. 23, 1901
	2 c. c. fresh blood	Fourth	Oct. 22, 1901	Positive	

By an examination of this table it will be seen that of the seven individuals who received subcutaneously the fresh or partially defibrinated blood in quantities of 0.5–2 c. c., six (85.7 per cent) developed an attack of yellow fever within the usual period of incubation of the disease.

These results are of very great interest as demonstrating that the specific agent of yellow fever is present in the blood, at least during the first, second, and third days of the attack.

Another important point brought out by these experiments was that the blood which conveyed the disease did not contain any bacterium which would grow on our usual laboratory media.

In order to establish this fact, as soon as blood had been injected into the nonimmune subject, additional blood was, at once, withdrawn in considerable quantity and transferred to tubes of nutritive bouillon. In one instance, where 2 c. c. of blood had been drawn into the syringe, 0.5 c. c. of this sufficed, when injected, to produce a severe attack of yellow fever, after 73 hours' incubation, while the remaining 1.5 c. c. transferred immediately to four tubes of bouillon gave no growth, except that from one tube we isolated on the fourth day *Staphylococcus pyogenes citreus*, found by us to be a common skin-contaminating organism in Cuba.

Table I further shows that the specific agent contained in the blood is destroyed or attenuated by heating the latter at 55° C. for 10 minutes, so that the injection of 1.5 c. c. of this heated blood was harmless (cases VII, VIII, and IX), while the injection of 0.75 c. c. of the same blood unheated sufficed to promptly induce an attack of yellow fever in a "control" individual (case VI).

Of not less interest was the fact brought out by these observations that yellow fever can be produced by the injection of a small quantity of bacteria-free serum filtrate, obtained by passing the diluted serum through a Berkefeld laboratory filter (cases X and XI), and further that the blood of a case of yellow fever, thus produced, when injected into a third nonimmune subject will promptly bring about an attack of this disease (case XII); thus demonstrating that the specific agent of yellow fever can find its way through the pores of a filter which ordinarily serves to prevent the passage of all known bacteria.

I have elsewhere (12) in conjunction with one of my colleagues (Carroll) discussed the facts here presented more at length and will limit myself, therefore, to the remark that these experiments appear

to indicate that yellow fever, like the foot-and-mouth disease of cattle, is caused by a micro-organism so minute in size that it might be designated as ultramicroscopic.

THE PROPAGATION OF YELLOW FEVER.

Prior to the time at which the foregoing observations were made the commission had already turned its entire attention to the possible solution of the problem of the propagation of yellow fever, being induced thereto, not only by the fruitlessness of the investigations made thus far along bacteriological lines, but, also, by reason of certain facts which seemed to call for a better interpretation than had hitherto been accorded them.

Without entering into details, I may say that, in the first place, the commission saw, with some surprise, what had so often been noted in the literature, that patients in all stages of yellow fever could be cared for by nonimmune nurses without danger of contracting the disease. The noncontagious character of yellow fever was, therefore, hardly to be questioned.

In the second place, it had been observed that patients discharged from the wards during early convalescence could be brought into intimate association with nonimmune individuals without thereby establishing fresh foci of the disease. This did not seem to indicate that any specific agent was present in the excreta of the sick.

Again, it has been noted that in certain cases of this disease no growth had been obtained on the ordinary laboratory media, either by frequent cultures from the blood during life or from the blood and organs after death.

Further, in the course of an investigation which the commission were able to make during the last week of July, 1900, concerning the origin and spread of a small epidemic of yellow fever that had appeared in a military garrison, numbering about 900 men, at Pinar del Rio, Cuba, they had seen that by reason of the false diagnosis of "pernicious malarial fever" which had been given to these cases no disinfection of bedding or clothing had been carried out; and yet there was no indication that this neglect had contributed in the least to the spread of the disease; nor had any harm come to those nonimmunes who had slept in the beds vacated by the sick, or washed the supposedly infected garments of those who had recovered or died of this disease.

Putting these various data together, it seemed probable that more progress might be made if attention should be turned to the mode of transmission of yellow fever, especially as our own observations had caused us to seriously doubt the usually accepted belief of the conveyance of this disease by means of fomites.

Then, too, the endemic curve of yellow fever in the city of Habana, and its well-known epidemic curve in the United States, appeared to be more intimately associated with and more affected by the rise and fall of the annual temperature curve than was to be seen in any of the acute infections, except malarial fever. The peculiar behavior of this disease (if I may use the expression) in rapidly spreading in certain localities, when introduced, as contrasted with its failure to propagate itself in other places, where the conditions for its increase were apparently just as favorable, seemed to point in the strongest

manner to the necessity for some special agent or intermediate host in the dissemination of its specific cause. If malarial fever—a disease so much affected by temperature conditions—required the agency of a special genus of mosquito for its propagation, as had in recent years been so brilliantly worked out by Ross, Grassi, Bastianelli, Bignami, and others, it did not seem unreasonable to suppose that yellow fever—a disease so plainly controlled by seasonal conditions—might also depend on some such agent for its spread. Influenced by this line of reasoning, the commission began, during the second week of August, 1900, its observations relative to the propagation of yellow fever by means of the bite of a certain species of mosquito—*Stegomyia fasciata.*

The work along this line was carried forward so rapidly that, within 30 days, 11 individuals had been bitten by infected Stegomyia, of whom two [1] developed well-marked attacks of yellow fever within the usual period of incubation, and under such circumstances as to positively exclude in one case any other possible source of infection.

Appreciating fully the importance of this discovery and in order to exclude all other possible sources of infection in our future observations, it was now determined to establish a special experimental station where further observations could be made on nonimmune human beings, both as to the propagation of yellow fever by means of the bite of the mosquito as well as by exposure to the most intimate contact with infected clothing and bedding, and this under the strictest enforcement of military quarantine. With the approval and assistance of the military governor of the Island of Cuba, this experimental station was ready for occupancy on November 20, 1900, and was continuously occupied until March 1, 1901.

As the results obtained at this station have already been published (13) in full elsewhere, I will here only present a brief account, first of the experiments with fomites and afterwards of those made with infected mosquitoes.

ATTEMPTS AT INFECTION BY FOMITES.

I quote from a paper which the writer presented for the commission at the meeting of the Pan-American Medical Congress,[2] held in Habana, Cuba, February 4–7, 1901:

> For this purpose there was erected at Camp Lazear a small frame house consisting of one room, 14 by 20 feet, and known as "building No. 1," or the "infected clothing and bedding building." The cubic capacity of this house was 2,800 feet. It was tightly sealed within with "tongued and grooved" boards, and was well battened on the outside. It faced the south and was provided with two small windows, each 26 by 34 inches in size. These windows were both placed on the south side of the building, the purpose being to prevent, as much as possible, any thorough circulation of the air within the house. They were closed by permanent wire-screens of 0.5 mm. mesh. In addition a sliding glass sash was provided within and heavy wooden shutters without; the latter intended to prevent the entrance of sunlight into the building, as it was not deemed desirable that the disinfecting qualities of sunlight, direct or diffused, should at any time be exerted on the articles of clothing contained within this room. Entrance was effected through a small vestibule, 3 by 5 feet, also placed on the southern side of the house. This vestibule was protected without by a solid door and was divided in its middle by a wire-screen door, swung on spring hinges. The inner entrance was also closed by a second wire-screen door. In this way the passage of

[1] One of these cases was that of Dr. James Carroll, Contract Surgeon, U. S. A., a member of the commission.

[2] *Loc. Cit.*

mosquitoes into this room was effectually excluded. During the day and until after sunset the house was kept securely closed, while by means of a suitable heating apparatus the temperature was raised to 92°–95° F. Precaution was taken at the same time to maintain a sufficient humidity of the atmosphere. The average temperature of this house was thus kept up at 76.2° F. for a period of sixty-three days.

November 30, 1900, the building now being ready for occupancy, three large boxes filled with sheets, pillowcases, blankets, etc., contaminated by contact with cases of yellow fever and their discharges were received and placed therein. The majority of the articles had been taken from the beds of patients sick with yellow fever at Las Animas Hospital, Habana, or at Columbia Barracks. Many of them had been purposely soiled with a liberal quantity of black vomit, urine, and fecal matter. A dirty "comfortable" and a much-soiled pair of blankets, removed from the bed of a patient sick with yellow fever in the town of Quemados were contained in one of these boxes. The same day, at 6 p. m., Dr. R. P. Cooke, acting assistant surgeon, United States Army, and two privates of the Hospital Corps, all nonimmune young Americans, entered this building and deliberately unpacked these boxes, which had been tightly closed and locked for a period of two weeks. They were careful at the same time to give each article a thorough handling and shaking, in order to disseminate through the air of the room the specific agent of yellow fever, if contained in these fomites. These soiled sheets, pillowcases, and blankets were used in preparing the beds in which the members of the Hospital Corps slept. Various soiled articles were hung around the room and placed about the bed occupied by Dr. Cooke.

From this date until December 19, 1900, a period of 20 days, this room was occupied each night by these three nonimmunes. Each morning the various soiled articles were carefully repacked in the aforesaid boxes, and at night again unpacked and distributed about the room. During the day the residents of this house were permitted to occupy a tent pitched in the immediate vicinity, but were kept in strict quarantine.

* * * * * * *

December 19 these three nonimmunes were placed in quarantine for five days and then given the liberty of the camp. All had remained in perfect health, notwithstanding their stay of 20 nights amid such unwholesome surroundings.

During the week December 20–27 the following articles were also placed in this house, viz, pajamas suit, 1; undershirts, 2; nightshirts, 4; pillow slips, 4; sheets, 6; blankets, 5; pillows, 2; mattress, 1. These articles had been removed from the persons and beds of four patients sick with yellow fever and were very much soiled, as any change of clothing or bed linen during their attacks had been purposely avoided, the object being to obtain articles as thoroughly contaminated as possible.

From December 21, 1900, till January 10, 1901, this building was again occupied by two nonimmune young Americans under the same conditions as the preceding occupants, except that these men slept every night in the very garments worn by yellow fever patients throughout their entire attacks, besides making use exclusively of their much-soiled pillow slips, sheets, and blankets. At the end of 21 nights of such intimate contact with these fomites, they also went into quarantine, from which they were released five days later in perfect health.

From January 11 till January 31, a period of 20 days, "building No. 1" continued to be occupied by two other nonimmune Americans, who, like those who preceded them, have slept every night in the beds formerly occupied by yellow fever patients, and in the nightshirts used by these patients throughout the attack without change. In addition, during the last 14 nights of their occupancy of this house they had slept each night with their pillows covered with towels that had been thoroughly soiled with the blood drawn from both the general and capillary circulation on the first day of the disease, in the case of a well-marked attack of yellow fever. Notwithstanding this trying ordeal these men have continued to remain in perfect health.

The attempt which we have therefore made to infect "building No. 1" and its seven nonimmune occupants during a period of 63 nights has proved an absolute failure.

INFECTION BY MOSQUITOES.

While the experiments with fomites were being carried out in "Building No. 1," certain nonimmune individuals who were lodged in tents, in a separate part of the camp, were being subjected, with their full consent, to the bites of mosquitoes which had previously fed on the blood of cases of yellow fever occurring in the city of Havana. Thus during the period from December 5, 1900, to February 7, 1901, we had subjected to this method of infection 12 nonimmune subjects,

who had previously passed their full record of quarantine in this camp. Of these 10, or 83.3 per cent, experienced attacks of yellow fever and always within the period of incubation of this disease.

The following Table II gives the necessary data concerning these observations:

TABLE II.

No. of case.	Days in quarantine.	Inoculation.		Method of inoculation.	Period of incubation in hours.	Result.	Order of occurrence.	Date of occurrence.
		Hour.	Date.					
I	15	2 p. m.	Dec. 5, 1900	Mosquito	81½	Positive	I	Dec. 8, 1900
II	9	4 p. m.	Dec. 8, 1900	do	137	do	III	Dec. 13, 1900
III	19	10.30 a. m.	Dec. 9, 1900	do	83½	do	II	Dec. 12, 1900
IV	21	4.30 p. m.	Dec. 11, 1900	do	91½	do	IV	Dec. 15, 1900
V	32	12 m.	Dec. 21, 1900	do	95	do	V	Dec. 25, 1900
VI	31	10 a. m.	Jan. 8, 1901	do		Negative	VI	
VII	22	11 a. m.	Dec. 30, 1900	do	94½	Positive	VII	Jan. 3, 1901
VIII	69	8.30 p. m.	Jan. 19, 1901	do	95½	do	VIII	Jan. 23, 1901
IX	74	10.30 a. m.	Jan. 25, 1901	do		Negative	IX	
X	6	9.30 a. m.	Jan. 31, 1901	do	74½	Positive	X	Feb. 3, 1901
XI	78	11 a. m.	Feb. 6, 1901	do	78	do	XI	Feb. 9, 1901
XII	25	2 p. m.	Feb. 7, 1901	do	70	do	XII	Feb. 10, 1901

The positive results obtained, therefore, by this mode of infection stand in striking contrast to the negative experiments made with fomites. Indeed, cases VIII and XI of Table II had each slept 21 nights in the garments of yellow fever patients while occupants of "building No. 1." As they had remained in perfect health at Camp Lazear for yet 30 days longer, they were at the expiration of this time bitten by infected mosquitoes solely for the purpose of testing their immunity and with the result that an attack of yellow fever promptly followed in each case.

It should be borne in mind, also; that of the nonimmune residents at Camp Lazear, while all lived under the same hygienic conditions, only those individuals developed yellow fever who were purposely bitten by contaminated mosquitoes, or injected with the blood of those sick with this disease. Moreover, the precision with which the infection of the individual followed the bite of the mosquito left nothing to be desired in order to fulfil the requirements of a scientific experiment.

Case V of Table II is of especial interest, when taken in connection with the failure to induce the disease by contact with fomites.

This individual, having been quarantined for 32 days at Camp Lazear, volunteered to enter a newly erected building in which 15 contaminated mosquitoes had just been freed. His first visit was at noon, December 21, 1900, and the length of his stay 30 minutes. At 4.30 p. m. the same day he again entered this building and remained 20 minutes. The following day at 4.30 p. m. he for the third time visited this room and remained 20 minutes. During each of these visits he was bitten by mosquitoes. He did not enter the building again, nor was he exposed to any other source of infection. Nevertheless at the expiration of 3 days and 23 hours, or at 6 a. m. December 25, 1900, he was suddenly seized with an attack of yellow fever, which proved to be severe in character. That the infection was occasioned by the bites of contaminated mosquitoes was plainly shown by the immunity from the disease enjoyed by two

nonimmune "controls," who, protected only by a wire-screen partition, had been present at each of the subject's visits and who under the same conditions of security against the bites of the infected mosquitoes continued to sleep in and breathe the commom atmosphere of this room for yet 18 nights.

To the positive cases contained in Table II, which were produced at Camp Lazear, we are now able to add 4 other cases of yellow fever occasioned by the bites of infected mosquitoes, thus making a total of 14 cases, in each of which happily recovery followed.

A very important point brought out by these observations is that an interval of about 12 days or more after contamination appears to be necessary before the infected *Stegomyia* is capable of conveying the disease to a susceptible individual. Repeated experiments made with insects which had bitten yellow fever patients 2 to 10 days previously were always negative, although these same insects were proven capable of conveying the disease after having been kept until 17 to 24 days had elapsed. Our observations (14) further demonstrate that mosquitoes that have been kept for periods varying from 39 to 57 days after contamination are still capable of conveying the disease, and further that infected *Stegomyia* may survive for a period of at least 71 days. This will explain how the contagion of yellow fever may cling to a building, although it has been vacated for a period of two or more months.

Bearing in mind that the observations made by means of blood injections (Table I) were only undertaken after we had succeeded in demonstrating that the disease could be conveyed by the bites of infected *Stegomyia*, it will be seen that our study of the method of propagation of yellow fever, at Camp Lazear, sufficed to prove very definitely that, while the natural mode of transmission of this disease is through the bites of infected mosquitoes, yellow fever may also be conveyed, like malarial fever, by the injection of a small quantity of blood taken from the veins of an individual suffering with this disease.

Per contra, our observations show that, notwithstanding the common belief in this mode of transmission, yellow fever can not be induced in the nonimmune individual even by the most intimate contact with contaminated articles of clothing and bedding.

Although the investigations made at Camp Lazear were only concluded one year ago, already confirmatory evidence of the strongest character has been furnished in a series of experiments carried out by Guitéras (15) at the inoculation station of the sanitary department of Habana.

I may be pardoned for quoting the paragraph with which Guitéras begins his contribution. He says: "The favorable results obtained by the United States Army commission in their experiments with yellow fever, the continued series of mild cases resulting from these experiments without a death, suggested very naturally the continuation of their work on a larger scale; not with a view to control or confirm the conclusions of the commission, for anyone who had followed their work with unprejudiced attention must have concluded that their solution of the problem of the etiology of yellow fever was final; but rather in the hope of propagating the disease in a controllable form, and securing amongst the recently arrived immigrants immunization, with the minimum amount of danger to themselves and the community."

Of a total of 42 individuals inoculated by Guitéras 25 were rejected by him by reason of having been bitten by insects that had been applied to cases of fever about which the diagnosis was in doubt. The following table, therefore, only includes 17 persons who were bitten by *Stegomyia* that had previously fed on unmistakable cases of yellow fever at intervals of 14 to 36 days before being applied to the non-immune subject.

TABLE III.

No. of case.	Date of inoculation.	Mode of inoculation.	Result.	Period of incubation.
1	Feb. 23, 1901	Mosquito	Positive	3 days, 10 hours.
2	Aug. 4, 1901	do	Negative	
3	do	do	do	
4	Aug. 7, 1901	do	do	
5	Aug. 8, 1901	do	Positive	4 days, 5 hours.
6	do	do	do	3 days, 3 hours.
7	Aug. 7, 1901	do	Negative	
8	Aug. 9, 1901	do	Positive	5 days, 3 hours.
9	Aug. 10, 1901	do	Negative	
10	do	do	do	
11	do	do	do	
12	Aug. 13, 1901	do	Positive	3 days, 19 hours.
13	do	do	Negative	
14	Aug. 14, 1901	do	Positive	3 days, 21 hours.
15	do	do	do	5 days, 21 hours.
16	Aug. 22, 1901	do	do	3 days.
17	Aug. 24, 1901	do	Negative	

A more complete confirmation of the results obtained by the American commission could not be furnished than the data contained in the foregoing table, since they show that of 17 individuals who were bitten by infected *Stegomyia fasciata*, 8 (47 per cent) developed the disease. Most unfortunately, in three of these cases very grave symptoms ensued, such as black vomit and suppression of the urine, which eventuated in the death of the patients. I may add that in the hands of Guitéras fomites failed to exert any effect on nonimmunes.

Whether other species of mosquitoes than *Stegomyia* are capable of conveying the parasite of yellow fever has not as yet been determined by the commission; nor have we been able to ascertain whether the parasite passes from the mother insect to daughter insects. The experiments which we have thus far been able to make for the purpose of determining these important points, although negative, have been too few in number to warrant any definite expression of opinion.

THE PREVENTION OF YELLOW FEVER.

The definite determination of the way in which yellow fever is transmitted from the sick to the well furnishes a solution at last of that much vexed problem of how to prevent the spread of the disease. Even in the absence of more definite knowledge concerning its specific agent—knowledge greatly to be desired from the scientific standpoint—we are now able, as sanitarians, to direct our efforts along certain well-defined lines, with a feeling of security heretofore unknown.

From the point of view of prevention the situation may be briefly summed up in the following conclusion, which was presented by the American Army commission to the Pan-American Congress of 1900,[1]

[1] *Loc. cit.*

viz, "The spread of yellow fever can be most effectually controlled by measures directed to the destruction of mosquitoes and the protection of the sick against the bites of these insects."

This conclusion was the logical outcome of the observations that had been made by the commission at its experimental station near Quemados, Cuba.

The importance of the discovery that yellow fever is transmitted by the bite of a certain species of mosquito did not fail to attract the prompt attention of the military governor of the island of Cuba, himself a physician and formerly a distinguished member of the Medical Department of the United States Army. By his direction the theory was at once subjected to a practical test in the city of Habana, in which city yellow fever had not failed to make its yearly appearance during the past 140 years.

Under the efficient management of the chief sanitary officer, Surg. Maj. Wm. C. Gorgas, United States Army, the sanitary regulations were so far modified as to require that every patient having yellow fever should not only be quarantined, but that his room should be promptly protected with wire screens, so as to prevent the possibility of mosquitoes becoming infected by sucking the blood of the patient. As a second important measure, a systematic destruction of all mosquitoes in other rooms of the patient's house, as well as in adjoining houses, was at once begun, the fumes of *pyrethrum* being relied upon to stupify the insects, after which they were carefully swept up and burned. In other words, Surg. Maj. Gorgas relying upon the well-known slow progress of yellow fever sought to destroy all mosquitoes, infected or noninfected, within a given radius of each case, while at the same time he effectually excluded all mosquitoes from access to the sick. If a secondary case occurred, the same hygienic measures were vigorously enforced along the lines above indicated.

As an illustration of what has been accomplished by these newer sanitary regulations, I may state that counting from the date when they were put into force—viz, February 15, 1901—Habana was freed from yellow fever within 90 days; so that from May 7 to July 1—a period of 54 days—no cases occurred. Notwithstanding the fact that on the latter date, and during the months of July, August, and September, the disease was repeatedly reintroduced into Habana from an inland town, no difficulty was encountered in promptly stamping it out by the same measures of sanitation intelligently applied both in the city of Habana as well as in the town of Santiago de las Vegas, whence the disease was being brought into Havana.

As a further illustration of the remarkable sanitary victory accomplished over a disease whose progress we had heretofore been powerless to arrest, I will close this paper by inviting the reader's attention, first to the accompanying Chart I, which shows the average monthly mortality from yellow fever in Habana for the 20 years 1880–1899, inclusive, and also the mortality by month for the years 1900 and 1901. I will then ask him to examine Chart II, which shows the progress of yellow fever in Habana during the epidemic year, ending March 1, 1901, when the sanitary authorities were putting forth every effort known at that time to sanitary science in order to control the march of the disease; and when he has satisfied himself that no effect whatever was produced upon the epidemic of that year, I will invite his attention to Chart III, which shows the occurrence of this disease

CHART I.

Showing monthly mortality from yellow fever in the city of Havana, for the twenty years, 1880–1899, and for the years 1900–1901.

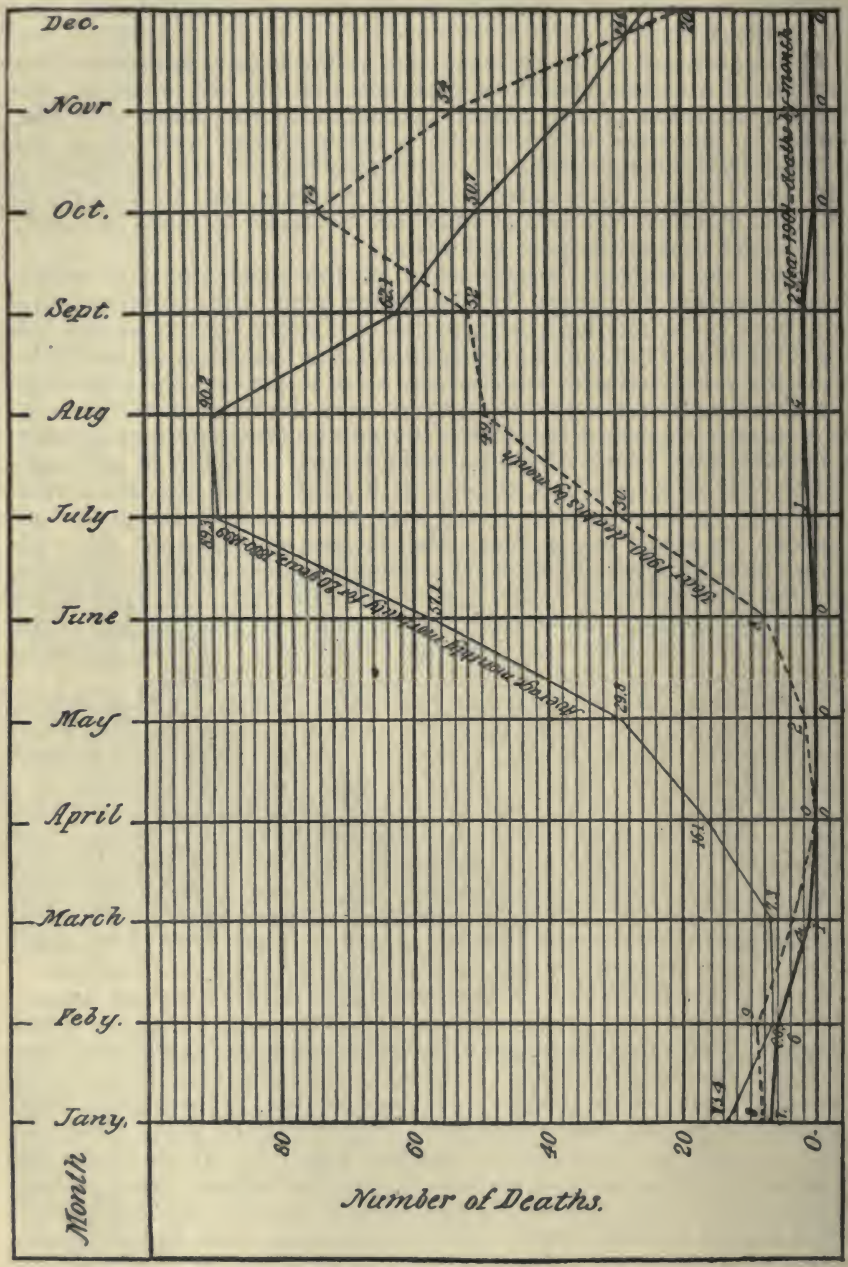


CHART II.

Cases and deaths from yellow fever in the city of Havana, for the epidemic year, March 1 1900, to March 1, 1901 (by month).

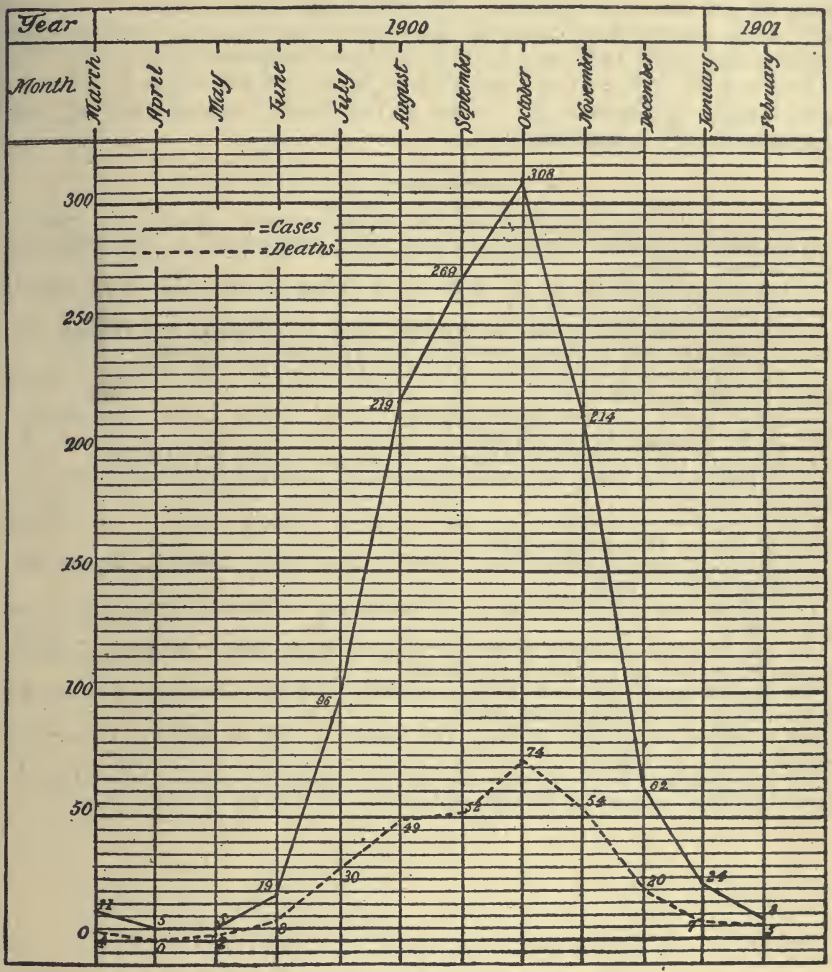
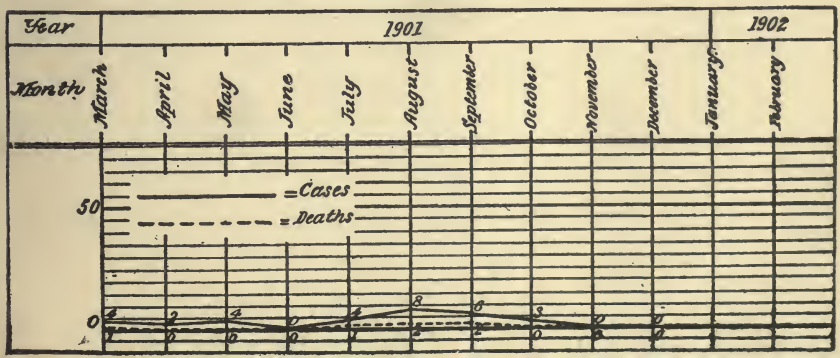


CHART III.

Cases and deaths from yellow fever in the city of Havana, for the epidemic year, March 1, 1901, to March 1, 1902 (by month).



in Habana for the epidemic year March 1, 1901, to March 1, 1902, during which year yellow fever was fought on the theory that the specific agent of this disease is transmitted solely by means of the bites of infected mosquitoes. By carefully comparing the figures both as to deaths and cases in these two charts, and recalling that between the years 1853 and 1900 there have been recorded in the city of Habana 35,952 deaths from yellow fever, he will then be able to more clearly appreciate the value of the work accomplished by the American Army commission.

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DR. JAMES CARROLL.

PART III.—THE PUBLICATIONS OF JAMES CARROLL, ASSISTANT SURGEON, UNITED STATES ARMY, IN REGARD TO YELLOW FEVER.

[Published after the death of Maj. Walter Reed.]

Chapter 1.

THE TRANSMISSION OF YELLOW FEVER.[1]

By James Carroll, M. D.,
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[Read at the forty-fourth session of the American Medical Association, in the section on practice of medicine, and approved for publication by the executive committee: Drs. J. M. Anders, Frank A. Jones, and W. S. Thayer.]

Several American observers have noted that during the yellow fever outbreaks mosquitoes were very numerous, among them Rush(1), at Philadelphia in 1797; Dr. Weightman(2), of the United States Army, at St. Augustine, Fla., in 1839; Dr. Wood(3), at Centerville, Miss., in 1853. Dr. E. H. Barton(3) states "that at Clinton, La., in 1853, mosquitoes were uncommonly numerous night and day." At Trinity, La., in the same year, when sawdust was used to fill up low places in the streets, the disease was not propagated, though many cases were brought there and no precautions were used(3). It is hardly necessary to note what the effect of this obliteration of puddles would be on the development of mosquitoes. Dr. Beyrenheidt(3), of Biloxi, Miss., in reporting a severe epidemic at that place in 1853, during which 533 cases and 111 deaths occurred in a population of 5,520, makes the interesting statement that "mosquitoes and fleas were very abundant." Dr. Bennett Dowler strongly urged drainage of the city of New Orleans, and spoke of the city and its environs as "mosquito lands"(4). La Roche(5) states that in 1793, during the epidemic in Philadelphia, "the narrow streets and alleys near the wharves, as, indeed, in many other parts, were in a foul state, and the gutters almost everywhere sadly neglected." In 1794 Rush and others ascribed the fever to exhalations from wharves, neglected gutters, and stagnant ponds(5). In 1797, during another outbreak in Philadelphia, the condition was practically the same; the Academy of Medicine called the attention of the governor to the putrid exhalations from the gutters, streets, ponds, and marshy grounds of the neighborhood of the city(5). While high temperature, low altitude, and the presence of standing water are the conditions most favorable to the development of a yellow fever epidemic, there are numerous instances on record where the disease after introduction spread from house to house throughout the town in places where the general conditions of sanitation and drainage were good. This is now explained by the habits of the mosquito (*Stegomyia fasciata*), which breeds in standing water, in houses as well as out of

[1] Journal of the American Medical Association, May 23, 1903.

doors. As a general rule, in ports where yellow fever epidemics first appear, the conditions are known to be favorable for the development of enormous numbers of mosquitoes.

A very interesting observation was made in 1839 in South Africa by William Ferguson, then a surgeon in the South African corps, in regard to the extension of yellow fever from Sierra Leone (where it had been brought on vessels from the West Indies) to Gambia, Goree, and Ascension, the subsequent ports of arrival of some of these infected vessels. After mentioning an unusually heavy accumulation of mud and filth in a pit at Ascension, which was said to have been the cause of the fever occurring after an unusually heavy fall of rain, he makes the following statement:

(6) It will be observed that at Ascension, at Goree, and at Gambia a period of three or four weeks always elapsed betwixt the landing of the sick and the epidemic outbreaking of the disease among the population, a degree of uniformity worthy of remark whether the conclusions at which I have arrived (that the disease was carried to these places on infected vessels) be mistaken or not.

These outbreaks were accompanied by black vomit and were undoubtedly yellow fever of imported origin.

Just 60 years later Carter (7) made a similar observation in the United States, shortening the period slightly and giving cases and data. In a later paper (8) he designates the interval between primary and secondary cases the period of "extrinsic incubation."

The known facts regarding the apparent noncontagiousness of the disease, the peculiar manner in which it has been seen to pass from one house to another without intercommunication of the inhabitants, and the numerous points of resemblance between yellow fever and malaria, led us to expect results from mosquito inoculations in yellow fever. After satisfying ourselves that *B. icteroides* (Sanarelli) was not to be considered, Drs. Reed, Lazear, and myself, in consultation, decided that the mosquito theory had many facts to support it and could be promptly decided one way or the other. This leads us to a consideration of the mosquito theory of Finlay.

At the session of the Royal Academy of Sciences, Habana, August 14, 1881, Finlay first gave to the world his memorable theory of the transmission of yellow fever by the mosquito, and reported five experiments, which are included in the accompanying table, comprising all of Finlay's and Delgado's positive cases published in 1891. (9)

Finlay believed (10) that the transfer of the specific agent of the disease from patient to nonimmune was effected mechanically by the insect's proboscis (14) and that the infection would be conveyed immediately if the insect chanced to bite a susceptible person a few moments after feeding on a patient in the proper stage of the disease. (11) He also thought that the graver forms of yellow fever might be produced by the bite of *Culex pungens*, because the insect ingested a larger amount of blood than stegomyia, and consequently a greater quantity of the virus would be retained on its proboscis (stylet). (11) He ventured the opinion that yellow fever was a sort of eruptive fever, and that the seat of the eruption was the endothelial lining of the blood vessels, and that the mosquito picked up the inoculable material from the interior of the blood vessels on its biting apparatus and transferred the same to the interior of the vessels of the person subsequently bitten.

TABLE 1.—*Mosquito inoculations reported by Finlay and Delgado in the Archives de Medicine Navale, tome 55, Paris, 1891.*

No. of case.	Patient.	Date of contamination of mosquito.	Date when the patient was bitten.	Period in mosquito.	Date of attack of fever.	Period of incubation.	Character of attack.	Albuminuria?	Remarks.
				Days.		*Days.*			
1	F. B. M.	June 28, 1881	June 30, 1881	2	July 14, 1881	14	Mild	Yes	Excessive period of incubation.
2	Aly. C.	July 16, 1881	July 22, 1881	6	July 27, 1881	5	Abortive	No	Insect bit Dr. Finlay July 20.
3	L. G. P.	July 26, 1881	July 29, 1881	3	July 31, 1881	2	Mild	No	Infection by mosquito excrement.
4	D. L. F.	July 29, 1881	July 31, 1881	2	Aug. 5, 1881	5	Abortive	?	Did not report himself sick. History of illness vague.
5	D. G. B.	July 31, 1881	Aug. 2, 1881	2	About Aug. 20, 1881	18	Mild	?	Excessive incubation period (15).
8	J. B.	June 20, 1883	June 22, 1883	2	July 9, 1883	17		No	Two mosquitos used. Excessive incubation period. Resided in Habana.
9	P. U.	Aug. 13 and 15, 1883	Aug. 17, 1883		Aug. 26, 1883	9		No	Excessive period of incubation. Jesuit priest, lived at Marianao near Habana.
13	J. S.		Aug. 18, 1883		Sept. 9, 1883	22		No	Excessive period of incubation. Lived at Marianao. Moved to Habana six days before his attack.
28	H. Oz.		Sept. 7, 1886		Sept. 23, 1886	16	Mild		Excessive period of incubation.
32	J. P.		June 16, 1887		July 11, 1887	25		Trace	Do.
42	P. Rem.		June 8, 1888		July 1, 1888	23		No	Do.
55	P. Go.	Not stated	Aug. 17, 1889		Aug. 26, 1889	9		No	Do.
66	H. Ola.	do	Aug. 14, 1890		Aug. 21, 1890	7		No	Lived at a country residence near Habana.

In a later paper he assumes that the picking up of these germs by the proboscis of the mosquito is selective, because there is nothing to prove that other inoculable diseases have ever been so transmitted. From four culture experiments, in each of which the head and the proboscis of a mosquito were dropped into a bouillon tube, he infers that the head and the proboscis of the day mosquito possess bactericidal properties for ordinary bacteria and fungi with the exception of a coccus, which was subsequently (12) claimed to be the specific agent of the disease. (13) The sting of the mosquito is suggested as the "intermediate host" necessary for some phase of development of disease germs. (14)

As late as 1899 Finlay mentions the isolation of the tetracoccus from culture media into which the heads and proboscides of contaminated mosquitoes had been dropped, as one of the three results of his experiments on yellow fever mosquitoes.

In a paper (13) published in 1895 he announced some very interesting results obtained with the "tetracoccus." A number of rabbits were inoculated intraperitoneally with cultures in bouillon; one of these cultures had been obtained from the head and the proboscis of a mosquito by placing them in a tube of bouillon five days after the insect had bitten a yellow-fever patient; the others came from the finger blood and milk of yellow-fever patients. All of the rabbits died; some of them showed infarcts of the kidneys, lungs, and liver. A rabbit obtained from the country was placed in the stable where some of the other rabbits had been kept, and at the end of eight days it was found dead. The tetracoccus was obtained from its heart's blood.

Eleven days after the rabbits had been removed from the house (the stable is usually a part of the house in Habana) a Spanish wet nurse came to spend some time there and on the third day following her arrival she was attacked with yellow fever. Mosquitoes had been unusually abundant in the house during the whole time the inoculated rabbits had been kept in it, and we are asked to keep this in mind in view of the possible transmission of the disease from animals to man. We are told that the blood from the finger of this woman on the third day of her illness gave the "pale yellow tetracoccus," and the milk from her breast gave a "white tetracoccus," which proved fatal to a rabbit in 15 days. (13)

While reading the accounts of these experiments one is constantly reminded of the pathogenic staphylococci. It is strongly suggested (13) that the rabbits died of yellow fever, and it is asserted that the experiments justified the assumption that the tetracoccus was the "specific germ of yellow fever."

The statement is also made in this paper that of 100 presumably susceptible persons who had received the mosquito inoculation during the 14 years previous, only 3 had subsequently died of yellow fever. (13)

I have been unable to find records of these 100 cases in the library of the Surgeon General's Office, and submit those of which the data are accessible to me. As these include the cases on which Dr. Finlay's claim is based they will suffice for the purpose. The 54 negative cases are omitted.

Case 3 was bitten by a mosquito that had been fed on bloody excrement from another mosquito that had been found inside the mosquito net of a fatal case. The material was allowed to dry for 27 days in the test tube and was then moistened with a little sugar and water to prepare it for feeding. (15) There is a marked difference between the method of procedure herein described and that given in 1901, (16) when Dr. Finlay said:

> I applied a nocturnal mosquito and allowed it to fill itself from a case of yellow fever. After pricking the side of the insect's abdomen I mixed the blood which escaped with a drop of sterilized sirup and fed with it a fresh culex mosquito, and finally applied the latter to a third soldier (July 29). Two days later, July 31, the soldier went to the hospital with a fever which was also recorded as "abortive yellow fever."

This case (L. G. P.) was omitted from the paper published in 1881, as stated, but was included in 1891 in the report from which the cases here recorded are taken.

Case 4 is further discussed in English in a footnote on page 368 of the Revista de la Asociacion Medico-Farmaceutica, Habana, February, 1902. (History of illness vague. Did not go to bed or report himself sick.) The first 5 cases were newly arrived soldiers, stationed at Cabanas and who were brought to the city of Habana for examination once in every 5 days.

Case 9 is cited by Finlay (17) in refutation of our conclusion (18) that the mosquito is not capable of infecting until about 12 days or more have elapsed after it has bitten the patient.

Case 55 was a Spaniard, newly arrived, who lived at a country residence. At both attempts to inoculate him the mosquitoes failed to bite; nevertheless he was taken sick August 26. Another nonimmune who occupied an adjoining room was taken sick with similar symptoms, a few days later. No further comment is necessary, except that the cases of the Army commission and of Dr. Guitéras were kept under close observation and strict control. Nearly all of Dr. Finlay's cases were exposed to infection in the city of Habana. Only four of them come within the recognized periods of incubation, viz, Nos. 2, 3, 4, and 66. The first three of these were inoculated in Habana in July, 1881, during which month there were 90 deaths from yellow fever in that city alone. The last was inoculated in August, 1890. In that month 60 deaths from yellow fever are recorded for the city of Habana.

Finlay has published a great many conjectures and speculations in regard to yellow-fever transmission. Some of these, such as the belief that the disease was transmitted by the mosquito, have been proven by our work, but not in accordance with his ideas. I can find no evidence that he has produced a single case of yellow fever by his inoculations. In the first place the mosquito is incapable of transmitting the disease in so short a period as 2 to 5 days after biting the patient. In the second place 7 days must be placed as the extreme limit of incubation in the human being. Our longest period was between 5 and 6 days. Finlay conveniently puts the ordinary limit of yellow-fever incubation between 5 and 22 days. (14) The efficiency of the 5-day quarantine regulation proves that incubation in man certainly does not extend over 6 days, or 7 at the extreme, and in the 30 experimental cases recorded by ourselves and Guitéras the former period has never been exceeded.

TABLE 2.—*Negative mosquito inoculations of the Army commission.*

No.	Character of attack and number of patients bitten.	Day of disease.	Interval in mosquito (room temperature).	Date of application of mosquito.	Number of mosquitoes applied.	Remarks.
			Days.			
1	Mild, 1	Seventh	5	Aug. 11, 1900	1	Negative.
2	Very mild, 1	Fifth	5	....do....	1	Do.
3	....do....	....do....	6	Aug. 12, 1901	1	Do.
4	....do....	....do....	6	....do....	1	Do.
5	....do....	....do....	8	Aug. 14, 1901	1	Do.
6	....do....	....do....	10	Aug. 16, 1901	1	Do.
7	Severe, 1	Second	3	Aug. 18, 1901	1	Do.
8	Very mild, 1	Fifth	13	Aug. 19, 1901	2	Do.
	Severe, 1	First	3			
9	Fatal, 1	Second	6	Aug. 25, 1901	1	Do.
	Mild, 1	First	4			
	Severe, 1	Second	2			
10	....do....	Third	3	Nov. 20, 1901	1	Negative; repetition.
	....do....	....do....	6			
	....do....	Fifth	11			
11	....do....	Third	6	Nov. 23, 1901	1	Do.
	....do....	....do....	9			
	....do....	Fifth	14			
12	Moderate, 1	Third	12	Nov. 26, 1901	1	Do.
	Well marked, 1	Second	10			
13	Moderate, 1	Third	15	Nov. 29, 1901	1	Do.
	Well marked, 1	Second	13			
14	Severe, 1	....do....	10	Nov. 26, 1901	1	Do.
15	....do....	....do....	13	Nov. 29, 1901	1	Do.
16	....do....	....do....	16	Dec. 2, 1901	2	Do.
	Fatal, 1	Third	12			
17	Well marked, 1	....do....	12	Nov. 26, 1901	1	Do.
18	....do....	....do....	15	Nov. 29, 1901	1	Do.
19	....do....	....do....	18	Dec. 2, 1901	2	Do.
20	Mild, 1	First	4	Dec. 17, 1901	14	Do.
21	....do....	....do....	11	Dec. 24, 1901	7	Do.
22	Very mild	Eighth hour	[1] 22	Jan. 25, 1901	12	Do.

[1] 82° F.

NOTE.—The subjects of Experiments Nos. 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, and 21 were proved to be susceptible by subsequent experimental infection. No. 22 declined a second test. In Experiments 20 and 21 the same set of insects and the same subject were used. Four of these insects infected this man six days later, on December 30, 1900.

In a letter of August 20, 1901, Dr. Finlay (19) states he was convinced that extension of the interval between the application of the mosquito to the patient, and subsequently to the nonimmune, would develop a severe attack, such as he was anxious to avoid. One can sympathize with the humane feeling that prompted him to forego positive proof of his theory rather than run the risk of producing a severe attack, but it is a fact that on August 22, 1901, two days later than the date of that letter, I saw Dr. Finlay apply to a nonimmune two mosquitoes that had been kept 34 days after contamination. (20)

I have been impelled to look up the literature of this subject because I have seen several times of late the statement of Dr. Finlay that the Army Yellow Fever Commission has tacitly ignored his right of priority. (21) It is too late, after facts have been proved and recorded by others, to claim priority unless one can point to unmistakable evidence, in print, as proof that the facts have been demonstrated and duly reported. In our preliminary report (22) Dr. Finlay has been given due credit for priority in advancing and advocating the mosquito theory. Nothing more is due to him. He states (21) that he had "many years ago discovered that yellow fever was transmitted by mosquitoes," when in reality he simply

assumes that to be the case, and the facts recorded by him do not sustain his claim. (23) He further states (21) that his own work had been singularly misrepresented before the American public, and that "among the facts and conjectures which are attributed to the recent investigators there is scarcely one which had not been asserted, demonstrated, or suggested by me, as the result of my personal experiments and observations." One can only express admiration for this eminent scientist's persistent adherence to his theory, but the unbiased observer, after a perusal of his numerous writings, must agree with us that while he asserted and suggested everything that intelligent reasoning and profound knowledge could suggest, he failed to produce a single case of the disease. Our results have been confirmed by Guitéras with eight cases and three deaths; (24) Dr. Finlay's assumed results have never been confirmed by a single investigator. In our "Additional note" (25) we report among other instances one in which the bites of 14 insects, applied 4 days after contamination, failed to infect, and the 7 remaining alive failed also to infect 11 days after contamination, but on the seventeenth day following contamination the bites of 4 of the same insects produced an attack of yellow fever in "the same individual." During the whole of this time these insects had been kept in a heated room at an average temperature of 82° F. If, as is claimed by Finlay, (26) protection is conferred by one or two bites of "recently contaminated"—two to five days (19)—mosquitoes, this individual, who had received 21 bites from recently contaminated insects, should have been able to resist the bites of 4 of the same insects 6 and 13 days later. Should one accept Finlay's extension of the incubation period to 22 days infection might then be erroneously attributed to the bites inflicted 13 days before the onset of fever.

The Army board worked on an entirely different hypothesis from Finlay, who believed that the infecting agent was retained on the biting parts of the mosquito, that infection was direct, and no interval was necessary. The board worked on the hypothesis that the specific agent of yellow fever was probably one of that group of strict parasites that in nature necessarily pass through two distinct and alternating cycles of development, one within the body of a vertebrate, the other within a blood-sucking invertebrate host. Finlay believed that the bite of a single insect would confer a mild infection and multiple bites a severe one. In my own case, produced by the bite of a single insect, a fatal result was looked for during several days. Dr. Lazear was bitten by a single insect and died.(27) I became so firmly convinced that the severity of an attack depended on the susceptibility of an individual rather than on the number of bites sustained, that on October 9, 1901, at Habana, I purposely applied to a nonimmune 8 mosquitoes (all I had) that had been contaminated 18 days before. The attack that followed was a mild one; the temperature never reached 103° F., and dropped to normal on the evening of the fourth day.(27)

The original theory of Finlay has been variously modified by him from time to time to meet possible contingencies. He now evidently inclines to the belief that development of the germ takes place in the salivary glands of the infected mosquito.(21)

TABLE 3.—*Positive mosquito inoculations of the Army commission.*

No.	Character of attack and number of patients bitten.	Days of disease.	Period in mosquito.	Number of mosquitoes used (room temperature).	Date of application of mosquitoes.	Incubation.	Character of attack.
			Days.				
1	Severe, 1	Second	12	1	Aug. 27, 1900	3 days 7 hours	Severe.
	Mild, 1	First	6				
	Severe, 1	Second	4				
	Mild, 1	do	2				
2	Fatal, 2	do	2–16	4	Aug. 31, 1900	6 days	Moderate.
	Mild, 8	First and second.					
	Severe, 7	First, second, and third.					
3	Fatal, 2	Second	2–15	5	Dec. 5, 1900	3 days 10 hours	Pronounced.
	Severe, 1	do	1–19				
	Mild, 1	Third	2–21				
4	Fatal, 1	do	17	4	Dec. 8, 1900	5 days 17 hours	Mild.
	Severe, 2	Second and third.	18–22				
	Moderate, 1	Third	24				
5	Fatal, 1	Second	19	1	Dec. 9, 1900	3 days 12 hours	Do.
6	do	Third	20	4	Dec. 11, 1900	3 days 20 hours	Moderate; relapse on third day.
	Severe, 2	Second and third.	21–25				
	Moderate, 1	Third	27				
7	Severe, 1	Second	1–24	[1]15	Dec. 21, 1900	3 days 23 hours	Pronounced.
	Well marked, 2	First	10–5 12				
	Mild, 1	do	4–8				
8	do	do	17	[1]4	Dec. 30, 1900	do	Mild.
9	Well marked, 1	Third	39	[1]3	Jan. 19, 1901	4 days	Moderate.
10	do	do	51	[1]2	Jan. 31, 1901	3 days 3 hours	Mild.
11	do	do	57	[1]2	Feb. 6, 1901	3 days 6 hours	Do.
12	Fatal, 1	Second	16	[1]3	Feb. 7, 1901	2 days 22 hours	Moderate.
13	do	Third	1–53	4	Sept. 16, 1901	3 days	Severe.
	do	Second	3–34				
14	Severe, 1	do	18	8	Oct. 9, 1901	3 days 8 hours	Mild.

[1] 82° F.

A complete proof or disproof of his claim of positive results for his recorded inoculations could easily be obtained by means of a series of innocent experiments. It is interesting to note that at the very time when this distinguished authority is in position to confirm the results of his first inoculations, if they are susceptible of confirmation, he takes the ground that inoculation experiments on human beings in Cuba must be strictly forbidden.(21)

TABLE 4.—*Positive mosquito inoculations of Dr. Guiteras.*

No.	Character of attack and number patients bitten.	Day of disease.	Period in mosquito.	Number of mosquitoes used.	Date of application of mosquitoes.	Incubation.	Character of attack.
			Days.		1901		
1	Severe	First	26	1	Feb. 23	3 days, 10 hours	Pronounced.
2	do	Third	19	4	Aug. 8	4 days, 5 hours	Fatal.
3	do	do	19	4	do	3 days, 3 hours	Mild.
[1]4	do	do	20	3	Aug. 9	5 days, 3 hours	Fatal.
5	do	do	24	1	Aug. 13	3 days, 19 hours	Mild.
6	do	do	24	2	Aug. 14	3 days, 21 hours	Fatal.
7	do	do	24	3	do	5 days, 21 hours	Moderately severe.
8	do	do	34	2	Aug. 22	3 days	Severe.

[1] Case 4 had been bitten with negative result 10 days previously by 4 mosquitoes 5 days after they had bitten a fatal case in the third day of the disease. See Case 33 of Guiteras's table, Amer. Med., Nov. 23, 1901, p. 811.

It is unfortunate that Dr. Finlay in his numerous contributions to this subject very seldom gives exact references that would enable one to compare his more recent assertions with his former statements. In regard to his expressed opinion that the great merit of our work consists in our having accurately defined the danger line, beyond which there is a risk of producing severe or fatal experimental cases when nonimmunes are inoculated with mosquitoes whose contamination is more than 10 days old (21), I desire to record my belief, based on experimental observation and on the results obtained by Guitéras, that it is impossible to confer protection or to produce infection of any grade, with an insect that has been contaminated less than a week, and that inoculations with a mosquito contaminated for a shorter period will be absolutely devoid of result. The accompanying tables, compiled from our and Guitéras's cases, afford a substantial basis for the assertion. I deem it a duty to the service to which I belong, to my dead colleagues (Reed and Lazear) and to the profession, to state the facts plainly and clearly. I do not expect that this paper will remain unanswered; nevertheless, I shall decline to engage in controversy and leave the final determination to those who are competent to judge, after they have carefully perused the publications herein referred to.

The mosquito theory has been practically demonstrated by the Army commission and Dr. Guitéras in two series comprising 22 cases in all. The noncommunicability of the disease by means of fomites has been a matter of common observation in certain localities, and has also been demonstrated practically by our own experiments and those of Havard and his associates. Yellow fever, therefore, is not a filth disease, in the strict sense of the term, and filthy accumulations are dangerous in this connection only when accompanied by sufficient moisture to breed mosquitoes under favorable conditions of temperature. Under such conditions standing water is a source of danger, within dwellings or without, and whether dirty or clean, unless it be kept covered or is changed every few days. Yellow fever is a preventable disease; quarantine, if effective, will exclude it, but if the quarantine be evaded and cases gain entrance to a city the disease can be absolutely controlled and finally exterminated by measures directed against the mosquito alone.

Carter (7) has well shown (8) that first cases are not dangerous until after the lapse of a number of days, for, in his experience, persons in direct contact with them for a few days only never developed the disease after being placed in quarantine. This applies only to the first cases occurring in a town or neighborhood. He found that secondary cases did not appear until the expiration of a number of days, varying from 11½ to 29, the average being 18. This interval represents the time necessary for the mosquito, after biting a patient, to become capable of infecting, plus the period of incubation in the person bitten.

The greatest obstacle to the control of this disease is the failure to recognize the first cases when they are not accompanied by black vomit. Some of these cases are so mild in character that no physician would dare to pronounce them yellow fever unless he knew the disease to be prevailing at the time. Susceptible persons visiting the house or living in adjoining houses would be bitten and develop the disease in near or distant localities several weeks later, forming

secondary foci of infection. From these secondary foci tertiary foci would in time develop. The diagnosis of bilious remittent fever, dengue, etc., would serve to cover the earlier cases until the appearance of black vomit, by which time the infection would have become more or less widely disseminated. Such is the history of many outbreaks.

The number of mosquitoes in infested districts can always be appreciably diminished by giving attention to surface drainage and the removal of standing water, no matter how small the quantity or how pure the quality may be. Rain gutters and conduits on buildings should be kept clear and free; cisterns, wells, flush tanks, and other permanent receptacles for water should be kept tightly covered or securely screened; privies and cesspools should be cared for; air vents to cisterns and wells protected by screens, and water should never be permitted to stand in any vessel or receptacle within a building longer than three or four days. Ditches and open drains containing water should be frequently flushed; old cans, crockery, etc., should be removed from the vicinity of dwellings; pools or ponds should be stocked with fish and deepened at the margins or treated with petroleum. As the stegomyia is largely a house-dwelling and a house-breeding insect, these and other similar measures will surely diminish their number and add to the general comfort and protection. In places exposed to yellow-fever infection all fever patients should be protected, night and day, from the bites of mosquitoes by the use of netting and wire screens. Strict quarantine measures, local and general, with the isolation of patients and extensive and thorough fumigation of the localities where they are found will insure suppression of the disease wherever it may appear.

In the suppression or control of yellow fever disinfection, apart from fumigation, is a waste of time and money. Natural yellow fever is transmitted by the mosquito, and always and only by the mosquito. The harmlessness of fomites has been fully demonstrated by our experiments in 1900 and 1901, in which three young Americans slept for 20 consecutive nights in a room garnished with articles soiled with black vomit, bloody fecal discharges and urine from fatal and other cases of yellow fever. Three and four large boxes were packed and unpacked with these articles night and morning by these nonimmunes, who suffered no disturbance of health from these exposures. The room was 20 feet by 14 feet, double walled, tightly ceiled, heated to above 90° F. and dark. Water was always present to keep the atmosphere moist. Two other nonimmunes then occupied the room for 20 nights while additional articles of bedding and clothing were added. They slept in the garments and between the sheets that had covered cases of yellow fever, some of which were fatal. The result of this second exposure was nil. A third attempt was then made with two additional nonimmunes equally without success. Not the slightest indisposition followed close and intimate contact with this repulsive material in any case. Temperatures and pulse rates were recorded at regular and frequent intervals. Four of these seven nonimmunes were subsequently infected by blood injections and by means of infected mosquitoes. A fifth resisted the mosquito once (28) and declined further attempts at inoculation.

Yellow fever has been eradicated from Habana, one of its endemic homes, by the institution of measures directed against the mosquito,

after extreme cleanliness and energetic disinfection had proved a dismal failure. Several cases subsequently imported into that city have been handled with impunity by guarding the patients against the bites of those insects. A small outbreak in Santiago de las Vegas in 1901 was promptly suppressed by Col. Gorgas by the use of mean directed only against the mosquito. On those who decline to accept such evidence must rest the burden of proving that the disease is transmitted in some other way before their position can be sustained.

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(11) Finlay: Ibid., pp. 362 and 369; also Edinburgh Med. Jour., Oct., 1894, p. 334.
(12) Proceedings of the International Congress of Hygiene and Demography, Budapest, 1894, p. 702.
(13) Edinburgh Med. Jour., vol. xli, 1 pp. 523 to 526.
(14) Finlay: Amer. Jour. Med. Sci., n. s., vol. xcii, 1886, pp. 402, 403.
(15) Footnote to p. 369, Revista de la Asociacion Medico-Farmaceutica, Havana, Feb., 1902.
(16) Medical Record, N. Y., Feb. 9, 1901, p. 203.
(17) The Journal A. M. A., April 13, 1901, p. 1041.
(18) Ibid., Feb. 16, 1901, p. 439; 3d conclusion.
(19) Medical Record, Aug. 31, 1901, p. 344.
(20) Case 8 of Dr. Guiteras' series, Amer. Med., Nov. 23, 1901.
(21) See reprint, p. 8, on "Method of Stamping Out Yellow Fever, Etc.," by Dr. Charles Finlay, M. D., Conference of State and Provincial Boards of Health, New Haven, Conn., Oct., 20, 1902, and Medicine, Detroit, March, 1903, pp. 175, 179.
(22) Phila. Med. Jour., Oct. 27, 1900.
(23) Sternberg, Amer. Jour. Med. Sci., new series, vol. cii, 1891, p. 627, and Nuttall, Johns Hopkins Hosp. Reports, vol. viiii, 1899–1900, p. 27.
(24) Amer. Med., Nov. 23, 1901.
(25) The Journal A. M. A., Feb. 16, 1901.
(26) Finlay: Edinburgh Med. Jour., Oct., 1894, p. 335.
(27) The Etiology of Yellow Fever, Amer. Med., Feb. 22, 1902, Case 2.
(28) Case 22, Table 2.

Chapter 2.

REMARKS ON EPIDEMIC OF YELLOW FEVER IN BALTIMORE.[1]

By James Carroll, M. D., surgeon United States Army, Washington, D. C.

Mr. President and gentlemen of the alumni association: Instead of a strictly technical theme, I have chosen one that may be of more general interest, and which formerly demanded the attention of two of the most brilliant minds among the early teachers of the university.

Dr. Nathaniel Potter, a former pupil of Dr. Benjamin Rush, and afterwards the first professor of theory and practice of medicine in the university, held in 1793 that yellow fever was not contagious, and he communicated this opinion to Dr. Rush in writing. According to his own statement, he believed that he was the only person in America who held that opinion, and in 1795 he prepared to defend his belief in an inaugural thesis to be read at the next commencement of the University of Pennsylvania, of which he was a student. He was dissuaded by Dr. Wistar on the grounds of propriety and expediency. Dr. Potter states that in 1797 Rush's contention that the disease was contagious was first publicly attacked by Dr. John B. Davidge, one of the founders and the first professor of surgery and obstetrics in this school, whose paper was published in the Federal Gazette, of Baltimore, on the 30th day of November, 1797. Dr. Davidge subsequently enlarged his paper and embodied it in a volume entitled "Physical Sketches," published in Baltimore in 1814. On account of the importance of this city as a seaport, in almost constant intercourse with the West Indies, yellow fever must have been introduced a great many times, yet the only important epidemic outbreaks of the disease took place in 1794, 1797, 1800, and 1819. It is notable that all the outbreaks began at Locust Point, or about the docks and wharves, and they can be traced directly or indirectly to the shipping. The relatively high ground upon which the city stood, and the distance from the city proper to the wharves and shipping, explain why the interurban residents suffered but little, while those living upon the poorly drained, low-lying districts near the river were compelled on such occasions to flee for safety.

It can be easily shown that yellow fever was frequently confounded with malaria; indeed, it was strongly contended that the two diseases were one and the same, the difference being only in the degree of intensity. Then, while many contended that the disease was imported, and though their contentions could be supported by sworn testimony, there were others among the leaders and teachers in the profession who held, with Rush, that since the infection was most prevalent in poorly drained localities, the water and decomposing vegetable matter must be necessary for the generation of the poison, which was manifestly conveyed through the atmosphere. The

[1] The Hospital Bulletin, University of Maryland, Feb. 15, 1905.

general restriction of the disease to the localities described, the observation that many persons who visited those localities for only a few hours became infected, while in other localities no infection took place, even among those who were intimately associated with the patients, proved the disease to be one of locality. With the observation that if the wind blew strongly from the direction of the infected locality toward the city, that within a few days the disease also extended toward the city, it was concluded, with reason, that the poison must exist in the atmosphere, that it was transported by the winds, and that infection could only result from the inhalation of this poison, which was believed to be gaseous in nature. This agreed with Sydenham's theory of the epidemic constitution of the atmosphere, which was supported by Rush and his pupils, and which then seemed to offer the only explanation of the recorded observations of centuries. If we admit the mosquito as the sole carrier of the disease, we will be prepared to acknowledge that their observations were, in the main points, strictly accurate; that their reasoning was logical, and the deductions fully justified by the premises. It then becomes very easy to understand how the disease became one of lowly situated and poorly drained localities; how it was transmitted by the atmosphere; how it failed to spread in certain locations; and how it disappeared upon the appearance of a heavy frost. The observation was actually recorded by a Baltimore physician that during the epidemic mosquitoes became an intolerable pest, while but a short time before no mosquitoes were observed.

How beautifully this observation agrees with our present knowledge that the yellow-fever-carrying mosquitoes can be conveyed on vessels; that in the warmer season of the year they will multiply on shore, gradually extending from house to house, breeding in and about the dwellings (for they are domesticated insects), and that they become infected only after feeding upon a patient. The importation of the mosquito explains the appearance of this insect in places where it usually does not exist; it explains the occurrence of the earlier cases among persons who either visited the vessels or wharves or docks, or who lived in the vicinity of them. It also explains why favorable localities were visited by the infection only, as a rule, when they received shipping; while localities equally favorable to the infection, but far from the shipping, remained free from it. Of course, the absence of the proper mosquito explains the failure of the disease to spread to any extent in the city proper. This stood upon ground that was high and dry, and it was at that time some distance from Fell's Point, the location of Sugar House Wharf where many of the vessels from the West Indies probably made their landing. Assuming that at the Sugar House Wharf cargoes of sugar were unloaded, we are reminded that sugar is a favorite food for the yellow-fever mosquito, and that it can subsist on this and water alone for months. Now Sugar House Wharf was at Fell's Point, and most of the outbreaks began at Fell's Point, where, presumably, the largest number of mosquitoes was imported.

During the epidemic of 1794, 360 deaths were recorded. Dr. Drysdale reported[1] that he saw his first case just before death on the 7th of August, at Bowley's Wharf, in the town, and on the 14th,

[1] The Philadelphia Medical Museum, 1805, I 26. Letters written by Dr. Drysdale to Dr. Rush.

20th, 22d, and 23d of the same month he saw five additional cases at the same part of the wharf. There were also at the same place some other cases which did not come under his care. Dr. Drysdale states that there was considerable sickness at Fell's Point after the death of his first case, and many deaths had occurred suddenly, or after a short indisposition. An investigation was made by three of the most respectable physicians, who reported that the prevailing fever was the common epidemic of the season which visited the Southern and Middle States annually, viz, the bilious remittent fever. The number of cases now rapidly increased, so that by September 25, in about seven weeks, five physicians were attacked and two of them died. The cases had become so numerous that Dr. Coulter visited and prescribed for more than 120 persons daily. By the end of the month many families had sought refuge in the country. During this time the city remained unusually healthy, and although some persons infected at the Point died in the city proper, in that location the disease failed to spread.

In his ninth letter of a series to Dr. Rush he states that yellow fever was first discovered at two points, remote from each other, viz, at Bowleys Wharf in the town, and at Fells Point. Many cases occurred throughout the town, but these originated either from communication with Bowleys Wharf or the Point, and the infection could be distinctly traced to one of those two places. Being puzzled to explain why the infection was confined to those two places, he found that the first cases on the Point were confined to houses whose cellars were filled with stagnant, putrid water, and he also found black, putrid, and offensive water beneath the stores in which the sick resided at Bowleys Wharf. Almost all those who were first affected were newcomers. Dr. Drysdale describes the Point as being low and flat; its streets generally not paved; its alleys filthy, and the ground around it marshy in many places. The frequent warm rains kept the noxious places constantly moist under a hot sun. We can easily recognize these as conditions favorable to the multiplication of mosquitoes, and the domestic habits of the *stegomyia* mosquito would tend to keep the infection rather closely confined to these localities. He further makes the significant statement that remittents were present from a very early period. It is more than probable that many of these remittents were true yellow fever, because under the belief then prevailing, that these were simply the prevailing types of summer fever, they would not be reported. It is also probable that if occasional cases were known to have been yellow fever, some physicians would have concealed them from the same motives that prevail to-day. He could discover no satisfactory evidence of the importation of the disease, though he states that the *Triumph* arrived at the wharf about the last of June, with almost all the crew indisposed, and previous to this there lay at the wharf a schooner whose captain had died on the voyage from the West Indies. The fact alone, however, that vessels from the West Indies came up to the wharf is sufficient to indicate to us the source from which the infection was received. The following sentence toward the end of the ninth letter is of extreme interest: "Locusts were not more numerous in the reign of Pharaoh than mosquitoes through the last few months; yet these insects were very rare only a few years past, when a far greater portion of Baltimore

was a marsh." With wonderful acuteness of observation he remarks that some families at the Point avoided yellow fever by carefully precluding all communication with the sick, and that vessels also preserved their crews in health by removing to a distance from the wharf and preventing the sailors from going ashore. As soon as one infected person came on board he quickly infected all or most of the crew. He instances one man who contracted the disease on shore and carried it on board the ship *Phoenix*, whose crew was healthy. These all became infected and 5 out of 12 died. As the result of these observations he very naturally concluded that in some instances the fever proved contagious. These, and other cases cited, are now so easily explained by the mosquito theory that we can not appreciate the perplexity of the problem as it formerly presented itself for solution. The most accurate and careful observation yielded results that were apparently contradictory. All honor to Dr. Drysdale, whose tenth and last letter of the series was written to Dr. Rush in December, 1794.

Some further interesting references to this epidemic were published by Dr. John B. Davidge in 1798 and subsequently rewritten by him in a treatise on yellow fever, published in 1813. He makes the interesting statement that the yellow fever first appeared in the last of August, but the common bilious fever prevailed at Fells Point from June. A lady from Philadelphia was attacked with yellow fever, on Charles Street, and she had black vomit, but no other person in the family or neighborhood was attacked during the whole season. He noted that the disease extended in the direction of the prevailing winds, and that it was conveyed by a northeast wind all along Federal Hill and the west end of the basin. A considerable number of cases occurred in the city and many who had attended the launching of a frigate (near the water, of course), subsequently suffered from yellow fever, and several of them died, but no single person in the city contracted the disease from them.

Concerning the prevalence of yellow fever in Baltimore at that time (1798), Dr. Davidge writes:

> A physician in conversation the other day told me that he had met with the yellow fever in Baltimore ever since he had lived there, which is 15 or 20 years. It is violating all obligations of decency and truth to say that it is of recent date.

This statement was probably correct, for every importation of the disease is not necessarily followed by an epidemic. In Baltimore and other places where the mosquito, *Stegomyia fasciata*, is not normally present, an epidemic is not possible, after the introduction of any number of cases, provided the mosquito be absent. For the production of an epidemic the introduction of infected mosquitoes alone during the hot season may suffice, because the mosquitoes deposit their eggs, and in a week or 10 days another brood will have become mature. The insects of this new brood must bite a patient in the first three or four days of the attack in order that they may become infected. Should only one or two infected insects be brought in and should they die (as frequently happens) immediately after depositing their eggs, then the disease would appear only in the persons first bitten by them, and these would have passed beyond the infective period by the time the new brood had matured. Should the infected insects, however, have remained alive, and should they have bitten other persons, at intervals of a few days in succession,

these persons would be in the proper stage of the disease at the maturing of the new brood to enable them to become infected. When the proper mosquito has been previously introduced into a favorable locality in the proper season, or when the mosquito, *Stegomyia fasciata*, is naturally present, the introduction subsequently of a single case may produce an epidemic. The facts above stated will readily explain the frequently reported appearance of sporadic cases without the occurrence of secondary ones.

We can now see that the immunity against the disease enjoyed by the city proper evidently depended upon its high and dry location, which rendered the conditions unfavorable for the multiplication of the mosquitos that were imported. In this regard Baltimore was more fortunate than Philadelphia, which was lower and contained more standing water. Hence, the mosquitos were more abundant and the disease spread uniformly. This led Dr. Rush to contend that the disease must be contagious, while Dr. Davidge held that the contagion was local, and existed only in the air of certain spots, from where it might be wafted by the winds in any direction. Dr. Davidge asserted (p. 84) that they had the most stubborn and irrefragable proofs, in those cases occurring about the wharves and at Fells Point, that the disease was incapable of supporting itself. When these cases were removed up into the city their virulence died with them, those who died; and, he writes, "from those who recovered, all mischief and supposed contagion evanesced into empty air, which bore it to the pages of medical writers, and not to the bodies of healthy attendants. This was the result in 1794 and 1797."

The importance of this observation can hardly be overestimated; it shows the sagacity and care with which the epidemic was studied by these devoted men. Dr. Davidge learned the truth, and that truth unfortunately still remains to-day a hidden mystery to many of our practitioners, notwithstanding the recent absolute demonstration of it beyond a shadow of a doubt.

In connection with the now known mosquito propagation of the disease, an observation recorded by Dr. Nathaniel Potter [1] in this outbreak of 1797 deserves mention. He tells us that previous to the 17th of September the fever had been confined to certain places and to such as had breathed the air evolved from them; on that day a strong southeast wind wafted the effluvia in a northwest direction and diffused it among the inhabitants of the upper parts of Frederick, Gay, South, and Calvert Streets, who became immediately implicated in all the horrors of the fever.

In 1800 there appeared the severest outbreak the city has known. The mortality from yellow fever is recorded to have been 1,197, or about 1 in 50 of the population of 60,000. Again the disease began at Fells Point, on the borders of the cove, which extended from Jones Falls to the interior. The faculty of medicine of the city, after investigation, reported to the mayor that in their belief the disease was not imported, but originated in the cove from the stagnation and putrefaction of filth under a summer's sun. The first two cases appeared on the 2d of May,[2] another on the 8th of June, one on the 9th, 10th, and 13th; then from the 22d they became more numerous.

[1] Memoir on Contagion, by Nathaniel Potter, M. D., Baltimore, 1818, p. 20.
[2] Medical Repository, New York, 1801, vol. IV. p. 351.

It is unfortunate that we have no detailed description of this epidemic, the most disastrous the city has ever experienced.

A few cases are reported for the years 1802–1805.

The next important outbreak took place in 1819 following the arrival of an infected ship from Habana.[1] In a letter to the editors of the Medical Repository, Dr. Pierre Chatard,[2] of Baltimore, writing October 19, cites the first cases as follows: The fever commenced raging at Fells Point in the beginning of July, and never ceased there until the end of October. It appeared also at Smith's Dock toward the end of July, carrying off five persons whose names are given, and others. The persons named had countinghouses on the dock or in the vicinity. No other cases appeared at the dock for two months, at the end of which time two more appeared. Dr. Chatard attributes the absence of cases during this time to the great quantity of lime that had been strewn on the ground by order of the mayor. The lime was again applied and the cases ceased. At Fells Point the disease raged for three months before it subsided. The greater part of the population retired to the healthier portions of the city, and many of them sickened and died there, but none of their friends or relatives suffered in consequence. We are told by Dr. Chatard that the epidemic focus on the Point never exceeded seven or eight thousand square feet. This information he regarded as precious because it demonstrated the noncontagiousness of the disease and the value of a local quarantine.

Among the most interesting records of this epidemic are the letters and other documents published by authority of the mayor in 1820. These contain the actual opinion and experiences of the physicians, and they show a remarkable unanimity in the belief among the Baltimore physicians that the disease was noncontagious. The persistency with which the infection originated and remained in the vicinity of shipping, wharves, etc., is generally commented on. Dr. Clendinen reports that his first cases were located at the southeast corner of Fells Point, and several of them appeared among foreigners on board the shipping, persons who had been healthy previous to their arrival. This invasion by the disease of healthy ships tied up to the wharves appeared to be indisputable evidence of the poisoned condition of the atmosphere. Of course it is hardly necessary to say here that these vessels were simply invaded by infected mosquitoes. Dr. Clendinen was a resident of the Point, and he states that his family had suffered from the disease and he had lost a student, an assistant physician, and some of his best friends. Dr. Samuel B. Martin, after enumerating 34 of his earlier cases, with their location about the wharves and shipyards, states:

> These will suffice, I think, to show the course the disease took in its commencement, traveling regularly along the course of the water and infecting the streets in the vicinity thereof. My most violent cases were near the water's edge or contracted there.

No mention of this epidemic would be complete without a reference to the little book by Dr. David M. Reese, entitled "Observations on the Epidemic of 1819," a book which every one interested in the subject should read. According to him, some persons attributed the epidemic to the arrival of the schooner *Adventure* from the West

[1] Carpenter on Yellow Fever, New Orleans, 1844, p. 18.
[2] Medical Repository, New York, vol. 20, 1820, p. 261.

Indies, laden with coffee, while others looked with suspicious eyes upon the schooner *Proserpine* laden with hides and coffee. Both vessels were ordered to the quarantine ground, but were soon permitted to return because, after a reexamination by the health officer, their cargoes were found to be in a sound condition.

Referring to the time when 1,016 cases had been reported by the physicians, Dr. Reese states that of all of these only 12 were supposed to have originated in the city. He calls attention to the remarkable fact that, in almost every instance where a person visited the Point at night the contracted they disease, while those who were there only in the daytime escaped with impunity. He further remarks that those of the Baltimore physicians who became infected suffered in consequence of paying a visit by night to the source of infection, or to the vicinity where the cause existed. Several physicians who had attended patients in the daytime in the very center of the infection, and through the whole course of the fever remained exempt until by visiting the district once in the night they contracted the disease. This accords perfectly with the mosquito theory and with the twilight habits of *stegomyia fasciata*, the particular mosquito now known to be concerned in the transmission of the disease. It is also in accord with the experience of the American troops near Habana. Soldiers who visited the city only between the hours of 9 a. m. and 4 p. m. remained free from the disease, while among those who became infected there were but few who did not acknowledge having spent a night or a part of a night out of the barrack. Let us now consider what evidence, if any, collected by these closely observant Baltimore physicians could be used to support the mosquito theory to-day. Firstly, they recorded the presence of an unusually large number of mosquitoes; secondly, they observed that the infection was localized in the low, wet districts near the river and shipping; thirdly, they noted that the infection was contracted mostly at night; fourthly, they showed that in the higher and drier ground of the city proper the disease was absolutely noncontagious; fifthly, they reported that the disease traveled in the direction of the prevailing winds, when these were strong and blew in one direction; and, sixthly, they were familiar with the fact that yellow fever was most apt to prevail when the mean temperature was high, and they knew perfectly well that the disease was stamped out by the frost. To this we can add nothing more than the direct implication of the mosquito.

Of course, a mistake was made in the failure to recognize the imported nature of the disease, and strong protests were written against the quarantine methods then in force against Baltimore by Philadelphia, Wilmington, and other places. These quarantines were established in the belief that the disease was contagious. The Baltimore physicians, having the strongest proofs that it was not, felt that they were treated with undue severity. In a low-lying city like Philadelphia, where mosquitoes were numerous, there was justification for the belief in contagion, so that, while both were partly wrong in their opinions, under the circumstances the method of quarantine was a justifiable and proper one to adopt for their safety. On the other hand, the lax quarantine system at Baltimore was a source of danger; still it was justifiable on the ground of the available evidence to show that yellow fever was not contagious and upon the belief then prevailing that all infectious fevers were the result

of putrefaction. Hence, if a vessel were clean and her cargo in good condition, it was assumed that she could not harbor the seeds of the disease and she was permitted to come into dock and unload.

In the management of the epidemic the wise policy was adopted of advising all persons to flee the infected location and seek a residence upon high ground without the range of the infection. This the majority did, many going to the country or remaining nearby, while some refused to leave their habitations, and these latter furnished the fuel for the continuance of the pestilence. This epidemic is said to have cost the city 350 lives.

The kindly concern shown for the welfare of the destitute poor stands out brightly in the history of this outbreak. It became necessary to remove the healthy poor from Fell's Point and provide means of shelter and sustenance for them until it was safe for them to return. A committee was appointed who visited a Mr. Owen Dorsey to solicit the use of a ropewalk owned by him. This was granted free of charge and the removal began. More room was soon needed, and a Mr. Christopher Chapman gave up another adjacent ropewalk, 1,000 feet long, for the purpose. This was not sufficient and more than 100 tents and marquees were then pitched and filled. Over 1,000 persons were received, made comfortable, and supplied with provisions and every necessity. The corporation appropriated $1,000, but this was returned, the donations of money and supplies being ample for all purposes. Notwithstanding the partial depopulation, business depression, failure of some of the leading commercial houses and one of the banks, over $4,000 in cash were contributed and liberal donations of food, clothing, etc., poured into the warehouses designated to receive them. The neighboring farmers contributed flour, fruit, and vegetables as well as money, and Georgetown, D. C., contributed $700. A soup house was established at the encampment, and this supplied over 100 gallons of rich, wholesome soup daily. This enterprise was undertaken by three energetic gentlemen—Messrs. Stewart, Mosher, and Coale—and through voluntary contributions of material and labor the total outlay required was only $10. The camp was maintained for 53 days, and when it was broken up, on the 25th day of October, each person was supplied with provisions for three days. There were only six deaths in the encampment and five additional in the hospital of persons who contracted the fever at the Point and were carried from the camp to the hospital for treatment. The sick among the poor were cared for at the hospital at the expense of the city. Food, luxuries, and stimulants were provided for distribution upon the order of any practicing physician. It is estimated that by these means several hundred lives were saved, and the record is one of which Baltimore should be proud. The mayor, Edward Johnson, was a man of Christian character, high courage, and strong determination. Disregarding protests, the mayor and many of the board of health visited the hospitals during the height of the epidemic, and by their example inspired others with confidence in the noncontagious nature of the disease. Dr. Reese wrote of him:

> Mr. Johnson is one of the few individuals with whom, when interest and duty are in opposite scales, the latter will ever predominate.

After this disastrous epidemic a few cases occurred annually until 1805, and perhaps later.

Ten cases are reported to have appeared at Fort McHenry in 1868, and the disease was believed to come from infected vessels in quarantine near by. It is probable, as has been stated by Dr. John Morris,[1] that sporadic outbreaks were frequent at Fells Point until 1855. In this year Dr. Kemp, of the board of health, had the infected district drained and cleaned. It is said to have been free from the disease from then until 1876 (except during the suspension of commerce during the Civil War), when a small outbreak of the fever undoubtedly appeared, though the cases were not officially reported.[2]

In this review of the epidemics at Baltimore, the literature of which is very scant, I have confined myself to a simple narration of the facts which seem to be of general interest, and I hope that some of you may be stimulated to read for yourselves the records written by men of this city, some of whom were teachers in our university and of whom you have every reason to be proud.

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[1] History of the Epidemic in Baltimore in 1876. Reports of American Public Health Association, Vol. IV, p. 244.

[2] Baltimore Physician and Surgeon, Vol. VI, No. 2, 1876, p. 37.

Chapter 3.

YELLOW FEVER: A POPULAR LECTURE.[1]

By James Carroll, M. D., assistant surgeon, United States Army.

Yellow fever, or yellow jack, as it is more familiarly called, is so far as our knowledge goes, strictly an American plague or pestilence, and our earliest authentic accounts of this disease record its occurrence in the West Indies at the middle of the seventeenth century. By one or two of the older writers it is reported to have been transported there from Siam, but this seems unlikely, because yellow fever has never been shown to be an oriental disease. Before the time of Sydenham, oriental plague, typhus fever, smallpox, cholera, pernicious malaria, and yellow fever were all called putrid or pestilential fevers; it was believed they were due to the same cause and that they were transmitted through the atmosphere as visitations from God. At that time the science of medicine stood upon such a low plane that the best English physicians were just beginning to learn that there were differences between measles and smallpox, typhoid fever or typhus fever, and malaria, etc. Harvey had only recently announced the circulation of the blood and Malpighi had followed him with a demonstration of the blood corpuscles in the smaller vessels (capillaries) uniting the arteries and veins. Peruvian bark, that blessing in malarial fevers, was barely known at the time when yellow fever first prevailed at Barbados, Jamaica, Santo Domingo, and Martinique, and later at Vera Cruz. In 1761 the disease was carried from Vera Cruz to Habana by the Spaniards, who lost 3,000 persons from it in that year alone, and in 1780, out of an army of 8,000, about 2,000 died of yellow fever within two months after landing at Habana. It is further reported that in 1794 there were over 1,600 victims to yellow fever in the Spanish garrison and squadron at Habana. More recently, for the 10 years from 1870 to 1879, inclusive, 11,746 deaths are recorded for the city of Habana from yellow fever alone. Spain paid dearly for the Pearl of the Antilles in both men and treasure, for, besides decimating her troops in Cuba, the disease followed them across the Atlantic and appeared in epidemic form in various cities of the Peninsula from time to time.

The fearful mortality attendant upon this disease is well brought out in the accounts of some of these epidemics. For instance we are told by an English physician, Dr. O'Halloran,[2] who studied the epidemic in Barcelona in 1821, that the general hospital received 830 patients suffering from yellow fever, and of these no less than 749, or 90 per cent, died. This keen observer contends the disease can not be contagious, but is due to some local infection of the atmosphere, and in support of his contention he cites numerous instances during the out-

[1] Delivered at Galveston, Tex., Apr. 12, 1905, under the auspices of the University of Texas. Reprinted from American Medicine, Vol. IX, No. 22, pp. 907-915, June 3, 1905.

[2] Remarks on the Yellow Fever, by Thomas O'Halloran, M. D., London, 1823.

break referred to, showing the disease was not and could not be directly contagious, because during the epidemic thousands of persons fled from the city to the country, including those who had slept with, nursed, and been intimately associated with the sick, traveling in many instances in the same carts or carriages that had been used for the transportation of patients, and even the dead, and after carrying with them the personal effects of those who had died of the disease. Still, no other cases followed in the districts to which these people fled and the evidence appeared to be indisputable that the disease spread by contagion in certain localities within the city or its environs, and the conclusion was arrived at that the contagion could not exist in the country, but originated de novo in certain localities in the cities, as a result of peculiar atmospheric and local conditions. It was observed that the nuns of the general hospital who were thrown into frequent and direct contact with the sick escaped the disease, while in the convalescent hospital the president, the head apothecary and the superintendent, none of whom had ever entered the rooms of the sick, and who had taken every precaution not to communicate with the sick nor with anything belonging to them, all fell ill. Of course, now that we know that natural or nonexperimental yellow fever can only be contracted through the bite of a contaminated mosquito, it is quite clear that the presence or absence of the disease in certain localities means simply the presence or absence of contaminated mosquitos. As we view the subject now, the yellow fever mosquito was brought to Spanish ports by vessels coming from Habana, and being a house mosquito, it multiplied in those cities during the warm season. It was then at hand to receive and transmit the infectious agent whenever it encountered cases of the disease, and these were frequently imported. Upon the appearance of frost the mosquito went into hibernation and the epidemic promptly ceased. As the insect was an imported one it was not present in the country districts, consequently there was no extension of the disease from patients treated there, and in the cities the epidemic could only spread where the proper mosquito chanced to be present. The introduction of the mosquito alone can have no ill effect unless it has previously bitten yellow fever patients, and in like manner, sufferers from yellow fever are absolutely harmless to others unless they are bitten by the proper mosquito.

As Dr. Howard, no doubt, told you last year, the female mosquito at certain periods in her existence experiences a physiologic need for blood. The hemoglobin of the blood seems necessary for the maturation of her ovums, and she will not deposit her eggs until she has obtained a meal of blood. The male insect can not transmit yellow fever, because, having no need for it, he never sucks blood, and while his proboscis will provide him with fruit juices, it will not penetrate the animal skin. The mysterious movements of the disease, passing from house to house, even at times when there had been no communication between the inhabitants; the remarkable immunity enjoyed by some groups of persons who were equally and fully as much exposed as others who were decimated by its ravages; these, as well as the peculiar way in which the infection clung to dwellings and ships, invested it with a mystery that puzzled physicians for centuries, and remained totally unexplained until the demonstration of the mosquito theory within the past five years. Even to-day, in our own country, where the results upon which it is based were first

published, the mosquito theory of the transmission of yellow fever still has many opponents, and some of its supposed friends are very weak-kneed and seem still to be looking for evidence that would justify them in deserting it. It is painful to read, in one of our most prominent and influential daily newspapers, the letters emanating from a well-known writer upon the subject of yellow fever, who a few years ago was looked up to as an authority and wrote for standard professional works, but who is now damaging his own reputation and retarding progress by asserting that the mosquito is not the sole medium for the transmission of this disease. It does not seem to have occurred to this widely known and most interesting writer that the burden of proof rests upon him, and that he should either remain silent or be prepared to prove by actual demonstration that there is some foundation for his claim. I take the liberty here to suggest to the paper in whose interest this writer was sent to Cuba, that it could hardly invest a few hundred dollars more profitably than to enable this gentleman to furnish the necessary evidence in support of his statements, if such evidence is obtainable, as it certainly should be if his assertions are well founded. Who would think to-day of advancing the old theory that malarial infection is contracted in any other way than through the bite of the mosquito? No one who is familiar with modern ideas on parasitology would entertain the idea for a moment, and there is no more ground for assuming that yellow fever is transmitted in any other way than there was formerly for entertaining that opinion in regard to malaria. In your own State during the last two years you have had abundant evidence of the power of measures, based upon the mosquito theory alone, to suppress this disease, even when that theory met only half-hearted acceptance. Do not understand me as intending to reproach those hesitating nonbelievers who were so slow to move; on the contrary, I sympathize with them and with their refusal to conform their ideas to all the new theories that were being constantly advanced, then denied, contested, and recontested with every reappearance of the disease.

But let us return again to the scenes enacted, and the conditions found, where the disease has prevailed in the past. Dr. O'Halloran, in summing up after studying the epidemic at Barcelona, calls attention to the House of Charity, a clean, well-ventilated building in the noninfected part of the city, and which was occupied by more than 1,100 persons during the height of the epidemic. These persons, men, women, and children, went out daily into various parts of the city, some visited the sick and entered the houses of the dying and the dead. Among all this number, only 2 contracted the disease. These were treated in the Seminario Hospital, where 1 recovered and the other died. The one that recovered was at once returned to the House of Charity, where she mingled with the other inmates; still none of them was affected. He then says:

> The foregoing is a true report, and may be regarded as an important one. Had the House of Charity been situated in the eastern extremity of Barcelona, or in Barceloneta, where the epidemic cause existed to a high degree, the destruction would have been in all probability great; but as the cause did not extend, or only in a very inferior degree, to that part of the city in which the House of Charity stands, the cause of the nonpropagation of the malady is easily accounted for. This case strongly tends to prove that the yellow fever will not multiply except where an epidemic cause exists in force; and it moreover proved that the disease is not contagious.

Further on, in speaking of the Casa Miserecordia, or House of Pity, he states:

> The building is low, but the apartments are spacious and well ventilated. It contained 150 girls during the rage of the epidemic. The nuns who teach them are 24 in number. They maintain themselves by washing, ironing, and other similar modes of occupation. They employ women to traverse the city from house to house to procure needlework, etc. These women went to all parts of the city; they communicated indiscriminately with the inhabitants, and they were not affected by the disease, nor did the nuns or girls suffer by communicating with them. This is a singular fact, and a strong one. It appears strange that a disease which was said to have been imported from Habana into Barcelona, from Barcelona to Intosa, and from thence to Asco, Mequinenza, Malaga, etc., could not be introduced into the House of Pity through numerous channels of communication.

Again, speaking of the House of Correction, a three-story stone building, in which were located 100 females during the epidemic season, he asserts:

> Nine of them were attacked with the reigning malady; 4 of them had been recently admitted as having committed some irregularity in sickly Barceloneta. They were all removed to the Seminario Hospital, where 4 died; the remaining 5, when cured, returned to the House of Correction; they communicated freely with the others, but no disease ensued. This house was visited daily by some of the female inhabitants of the city, who, through charity, brought eatables, etc., but without detriment to the inmates.

Had this been a contagious malady, the persons who returned to the House of Correction after being cured in the Seminario Hospital, which was then the seat of pestilence and of death, and to which hundreds were sent to die, could scarcely have failed of communicating the disease to the numerous females who had intercourse with them at all hours of the day.

Of 50 persons who were constantly employed burying the dead, only 2 died, although they communicated freely with the inhabitants of the city in the nighttime.

Later he mentions the lazaretto called Marine, a mile to the east of Barcelona and within 150 yards of the sea. It was opened for the sick on August 7; 79 sick were admitted, of whom 58 died; 32 persons were employed in various duties of the establishment as doctors, friars, servants, and washerwomen, and not one of them took the disease. Of the above number, 6 were employed in burying the dead, and 3 in washing the bedding. After this establishment was broken up, 5 women remained in it, employed in washing the bedding of the Seminario Hospital, but without being affected by the disease.

In his conclusions, he finally observes in discussing the epidemic:

> Its fatal and malignant nature in unventilated places; the exemption of parts of the city from its influence, when no precautions were taken; the sickening of persons who observed the strictest seclusion; the sudden impression of contaminated air on persons recently from the country, without communication with the inhabitants of the city; the greater exemption of nurses and other attendants on the sick from the disease, than those who were simply exposed to the contaminated air of sickly houses; the almost absolute exemption of washers of bedding, clothes, etc., which had recently been used by the sick; the circumstance of the attendants in the hospitals and lazarettos having generally escaped the impression of the malady; the impossibility of diffusing the disease in the country, where no epidemic cause existed; and, finally, the death of some hundreds of persons who communicated with Barcelona, and who sickened in the neighboring villages and country houses without a solitary instance of its affecting the most assiduous of its attendants, however circumstanced, are ascertained facts and convincing proofs of the noncontagious nature of the yellow fever.

The evidence that Dr. O'Halloran offers in support of his contention that yellow fever is not contagious is most conclusive. After

reciting the appearances found upon dissecting the bodies of those who had died of the disease, he publishes a letter written by Dr. Salvador Campmany during the following year. Dr. Campmany was in charge of the Virreina Hospital at Barcelona during the outbreak of 1821, when, between September 1 and December 20, this hospital handled the bodies of no less than 8,649 persons dead of yellow fever. O'Halloran states that Dr. Campmany was at first of the belief that the disease was contagious, and when he began to take care of the sick he wore an oilcloth dress. The letter is so interesting that I shall give you the last paragraph verbatim.

> The above sketch does not afford grounds for argument as to the contagious or non-contagious nature of the disease. I shall only state that out of 30 persons of all descriptions who were destined to assist the sick not one took the disorder. The nurses continually communicated with the sick. When delirious patients escaped from their beds the assistants had to take them on their shoulders and replace them in their respective quarters. On the opening of the bodies the anatomists, in my presence, involuntarily cut their fingers and hands, and not one was inoculated with the yellow fever. When the gravediggers carried the dead bodies to the church yard they had to handle them a great deal before throwing them into the pit, and not one suffered in his health. In short, not an individual employed in the lazaretto either took the disorder or was infected by those who were sick of the yellow fever.

One could scarcely desire more complete confirmation than this of the subsequent demonstration, almost 60 years later, by the army board, of the noninfectiousness of the clothing, bedding, and dejecta of yellow fever patients.

These were the opinions in 1823 of an observer who had seen and himself suffered from yellow fever in the West Indies some years before. Others, however, who were equally qualified to observe, insisted, and advanced evidence to show, that the disease was imported and that it was contagious. In short, the same differences of opinion and the same dissensions among the highest authorities in regard to this disease prevailed then as before and since, even to the present day. O'Halloran states that the disease was not declared to be the American yellow fever until August 14, 1821; that in April a fleet of 52 vessels sailed from Habana for various Spanish ports, 20 of them for Barcelona. Cases of yellow fever occurred on some of these vessels after their arrival in Spain, but for commercial reasons every effort was made to conceal them and deny their real nature. Many of the sailors on the infected vessels were, of course, immune, and of those who were susceptible the larger number had suffered attacks during the voyage, so that while they were lying in the Spanish harbors the first persons to become infected were those who visited the ships for the purpose of unloading, making repairs, etc. Some of these vessels lay at Barcelona early in June, and we are told that during this month "the bilious remittent or gastric fever was common, and ultimately predominated in so high a degree as in a manner to supersede all other diseases; and that during the month of July the bilious remittent fever, with hemorrhagic affection, was common and obstinate." The following sentence, quoted verbatim, is of much interest to us at present:

> It is worthy of remark that during this month (July) the flies and mosquitoes were infinitely multiplied.

How well this reminds us that the same unusual prevalence of mosquitoes during an epidemic of yellow fever has been noted by a number of American physicians, including Dr. Rush, at Philadelphia,

in 1797 and 1805; Dr. Vaughan, at Wilmington, Del., in 1802; Dr. Weightmann, at St. Augustine, Fla., in 1839; Dr. Wood, at Centerville, and Dr. Beyrenheidt, at Biloxi, Miss., as well as Dr. Barton, at Clinton, La., and Dr. Dowler, at New Orleans, all in 1853. What interest these observations add to the now well-known mosquito theory of the transmission of the disease, and how well do modern experiences and knowledge add confirmation to Sydenham's theory that certain diseases resulted from an "epidemic constitution of the atmosphere."

I would like here to call your attention to some statements made by a well-known Galveston physician in 1876. Dr. Greensville Dowell, at that time a member of the Galveston Medical Society and professor of surgery in the Texas Medical College, wrote of yellow fever, of which he was a wonderfully close student, as follows:

> Its history shows that no ship, however filthy, can develop it while it remains out of its endemic or epidemic influence. No heat or moisture can alone produce it, or we would have it as often in the East Indies as in the West Indies, and if the conditions in the East Indies were the same as in the West Indies it would be introduced there, as well as in the West Indies, by ships. Hence there must be some cause, specific and sui generis, that produces it. This cause, I have assumed, is animalcular or fungotic, and partakes of the nature of the grasshoppers of Egypt and the western prairies, or the smut in cereals; but these are too small to be observed with any instruments we now have, and have so far eluded demonstration; but if we compare the effects of heat and cold on gnats and mosquitos with yellow fever, it will not be difficult to believe it is of the same nature, as it is controlled by the same natural laws.[1]

So far as I know, Dr. Greensville Dowell was the first even indirectly to incriminate the mosquito by pointing out the fact that it is governed by the same natural laws as yellow fever. And five years after, in 1881, Dr. Finlay enunciated his theory that the disease was transmitted by the mosquito, but his theory was not proved until 19 years later.

O'Halloran's observation that bilious remittent fevers prevailed for two months prior to the appearance of yellow fever has been duplicated in the United States hundreds of times, and we are forced to the conclusion that there must be some relationship between bilious remittent and yellow fever. O'Halloran thought that these bilious remittent fevers were of local origin and that they gradually merged into yellow fever. The same opinion has been held by many in our own country, but this has been offset by evidence, on the other hand, that bilious remittent fever was undoubtedly imported from the Tropics, and was simply a milder form of yellow fever. The truth is that practically all such cases were genuine yellow fever that were not recognized because of the absence of black vomit, which has been erroneously regarded as a necessary symptom. In the work of the Army commission 14 cases of experimental yellow fever were produced by means of the mosquito, and some of them were severe, but black vomit was not present in a single instance. This led some persons to the conclusion that cases produced by only one or two mosquitos were necessarily mild, but the experience of Dr. Guitéras in August, 1901, proved the contrary. Out of seven cases that he produced by the bites of one or two mosquitoes, three died with black vomit.

I have purposely cited from Dr. O'Halloran's account of the epidemic at Barcelona in order to show that other careful observers,

[1] Yellow Fever and Malarial Diseases, by Greensville Dowell, M. D. Philadelphia: 1876, p. 13.

working in other fields, have recorded the same observations and the same opinions as the older American physicians.

The literature of yellow fever in the United States shows that in nearly every outbreak a number of cases, usually the first ones to occur, have escaped recognition. This has happened from the time of Rush until to-day, and has been due to (1) the comparative mildness of the cases, which led to the diagnosis of "bilious remittent fever;" (2) the dread on the part of the physician attending these cases to assume the responsibility for diagnosing the first case of yellow fever, because, in the event that black vomit did not supervene, the correctness of the diagnosis would be called into question, and the physician would be branded an enemy to the community. The Eleventh Annual Report of the Florida State Board of Health, published in 1900, furnishes an admirable illustration wherein it is shown that in the outbreak at Key West in August, 1899, there were already 11 cases unrecognized in the town before a single one was correctly diagnosed. Is it any wonder, then, that under such circumstances the disease was able to gain a firm foothold? The occurrence of a number of cases of the so-called "bilious remittent fever," of short duration, should always excite suspicion, for such cases, when found in groups, are almost invariably cases of genuine yellow fever. At the present day nothing less than the absolute demonstration by an experienced observer of the presence in the blood of malarial parasites or spirillums would justify any other diagnosis than yellow fever; and even if they were shown to be cases of malarial or relapsing fever, modern scientific medicine requires that, in the case of the former at least, the patients should be rigidly protected against the bites of mosquitoes, since we know that malaria, like yellow fever, can be transmitted in no other way than through the bite of that insect, if we except experimental inoculation. In the case of relapsing fever, of the manner of transmission of which we know absolutely nothing, it would be wise to take the same precaution.

The epidemics that have ravaged the city of Philadelphia have been so graphically described by Rush and later by La Roche that one is apt to conclude that the only serious outbreaks this country has experienced were those occurring at Philadelphia, New Orleans, and one or two other seaports. It is only when we search the literature of this disease, that we can appreciate the general devastation and terror created by it, and the enormous losses sustained by the communities it has visited. In a treatise on yellow fever by Dr. Samuel Brown, of Boston, which was published in 1800, he says in speaking of the disease: "This is a foe against which neither ramparts nor intrenchments afford any security: 'It wasteth at noonday;' and every principal town throughout the United States exhibits recent and mournful testimonials of its ravages. We will not enter upon a particular detail of the distresses which Philadelphia, New York, Boston, and other commercial places have experienced; the tale of woe would be too afflictive for even the dullest sensibility to bear and the feelings of humanity would be agonized to overexcitement."

In order to show the manner in which yellow fever invades a seaport town, and the mystery attendant upon its appearance and spread, I will quote from the report of the committee of medical men appointed to investigate the outbreak that occurred at Mobile, Ala., in 1819. After giving in detail the condition of the wharves and

docks, the direction of the prevailing winds, and the degree of temperature and moisture, they state that during the previous winter, spring, and summer up to July 1, the city was healthy. "In the latter part of July a number of violent cases of bilious fever occurred among persons unaccustomed to the climate, and some of a more questionable character; several persons employed as workmen in filling up one of the new wharves were taken violently ill, and died after a short illness of two or three days. About the same time two persons usually employed about Dauphin Street Wharf were taken in like manner, and died after a short illness. A number of carpenters and sailors employed about the wharf, and who were much on board the schooner *Sally*, filled with stagnant water, and about the steam sawmill, where there was a pond of like offensive water, were taken with violent fevers, and several of them died. The physicians who attended these persons died, but it is stated that one of them, Dr. Lawton, spoke of them as cases of malignant fever. An engineer at work on a steamboat at the same wharf died soon after, his illness lasting 5 days. A man who attended him, and a servant boy living in the same house, were taken down with a similar fever, and died on the third and fourth days. All these persons died with black vomit, and were declared by the attending physicians to be cases of yellow fever. At about the same time other fatal cases occurred among persons whose time was spent about the river and wharves or stores in that neighborhood. Within a few days after the prevalence of yellow fever was known an exodus took place, and the population became reduced from 1,300 in July to 500. Of these, 133, or over 25 per cent, died."

The report states that the suburbs of the town, at no greater distance than a mile from the river, were as healthy during the prevalence of the fever as more distant parts of the country; and the disease was not known to be communicated, in any instance, to persons out of the town by the removal of and attendance upon the sick. Hence, it was concluded that the disease was only communicable in the atmosphere in which it originated, and even then some other cause, not understood, appeared to be necessary, because "a number of persons frequently in the room with the sick, dying, and dead, in circumstances of the greatest exposure, never took the fever." It is further remarked that Natchez and other ports on the Mississippi below suffered heavily, and practically every seaport on the Atlantic and Gulf coasts appeared to have suffered more or less that summer from yellow fever. It is very interesting to note how the disease almost invariably first made its appearance in the vicinity of wharves and shipping, in parts of the town where surface drainage is usually more or less defective, and decaying wood and vegetable refuse are necessarily present. As these were the only special conditions found to prevail in these localities, it was quite generally conceded that to them the disease owed its origin. When vessels with yellow fever on board arrived in port, efforts were made to conceal the nature of the disease, and by false entries when patients were buried at sea, or by burial at night where death occurred in port, many cases are known to have been concealed. Again, a vessel with an immune crew, but infected mosquitoes on board, would infect persons from shore who visited the ship for various purposes, yet, there being no sickness on the vessel, she was relieved of suspicion and the disease was assumed to be of local origin. Cases resembling

yellow fever, but without black vomit, were called bilious fever, and under this guise, aided by the occasional concealment of an undoubted case, the disease frequently escaped detection for weeks and months.

In the description of the epidemic at Baltimore, also in 1819, as observed by various practicing physicians, we find many statements that must now be regarded with special interest. For instance, it was conceded by all that the first cases appeared at Fell's Point, where the principal docks and wharves were located. One observer states that the disease never originated more than two or three hundred yards from the water, and it was six weeks from the commencement before the disease had spread much more than 100 yards from the place of origin. The transmission of the contagion was rightfully attributed to some unknown agent present in the atmosphere, for in speaking of the infection it is said, "upon this ground, then, it may be asserted that some matter which was foreign to the natural composition in the air of this place floated about with it at this time. Some portion of whatever this air contained was therefore of necessity breathed or swallowed by the people who came within its limits. And the properties of the foreign matter in this air must be decided upon by the effects which it has had on those who receive it into their habits." We have only to add the mosquito now, and the general truth of the above statements becomes manifest. And with the mosquito we necessarily include the insect's bite as an additional and at that time unknown avenue of entrance for disease. Conceding this, how easily one can explain the first appearance and prevalence of the disease in the localities where the conditions are favorable for the multiplication of mosquitoes, viz, in the low-lying and generally poorly drained districts in the vicinity of the wharves and shipping. When we consider further that the mosquito that transmits yellow fever is a tropic and subtropic insect and that, practically speaking, it is not found north of Mason and Dixon's line, it then becomes absolutely clear that yellow fever in epidemic form can be introduced into that section only when the presence of high atmospheric temperature and moisture afford conditions favorable for the propagation of this insect. But the yellow-fever mosquito is a tropic insect, and yellow fever is a tropic disease; it follows, therefore, that, given the proper conditions as to temperature and moisture, there must have been introduced at that time both the proper insect and cases of the disease. These must necessarily have come originally from infected localities within or near the Tropics.

In the days when yellow fever prevailed in our northern seaports outbreaks invariably followed the arrival of one or more vessels from Habana or some other infected port, but the interval elapsing between the entry of the vessel and the recognition of the disease was so long and the manner of extension of the disease was so mysterious that it became impossible to trace the connection between the one and the other. Let us suppose, for example, in the month of July, at a time when yellow fever prevailed and before the days of rigid quarantine, a sailing vessel lying at Habana and bound for Baltimore. She is tied up at a dock, and numbers of the yellow-fever mosquitoes, which are the prevailing house mosquito at Habana, fly aboard. They deposit their eggs in open casks, pitchers, or other receptacles containing fresh water exposed to the air. The crew are immune with one exception, and this man is taken sick three or four

days out from Habana on the journey northward. He has yellow fever, but his temperature is only moderately high, and although he is deeply jaundiced there is no black vomit. The captain insists the case is one of bilious remittent fever and not yellow fever. No one could question his statement, because even the best physicians were unable at that time to draw the line between yellow fever and malarial fever, and it is not always easy to do it to-day. The hypothetic case of genuine though unrecognized yellow fever is bitten by a number of mosquitoes during the first three days of his fever, but no one is aware of it, or would attach any importance to it if they knew. In two weeks the patient is practically well, and in another week or two the vessel arrives in port with a clean bill of health. There is no sickness on board, she is in fairly good condition, and ties up to the dock in Baltimore—say 25 or 30 days after leaving Habana, and with several infected mosquitoes on board.

Perhaps these mosquitoes are disturbed by the unloading of the ship or cleaning of the cabins, and they may fly onto another ship tied up at the same wharf or travel along the wharf to a watchman's house or some other dwelling in the immediate vicinity. The first cases of the outbreak may appear on the other ship tied up at the dock, and this latter vessel may have come from Europe and be in rather foul condition. The infection in that case would be attributed to the foul air generated by the action of a hot atmosphere upon the decomposing matter present in her hold. The next case may appear in some one sleeping or employed on the dock or on a neighboring vessel. In the month of August conditions would be favorable for the propagation of mosquitoes, and in addition to those hatched out on the trip from Habana another brood will soon have appeared on shore. The mosquito may also have been introduced by other vessels earlier in the season, and the conditions will then be suitable for a further extension. The continuance of the outbreak necessarily depends on the coming together of the imported mosquitoes and cases of yellow fever in the first three days of the disease; consequently in numerous instances only one or two cases occur, and none follows unless fresh cases are introduced by other vessels from infected ports. The frequency of the occurrence of cases of bilious remittent fever in American ports during the last century shows that during the early part at least yellow fever was being constantly imported, though it only occasionally assumed epidemic proportions. Let us suppose that the vessel leaving Habana sailed for New Orleans, Mobile, or Galveston, instead of Baltimore. Here the case will be different, because in these places the conditions are favorable for the propagation of the yellow-fever mosquito throughout the greater part of the year, and the introduction of a single case might prove sufficient to light up an epidemic, because the proper mosquito is at nearly all times present in the houses in abundance. Frequent severe outbreaks have occurred at New Orleans until a large part of the population had become immune, and those who were nonimmunes and could afford it habitually left the city during the warm season. Among the few who remained and chanced to be bitten by the proper infected mosquitoes, cases would occur from time to time as bilious fever, often suspected to be yellow fever, but for reasons of policy they were not so reported. Finally, after a few years had passed, confidence would be restored, and a

larger proportion of nonimmunes would supply the material for a fresh outbreak, which was certain to appear sooner or later. Then came a sudden exodus, with the wrecking of commercial interests, neglect of the sick, and the untold suffering known only to those who have passed through a severe epidemic. Here let me remark with emphasis that for the production of an outbreak of yellow fever three factors are necessary: (1) Preexisting cases of the disease, (2) mosquitoes of the genus Stegomyia, and (3) nonimmunes or persons who are susceptible to the disease. I would impress upon you the fact that the absence of any one of these factors will render it absolutely impossible for an outbreak to occur. An epidemic of yellow fever is impossible in the absence of preexisting cases, for the disease can not be generated by any amount of filth, heat, moisture, or decomposition without the intervention of the three factors named. Excluding experimental inoculation, the occurrence of cases of yellow fever is not possible under any conditions without the presence of the proper mosquito to transmit the infection from the sick to the well. And, finally, given any possible local conditions, any number of cases of yellow fever and any number of infected mosquitoes, in the absence of susceptible persons, cases of the disease must disappear.

But I am going faster than I ought. Here in Galveston you are in the epidemic zone of the disease; you have had your epidemics, and you have reason to guard against them in the future. Your city was described 30 years ago as being built upon an island composed of shingle, and this shingle so saturated with water that the latter could be found at a depth of a few inches. The mean temperature is about 74°, and the rainfalls are usually heavy in April, May, and June. Owing to the saturation of the deeper layers of the soil, the rain water lay upon the surface in pools until it disappeared by evaporation in the dryer months of the late summer and autumn. The surface pools of fresh water were ideal breeding places for mosquitoes, as also were the receptacles for rain water, which the early inhabitants collected and used after the custom at New Orleans. Yellow fever paid its first notable visit here in 1839, only a few years after the establishment of the first settlement. The population was about 1,000, and the people were located mostly along the Strand, in close proximity to the wharves and vessels. The first case reported occurred late in September on a steamer recently arrived from New Orleans. At about the same time another case occurred on a vessel anchored only a few yards from her. Both cases were fatal. As others were reported on land at the same time, it is more than likely that these were not the first cases, but as they were the first in which black vomit appeared they were probably the first in which a diagnosis of yellow fever could no longer be withheld. In this epidemic, which lasted less than two months, we are told that there were 250 deaths, which means the occurrence of at least twice as many cases among the population of 1,000 persons. It is further stated that the epidemic died out because "every unacclimated person had either fled from the town or suffered an attack. This was proved by the fact that when the refugees began to return the disease broke out again among the newly arrived, and there were a number of deaths." How beautifully this all fits in with the mosquito theory, now that we know that the bite of the mosquito can convey the disease as long

as two months after it has bitten a yellow fever patient. I have good reason to be a firm believer in the theory of the transmission of the disease by the mosquito, for I have seen 16 cases of experimental yellow fever produced by the application of infected insects, and it was my good fortune to be the first case among them. Among other experiments it was my privilege to apply two mosquitoes of the proper genus (Stegomyia) to a patient suffering with yellow fever, and 57 days later I applied the same mosquitoes to a soldier volunteer, who had been kept in strict quarantine for 78 days. In four days he was taken ill with a typic attack of yellow fever, from which he made a good recovery.

Returning to the subject of Galveston, a few cases are said to have appeared in 1842, but in 1844 a violent outbreak raged for about six weeks, and then ceased suddenly from the absence of susceptible persons. Here it was again noticed, however, that nonimmunes who visited the town but once for the purpose of shopping, etc., occasionally returned home to be taken ill with yellow fever a few days later. This continued until the appearance of a white frost, which we know benumbs the mosquito and forces it to go into hibernation. This, therefore, affords a rational explanation of the effect of the first sharp frost, which has so long been welcomed as the savior of districts afflicted with yellow fever. During the epidemic just mentioned nearly 400 deaths occurred in a population of about 4,000.

Three years later, in 1847, an epidemic was declared to be present in the month of October and there were about 200 deaths in a population of 4,800. In 1853, after an immunity of six years, the deaths from yellow fever were 535; in 1854, 404; in 1858, 873; and in 1859, 183 in a population of about 10,000.

In September, 1864, the disease was again epidemic, the deaths being 259 and the population 5,500. Three years of exemption followed, and in 1867 a severe epidemic is estimated to have produced 8,000 cases and 1,150 deaths in Galveston in a population of 15,000. From Galveston it was carried to a number of smaller towns, among which Alleytown on the Colorado River was afflicted with 200 deaths and about 800 cases in a population of 1,500.

During the same season Indianola is said to have received the infection from Vera Cruz, and we are told that "in less than a week the whole business part of the town was struck down as by lightning, there being no less than 125 to 150 cases taken during that time out of a population of less than 1,000." The extension of the disease was checked by a rapid depopulation of the town. The number of deaths among the citizens was about 75. From Indianola the disease is said to have been carried to various points throughout the State and even beyond. In 1870 and 1873 a few cases occurred, but the disease did not assume epidemic form. There is reason to believe, also, from the report of Dr. H. A. West, of this city (Galveston), that there were a few mild cases in 1897. I can find no record of any outbreak in Galveston since that time, although two cases were introduced on December 31 last, but as you well know there were in the State of Texas in 1903 over 1,200 cases of yellow fever, with nearly 140 deaths. Over 1,000 cases and 107 deaths are recorded for Laredo alone, and if it were not for the energetic measures instituted against the mosquito there would undoubtedly have been

another fearful epidemic to record for the United States similar to that of 1878, during which, according to the Board of Experts appointed by Congress, more than 100,000 persons were stricken in their homes, and 20,000 lives were sacrificed in a single season. In Memphis alone, according to Keating, there were in 1878, 17,600 cases of yellow fever, with 5,150 deaths, a mortality rate of about 1 in 4 of the reduced population. Scenes were enacted there similar to those described by Rush in his account of the epidemic at Philadelphia almost a century before, when the streets became deserted, bodies remained unburied, friends no longer shook hands upon meeting, husbands deserted their wives, wives their husbands, and parents their children. So, in Memphis, we are told of a prominent man who fled the city and refused to return when his wife and children were stricken and who still remained 50 miles away when notified of their death. These deplorable incidents, however, were more than offset by numberless instances of heroic devotion on the part of Sisters of Charity, nurses, and physicians who died at their posts of duty. As one illustration I might cite from the little book on yellow fever published in 1898 by Dr. W. L. Coleman, of Houston. Dr. Coleman was present during the Memphis epidemic and took down the names of 45 volunteer physicians immediately after their arrival. Most of them came from the Northwest, and one did not remain. The others all contracted yellow fever and 30 of them were dead within a month.

At that time no one could say how the disease was contracted; some held that it was of local origin and contagious, others that it was not contagious; many believed it was imported, that it was infectious but not contagious, and was carried in some mysterious way by the atmosphere. We are told by Keating that "Dr. Dowell, of Galveston, says that in 19 cases out of 20 it will be found to have been introduced or imported," which was wonderfully near to the truth as we know it to-day.

It may surprise you to learn that yellow fever experimental inoculations began in the United States in Philadelphia, during the yellow-fever epidemics in the years 1802 and 1803. It is a fact that in those years Stubbins Firth, a medical student of the University of Pennsylvania, deliberately experimented upon himself by placing fresh black vomit and blood serum obtained from yellow-fever patients into wounds made in his arms and legs. Failing in this, he inhaled the fumes from black vomit, which he heated over a sand bath in a small room, and then, making the residue into pills, he swallowed them. He administered black vomit to animals, injected it into their circulation, and deposited it in their tissues. As the results of these and other experiments were negative, he concluded that yellow fever was neither infectious nor contagious, and reported his work and conclusions in a graduation thesis in 1804.

But little more was done or could be done until the advent of the new science of bateriology encouraged the belief that this mysterious malady might be caused by a bacterium. The first to claim the discovery of the specific cause of yellow fever was Dr. Domingo Freire, of Brazil, who went further than this, and claimed also that he had conferred protection against the disease by inoculations with specially treated cultures. He was followed by Dr. Carmone y Valle, of Mexico; Dr. Babes, of Brazil; Dr. Gibier, of Paris; and Dr. Finlay, of Habana,

each of whom believed that he had found the cause of yellow fever in a different organism. It remained for Dr. Sternberg to show that these investigators were all mistaken, and that the bacteria found by them were not in any way related to the disease. Dr. Sternberg, himself, subsequently exhausted the field so far as the search for bacteria was concerned; he also made extremely careful and thorough examinations of the blood and tissues obtained from patients with yellow fever. He announced finally that his search had proved unsuccessful, and his work stands as the best that has ever been done in the study of the bacteriology of the disease.

In 1897 the sensational announcement was made that Dr. Guiseppe Sanarelli, an Italian bacteriologist, working upon the island of Flores, in Montevideo, had discovered the cause of yellow fever in a bacillus that he had found in about 50 per cent of the patients examined by him. He reported also that the injection of pure cultures of this bacillus into the circulation of dogs brought about an infection similar to yellow fever in the human being, with the vomiting and other symptoms of that disease, and a similar condition of the organs after death. This announcement naturally interested Dr. Sternberg, who at this time had become Surgeon General of the Army, and he immediately turned to an organism that he had obtained from about 50 per cent of the patients examined by him, that he had found to be exceedingly virulent for the small laboratory animals, and which he had called Bacillus X, because he had been unable positively to identify it. He obtained a culture that had been preserved by one of his former assistants, and directed Dr. Reed and myself to undertake certain experiments with it. As Dr. Sternberg had never injected it into dogs, one of the first steps in our work was a duplication of some of Dr. Sanarelli's experiments, viz, to inject it into the circulation of dogs. We obtained the same effects as Sanarelli had recorded for his yellow-fever bacillus, and this seemed to indicate that the organisms must be identical. Dr. Sternberg then procured a culture of Sanarelli's bacillus from Prof. Roux, of Paris, and handed it to us for comparative study. It is amusing now to think of the fearful respect with which we handled the culture from Dr. Sanarelli's laboratory, because we were fully prepared to accept it as the cause of yellow fever from what we knew of Dr. Sanarelli's reputation as a bacteriologist. After several months it became apparent that this supposed yellow-fever bacillus of Sanarelli was nothing more nor less than the common hog-cholera bacillus, an organism that was much better known in America than abroad. Sanarelli was evidently at that time not familiar with the bacillus of hog cholera, for he pronounced the germ obtained by him "the strangest of all microbes that are known." A bitter controversy arose upon the publication of our reports of the work in which we had found that Dr. Sanarelli's bacillus when fed to young hogs would produce the symptoms and lesions of hog cholera. Indeed, Sanarelli still contends in his own country that he found the bacillus of yellow fever, a contention that finds no support to-day among reputable bacteriologists in this country or in Europe.

It is a remarkable fact that upon his own demonstrations alone, Dr. Sanarelli was awarded large pecuniary prizes and honors as the discoverer of the causative agent of yellow fever. Unfortunately, Archinard and Woodson, and a commission from the Marine-Hospital Service, working in the United States, reported that their results con-

firmed the claims of Dr. Sanarelli. In 1897 and 1898, the latter commission, consisting of Drs. Wasdin and Geddings, continued their investigations in Habana, and in 1899 an elaborate report was issued, in which it was claimed that dogs, rabbits, mice, and other animals could be given yellow fever by infecting them with Sanarelli's bacillus, that infection took place through the lungs, and that a diagnosis of yellow fever could be made by isolating the bacillus from the blood of the patient. This made matters rather interesting for us, but did not shake our confidence in our results. Bacillus X (Sternberg) was found to belong to the group of colon bacilli.

Finally, in 1900, during the American occupation of Cuba, yellow fever became epidemic in Habana. To take advantage of the opportunity thus offered, Gen. Sternberg designated a board to meet at Habana, for the purpose of continuing the study of that disease. The members of that board were Drs. Walter Reed, James Carroll, Aristides Agramonte (a Cuban immune), and Jesse W. Lazear. Drs. Lazear and Agramonte were already at Habana, and we joined them there in June. Our first aim was to confirm or disprove the claim for Sanarelli's bacillus, which he had called *B. icteroides*, and after a most painstaking and careful investigation of the blood obtained during life from 18 undoubted cases of yellow fever, and of the blood and tissues of 11 fatal cases after death, we were compelled to report that we had failed to find *Bacillus icteroides* in a single instance.

Having thus disposed of *B. icteroides*, two lines of work now presented, one an investigation of the mosquito theory, so long advocated by Dr. Carlos Finlay, of Habana, the other a study of the microorganisms present in the intestinal canal of yellow fever patients. The former was chosen, because of the numerous points of resemblance between yellow fever and malaria, which was known to be conveyed by the mosquito. Both diseases are airborne; both are contracted mostly at night; both jump from house to house in a mysterious way; both are noncontagious; both prevail in the season when mosquitoes are numerous, and infections cease to occur upon the appearance of a sharp frost; the interval of time elapsing between the occurrence of the first case and secondary ones in primarily infected dwellings suggested the necessity for an intermediate host in the conveyance of yellow fever; it was noted that in a large military command at Columbia Barracks, near Habana, the only persons who contracted yellow fever were those who left the camp after sundown, and these, after recovery, although they mingled freely with their comrades, never infected them. This latter observation seemed to show that the cause of the disease was not present on the body, in the clothing, or the dejecta. A consideration of all these points led us to decide that the next step should be to test the mosquito theory. In the early consideration of this line of work the members of the board paid a visit to Dr. Finlay, who received them most courteously, showed them the common house mosquito that he believed to be responsible for the disease, narrated the work that he had done, and kindly supplied them with some dried mosquito eggs for the purpose of hatching them out for study. The moral responsibility was next considered, and in a later conference it was agreed that the members of the board would themselves be bitten, and subject themselves to the same risk that necessity compelled them to impose on others.

Dr. Lazear was given charge of the mosquito work, because he already had had experience with other mosquitoes. I was to continue my work with the cultures, and Dr. Reed returned to the United States. Dr. Lazear made a number of unsuccessful attempts with mosquitoes, applied one or several days after biting a patient as Dr. Finlay had done, and he himself was bitten by a mosquito that he had applied to a mild case of yellow fever 10 days before. I reminded Dr. Lazear that I was ready, and he at last applied to my arm an insect that had bitten a patient with a severe attack 12 days previously. Four days later I had fever, and on the day following I was carried to the isolation camp as a patient with yellow fever. On the day that my fever appeared, Dr. Lazear applied the same mosquito, with three others, to a soldier, X. Y., who was taken sick on the fifth day following, and passed through a comparatively mild attack. Scarcely more than a week later, Dr. Lazear was applying mosquitoes, as usual, late in the afternoon, to patients in the yellow fever hospital, known as Las Animas, and while thus engaged a mosquito alighted upon his hand. He allowed it to take its fill, and concluded it was one of the common culex mosquitoes which were present in the hospital in large numbers. So little importance did he attach to the incident that he made no note of it, and related the circumstance to me when he was first taken sick, five days afterward. A week from that date he died, having been delirious and affected with black vomit for several days. Thus ended the first set of experiments, with the death of our esteemed and unfortunate colleague.

Two months later a new series of experiments was instituted for the purpose of confirming the results already obtained, to see, also, whether the disease could be contracted from exposure to soiled or contaminated articles of bedding, clothing, etc., and to determine whether or not the infectious agent was present in the blood.

For the first-mentioned experiments an isolation camp, called after our deceased comrade "Camp Lazear," was established in a secluded spot about a mile from Columbia Barracks and apart from any habitation. In this camp there were placed three immunes and nine nonimmunes, including one immune and one nonimmune physician. A strict quarantine was maintained and only the immunes were permitted to leave the camp. If a nonimmune left, he was not permitted to return. As newly arrived nonimmune Spanish immigrants could be obtained from the immigrant station at Habana they were brought out and added to the command in quarantine. The camp consisted of seven large hospital tents, separated by a wide interval and pitched in the arc of a circle. The nonimmunes distributed through the tents were required to sleep beneath mosquito bars, and the rule was rigidly enforced. The plan was to pick out men here and there in the line of tents, bring them down with infected mosquitoes, and in that way establish the fact that cases could be produced at will by the application of infected mosquitoes. It was further desired to show that an infected house was simply one that contained active infected mosquitoes, and that nothing more was necessary for the production of an epidemic in a susceptible community. A new, tightly ceiled frame building was constructed, 20 feet by 14 feet, provided with two small windows, tightly closed with fine-mesh wire screens; also with two vestibules protected by an outer door, and an outer and an inner tightly fitting screen door, so as

to guard against the ingress of mosquitoes from without or their egress from within. Upon entering the vestibule the screen door through which one passed was closed, and the other was not opened until it was made certain that no mosquitoes were passing in or out. The lumber used in the building was tongued and grooved; the walls were battened on the outside and lined with white cotton cloth within. The walls and floor were double, and all crevices were stopped; the ceiling was covered with cloth and made so low that mosquitoes resting upon it could be captured with ease. Across the middle of this room there was built a wire-screen partition extending from floor to ceiling and dividing it into two compartments, each with a separate entrance. Beds were placed in each of these rooms, and one of them was occupied by two nonimmunes for 18 consecutive nights. The bedding and other articles admitted to the room were all disinfected. On December 21, 1900, the date of the first occupation, 15 contaminated mosquitoes were turned loose in the unoccupied compartment, and then a nonimmune entered and lay upon one of the beds, with his chest and limbs exposed for 30 minutes. During this time he was bitten by several insects and others bit him again later in the day, when he lay there for 20 minutes. This procedure was repeated again on the following day, the last of exposure. On December 25, four days after his first exposure, this man who had remained in strict quarantine, was taken ill with a severe attack of yellow fever, from which he recovered. The other two men, who slept in the same room but in another compartment, separated from the mosquitoes only by the screen partition, remained in their usual health.

Another building had been constructed similar to the above, but provided with only a single vestibuled entrance. It was equally protected against the entrance of mosquitoes and had two small screen-protected windows provided with shutters, so as to exclude sunlight as well as mosquitoes. It contained a coal-oil stove, by means of which the temperature was kept above 90° during the day, and the atmosphere was provided with moisture. Into this room, which was warm, dark, and moist, like the hold of a ship in the Tropics, several boxes containing sheets, blankets, pillow slips, and garments direct from the yellow-fever hospital were placed. These had been soiled intentionally with black vomit and other repulsive material from cases of yellow fever. This room was then entered each evening at sundown by two nonimmune Americans, one of them a physician, who unpacked the boxes, handled and shook the articles, then hung them up on nails in the walls, and retired for the night. Upon rising in the morning they removed the articles from the walls, handled them freely, and repacked them in the boxes, where they remained until evening. This procedure of unpacking and repacking, handling, and sleeping in the presence of the soiled materials was kept up for 20 consecutive nights, and in the meantime fresh supplies were added as fast as they could be obtained. On one or two occasions the stench drove the occupants out, but they returned again and slept there. They spent the daytime in a tent nearby, but were strictly quarantined. The pulse rate and temperature of all nonimmunes in the camp were recorded three times daily, and showed that the health of these men was not affected in the slightest degree; on the contrary, they gained in weight.

These were succeeded by two other nonimmunes after the addition of more soiled garments, etc., and they in turn were followed by another two for the same period. Some of these men slept between the sheets and in the garments used and soiled by yellow-fever patients at the time of their death, and they even slept with their faces upon towels soiled with blood that had been shown by inoculation to be capable of infecting with yellow fever. In no single instance did any disturbance of health follow these exposures; the conclusion was therefore arrived at that yellow fever can not be contracted through exposure to fomites. If one stops to reflect that the mosquito is not able to infect until 12 days or more after contamination, one is forced to the conclusion that the yellow-fever parasite, which has never been seen, must, in all probability, pass through a distinct cycle of development in the mosquito before the insect becomes dangerous. As Dr. Howard has told you, a corresponding but slightly shorter interval is seen with the mosquito that transmits malaria. The developmental phases of the malarial parasite in the mosquito are well known and have been demonstrated. Judging by analogy, therefore, it seems justifiable to assume that the parasite of yellow fever appears also to belong to that group of obligate parasites whose whole existence is passed within the bodies of two living hosts, one of which, man, is a vertebrate, and the other, the mosquito, an invertebrate. This affords an explanation of the uselessness of disinfection against yellow fever as well as malaria, and it also explains the instances occasionally noted in the literature, where a prompt suppression of the disease followed the use of fumigation as well as disinfection.

Returning to the subject of the experiments at Camp Lazear, the susceptibility of the men exposed to the fomites or soiled articles, was shown by the fact that four of them were subsequently infected by means of mosquitoes and blood injections. Four nonimmunes in all were infected by the subcutaneous injection of small quantities of blood drawn in the first and second days of the disease. This established another point of analogy between yellow fever and malaria, and demonstrated the presence of the infectious agent in the blood, notwithstanding that we had failed to discover anything upon careful microscopic examination of the blood from many patients, including those in whom the blood, drawn at the same time, produced yellow fever in persons into whom it was injected.

Nine additional cases were produced in Camp Lazear by the application of infected mosquitoes, making in all 10 cases of yellow fever brought about at will. All were taken sick within the usual period of incubation, never more than six days. They were selected here and there in the different tents, and no other cases occurred than those purposely inoculated. As soon as a case appeared the patient was immediately removed to the yellow fever isolation camp, a mile distant, to avoid the possibility of any stray mosquitoes becoming infected from him. In no instance was the mosquito found to be capable of infecting in a shorter period than 12 days after biting the patient, and one patient was infected with two mosquitoes kept as long as 57 days.

This work was concluded by the end of February, 1901, when confirmatory experiments were taken up by Dr. John Guiteras, of Habana. His first patient was infected in February with a mosquito

obtained from the Army commission, and his subsequent inoculations were unsuccessful until August, when he succeeded in infecting seven persons with mosquitoes. Of these cases, three, unfortunately, proved fatal. Among the latter was a young American nurse, Miss Maas, of Baltimore, who voluntarily submitted herself to the experiment.

In August, 1901, I returned to Habana, and obtaining some of Dr. Guiteras's mosquitoes, infected two Spanish nonimmunes. Drawing blood from one of them and separating the serum, I passed the latter through a filter, which was shown to be capable of holding back the ordinary bacteria. Injection of the filtered serum into two Americans infected them with yellow fever. In this way it was shown that bodies smaller than ordinary bacteria were capable of producing yellow fever upon injection, and our failure to discover anything upon microscopic examination of the blood of yellow fever patients was thus satisfactorily explained. It was further shown, as a point of great scientific interest, that blood that was known to be capable of producing the disease was found to be absolutely harmless after it had been heated to 131° F. for 10 minutes. At this time I produced six additional yellow fever cases, all of whom recovered.

Such were the results obtained by the Army board, and they can be summarized as follows:

1. *Bacillus icteroides* of Sanarelli was shown to be practically identical with the bacillus of hog cholera, from which it differs only in the source from which it is obtained.

2. Yellow fever is transmitted by a mosquito of the genus Stegomyia, and all attempts to bring about the infection through contact with bedding, clothing, and dejecta of yellow fever patients have resulted in failure. Hence it follows that disinfection against yellow fever is valueless.

3. Yellow fever can be produced experimentally, by the injection of blood drawn in the first and second days of the disease, but this has no direct bearing upon the transmission or prevention of the disease in its epidemic form.

4. The specific germ of yellow fever is sufficiently minute to pass through the pores of a bacteria-proof filter, and it is destroyed by a temperature of 131° F.

Confirmation of the mosquito inoculations has been furnished by Dr. Guiteras, in Habana; Drs. Ribas and Lutz, as well as the French commission, in Brazil, and by a commission of the United States Public Health and Marine-Hospital Service, at Veracruz. It is especially gratifying that a French commission from the Pasteur Institute, working recently in Brazil, has confirmed practically all the results of the American Army commission.

The following, therefore, may be safely assumed:

1. Disinfection in the prophylaxis against yellow fever is effective only when it takes the form of fumigation and destroys mosquitoes.

2. Yellow-fever patients can be the source from which other cases spring only when they have been bitten by the proper mosquitoes; consequently, in the yellow-fever zone all acute febrile cases not diagnosed should be handled as though they were yellow fever, and should be kept rigidly behind safe mosquito screens and netting. So far as has been shown the yellow-fever patient is dangerous when bitten by mosquitoes during the first three or four days of the fever

only, but since relapses may occur, every precaution should be maintained as long as the temperature remains elevated.

3. The hospitals intended for the treatment of suspected cases of yellow fever should be located upon ground that is high, well drained, away from creeks, pools, or standing water of any kind, free from mosquitos, and not surrounded by grass or shrubbery. All entrances and exits to such hospitals should be provided with close-meshed wire screen spring doors, and similar screens should be fixed immovably over every window and other opening communicating with the exterior. Standing water should not be permitted in barrels or vessels of any kind, and broken crockery, tin cans, or other possible retainers of rain water should be systematically searched for within a radius of several hundred yards, and removed.

4. In general sanitation, all surface pools should be promptly drained and filled in with gravel, or covered with petroleum. Petroleum should be applied systematically to standing water in all ditches, pools, rain-water gutters, etc., that can not be filled up or emptied. The margins of ponds should be deepened, to enable the fish to reach mosquito larvæ.

5. Water should not be permitted to stand uncovered in houses; and rain water in cisterns or barrels, when not used for drinking purposes, should be treated with petroleum; if the water is used for drinking, all openings, vents, etc., should be closed with wire screens or tightly fitting covers. Periodic examinations should then be made for wigglers (larvæ) or mosquitoes, because the female mosquito may pass through a very minute opening when seeking water on which to deposit her eggs. By means of these and other similar measures, the number of mosquitoes may be greatly reduced, and the chances for the conveyance of the infection, should it happen to be present, will be thereby greatly diminished.

Stegomyia fasciata, the yellow-fever mosquito, is a house-dwelling and house-breeding insect; particular attention should therefore be paid to the smallest as well as the larger collections of standing water within and about habitations.

6. After the removal of a patient, his room and the adjoining ones should be at once tightly closed by pasting paper over all cracks and openings, and then fumigated with insect powder, tobacco, or sulphur, to destroy mosquitoes. When the room is opened after a few hours these should be swept up and burned.

7. Experience at Habana has shown that patients suffering from yellow fever upon their arrival at a port can be carried through a thickly populated city to a properly screened hospital, and there treated without the slightest danger to the community, so long as they are rigidly protected against mosquitoes. Money spent for the purpose of disinfection against yellow fever is wasted, for yellow fever in epidemic form can only be contracted through the bites of mosquitoes of a single genus.

8. The noncontagiousness of yellow fever was clearly shown in certain localities years ago before the use of disinfectants, in places where the yellow-fever mosquito did not exist. The belief in the supposed contagiousness of this disease arose from its transmission through the atmosphere by the mosquito at a time when this insect was not suspected or known to be concerned in the transmission of any disease.

9. When a house is infected with yellow fever, it simply contains infected mosquitoes; in the absence of this insect, no amount of filth, heat, or moisture is capable of generating the disease.

10. Vessels from infected localities should be compelled, upon entering port, to anchor at least a fourth of a mile from shore; they should never be permitted to tie up to a wharf or dock in the city, except in northern latitudes during the cold season of the year. In this way, the chances for contaminated mosquitoes reaching the city can be reduced to a minimum.

11. As the yellow-fever mosquito does not bite, as a rule, between the hours of 9 a. m. and 3 p. m., it is practically safe for nonimmunes to visit infected localities between these hours for the transaction of business. Before 9 a. m. and after 3 p. m. they will run a greater or lesser risk of being infected.

12. It is now certain that before the lapse of many years, the disease, yellow fever, will have become extinct. The length of time necessary for its complete eradication will depend upon the readiness of our southern neighbors to accept the mosquito theory in toto, and institute in their infected seaports vigorous and energetic measures based upon it.

13. Another epidemic of yellow fever should never be seen in the United States. An example has been shown in Cuba, and the measures necessary to prevent the extension of the disease are so simple, so plain and practicable for persons in authority, that the existence of an epidemic of yellow fever in our country should alone be regarded as prima facie evidence of the culpability of some responsible person.

In conclusion, I can not refrain from asking you to pay no attention to the sensational letters, already referred to, as recently published from a well-known American physician on the island of Cuba. This gentleman was at one time regarded as an authority upon yellow fever, of which he has seen a great deal, but he is now five years behind the time. His insinuation that cases of yellow fever are still frequent in Cuba, and that they are called typhoid fever, is a scandalous misrepresentation of the actual truth, and an unjustifiable reflection upon the intelligence and zeal of Cuban physicians, like Drs. Finlay, Guiteras, Agramonte, Albertini, and others, who realize fully the responsibility that rests upon them, who have suppressed yellow fever on the island for three years, and who are fully competent to deal with the situation there, now and in the future.

Chapter 4.

LESSONS TO BE LEARNED FROM THE PRESENT OUTBREAK OF YELLOW FEVER IN LOUISIANA.[1]

By James Carroll, M. D., Assistant Surgeon, United States Army, Washington, D. C.

The present seems to be a suitable occasion to invite attention to several points in connection with the epidemic occurrence of yellow fever in the United States at the present as well as at other times. In the discussion of the symposium on yellow fever at the meeting of the American Public Health Association in Washington in 1903, I called attention[2] to the necessity during the epidemic season for requiring physicians, in cities where yellow fever is prevailing or likely to prevail, to report promptly to the authorities all cases of fever of any kind coming to their notice. This is necessary in order that there may be no delay in the institution of proper measures to protect the community against extension of the disease if it be yellow fever, for this extension will almost surely take place in the more southern latitudes if the patients are not protected from mosquitoes at the outset. If all cases of undetermined fever were promptly reported and at once protected from mosquitoes[3] it would hardly be possible for the disease to spread if it were yellow fever; on the other hand, where the physician waits for the appearance of black vomit, the golden opportunity passes by, for it has been shown that in practically all cases the disease can not be communicated after the fourth day of the fever. For this reason the diagnosis should be anticipated, and all febrile patients should be immediately protected from mosquitoes until it is shown by actual demonstration that they are not suffering from this disease. Epidemics do not follow every introduction of yellow fever; mosquitoes becoming infected may die before they bite a nonimmune, or the patients may happen to be treated in a locality free from Stegomyia. A group of cases of yellow fever occurring without black vomit usually receives the designation bilious remittent fever, a diagnosis that should be erased from our text books. Bilious remittent fever, acute in type and of short duration, appearing in the United States, is yellow fever, and it should be so regarded. Bilious remittent fever was formerly regarded as a type of malarial remittent, but that was before the use of the microscope was found to be necessary for a positive diagnosis of malarial infection. We know now that malarial fever is not a disease of cities, but of outlying districts, while the bilious remittent fever, so called, has been recorded in the cities, in epidemic form, and in such intimate association with yellow fever that by some the diseases were declared identical, and by others the latter was said to be only a modification

[1] Read at the thirty-first annual meeting of the American Public Health Association at Boston, Sept. 25-29, 1905.

[2] Report of the Proceedings of the American Public Health Association, vol. xxix, p. 291.

[3] Since this paper was read, I have been informed by Dr. E. Liceaga, president of the Superior Board of Health of Mexico, that the line of procedure indicated is now being followed in his country.

of the former. Most interesting and important in this connection is the statement cited by La Roche,[1] in his chapter on bilious remittent fever, that "the morbid appearances revealed on dissection are the same in remittent as in yellow fevers." This statement, however, was not wholly accepted by him, for he calls attention to the bronzed appearance of the liver in certain remittents, a condition that we know results only from malarial pigmentation. Now that we can so easily differentiate malarial remittent and typhoid from yellow fever, the diagnosis is much less difficult, except where yellow fever occurs as a complicating infection.

Our confreres in Havana have demonstrated to us that it is possible to prevent the epidemic occurrence of yellow fever, while occasionally admitting cases of the disease into the heart of a city in which the climatic and other conditions are known to be most favorable for its extension in epidemic form, and in which there are more susceptible persons now than ever before. The method suggested here is in many respects similar to, and is based on, the one adopted during the American occupation of Havana.

Since then it has been sufficiently demonstrated, in 1903 and again in 1905, that under the lax system heretofore and now in vogue, yellow fever can easily secure a firm foothold in certain of the southern states and escape recognition until it has passed almost completely beyond control. On both occasions cited, the outbreak was suppressed or limited only by the intervention of the General Government, which, through the energetic action of the United States Public Health and Marine-Hospital Service, finally succeeded in checking two epidemics that threatened to become little less than national calamities. Great credit is due to those officials for the success that was attained in spite of the extreme delicacy of the situation and the passive opposition encountered from many quarters.

Our experiences in Cuba have shown that for the exclusion and suppression of yellow fever absolute hygienic control is necessary not only of the people at large, but of the patients as well, and especially of the practicing physicians. The aim of modern medicine is the prevention of disease rather than its cure, and the safety and welfare of the thousands of persons exposed demand that the proper measures be instituted and rigidly enforced. No valid argument can be brought forward to show why the United States should not be kept as free from outbreaks of yellow fever as the city of Havana, its former endemic home, has been during the past four years.

To attain this result the following requirements seem to be essential:

1. Our physicians, or at least those who are in control, must disabuse their minds of the impression that black vomit necessarily occurs in the majority of cases of yellow fever.

2. During the epidemic season, viz, from about May 1 to October 31, and in the epidemic zone, physicians should be required to report to the health authorities, immediately, all cases of fever of any kind that come under their observation, whether among their patients or not, and failure to do so should be made punishable under the law.

3. The board of health should be authorized to appoint, with proper compensation, a commission of three experts, all of whom should be men of high reputation as diagnosticians. It should be the

[1] Yellow Fever, La Roche, Philadelphia, 1855, vol. i, p. 590.

duty of this commission to visit without delay all cases of fever reported to the health authorities, and the onus of diagnosis should rest on the commission and not on the attending physicians. They (the commission) should visit each patient daily until the diagnosis is established or the patient sent to hospital, and they should forward promptly to the health department a written report at each visit. The commission should determine whether or not the patient shall be treated as a possible case of yellow fever, and their decision should be final and obligatory on all concerned.

4. All patients presenting the symptoms of yellow fever, and all cases not diagnosed but remaining under suspicion, should be promptly removed for treatment to a hospital especially located and provided with wire screens and mosquito nets, and the whole or a portion of which has been set apart for that purpose. The yellow fever wards or hospital should be under the direct control of the senior diagnosis commission, and the patients should be treated by physicians appointed only on their recommendation and acting under their direction.

5. In exceptional cases, to be determined by the commission, patients under observation awaiting diagnosis could be treated in their homes beneath mosquito netting, and in rooms properly protected with wire screens, until the nature of the case had been finally settled to the satisfaction of the commission.

The commission and not the attending physician should be held responsible for the enforcement of all clinical measures necessary for the protection of the community, and they should be empowered to employ such help as seemed in their judgment to be required. They should also be assisted at times by subcommissions appointed on their recommendation.

Under such a system, conscientiously carried out, the occurrence of an epidemic of yellow fever in any city would become an impossibility. Objection can not be made on the ground of expense if the members of the diagnosis commission are paid only for every visit to a patient; under such an arrangement the cost to the city would be trifling when compared with the losses now sustained by individuals and the whole community through the failure of practicing physicians to recognize and report mild cases of the disease. And herein lies the crucial point. The diagnosis must be anticipated and the proper precautionary measures be taken before the disease has fully declared itself. Diagnoses of malarial remittent, and above all of bilious remittent fever, must not be accepted as conclusive until the presence of malarial or other parasites has been demonstrated to the satisfaction of the members of the diagnosis commission. Attention was called two years ago [1] to the fact that over and over again, since the time of Benjamin Rush, yellow fever has stalked abroad in our cities, unrecognized, under the guise of bilious remittent fever. The time has come when a diagnosis of bilious remittent fever should no longer be accepted, for there is no such disease per se. We may have malarial fever complicated with jaundice, but this should not change the diagnosis of malaria any more than an accompanying icterus would change a diagnosis of typhoid fever. Similarly a complication of malaria no longer justifies the diagnosis of

[1] Journal Association of Military Surgeons, 1903, No. 4, vol. xiii, pp. 193, 199, and 200.

typho-malarial fever, and that term has properly been discarded. In numerous instances it is stated in the records of the older epidemics of yellow fever that the disease was preceded by, or began as, a bilious remittent fever, just as in more recent times physicians have believed that typhoid fever began as malarial fever. The conclusion is equally untenable in both cases, and the deduction is obvious that cases of so-called bilious remittent fever must be regarded and treated as cases of yellow fever, unless a satisfactory specific cause for the condition can be demonstrated beyond a doubt. It is proper to mention here that in every one of the 22 cases of yellow fever purposely inoculated by the Army Board in Cuba, a diagnosis of bilious remittent fever would have been justified if it had not been known that they were produced from true cases of yellow fever, for, although some of them were severe, black vomit was absent from all.

It may seem unnecessarily severe to require physicians, under a penalty, to report all cases of fever coming under their observation, but no other means will attain the desired result, and the enormous interests at stake demand that the methods instituted be thorough and that they be rigidly carried out. The appointment of a board of diagnosis, as has been suggested, will relieve the attending physician from the odium that accompanies a diagnosis of yellow fever in a doubtful case, and the board, fully appreciating the responsibility that rests on them, may be relied on to do their duty. During the discussion on yellow fever before the American Public Health Association at its meeting in Washington two years ago, already referred to in my remarks, which were badly misquoted,[1] I urged the necessity for requiring physicians, under a penalty, to report all cases of fever, in order that they might be examined by a board of experts (as was done in Cuba) and treated as cases of yellow fever until the diagnosis was established. Only last month, in a conversation on this subject with a physician from a large city in Texas, he laughingly remarked: "We never report our cases of yellow fever until we have about a dozen of them."

The present epidemic in and about New Orleans only serves to emphasize the necessity for such regulations as are here suggested, and this necessity is further emphasized by the statement in the public press of September 5 that "Inspector Brady attributed the continued spread of the disease to the unwillingness or inability of physicians to diagnose mild cases of yellow fever, and that physicians of standing and ability look for black vomit before making a diagnosis." We have elsewhere [2] cited the occurrence of the same difficulty at Key West in 1889, and we again assert that these physicians may be thoroughly conscientious and able men, but they are baffled by the differences between the aspects of the disease as they actually find it and as they have been taught by the best authorities to expect to find it. It is the manifest duty of local health authorities, therefore, to relieve the physician of the burden of diagnosis and to leave that and the adoption of protective measures to the board of expert diagnosticians.

In this connection I beg to be permitted to call attention to the present situation at Jackson Barracks, a station of two batteries of Coast Artillery, in New Orleans. By the seventh day of the present

[1] Reports of the Proceedings of American Public Health Association, vol. xxix, 1904, p. 291.
[2] Journal Association of Military Surgeons, 1903, vol. xiii, No. 4, p. 201.

month a number of cases of yellow fever had appeared in the neighborhood and seven of them in a block that approached within 100 feet of the officer's quarters. Still the garrison has not been removed and up to the present time no single case has occurred among them; even should a case or two appear an epidemic is not feared. The reason for this is simply that the medical officers know that it is absolutely within their power to prevent any epidemic extension of the disease; they are constantly on the alert, and all cases of fever are handled in the beginning as though they might be yellow fever.

Again, at Fort McIntosh, in Laredo, Tex., in 1903, there were only 5 cases of yellow fever in a command of 111 officers and men, while in the town alongside them over 1,000 cases and more than 100 deaths occurred. It was found that the 5 men who became infected had violated orders by visiting the town at night without wearing the prescribed mosquito head-nets, leather gauntlets, and leggings.

If, in the presence of cases of yellow fever among and around them, garrisons of soldiers can be protected from the infection in anything like epidemic form, it necessarily follows that the same measures and the same degree of vigilance will protect a community, provided the physicians do their full duty and they are properly assisted by the authorities. The subject is one involving the lives and interests of thousands of innocent persons, and the secret of success lies in eternal vigilance, with the determination to allow no case, however mild and doubtful, to escape the fullest precautions.

DR. ARISTIDES AGRAMONTE.

PART IV.—REPORTS FROM SANITARY OFFICERS IN HABANA, CUBA, DEMONSTRATING THE PRACTICAL VALUE OF THE SCIENTIFIC FINDINGS OF MAJ. REED AND HIS ASSOCIATES ON THE YELLOW-FEVER COMMISSION.

Chapter I.

SANITATION AND YELLOW FEVER IN HABANA.

Headquarters, Department of Cuba,
Office of Chief Surgeon,
Havana, February 8, 1901.

The Adjutant General of the Department.

Sir:

* * * * * * *

YELLOW FEVER, ESPECIALLY FROM THE VIEWPOINT OF THE SANITARIAN.

Yellow fever has played such a conspicuous and important part in the mortality of Habana that it deserves special consideration. This infectious disease may claim Habana as one of its oldest and most favored haunts. It was here as early as 1720, if, as I believe, we are justified in so regarding the outbreak of that date described by the historian Pezuela, apparently imported from Vera Cruz. It thereafter broke out in occasional epidemics like the historic, ones of 1749 and 1762, the latter being particularly fatal to the Anglo-American army which had just captured the city, and causing the conquerors to relinquish their prize in 1763. From that day to this yellow fever has been endemic in Habana, hardly noticeable in some years, a mere smouldering fire when nonimmunes were few, but quickly lighting up into a blaze as soon as the fuel of immigration came within its reach. The result has been a thoroughly infected city, a source of danger not only to its own inhabitants and the rest of Cuba, but as well to all countries having commercial relations with it.

During the decade 1890–99, the recorded number of deaths was 4,831, giving an annual average of 483, with a wide range from 1,282 in 1896 to 103 in 1899. In 1900 the number of deaths was 310. Thus yellow fever is not nearly as fatal in Habana as typhoid fever in the United States, and its importance would seem to have been very much exaggerated, did we not realize that its mortality is not furnished by the whole population, but only a small proportion thereof, that is, the nonimmunes probably never averaging more than 1 in 10.

Until a few months ago the mode of propagation of yellow fever was uncertain; we were fighting an unknown enemy in the dark, an

enemy so wily and elusive that we never knew to what extent our clumsy and expensive methods of warfare were successful. But, very recently, much light has been thrown upon the subject as the result of one of the most brilliant medical discoveries of the age. The announcement long ago made by Dr. Carlos Finlay, of Habana, that mosquitoes were the agent of transmission in yellow fever has been verified and scientifically demonstrated by Maj. Walter Reed, Surgeon, United States Army, and his colleagues, in the most conclusive manner. It is true that the germ itself, in spite of the claims of Sanarelli and his partisans, has not yet been isolated, but this is of comparatively little moment to the sanitarian, more concerned with prevention than cure. For our purpose, the mosquito is the enemy, and all our efforts must be directed against it. This war should be waged with a twofold object: the destruction of the malaria-bearing anopheles and that of the yellow-fever bearing culex; thus, at the same time, eradicating the two diseases which have contributed so much to make Habana a byword of reproach among civilized nations. Practically, then, the problem consists: First, in finding the haunts and breeding places of mosquitoes and the best means of extinguishing them; second, in carefully protecting yellow-fever patients and all nonimmunes with mosquito bars, so that mosquitoes may not be infected by the former and carry the infection to the latter; third, in isolating patients, and also, as much as is possible, nonimmunes, so that mosquitoes biting the former may not be able to reach the latter. The knowledge that mosquitoes do not travel far, seldom more than a few hundred feet if shelter exists, and that each house practically breeds its own, simplifies the question. The data being thus plainly stated, there does not appear to be insurmountable obstacles in the way, and we may confidently expect to see yellow fever stamped out in Habana in the course of three or four years after the construction of a good sewerage system, provided the same unremitting efforts are continued under intelligent medical supervision and with the unrestricted help of the State.

The isolation and protection of patients is a most important measure, but hard of successful accomplishment on account of the difficulty of discovering and recognizing all cases. Many patients among the poorer classes are not seen by physicians, and the experience of the last two or three years has led us to believe that many cases, especially among young children, are so mild that they pass unrecognized or are wrongly diagnosed. From these mild, ambulatory, and consequently unprotected cases the fever is mostly spread. It is only when the profession becomes convinced that such cases really exist, and that, as foci of infection, they are as dangerous as severe cases, that perfect results will be obtained.

Our present knowledge concerning the agency of the mosquito in yellow fever explains much that was obscure before and furnishes useful indications to the sanitary physician. For instance, the part played by dirt and filth in the breeding and propagation of the fever was always problematical; now we know that they have nothing to do with it, except inasmuch as they may attract and feed mosquitoes. It is certain that in Habana, in 1900, no visible correlation could be seen between dirt and yellow fever; the district which first became strongly infected lies east and south of the Parque Central, and is one of the cleanest and best constructed, while the most insanitary

wards became infected late in the season and only to a slight extent; the malodorous district reserved to houses of ill fame did hardly have a case. Yellow fever has not followed the poor and unclean, or the march of previous infections, but rather the movement of nonimmunes; wherever these located, there the infection searched and found them, regardless of the hygienic conditions of their premises, the most aristocratic apartments on the second and third floors being as liable to its invasion as any of the hovels crowded around a patio.

We also know that digging the ground, either for purposes of cultivation or construction or, for instance, the laying of sewers, is a perfectly harmless operation so far as yellow fever and malaria are concerned, provided no water is allowed to stagnate in any of the cuts and ditches. The value of this knowledge on the eve of undertaking our great work of sewerage can not be overestimated.

The positive agency of the mosquito in propagating yellow fever would naturally argue the noncontagiousness of the disease and the inertness of fomites; but in order that the demonstration might be complete, Maj. Reed and colleagues also conclusively proved by direct experiment that infected linen, bedding, and effects of all kinds are powerless to convey the disease. This discovery must bring about a revolution in our methods of disinfection and quarantine in yellow fever. Disinfection becomes completely useless, since there are no infectious germs to destroy. In a house where a case of yellow fever has been under treatment the problem is how to reach the mosquitoes which have become infected by biting the patient and are still lurking in the vicinity. It is probable that a certain proportion of mosquitoes, after feeding, fly out in search of water wherein to lay their eggs, in the immediate neighborhood, but enough remain in the patient's and contiguous rooms to require action. The best way to destroy them, so far as now known, is by fumigation. Sulphur fumes are most efficacious, but otherwise so objectionable that preference should be given to formaldehyde, which, as we know, is much safer and more convenient. It kills mosquitoes in from 10 to 15 minutes, so that rooms treated with it need not be closed more than three or four hours. The good effects of such fumigation seem to have been proved in preventing the recurrence of a second case in 694 out of 885 infected houses in Habana, and by the absence of a single case in Santiago de Cuba in 1900, after the epidemic of 1899.

The duties of quarantine officers have also become singularly simplified. Since we may assume in practice that the infectious germs do not exist outside of man and the mosquito, the disinfection of trunks and baggage on account of yellow fever is no longer justifiable; all that is required will be the examination of nonimmunes within the five days immediately following their last exposure to infection, the danger of transmission being from their own persons and in no wise from their clothing or baggage. Ships, like houses, are liable to harbor infected mosquitoes and will continue to require fumigation.

From what precedes it must be evident that the two chief factors in the propagation of yellow fever are mosquitoes and nonimmunes. Nonimmunes are almost entirely furnished by immigration. Were it possible to completely stop it, especially from Spain and the Canary Islands, for two or three years, it is almost certain that during that short period all germ-bearing mosquitoes could be destroyed, and the city thereafter kept as free from infection as Kingston in Jamaica

and San Juan in Porto Rico. Immigration, however, is too valuable to the interests of the island to be stopped, or even checked, for the sake of stamping out yellow fever, a disease without terror and of little consequence to Cubans. It is only possible, then, to take such measures as will protect as many nonimmunes as possible without interfering in any way with business interests. The plan lately adopted is practical and efficient: All nonimmune immigrants who do not come in answer to a call from Havana are taken to a detention station on the healthiest site around the bay, where they await in comfort and safety offers of employment. All employers of labor, or as many as it is possible to reach, have been notified of the existence of this station and invited to engage there all the hands they need. Earnest efforts are made to send as many as possible of these immigrants to the rural districts where most wanted. In this way all are benefited: the immigrant who procures work without hardship or danger, the city of Havana, which is rid of dangerous nonimmune agglomerations, and employers who are enabled to get as many hands as they may require with the least trouble and expense.

The relation which Spanish immigration has borne to yellow fever is important and interesting. It has been most active in periods of peace and prosperity, becoming small or stopping altogether in years of political disturbance and insurrection, and statistics show that the spread of yellow fever among civilians is directly proportional to the number of immigrants.

Soldiers, on the contrary, were few in years of peace and contributed little to the yellow fever mortality, but in troublous times they were greatly and rapidly increased, beginning to arrive as the civil immigration began to stop, so that their mortality curve rose as that of the civil population fell. Thus, when the last insurrection broke out, in 1895, immigration stopped; on the contrary, troops poured into Havana, and the result was a very high military mortality in 1896, 1897, and 1898. When the American troops took possession of Havana on January 1, 1899, the whole population was practically immune, and, the Spanish troops having departed, cases of yellow fever ceased. The American troops formed the only susceptible or nonimmune element and disciplinary measures were successful, with one slight exception, in preventing their contagion. It therefore happened, naturally enough, that only few scattered cases were observed during the spring and summer of 1899. As soon as peace was assured the current of immigration was resumed, and in greater volume than ever. The result was immediately seen in the number of cases, which steadily increased from August to December, the number for December being larger than for the same month in any previous year; this is more striking because the death rate of yellow fever generally rises to its maximum in August and September and shows a marked decline from October to December.

During the years 1899 and 1900, 40,384 immigrants arrived at Habana, namely 16,260 in 1899 and 24,124 in 1900, a great majority of them nonimmunes and at least 50 per cent remaining in the city of Habana. They still continue to come at about the same rate. With these figures of the largest immigration on record in the same space of time, what happened was to be expected and unavoidable, namely, an usually large number of cases of yellow fever in the summer and fall of 1900 and corresponding high mortality, although

the deaths (310) did not reach the annual average of the past decade. The effect of cold weather on the infection was, as usual, well marked; from 74 in October the number of deaths decreased to 57 in November, 20 in December, and only 7 in January, 1901.

The subject of immunity against yellow fever is very interesting and deserves a few remarks. Immunity is not enjoyed by all Cubans, as popularly believed, but only by those residing in cities, not by those who have lived from infancy in the interior rural districts. In other words, immunity is only enjoyed by the residents of centers where yellow fever is endemic; it is not enough to have lived in a tropical climate; one must have lived in an infected locality. The inference therefore is strong that immunity is acquired only by an attack of the disease; there is no other infectious disease against which immunity is obtained in any other way, and there is no reason to believe that yellow fever is an exception to the rule. Under the former belief that it was acquired by the absorption of germs through the respiratory passages, it was possible to conceive the possibility of a very slow but constant infinitesimal absorption which might in time produce immunity without any apparent fever, but such a conception is no longer tenable if the germs are introduced directly into the blood by the mosquito. Those physicians who assume a priori that Cubans, whether they live in the city or country, can not have yellow fever, decline to recognize it when they find it in natives; they call it "fiebre de borras" and consider it a special form of malaria, which, strangely enough, only occurs in this island.

Since the great majority of Cubans are immune and immunity is only acquired by an attack of the disease, we are compelled to the conclusion that nearly all natives of Cuba must have yellow fever in their youth—probably in the first few years of their lives. At that age the disease appears to be mild and comparatively harmless, and we may fairly assume that the 5,000 children annually born in Habana have it in such form that it is generally unrecognized by physicians who diagnose it under the comprehensive headings of malaria, calentura or meningitis. In this connection it is interesting to observe that in epidemic years the proportion of deaths among children, not diagnosed yellow fever, is noticeably greater.

Here an interesting question suggests itself. If Cubans have yellow fever in infancy in such a mild form as not to endanger life and remain immune thereafter, why should they endeavor to eradicate the disease in the island, so that their descendants will lose immunity and become liable to any epidemic that may break out hereafter? The answer is that foreign visitors and immigrants have natural rights that Cubans are bound to respect; that epidemics can be guarded against and avoided; and lastly, that although Cuban infants have the disease in an apparently mild form, it will probably be found, when the matter is investigated and the obscure diagnoses of many of the reported cases of death carefully analyzed, that a larger proportion of deaths among children than is generally believed is due to yellow fever or complications therefrom.

A few words in closing upon the result of treatment of yellow-fever cases at Las Animas hospital, an establishment intended for the reception and treatment of all contagious diseases, but chiefly yellow fever. During the year 1900 it was under the direction of Maj. W. C. Gorgas, chief sanitary officer, who devoted to it much of his

valuable time. The hospital is pleasantly situated in the outskirts of the city and as completely equipped with material and personnel as any hospital of its kind in the United States, American trained nurses being in attendance. An ambulance, carrying physician and nurse, is always in readiness to go when summoned, and the greatest care is taken to save patients all unnecessary fatigue or exertion in transit.

The patients sent to this hospital may be divided in two classes: First, Americans (including few other foreigners), the majority of them brought there at their own request early in the disease, but including also not a few homeless vagabonds and drunkards; second, Spaniards, mostly of the lowest classes, too poor and thriftless to belong to any of the quintas de salud.

It can easily be seen therefore that Las Animas receives most of the worst cases, generally after the disease has lasted several days, not infrequently the patients being unconscious and occasionally moribund, as shown by the fact that out of 58 deaths, 18 occurred within three days after admission. During the year, 272 cases of yellow fever were admitted; 167 Americans, 74 Spaniards, and 31 of other nationalities; 214 recovered and 58 died, giving a general death rate of 21.33. Taking the three leading and best conducted private hospitals in Habana for comparison, namely, the Dependientes, Covadonga, and Benefica, we find that during the year their yellow fever death rates were 24.35, 27.51, and 24.35 respectively, each higher than that of Las Animas, although their patients, being members of the centros or clubs to which the hospitals belong, are generally admitted early in the course of the disease and therefore in much more favorable conditions for successful treatment.

At Las Animas the death rate of Spaniards was 36.48 and that of Americans 12.57, a most remarkable difference when we bear in mind that all patients there receive the same identical treatment in the same wards. This difference is partly due to the fact that Americans are in better physical condition, with greater power of resistance, but chiefly to the circumstance that they are admitted early and have the full benefit of the treatment. In this respect the status of Americans at Las Animas may be fairly compared to that of the Spaniards received at the above-mentioned hospitals, and yet their mortality is only one-half that of the latter. Such results furnish food for reflection. At Las Animas patients are treated almost entirely on the expectant plan; medicines are avoided until there is a clear indication for their use; absolute rest, very careful dieting, and the constant attention, day and night, of trained nurses have been the main features of treatment. The key to success in the treatment of yellow fever, I believe, is good nursing at the hands of specially trained women. Such nursing is expensive, and in Cuba has been practicable, so far, only in few other hospitals, but any method of treatment which saves lives is always found to be the cheapest.

V. HAVARD,
Major and Surgeon, United States Army, Chief Surgeon.

Chapter 2.

REPORT OF THE HABANA YELLOW FEVER COMMISSION.

HABANA, *January 3, 1902.*

SIR: In compliance with your request that I should make a report of my department, as chairman of the Yellow Fever Commission, for the six months ending December 31, I have the honor to inclose the said report.

Very respectfully,

CHARLES FINLAY,
Chairman of the Yellow Fever Commission.

Maj. W. C. GORGAS,
Surgeon, United States Army,
Chief Sanitary Officer of Habana.

HALF-YEARLY REPORT OF THE HABANA YELLOW FEVER COMMISSION, JULY TO DECEMBER, 1901.

During the present term (July 1 to Dec. 31, 1901) the Yellow Fever Commission of Habana has examined and investigated 118 cases, reported as follows: 94 yellow fever suspects (37 of which were confirmed as "natural yellow fever" and 10 as "experimental yellow fever"); 7 suspected glanders (the diagnosis was confirmed in 4); 4 leprosy (confirmed in 3); 6 suspected smallpox (none of which were confirmed); 1 typhus fever (not confirmed); 1 relapsing fever (not confirmed); 5 reported as "infectious fever" (in 2 that diagnosis was maintained, inasmuch as these cases, while presenting clinical characters suggestive of an infection, could not be identified as malaria, typhoid, influenza, and Malta fever, and were therefore considered as belonging to the group of "Tropical unclassed fevers).

The 37 cases diagnosed as "natural yellow fever" have been distributed in Table I, so as to differentiate those whose infection had originated in this city from others who were brought to Habana, already sick or infected, from other parts of this island, and also from those who came from foreign ports.

TABLE I.—*1901.*

	July.		August.		September.		October.		November.		December.		Totals.	
	Cases.	Died.	Cases.	Died.	Cases.	Died.	Cases.	Died.	Cases.	Died.	Cases.	Died.	Cases.	Died.
Habana.....	7	3	7	1	9	2	0	0	0	0	0	0	23	6
Other towns (Cuba).....	6	1	3	0	0	0	1	0	0	0	0	0	10	1
Foreign ports..	0	0	1	0	0	0	1	0	2	1	0	0	4	1
	13	4	11	1	9	2	2	0	2	1	0	0	37	8

TABLE II.—*Experimental cases.*

August.		October.		November.		Totals.	
Cases.	Died.	Cases.	Died.	Cases.	Died.	Cases.	Died.
7	3	2	0	1	0	10	3

The wonderfully small number of yellow-fever cases and deaths in Habana during the epidemic season of the present year is an unprecedented event, and since it can not be accounted for by any climatic variations nor by a lack of nonimmunes or of opportunities for a reproduction of the yellow-fever germ through the introduction of cases from outside, we are bound to admit that it must be attributed to the killing of contaminated mosquitoes wherever they were supposed to exist, and to the protection of nonimmunes in the vicinity of infected houses against the bites of those insects, as the sanitary department has been doing since February.

MANNER IN WHICH THE INVESTIGATION HAS BEEN CONDUCTED.

The conclusive demonstration of the mosquito theory—by Dr. Reed, a year ago, and by Dr. Guitéras this summer—has made it all the more necessary that the investigation of yellow-fever cases should be carried out with great care, so as to secure a reliable diagnosis, and to discover, if possible, the source whence the infection has been derived.

The method practiced by the commission has been as follows: The data contained in the original report are carefully gone over at the bedside of the patient and additional particulars inquired into in order to discover, if possible, the probable source of his infection. A clinical history of the case having been obtained from the physician in charge, it is minutely scrutinized, and the patient is then carefully examined by each of the members present. Particular attention is given to the examination of the urine for albumen, and it is believed that, while sources of error are avoided, so small a quantity as 10 centigrams of pure albumen per liter would not escape detection, as a recognizable trace, by the methods employed. The different organs are explored to detect or exclude any lesion to which some of the symptoms might be attributed, and every circumstance in antecedents of the patient is duly taken into account.

As a rule, the secretary of the commission, before the meeting of the board, has collected blood, sputa, pus, or other available material, according to the nature of the disease reported, and the said material has been examined for malarial parasite or bacteria, tried with the Widal test, etc. In the case of private patients, supplementary information has been obtained by the secretary from the attending physician, and, if necessary, the latter is requested to be present at the meeting of the board. Whenever any doubt remains in the minds of the members the decision is deferred and the patient reexamined as often as may be necessary. In fatal cases, provided the family or friends of the patient do not object, an autopsy is made, notes of the findings recorded, and hystological specimens preserved or cultures prepared for subsequent examination. The physician in charge is always expected to notify the commission or to report the case again

if the subsequent course of the attack should throw some doubt upon the decision of the board, in which event a reversal of the first diagnosis would be voted if the majority of the members decided that there was occasion to do so.

USEFULNESS OF EXPERIMENTAL CASES FOR DIAGNOSIS.

In the diagnosis of mild cases of yellow fever it has been of great advantage to the commission to have the support of Dr. Reed's observation in one of his experimental cases, showing that an undoubted attack of the disease may run its full course without presenting any trace of albumen in the urine. Similar cases had been observed in private practice by members of the commission, and some of them have come before the board. The same may be said with reference to the importance of the typical fever curve as an element of diagnosis in nonalbuminuric cases.

SOME KNOWLEDGE OF THE LIFE CYCLE AND HABITS OF THE STEGOMYIA NECESSARY IN ORDER TO FOLLOW TRACK OF AN EPIDEMIC.

The importance of ascertaining the source of the infection in every confirmed case of yellow fever is self-evident, since the sanitary department is thereby enabled to take prompt measures calculated to control the propagation of the disease. But that investigation, according to the now accepted etiology, can not be successfully accomplished without a knowledge of certain details concerning the life of the yellow-fever mosquito which are not easily found in the current literature on that subject, and it may not be considered out of place to recapitulate them in this report.

The species of gnat which transmits yellow fever (*Stegomyia tæniata*, Theob.-Culex mosquito, R. D.) is diurnal and crepuscular, for it may be met with at any hour between daybreak and nightfall, and takes its rest during the night. The males never bite nor suck blood; the females only do so after they have mated, and never lay their ova before having sucked blood. After a complete feed of blood the insect will not bite again until all the contents of its stomach have been digested or discharged; this process requires from 48 to 60 hours in summer, but may be delayed 2 or 3 days more in cool weather. The wings of the Stegomyia are so small that after a full meal it must be unable to fly to any height or even to any considerable distance on a level. It shuns the sunshine, avoids flying across open waters, and keeps away from the wind. Its eggs are laid in a peculiar manner, some entirely out of the water, so that they are apt to remain unhatched during several weeks or months, and yet may develop a brood after that lapse of time when they happen to be covered with water of a suitable temperature. It is probably by this means that the species is propagated during the cooler months of the Cuban climate. The Stegomyia breeds in any collection of water (a very small quantity is needed) in the yards, gardens, basements of houses, often in the lye water used by washerwomen in this country; but also inside of rooms when water has been allowed to stand several days in basins, jugs, or open bottles. A new brood may develop in 9 or 10 days if the larvæ are abundantly provided with food (bread crumbs seem to agree very well with them), otherwise several weeks may elapse before the winged insect emerges from its pupa case.

When the temperature falls to 20° C. the insect is disinclined to fly, and below 15° or 10° C. it is benumbed and unable either to fly or to bite. It is killed by temperatures below freezing point or above 45° C.; probably 30° to 32° C. is its optimum temperature.

The Stegomyia is very domestic in its habits and will not be likely to leave the premises on which it has taken up its quarters so long as it finds in it the necessary conditions for the completion of its life cycle (opportunities for satisfying its craving for human blood, water in which it may lay its ova, and an agreeable atmosphere suited to its tastes and of the required temperature) In the absence of any of those requisites it will migrate into the nearest place where they may be satisfied.

The Stegomyia becomes contaminated and acquires the faculty of transmitting the disease only after having bitten a yellow-fever patient within the first 5 or 6 days of his attack. During the first 2 or 3 days of its contamination its bite may sometimes occasion an attenuated form of the disease, but after that period the insect loses for a while the faculty of inoculating the disease in any form, and it is only when 12 or more days have passed since its contamination that it acquires the power of producing a well-marked attack of yellow fever, the virulence of its bite being then considerably greater in summer than in winter. The contaminated Stegomyia retains thereafter, during its lifetime (which may last 70 days), the faculty of reproducing the disease every time that it chances to bite a nonimmune.

The manner in which a nonimmune may become infected is apparently under the following circumstances:

(1) By visiting a place where contaminated mosquitoes exist, at a time when those insects happen to be in a condition to bite and prepared to inoculate the disease.

(2) By the fact that a case of yellow fever has occurred in the neighborhood and mosquitoes contaminated from that patient have, for some reason, been induced to migrate into the nonimmune's dwelling.

(3) By the conveyance of contaminated mosquitoes in parcels, boxes, etc., or, possibly caught under a hat while biting the head of a visitor on his way to the nonimmune's house.

(4) During the hot summer days the Stegomyia is apt to fly out into the street, under porches, etc., suggesting the possibility of their biting a yellow fever patient on his way to the hospital if the carriage or the unprotected ambulance happens to be detained. In such a case, the insect, thus contaminated, would afterwards take refuge in one of the houses on the road to the hospital, and the nonimmunes in that house might, in due time, be inoculated by the infected mosquito.

A PRACTICAL ILLUSTRATION OF THE MOSQUITO THEORY.

As an illustration of the ways in which the yellow fever may be acquired, according to the preceding statements, and of the difficulties with which the sanitary department has had to contend this year in preventing the disease from spreading over the whole city, the following instance may be given as one in which the yellow fever commission was deeply interested.

In one of our best hospitals in this city (Quinta de Dependientes) the upper story of a new building is reserved for yellow fever patients and suspects. That floor being divided into a right wing for confirmed cases and the left wing for cases under observation, the landing of the stairs occupies the space between the two large screened doors, facing each other and opening into each of the two departments. Though well provided with wire netting, two defects were subsequently noticed in the disposition of these wards: the height of the ceilings, which prevents mosquitoes from being seen when they occupy the upper part of the rooms, and the absence of any syphon or trap in the pipe leading off the water from a basin under the hydrant. Under these conditions, mosquito larvæ might be bred outside the building where the defective pipe opens and the winged insect might find its way into the yellow fever ward, remaining there unseen after having bitten some of the patients. In fact, larvæ were observed by us, on one occasion, in the water jug used in that ward.

On the 14th of August of this year, two nonimmunes were admitted into the observation ward with a fever which appeared suspicious but only turned out to have been a mild attack of influenza. Both were discharged on the 18th. One of them lived at Florida Street, No. 24, the other in a bakery in Aguila Street, No. 185, opposite the Tacon market. The man from Florida Street was attacked, on the 20th (two days after leaving the hospital) with fever and developed a mild yellow fever. His house was duly fumigated and all the contaminated mosquitoes must have been killed, for no other case occurred in that neighborhood. The other man (No. 1), who lived at the bakery, was also attacked with yellow fever, but not until the 24th (six days after leaving the hospital), and two other men (Nos. 2 and 3), who worked in the same bakery and slept in rooms near his own, were also attacked, on the same day and the next respectively (Aug. 24 and 25). We must therefore infer that No. 1 had brought with him from the hospital some of the contaminated mosquitoes which had inoculated him, and the incubation was shorter in the two other men than in his own case. The bakery was, of course, fumigated and most of the contaminated mosquitoes probably killed; but the disposition of the house and of its neighborhood was particularly unfavorable, and some of the numerous insects which had had a chance of biting one or other of the three simultaneous cases must have escaped and flown across the narrow street into the porch of Tacon market, where fruit and flower venders lay out their goods on the floor under the porch and sit or stand the greater part of the morning waiting for purchasers. Two of those flower venders (Nos. 4 and 5) were attacked with yellow fever on the 7th and 11th of September, respectively; the last of these developing into a fatal case, the first of the series. These two men lived in the Cerro, where they had their garden near Tulipan Park.

Their dwelling was fumigated effectively, for no other case of yellow fever occurred in the neighborhood. The owner of the bakery on Aguila Street lived in a house at the back of it, on Amistad Street, No. 136, and (No. 1), when questioned by the members of the commission at the hospital, had told them that after his attack of influenza he had first gone to the owner's house. That house was therefore probably infected and duly fumigated; but from here also some

of the contaminated insects must have escaped and taken refuge in a café close by, Amistad Street, No. 130, where the bartender (No. 6) was attacked with yellow fever on the 12th of September. This house was also fumigated, but the same contaminated insects which had bitten this case or others from the same source must have crossed Dragones Street and entered another house in the next block, Amistad No. 95, where a man servant (No. 7) was attacked with fatal yellow fever on the 14th of September. The next two cases occurred in two newly arrived immigrants (No. 8 and No. 9) who lived together in a room at Ricla, No. 32, a food distance from the infected quarter; but they informed us that they were in the habit of going almost every evening to a house in the block next to that of (No. 7) Amistad, No 96, but on the other side of the street, to chat with an immune friend of theirs. These two men were attacked on the 21st and 22d of September. The killing of mosquitoes at their dwelling proved efficacious, for no other cases occurred near Ricla 32; but a few of the contaminated insects still remained in the block of (No. 7), for in a large tobacco factory occupying the south front of that block two of the workmen (No. 10 and No. 11) were attacked on the 28th of September. This time, however, the fumigation and killing of the mosquitoes within and around the tobacco factory must have killed the last of the infected insects, for no other case of yellow fever has been reported since in Habana.

DESIDERATUM.

The danger of new invasions which might insidiously acquire such proportions that they should prove difficult of control, comes principally from the want of a sure landmark by which to recognize even the mildest forms of the disease, a want which, it is feared, must subsist so long as the germ of the disease has not been definitely identified. With the certainty that the said germ is contained in the blood of the patient and also in the head of the contaminated stegomyia, it was thought that Drs. Reed and Carroll could not fail to discover that germ, knowing that they had apparently the best of materials to work upon and the assistance of experts well trained in the investigation of animal and vegetable germs. Their failure to do so has therefore caused general disappointment. The Yellow Fever Commission, howerer, considers it one of its duties not to let the matter drop, and to avail itself of Dr. Guiteras's permission and valuable cooperation for pursuing the search for the yellow-fever germ at the laboratory of his experimental station whenever a favorable opportunity for doing so presents itself.

CHARLES FINLAY,
Chairman of the Yellow Fever Commission.

HABANA, *January 3, 1902.*

Many years before the Yellow Fever Commission was organized, Dr. Carlos J. Finlay, of Habana, had formed the opinion that yellow fever was conveyed by the bites of mosquitoes and had fixed upon the *Stegomyia calopus* as the culpable agent. On June 30, 1881, he began a series of experiments to prove the transmission of the

disease by this insect, believing that he could in this way produce a mild type of fever which would convey immunity. He bred the mosquitoes in captivity and developed a technique for transporting them and placing them upon the patients, and between the date above mentioned and the arrival of the Yellow Fever Commission in Cuba he had made 103 experiments of which he regarded a considerable number as successful.

In the light of our present exact knowledge of the length of incubation of yellow fever in man and the considerable period of incubation in the mosquito between the time of biting and when she becomes able to transmit the infection, and also the very brief period (three days) at the begining of the disease during which alone the patient is able to infect the mosquito, it must be recognized that probably none of Dr. Finlay's experiments were successful, but none the less must credit be given for what Col. Gorgas has termed the "scientific clairvoyance" with which he had conceived his theory and the enthusiasm with which he maintained it.

When Maj. Reed went into Habana to consult him, before beginning the work of the board, he gave him eggs of *Stegomyia calopus* which he specifically stated were those of the mosquito which conveyed the disease, and the first experiments of the board were made with mosquitoes grown from these eggs. As Dr. Finlay was the originator of this theory, and was of great assistance to the commission, the above report of his, which is of scientific as well as historical value, is published in this place, although it is recognized that some of the views expressed by him are at variance with the findings of the commission.

Chapter 3.

REPORT OF MAJ. W. C. GORGAS, MEDICAL CORPS, UNITED STATES ARMY.

HEADQUARTERS DEPARTMENT OF CUBA,
OFFICE OF CHIEF SANITARY OFFICER OF HABANA,
July 12, 1902.

GENERAL: I herewith forward the report of the sanitary department, bringing the account of the work up to May 20 of the present year.

This being the final report of the sanitary department of the city of Habana under the military government, it might be useful to review, in a general way, the work of the department since its inception in 1899.

The great object of sanitation for Cuba, and particularly for Habana, as far as the United States was concerned, was the eradication of yellow fever. For over 200 years this disease had, at short intervals, devastated the Atlantic and Gulf coasts of the United States, causing great loss of life, and still greater financial loss, due to the entire cessation of commerce which occurred during the epidemic. It is estimated that the money loss caused directly by the epidemic of 1878, which affected particularly the lower Mississippi Valley, amounted to $100,000,000, and in years when there was no epidemic quarantines had to be kept up against the infected regions around the Gulf of Mexico, which stopped almost all travel and greatly interfered with commerce. The United States had come to look upon Habana as the particular point from which infection was spread. Yellow fever has been continuously present in this city since 1762. Every month in every year during that time there have been some cases. In all other localities of North America where yellow fever occurred, it occurred epidemically; that is, the locality was free from the disease for a longer or shorter time. In places above the frost line winter always puts an end to the disease, and in localities in the Tropics it always terminates after a greater or lesser period of years from the exhaustion of the nonimmune material. It was therefore hoped by the military authorities that if yellow fever could be controlled in Habana the United States would be free from danger of epidemic invasion.

One of the most prominent objects, then, that the military government had before it during its stay in Cuba was the control of yellow fever, and for this purpose we paid great attention to the improvement of the hygienic conditions all over the island. But Habana being the only endemic focus in the island, and, for that matter, anywhere else in North America, the energies of the military government were concentrated at this point.

None who knew anything of yellow fever had any clear idea how its eradication was to be accomplished, but there was a general belief and hope that by improving the sanitary conditions the disease

here could be greatly decreased, and possibly in the course of a number of years gradually gotten rid of, as has been the case in the cities of the United States. But no one, I think, who knew anything of yellow fever practically would have ventured to predict that much could have been done in this line in the course of three years.

In Habana the government went vigorously to work, rapidly organizing street cleaning, disposal of garbage, and the cleaning of premises. In a very few months the streets were as clean as those of any modern city and the garbage regularly disposed of. But the internal sanitation of houses and the organization of the sanitary department for the reporting and control of contagious and infectious diseases, and similar matters, took a longer time.

In the early part of 1899, the first year of the military occupation, very little yellow fever occurred. The preceding five years had been years of war, and for the last few months the American blockade had practically put an end to immigration into Habana, and the nonimmune population was pretty well exhausted, so that there were few left capable of having this disease. In January, there was one death; in February, none; in March, one; in April, two; in May, none; in June, one, and in July, two. That is, in the first seven months of 1899 there were only seven deaths from yellow fever. The military governor of the city, Gen. Ludlow, felt sure that the measures which were being taken had pretty well eradicated it.

But about the 1st of August, Spanish immigration began to pour into Habana, and between August and December some 12,000 immigrants arrived in the city, about 60 per cent of whom settled in Habana. This at once started up yellow fever, and by December of 1899 we were having a severe winter epidemic. This continued right along through 1900, during which year we had a very sharp epidemic, having in all some 1,400 cases.

The general sanitary conditions had improved, as indicated by the falling death rate, in a very satisfactory manner; but our work was evidently having no effect upon yellow fever. This disease was under control everywhere else in the island, but the principal means of reducing it, the deportation of the nonimmune population, so successful everywhere else, was not practicable in Habana.

By the beginning of 1901 the sanitary department was pretty well satisfied that ordinary sanitary measures were having no immediate effect upon yellow fever. The city during the year 1900 was as clean and in as good sanitary condition as it was possible for labor to make it, and affairs could not be gotten into better condition until after the completion of a sewer system.

In the summer of 1900 a commission of Army medical officers headed by Maj. Walter Reed, United States Army, had been sent to Cuba for the investigation and study of yellow fever. Due to the financial assistance given by the military governor to this commission, they were enabled to experiment on the human subject. They took up the theory advanced by Dr. Carlos Finlay of Habana, in the year 1880, that the *Stegomyia* mosquito was the sole means of the transmission of yellow fever. Dr. Finlay had maintained this theory for some 20 years, and had done considerable experimental work in this direction.

The commission, through elaborate and careful experimentation, proved this to be correct, and in February, 1901, Dr. Reed read a

paper before the International Sanitary Congress, in Habana, giving the results of their work. This idea was so new and so entirely contrary to all former theories on the subject, and, apparently, to all former experience, that the paper was received with scant belief. I myself had seen the work, and was convinced that the mosquito could convey yellow fever, but I was hardly prepared to believe that it was the only way, or even the ordinary way, of conveying the disease.

But all ordinary sanitary measures for the preceding two years had been flat failures. Yellow fever at the beginning of 1901 was about as bad as it had ever been in Habana at that time of the year. The city was infected in every part, and there was present probably the largest nonimmune population that had ever before been in Habana.

I had very little hope of accomplishing much; it seemed to me that even if the mosquito did convey yellow fever, he could not be gotten rid of, and, apparently, from all past experience, the mosquito was not the only way, or even the principal way, of conveying the disease; but, as he evidently could convey the disease, it was our duty to take precautions in this direction.

The military governor readily granted the necessary appropriation and authorized the employment of as large a force as needful for mosquito work. Work was commenced on this line February 4, 1901, and pushed in every direction. The results soon began to be apparent. In January there were seven deaths from yellow fever; in February, the first month of mosquito work, five deaths; in March, one death; none in April, May, or June; one in July; two in August; and two in September, and for the nine months following September, 1901, not a single case nor a death has occurred from this disease. This result convinced the sanitary department that the mosquito not only could convey yellow fever, but that it was the ordinary way, and the only way, at least in Habana, for the conditions in Habana during 1901 were as favorable for a yellow fever epidemic as they had ever been. The city had the largest nonimmune population, probably, that it had ever contained. Infection was scattered in every part of the city; not only so, but the small towns surrounding the city were thoroughly infected, and were constantly sending cases into the city. We continued the same sanitary measures that had been taken during the preceding year, and which had not had the slightest effect upon the march of yellow fever; but, in addition, we we took measures looking to the Stegomyia mosquito as the means of conveying the disease. Immediately after the adoption of these measures, yellow fever began to decrease, and by September had been entirely eradicated from the city.

The demonstration is the more effective in Habana from the fact that in all other cities of North America yellow fever lasts for a greater or lesser number of years, and then disappears from natural causes, to reappear again when conditions are favorable. In Habana the conditions have been different. For 150 years yellow fever has been constantly present in the city. From September, 1901, to July, 1902, not a single case nor a death has occurred. In the 150 years referred to, not any year, probably, can be picked out in which during the same period there were less than 100 deaths.

This, it seems to me, is a practical demonstration, given in the only endemic focus for yellow fever in North America, and in a year when

the conditions were most favorable for the development of the disease, of the fact that the Stegomyia mosquito is the only method of transmitting it—a fact proved by the Army commission.

Under Army administration the death rate in Habana has decreased in a marked degree. In 1898, the number of deaths was 21,252, giving a rate of 91.03; in 1899, the first year of our occupation, we had 8,153 deaths, giving a rate of 33.67; in 1900, we had 6,102 deaths, giving a rate of 24.40; in 1901, we had 5,720 deaths, giving a rate of 22.11; for the first four months of 1902 there occurred 1,896 deaths, which if kept up for the year would give 5,688 deaths, a rate of 20.68 for the year.

Thus it can be seen that under the military government, in a little over three years the death rate was reduced from 91.03 to 20.68. The latter rate would be a favorable one for the better class of cities in Europe or the United States. And this has come about without making any permanent sanitary installations, such as sewage. The city was kept as clean as it was possible for labor to make it, with regard to the streets, disposal of garbage, and the interior of the houses. But every house in Habana, somewhere under the house, still has a cesspool, the flow from which sinks into the surrounding ground, and as this has been going on for 400 years, the ground itself is as thoroughly saturated with organic matter as is possible.

The authorities had hardly hoped for such marked improvement until this system of cesspools has been done away with by a good system of sewage. But apparently the condition referred to has no very great effect upon the general health of the city; the improvement has come about from a careful street cleaning, disposal of garbage, internal sanitation of houses, and rigid control of infectious and contagious diseases.

Our work down here has been a useful lesson in municipal sanitation. The same thing could be accomplished by any community anywhere else, if they were willing to spend money and labor upon it. No elaborate machinery of any kind is necessary; merely men and brooms.

The primary object of the war with Spain was the liberation of Cuba from Spanish domination, but, at the same time, the United States had hoped to accomplish a good deal in improving the sanitary condition of the island. In this she has succeeded beyond her utmost expectations, and the results in Cuba have been a new departure in military conquest. The only other people who bear comparison with us in attempting to improve the sanitary conditions of a tropical country are the English, and neither in Jamaica nor in India have they been very successful in this respect.

Much to our surprise, we find that not only can a native city like Habana be made as healthy as the better class of cities in the United States, but that our own troops, with proper care, thrive just as well in the Tropics as they do in the Temperate Zone. With the troops, the health conditions have steadily improved, until at the evacuation of Cuba the health rate was better among them than the average of troops in the United States.

Our first year in Cuba, 1898, with an average of 8,345 men, we had a death rate from disease of 67.94 per thousand. The health conditions steadily improved during the four years of our occupation, and for the last three months of 1902, with an average strength of

5,000 men, we had a death rate from disease of 1.76 per thousand. This means that the first year of our life in the Tropics we lost 67 men out of every thousand, from disease; the last year of our stay, we had profited by our experience to such an extent that we lost only 7 men per thousand.

From our experience in Cuba, several useful lessons can be deduced. We find that the native in the Tropics, with the same sanitary precautions that are taken in the Temperate Zones, can be just as healthy and have just as small a death rate as the inhabitants of the Temperate Zone; that to bring this about, no elaborate machinery of any kind is needed; that it can be attained by any community, no matter how poor, if they are willing to spend sufficient labor in cleaning, and observing well-known rules with regard to disease; that the North American Anglo-Saxon can lead just as healthy a life and live just as long in the Tropics as in the United States.

But by far the most important sanitary lesson is with regard to yellow fever—that this disease is only conveyed by the stegomyia mosquito; that the disease can readily be eradicated, even when it has gotten a firm hold, and easily kept from establishing itself by taking measures looking to the mosquito as its cause.

I look forward in the future to a time when yellow fever will have entirely disappeared as a disease to which mankind is subject, for I believe that when the yellow fever parasite has once become extinct it can no more return than the dodo or any other species of animal that has disappeared from the earth.

Very respectfully,

W. C. Gorgas,
Major, Medical Corps, United States Army.

Brig. Gen. Leonard Wood,
United States Army, Washington, D. C.

PART V.—A FEW GENERAL DIRECTIONS WITH REGARD TO DESTROYING MOSQUITOES, PARTICULARLY THE YELLOW-FEVER MOSQUITO.

By W. C. Gorgas,

Colonel, Medical Corps, United States Army.[1]

As this article is not intended for the reading of people who have given any particular attention to the facts at present known of the way in which the mosquito carries disease from one person to another, I think it best to briefly call attention to the leading points in our present knowledge of this subject.

Malaria and yellow fever are the two great diseases with which the mosquito is concerned. They are by far the most important diseases in the tropical countries of the Western Hemisphere, and play a great part in the sickness of the southern part of the United States. Up to 25 years ago it was universally believed that malaria was caused by a gas, or miasm, arising from the decomposition of dead vegetable matter in hot countries, but about that time a French army surgeon in Algeria, Laveran by name, noticed that if he looked sufficiently carefully with his microscope, in the blood of persons suffering from malaria, he could almost always find a very small animal parasite. This little, living being got into the blood in some way, Laveran did not know how, fed upon the red blood corpuscles, and was apparently the cause of the disease which we call malaria. Laveran's discovery was a great advance in our knowledge of the disease, and it was gradually accepted by all the medical world.

A careful search was made for the parasite by many investigators, but it could only be found in the blood of human beings suffering from malaria. Where else it was bred and how it got into the blood of man no one could find out. About this time it was discovered by an English army surgeon, Dr. Manson, that a small worm—the *Filaria sanguinis hominis*—was introduced into the body by the bite of a mosquito. (This worm causes the disease among human beings known as filariasis, and to it are due the enormous and unsightly swellings of the legs and other parts of the body seen by our people in Cuba and the Philippines. It is, however, a disease very rarely found in the United States, and not of much importance to us. I only mention it here in connection with my story of the mosquito.)

About 15 years after the discovery of Laveran that malaria was due to an insect in the blood, and of Manson, that a certain worm which caused disease was introduced into the human blood by the bite of a mosquito, another great English army surgeon, Ronald Ross,

[1] Washington, Government Printing Office, 1904.

discovered that the malarial parasite was found in a certain species of mosquito—the anopheles—after the insect had bitten a human being suffering from malaria. With his microscope he followed the life history of this parasite, from the stomach of the mosquito, through the walls of the stomach into the mosquito's body, and finally into its salivary glands. In the saliva of the mosquito, the little organism was found in large numbers, and when biting man, for the purpose of getting blood, the mosquito injects her fatal saliva, just as does the rattlesnake when he bites. This discovery of Dr. Ross was demonstrated in the most positive manner.

An Italian living near Rome, in Italy (malaria is very bad in the neighborhood of Rome), while suffering from a malarial attack was bitten by an anopheles mosquito. This mosquito was then taken to London, England, where they have no malaria, and a healthy young man,who had never had malaria,was bitten by her. In a few days the young man had a well-marked attack of malaria, with the usual symptoms, and the malarial parasite was seen by the microscope circulating in the blood of the patient and feeding upon the red blood corpuscles of his blood. And, again, men were taken, put into houses, screened so that mosquitoes could not get in, and spent weeks in this unhealthy part of Italy without getting sick. Yet this particular part of Italy is considered so unhealthy that during the summer season neither native nor foreigner, who can avoid it, spends a night there.

A night spent in the Campania used to be thought a certain way to contract malaria, the idea being that the foul air from the marshes caused the disease. Yet it is now seen that entirely unacclimated men can breathe this air with safety, provided only that they live in screened houses and are not bitten by mosquitoes. These and similar facts convinced the scientific world that the malarial organism gets into the blood of the human being through the bite of the anopheles mosquito, and in no other way.

Before the year 1900 it was universally believed that yellow fever was carried from person to person and spread generally by a germ which up to that time had not been discovered. The germ was supposed to travel from person to person by contact with those sick of the disease, or by means of clothing or other articles which had been near the sick, and its development was believed to be greatly favored by all conditions which increased filth. There were a good many facts in the spread of the disease which were difficult to account for under this supposition, but nevertheless it was the best explanation possible, and, as I said, was almost universally accepted, both by physicians and people generally.

During the year 1900 the Army of the United States had entire control of Habana, at that time the great center of yellow fever for the world. An excellent opportunity for investigating the disease therefore existed. The Surgeon General of the Army sent to Habana a board of Army medical officers for the purpose of investigating yellow fever. This board was made up of the following Army doctors: Dr. Reed, the president, and Drs. Carroll, Agramonte, and Lazear. After much investigation they determined to study the relation of the mosquito to yellow fever. Their attention was called to this matter by the part that the mosquito had already been proved to play in malaria and filariasis, as mentioned above, and also by certain facts known in the history of yellow fever epidemics. Dr. Finlay, a prom-

inent physician of Habana, reasoning from certain peculiarities of yellow fever and from experiments which he made, had maintained for many years that a certain kind of mosquito in Habana, the stegomyia, was the cause of yellow fever, but he had not been able to prove it.

DIRECTIONS WITH REGARD TO DESTROYING MOSQUITOES.

The Army board of which Dr. Reed was president recognized that in Cuba, where they did their work, it would have to be entirely evident that the men experimented upon could not get yellow fever accidentally in Habana, or anywhere else, but only, if at all, in the course of the experiment. They therefore took a piece of unoccupied ground about 6 miles from Habana and built there a camp of material which could not have been infected with yellow fever. They then got men who had never suffered from yellow fever and placed them in these tents. It was known that if a man exposed to yellow fever was going to have it the disease would develop in less than six days, and if he passed through six days safe and sound he was known to have escaped that particular exposure.

The board therefore argued that if they kept their men in this camp for a period of two weeks they would be safe from any exposure which might have occurred before their coming to the camp. They also had to provide means which would insure their men not leaving the camp, contracting the disease outside, and thus bringing infection into the camp. This was done by a military guard, who allowed no one to go out or come in without Dr. Reed's permission. Things were now so arranged that if a mosquito was allowed to bite a man, and yellow fever developed, the board could be certain that the yellow fever was due to the bite of the mosquito alone. They did a great deal of experimenting here before they worked out all the details of the way in which the mosquito actually conveys yellow fever. They finally found out that if a female mosquito of one particular species, the stegomyia, was applied to a yellow-fever patient in the first 3 days of his sickness, and then kept from 10 to 20 days and allowed to bite a human being who had never had yellow fever, he would very generally develop the disease within 6 days after the bite.

They also found out that this same man, before he had been bitten by the yellow-fever mosquito, could sleep in the bed in which a patient had died of yellow fever, could be covered with a black vomit from a yellow-fever patient, or be exposed to the emanations from yellow fever in any other way, and as long as he was kept safe from the bite of the mosquito he would not have yellow fever; but this same man, after all this exposure, if afterwards bitten by an infected yellow-fever mosquito, would very certainly catch the disease. I think it would be interesting to give some of the details of the work by which this great discovery was demonstrated.

They had a little frame building built in this camp furnished with jars and the necessary simple material for breeding mosquitoes. The building was carefully screened and guarded, so that mosquitoes could not get in nor out. Eggs of this particular species of mosquito were obtained and hatched in one of the jars. A female mosquito was taken from the brood thus hatched. The male mosquito will not bite, and can readily be distinguished from the female with a magnifying

glass by the fact that the male has very heavy feathery feelers (antennæ) growing from his head. The female mosquito selected was put into a small glass tube, stoppered with a little cotton, so that she could get air freely but not escape, taken to Habana, placed on the hand of a patient in the first three days of an attack of yellow fever, and allowed to fill herself with blood. She was then brought back to her former home, placed in a large glass jar, and allowed to digest the blood she had obtained. The jar, covered with a piece of mosquito netting, had in it a small saucer with a little water, and a lump of white sugar was also provided. Under these conditions the mosquito was furnished with all the necessities of life.

So confident were the men in charge of the mosquitoes that I have known them to put their hands in the jars and let the mosquitoes feed upon them, up to the fifth or sixth day after the mosquito had bitten a yellow-fever patient. The mosquito, you recollect, can not convey the disease till from 12 to 20 days have passed from the time of her biting the yellow-fever case from which she becomes infected.

On the other hand, I once saw a party of 12 or 15 doctors in the mosquito room one day, when the mosquito-bar covering of the jar accidentally came off and the insects escaped into the room. These doctors had come from other countries to investigate the subject, and were not then convinced that the mosquito carried yellow fever. Still, they did not care to put the matter to a practical test in their own persons, and got out of the room so rapidly that the wire-screen door was broken down during their exit. It happened that the mosquitoes in this jar had never bitten a yellow-fever patient and were not infected.

After the mosquito had been left in this condition for from 10 to 20 days, it was known that her saliva was capable of transmitting the disease. When she was wanted for the purpose of giving somebody yellow fever, a man would take a glass tube, slip his hand under the mosquito netting, put the mouth of the tube over the mosquito, and then fill the mouth of the tube with a cotton stopper, as above described. She would then be taken to the man to whom it was desired to give yellow fever and who had bravely volunteered for the purpose, the cotton stopper taken out, the tube turned upside down with its mouth resting on the skin, and the mosquito allowed to settle. She would then introduce her biting apparatus and slowly fill herself with blood. But before she fills with blood she injects her saliva into the wound, just as does the snake in biting. It is this injection of the saliva that causes the swelling and the burning sensation that is felt at the point where the mosquito bites and which lasts some time after she has finished. The injection of the irritating saliva probably has the effect of making it easier for the mosquito to get blood.

Now, it will be remembered that this man who was bitten had been kept in the camp for two weeks before he was bitten, and isolated in such a way that he could not possibly have contracted yellow fever. There were 30 or 40 men in the same camp under exactly the same conditions. Three or four days after he was bitten by the mosquito he developed a well-marked case of yellow fever, although everybody else in the camp remained well. Dr. Reed and his fellow workers therefore very naturally believed that that particular mosquito gave the man yellow fever. They repeated this test 12 or 15 different times with the same result. Nobody else in the camp had yellow fever.

Always within six days after the bite of the mosquito known to be infected the man experimented upon had yellow fever.

To show how a house could become infected with yellow fever the board conducted the following experiment: They built a large room and screened it so that mosquitoes could not get in or out. (Whenever I use the word "screen" here I mean the ordinary wire netting or mosquito bar.) The purpose is of course to leave a perfectly free circulation of air, but to have the meshes of the wire or mosquito bar netting so small that a mosquito can not get through. They then divided this room into two parts by a wire netting extending from top to bottom, so that a mosquito could not pass from one side to the other, but at the same time leaving the circulation of air entirely free, the desire being to show that if it were any miasm, or emanation, or germ floating in the air which caused yellow fever it could freely pass from one side to the other of this netting, and that both rooms, as far as these emanations were concerned, were in the same condition.

Now, to show that the building was uninfected, four men were put in it who had never had yellow fever, two sleeping on each side of the wire netting. They were left there for two weeks and remained perfectly well. Reed then said, "I am now going to infect the room on one side of this wire netting with yellow fever and not infect the other side." He took the two men out of one side and liberated a half dozen infected female Stegomyia mosquitoes on this side. The two men still slept and lived on the uninfected side. He then put a volunteer on the side with the mosquitoes and left him there for half an hour, took him out, and within six days this man developed yellow fever, the two men on the other side of the room remaining well.

He therefore argued that, as the two men who had been for so long a time on one side of the wire netting and remained well were breathing the same emanations, and the only difference was that there were mosquitoes on the infected side to which the man had been exposed for half an hour, it was very good proof that the mosquito was the factor which gave yellow fever. He then said, "Now that I have shown you a house infected with yellow fever, I will demonstrate how it can be disinfected and rendered safe." He then caught his half dozen mosquitoes, bottled them up and put them back into their jars, and announced that the building was entirely safe and uninfected, put the two men back into the side which had been infected, and the four continued to sleep and live as safely in these quarters as they had before the infection.

The board had another room built and got all sorts of material infected by yellow-fever patients from the hospital, clothing worn by patients at the time they died of yellow fever, such as mattresses on which they died, soiled in every possible way, pillows and pillowcases saturated with black vomit, and blankets over which basins of black vomit had been poured; in short, material infected by yellow fever in every possible way that could be thought of. All this material was placed in the room, which was made close and tight with very little ventilation, so as to make the conditions most favorable for what was ordinarily considered the best way of insuring the spread of yellow fever. Volunteers who had never had yellow fever were placed in this room, lived and slept there for two weeks at a time, wore this clothing, slept on these mattresses, under these sheets, and yet not a single case of yellow fever was developed from this contact. The

men who had undergone this exposure were taken out and kept for two weeks so as to insure that they had not contracted yellow fever from the exposure, and then bitten by infected mosquitoes. They always got yellow fever from the bite of the mosquito, but never in any other way.

At this time the military authorities had had entire control of Habana for about two years. An Army doctor had been placed in charge of the health department and given the means and power to do what he thought most likely to free the city from yellow fever. Yellow fever in Habana was a disease like consumption in Galveston or New Orleans—always there, and always one of the principal causes of death in the city. And this had been the state of affairs as long as anything had been known with any accuracy, either about yellow fever or about the health conditions of Habana; and these things were pretty accurately known for more than a hundred years immediately preceding the time I refer to. When we organized our health department, we believed, as did everybody else, that yellow fever was caused by filth, dirt, and general insanitary conditions, so we went to work doing our very best to correct these conditions. With these efforts Habana very rapidly became a healthy city, as much so as many of our large cities in the United States, but yellow fever did not seem to be affected.

The second year of our control yellow fever was very severe in Habana, but did not attack the native Cuban because he was generally acclimated. Only the foreigner, therefore, was subject to the disease. During the year 1900 many of our prominent American civilians and military officials died of the disease, and the very cleanest and best parts of the city and the people who lived best and took the best care of themselves were most affected. When the Army Board published their discovery to the world the health department of Habana recognized that it and all the rest of the world had been on the wrong track with regard to yellow fever, and they determined to change their methods and attack the mosquito as the cause of the disease.

They had been convinced by the work of the Army board that a human being could only get yellow fever by being bitten by a particular kind of mosquito—the stegomyia—which had previously bitten a man suffering from yellow fever. They therefore arranged that as soon as a man sickened with yellow fever employees from the department went to the house and screened it with wire netting so that those mosquitoes that were in the house could not get out and those outside could not get in. A smudge was then made of sulphur, tobacco, or insect powder, as best suited to the circumstances, in the affected house, and in all those immediately around it, with the intention of killing all mosquitoes present. By this method it was hoped that both the mosquitoes that had bitten the man and caused the disease would be killed, and also those that had bitten the man after he was taken sick, and had thus become themselves infected and able to spread the disease. For the purpose of doing this screening a building was arranged very much like a fire station in one of our cities, where wagons, wire screens, carpenters, and men with material for making a smudge, were always kept on duty, who proceeded at once to the place where a yellow fever case was reported to exist.

This method was very successful in its results. After its adoption very few cases occurred where the disease spread from the person infected to others in the neighborhood. It was also determined to destroy as many as possible of the yellow fever mosquitoes in the city. It was known that the female mosquito had to have water on which to lay her eggs, and that these eggs could not hatch without water; that this water had to be very quiet and well protected for the hatching process to take place; that the eggs took about three days to hatch; that after hatching the insect had to live the life of a fish in this water for five or six days. During this fish stage they are known as larvæ, and are well known to everybody in the South, for they are nothing but the common wigglers always found in standing rain water during the summer months. Now, while in this wiggler stage the insect has to have air, and for this purpose must every little while come to the surface. At the end of five or six days the wiggler changes into the full-grown mosquito.

It is known that this particular species of mosquito—the stegomyia, or the yellow fever mosquito—lives and breeds almost altogether in houses and in their immediate neighborhood, and does not leave the house for any great distance. With this knowledge of its life history, the department found it easiest to destroy the mosquito in its wiggler stage, and the most useful means in this direction they found to be the doing away with all the little deposits of water in and near inhabited houses, which the wiggler must have in order to develop into the mosquito. The methods herein described were not settled upon, as might appear from this account, all at once and at the beginning, but many other methods of waging war against the mosquito were tried, found impracticable, and dropped.

With the object of doing away with the breeding places of the yellow-fever wiggler, all the houses and yards of Habana were carefully examined and all tin cans, empty bottles, and trash of the same kind, which were generally found filled with rain water and full of yellow fever mosquito larvæ, were carefully carted off. Then the necessary openings in all cisterns were covered with mosquito netting, so that the mosquitoes could not get in to lay their eggs. Among the poorer people, who had only barrels and other similar receptacles for rain water (and in Habana every family had something of this kind), the health department arranged these necessary receptacles for them by placing a wooden cover on the barrel, leaving a hole in the center of this cover for the entrance of water, and covering the hole with wire netting, so that mosquitoes could not get in. To enable them to draw off the water without opening the barrel a cheap wooden spigot was placed in the lower part.

Now, from the peculiarity of the wiggler, that he has to come to the surface of the water every few seconds to get air, if we put anything on the surface of the water that prevents him getting this air, he drowns just as certainly as a man would who is kept under the water. Ordinary kerosene oil, a tablespoonful or two to a cistern, spreads over the surface of the water and kills the wiggler in this way. He can not break through the scum of oil to get air. But oil very rapidly evaporates and has frequently to be renewed. So oil was only used in Habana where no other method was successful. The privy pits in all the houses there were in the center of the court, covered generally with heavy flagstone. These pits, not being in general accessible to the

inspectors, had to be treated with oil. Once a month a couple of ounces of oil were poured into the pipes leading to the pits.

To insure that these methods and ordinances were carried out, the city was divided into districts of about a thousand houses each, so that an inspector would get over each district in the course of a month, inspecting at the rate of about 30 houses a day. This inspector had with him two men who used the oil as above described. He had with him printed blanks on which he entered the condition of the premises as to wigglers. These reports were turned in every night to the office of the health department and were consolidated from day to day. At the end of the month we could therefore tell the condition of Habana as to wigglers. At the first report on this subject (I think in March, 1901) we found that we had in Habana in the neighborhood of 26,000 different water deposits which contained wigglers, most of them of the yellow-fever variety.

After once going over the city and carefully explaining to the people the dangers of allowing wigglers on their premises, and after having fixed up for the poor all the water barrels which they were obliged to keep for holding their rain water, the mayor of the city issued an ordinance stating that anybody who bred wigglers on his premises would be fined $10. These two methods of destroying yellow fever mosquitoes, namely, that of killing the grown mosquito in the neighborhood of every yellow fever patient with a smudge and of looking after the wigglers in all rain water deposits about the house, were steadily enforced during the year 1901. The results were better than we had dared to hope. Few cases occurred in which yellow fever spread from a case cared for in this way. Yellow fever rapidly decreased, and on September 28, 1901, the last case of yellow fever occurred in Habana, and since that time—now more than two years—not a single new case has developed in the city.

There were still, of course, a great many yellow fever mosquitoes in Habana, but these methods of destroying the wigglers had greatly decreased the numbers of mosquitoes. The report of January, 1902, after about ten months of this mosquito work, showed that within the city limits less than 300 premises had wigglers upon them. This I think a very fair measure of the results accomplished by one year's work, namely, that the number of deposits containing wigglers had been decreased from about 26,000 to about 300.

I think it is evident that the disappearance of yellow fever from Habana was due solely to this mosquito work. Remember that it was an every-day disease in Habana, and had been so for more than a hundred years, just as consumption is in New Orleans, a city of about the same size as Habana. Now, if some method should be adopted against consumption in New Orleans, and systematically put in operation in the city against that disease, and at the end of a year it could be shown that no new cases of consumption were occurring in New Orleans, and at the end of two years and a half it could be further shown that under the continuance of the same measures the disease had entirely disappeared from the city, and no new cases had occurred, I should think that we would all be at once convinced that the disappearance of consumption from New Orleans was due to the efficacy of the measures adopted.

In Habana, even now, a case or two of yellow fever comes in every month from Mexico and other infected regions which have a con-

siderable trade with Habana. The ships are carefully inspected by the quarantine authorities, just as is done in our country. If a person sick of yellow fever, or suspected yellow fever, is discovered, he is landed at the city wharf, in the heart of the business district, placed in an ambulance, carried to the yellow fever hospital, which is well within the city limits, and treated there. The only precaution taken is to see that Habana mosquitoes do not get an opportunity to bite him. The authorities at Habana thoroughly believe that if they can prevent mosquitoes from biting a yellow fever patient the city will be entirely safe in handling him and taking care of him.

In 1901, during the height of the yellow fever work at Habana, a town of about 5,000 inhabitants, some 12 miles from the city, became badly infected with yellow fever. This town, Santiago de las Vegas, was practically a suburb of Habana, and the business communication with the city was very intimate. We found that people who were working at Santiago de las Vegas were constantly getting sick of yellow fever, and as soon as they found themselves sick would come into Habana to the homes of their friends and relatives to be taken care of. In order to do away with this source of danger, a large force of men was put at work at Las Vegas, on the lines above described. The whole town was systematically gone through from house to house, and at the end of about six weeks of this work the disease was entirely wiped out and we had no more trouble with infection from Las Vegas. I mention this as showing the possibility of taking a small town and getting rid of the disease rapidly by mosquito work.

We had other mosquito work going on in the suburbs of Habana, among the truck gardens and irrigated fields where grass was grown. But the yellow-fever mosquito does not breed to any great extent in such places, and I do not think this work had much effect upon the yellow fever. But malaria, as I have above mentioned, is also carried exclusively by a mosquito named the "anopheles." Now, this malarial mosquito likes to breed in places where there are little puddles of water, cow tracks, horse tracks, and similar depressions in grassy ground, and the work in the suburbs had its principal effect upon this mosquito. It was not desirable to stop irrigation, as the livelihood of all these small farmers depend upon it, but by taking advantage of the fact that a deposit of water had to remain undisturbed at least 10 days to breed a mosquito, we could allow them to irrigate freely, provided the water did not remain longer than a week. The health department had all this area arranged with shallow, superficial ditches which would not interfere with irrigation, but would allow rapid drainage when the water was taken off. All pools and puddles which had no economic use were kept drained, and ditches and streams kept clean of grass and obstructions.

After once getting the country cleaned up at public expense, and the matter explained to the farmer, he was fined in the same way as the householder in the built-up portion of the city, if wigglers were discovered on his premises. While I do not think that these measures aided us particularly in yellow fever, they had a marked effect upon malaria. In 1900, the year before the mosquito work commenced, we had in Habana 325 deaths from malaria. During 1901, the year in which mosquito work was commenced, we had 151 deaths from malaria. In 1902, the second year of mosquito work, Dr. Carlos Finlay, the health officer of Cuba, reported 77 deaths from malaria in

Habana, and up to the 1st of November in 1903, the third year of mosquito work, Dr. Finlay reported 45 deaths from malaria.

This mosquito work of the Habana health department, I hold, demonstrates the practicability of eliminating in the Tropics the two diseases malaria and yellow fever, and I believe if the attention of the people at large in our own country were generally attracted to the danger of transmitting disease by the mosquito, and the practicability of destroying them, we could very generally eliminate these two diseases from our own country.

And now to the reason for writing this article. I thought an account of the relations of mosquitoes to disease, given in simple terms, readily understood by those who are not doctors, might held people generally in making an attempt to get rid of mosquitoes, each man about his own house. I will now proceed to make suggestions in this direction. And in order to make myself entirely clear will repeat a good deal, and enlarge upon what I have already said.

The work of the Army medical board of which Maj. Walter Reed was president, showing that a particular species of mosquito was the only means of transmitting yellow fever, is now pretty generally accepted by all the scientific world. Based upon this knowledge, certain methods were adopted by the Army medical officers in Habana, Cuba, which resulted in eradicating yellow fever from that city. During the fall of 1903 yellow fever was introduced from Mexico and became quite widely spread through western Texas. It is thought that a few general rules, based upon the knowledge acquired by the Army board and the experience of the Army medical officers in Habana, may be of use in assisting individuals and towns in freeing themselves from infected mosquitoes during the present winter and coming spring. Otherwise, it seems highly probable that yellow fever, at some point in Texas, will again develop as the warm weather comes on. This would come about from the fact that the infected mosquito can very readily live through the winter in the latitude of Laredo.

As yellow fever can only be spread by a particular species of mosquito, it follows that if there are none of these mosquitoes about, yellow fever can not spread. The danger in Texas is that the stegomyia mosquitoes, that have bitten people with yellow fever, will live through the winter and spread another epidemic as the warm weather comes on by biting people who have not had the disease. This mosquito, from its nature, stays immediately about the house and in the rooms, and seldom or never wanders far. It was found in Habana that by destroying all the mosquitoes in each house where yellow fever occurred the disease was always stopped in that particular neighborhood. It is probable, therefore, that if each householder in whose house yellow fever has occurred during the past fall will destroy all the mosquitoes in his house he will be free from the old infection next spring. This can readily be done by closing the room and making a smudge in it of sulphur or tobacco. Care should be taken to paste all the cracks up with paper, so that the smudge will be confined to the room fumigated, and the pan in which the smudge is made placed on a little earth, so that it can not set the floor on fire.

With sulphur, about a pound to a room 10 feet square, should be used, and with tobacco, about half a pound. To start the sulphur burning a couple of tablespoonfuls of alcohol should be poured on before applying the match. Sulphur should be used unless the room

contains valuable material which might be injured by it. The fumes of tobacco hurt nothing, but leave a disagreeable odor. The fumes of ordinary Persian insect powder hurt nothing and leave no odor, but it does not always kill the mosquitoes and care has to be taken to sweep them up afterwards. A couple of hours will be time enough to keep the room closed. After that time it can be opened, aired, and occupied. In towns, this method should be carefully carried out during the winter by the town authorities. Not only the houses in which yellow fever is known to have occurred, but every house in the infected town should be treated in this way. We found in Habana that a squad of five men, under intelligent direction, could easily fumigate a 10-room house in two hours. It should be arranged so that the whole of the infected town should be gone over before the 1st of April.

The above directions cover the points with regard to killing infected mosquitoes, and thereby preventing the liability of a new epidemic next summer from the old mosquitoes left over from last year. But it is even more important to prevent the breeding of a new crop of stegomyia mosquitoes, and this can be very readily done without very great effort.

The female stegomyia mosquito always seeks some small body of well-protected fresh water in which to lay her eggs. On the surface of this water she lays about 60 or 70 eggs. These, in warm weather, in three days hatch out into the ordinary wiggler, and the wiggler in five or six days develops into the full-grown mosquito. From the laying of the egg to the development of the full-grown mosquito takes about eight days in hot weather. Water is as necessary to the insect as it is to a fish. It is essentially a water insect during this period, though it is an air-breathing insect, too, and has to come to the surface of the water every few seconds to get air.

As I stated above, the stegomyia seeks particularly deposits of clean water, and is essentially a house mosquito, breeding either in the house or very close to it, in such places as cisterns and rain-water barrels, and in anything likely to catch and retain rain water, such as old bottles or cans, or gutters under the roofs of houses, etc. Now, if every householder will give a little attention to see that there are no such deposits about his house, he will be free from the stegomyia mosquito, and no one will contract yellow fever in his house, even if cases are introduced into it from elsewhere. If necessity obliges him to keep a cistern or barrels of rain water, if he will arrange the receptacle so that the mosquito can not get in to lay her eggs, it will be entirely safe. In the cistern this can be done by covering the top tightly, with the exception of a hole for ventilation, and one for the entrance of the water, and these two holes should be covered with wire netting. The netting should be not larger than 16 meshes to the inch. A larger mesh than this will allow the smaller size of stegomyia to pass through.

Water barrels can be arranged in the same way, a tight-fitting top put on, with a wire mesh over the hole for the entrance of the water, and a cheap spigot put in the bottom for drawing off water. If he finds wigglers in any of the vessels of water which he is obliged to keep, he can know that his cover is imperfect, and that the female mosquito has gotten in there in some way to lay her eggs. Small deposits about the yard and in the immediate neighborhood should be swept out or drained away. A deposit of water in Texas would have to stand at least 10 days to breed a mosquito. For this reason, if the

householder is not able to arrange his water vessels as above suggested he could avoid breeding stegomyia mosquitoes by having these vessels emptied once a week. But if the method of emptying is used, the larvæ should be carefully washed out or the vessel left to stand empty for more than an hour. If this precaution is not taken, a considerable number of the larvæ will be left adherent to the bottom and sides and will live if the vessel is at once refilled. Kerosene oil is fatal to the larvæ if two or three tablespoonfuls are spread over the surface of the water.

As I said before, the larvæ have to come to the surface every few seconds to get air, and as they are unable to break through the film of oil they die of suffocation, but the oil evaporates very rapidly and should be renewed every week. Much the better method is either to get rid of the deposit of water or protect it in the above-mentioned manner. Oil should only be relied upon in treating deposits in a building or its immediate neighborhood which can not be managed in one of the above-mentioned methods. Privy pits which contain water were the only places in Habana in which we habitually resorted to oil.

In towns these methods should be enforced by regular and systematic inspections. In most towns there are ordinances against pigs and pigsties. A hog is considerably larger than a mosquito wiggler, but with a little care an inspector will soon learn to discover the wigglers almost as easily as the hogs. And the householder should be taught that the wiggler causes a great deal more annoyance to himself and his neighbors than the hog does, and is infinitely more dangerous to health. And the ordinances should hold the householder as strictly to account for breeding wigglers on his premises as for having a pigsty with a litter of pigs. The larger deposits, a hundred yards or more away from the house, such as small ponds and swampy places, while breeding mosquitoes that cause a great deal of annoyance, will not breed the stegomyia to an extent sufficient to be dangerous to the house. They should be managed by the town authorities on the same general principles—to drain wherever possible.

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