Carlos J. Finlay and Yellow Fever

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"I admit the existence of a material transportable cause which may be either an amorphous virus, an animal or vegetable germ, bacterium, etc., but which consists in all cases of a tangible something which has to be communicated from the sick to the healthy in order that the disease may be propagated. What I propose studying is the medium or agent by which the pathogenic material of yellow fever is carried from the bodies of the infected to be implanted in the bodies of the non-infected.

. . . It seems natural that this agent could be found in that class of insects which, by penetrating into the interior of the blood vessels, could suck up the blood together with any infecting particles contained therein, and carry the same from the diseased to the healthy.

. . . Three conditions are therefore necessary in order that the yellow fever poison may be propagated:

First—A yellow fever patient in whose capillaries the mosquito may bury its lancets, and impregnate them with the virulent particles at the proper period of the disease.

Second—Prolongation of the mosquito's life from the time of the original sting, from which the inoculable material was obtained, to the moment in which it is applied to the selected subject.

Third—Coincidence of inoculable sting with the favorable subject."

These were the essential points of the theory for the propagation of yellow fever given the 14th of August, 1881, in the Academy of Sciences of Habana, Cuba, by a Cuban physician, Dr. Carlos Juan Finlay y Barres.

Dr. Carlos J. Finlay was born on December 3, 1833 (126 years ago), in the city of Puerto Príncipe, what is today Camaguey.

His father, Dr. Edward Finlay, originally from Scotland, obtained his Medical Degree at Rouen, France. When making a trip to South America to join Simon Bolivar's troops his ship wrecked and he landed safely on the island of Trinidad. There he began practicing medicine and was later married to Miss Elizabeth de Barres who was originally from France.

Dr. Finlay decided to go to Cuba. He settled in Puerto Príncipe, where Carlos was born. Some years later he changed his residence to Habana, the capital of the country, then a Spanish colony, taking over the practice of Dr. Belot; his major interest was opthalmology. Carlos and his older brother Eduardo, who was born in Trinidad, were raised in that Cuban capital.

Dr. Finlay sent both boys to France in 1845 for their education; Carlos was then 12 years old. One year later they returned to Habana because of

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a severe attack of chorea suffered by Carlos in LeHavre. In 1848 the Finlay family went to England on a trip, thinking of the education of their two sons. They visited London and from there Carlos and Eduardo were taken to Maguncia, Germany, where they stayed for one year. The following year they went back to Rouen, France, where they entered the Rouen Lyceum for their studies. In 1851, two years later, Carlos had an attack of typhoid fever and returned to Cuba with his brother. Carlos, however, later entered the Jefferson Medical College of Philadelphia and received his Medical Degree in 1855.

While at Jefferson Medical College, Carlos met Dr. John Kearsley Mitchell and his son Dr. Silas Weir Mitchell, both of whom were professors at the Medical School at that time. Dr. S. Weir Mitchell, Carlos' preceptor, tried to convince young Dr. Finlay to practice in New York, but Carlos wished to return to his native country.

Young Dr. Finlay returned to Cuba and obtained his second degree at the University of Habana Medical School on March 15, 1857. He, like his father, who had been a very successful opthalmologist in Cuba, was inclined to opthalmology, and later received his post-graduate training in opthalmology in Paris in 1860-61.

He returned to Matanzas, Cuba, a town 60 miles from Habana, and practiced for a short time. Then returning to Habana he married Miss Adela Shine, originally of Puerto España, Trinidad.

The Finlay's had a nice family, based on very strict Catholic principles. They had three children, Carlos Jr., later a physician and professor of opthalmology at Habana University, Jorge and Frank. All of them were prominent in Cuban society.

In the year 1867-68 a very severe cholera epidemic took place in Habana. Dr. Finlay became interested in bringing some relief to the population. He found the sanitary conditions of Habana to be terrible and suggested the possibility of transmission of this disease through fecal contamination of water and formites. This was not proven until 20 years later, when Petenkofer and Emmerich proved the pathogenicity and epidemiology of this disease.

Dr. Finlay expressed his desire to join the Academy of Medical, Physical and Natural Sciences of Habana. There he presented several papers concerning such varied fields as, exophthalmic goiter, inguinal hernia, cholera, etc. In 1865 he presented his first paper on the etiology of yellow fever. He became a member of the Academy on September 22, 1872. His thesis was on the atmospheric alkalinity in Habana. He published papers concerning his studies on the force of gravity, and later, in 1874, on cancer. His feeling towards treatment of cancer of the eye pointed to the importance of enucleation before the malignancy had been reproduced in regions of the body not accessible to the surgeon of that time, and before the patient had signs of cachexia.

Multiple papers were presented by Dr. Finlay concerning the surgical and pharmacological aspects of opthalmology, his major interest. He be-

lieved in the contagiousness of leprosy, and in 1879 stated that although this was not of a high degree, it did warrant hospitalization and isolation of those afflicted with the disease. These measures were not adopted until a later date in other countries. Other publications dealt with osteomyelitis, newborn tetanus, tuberculosis, and others on his philosophical viewpoint.

Dr. Finlay, as stated, made his first study of yellow fever in 1865. He was considered an expert clinician in the management of yellow fever, one of the leading causes of death in the country at that time, and in other tropical areas of the world. Some idea of the magnitude of the effects of this disease can be indicated by the estimate of 100,000 deaths occurring in Cuba from 1854 to 1898 from this dreaded disease.

Yellow fever existed in America before Columbus' time, according to Mayan Indian history. The first authentic report in America was made in 1495 when Columbus was in Hispaniola, today the Dominican Republic. In Cuba the first report dates back to 1649 when, according to Pezuela, "by an unknown horrible epidemic imported from the American continent, one-third of the population was devoured by a sort of putrid fever." In the years of 1653, 1667, 1668 and so on, Cuba was attacked by the so called "Yellow Jack." Habana was the most dreadful focus, because of the innumerable visitors who came to this city; an important spot for all travelers from Europe to Central and South America. The natives were considered immune to the disease, not because of the climatological conditions, as was previously thought, but by a mild, or severe, attack of this disease in early life, as was stated by Drs. Chaillé and Guiteras after their studies in Key West and Matanzas.

In 1762, Habana, then an English possession, suffered a terrible epidemic. Of the 15,000 men of the victorious English Army of Earl of Albemarle, only 7,000 overcame the disease.

In America the first report of yellow fever dates back to 1693. In New Orleans the first report dates back to 1769, although this is not authenticated; the first distinct report being made in 1796. In 1819 New Orleans had 2,000 deaths among 26,000 inhabitants then in the city Several epidemics were reported, the principal ones in 1853 with 8,000 deaths, 1877-78 with 16,000 deaths and others up to 1905, when the Finlay theory was put into practice.

In the Panama Canal Zone, of 86,000 employees of the French company which was constructing the canal, 52,000 were attacked by this disease and malaria, with 22,000 deaths.

One can easily grasp the impact of the so-called "Yellow Jack" on the peoples of the Americas. The U. S. Government perceiving this same matter sent the first American Yellow Fever Commission to Habana in 1879. This commission was formed of: Dr. Stanford E. Chaillé, then Professor of Pathology, Physiology and Hygiene at our Tulane Medical School, a former graduate and later Dean of the then called University of Louisiana. Dr. Chaillé had worked in Paris under Claude Bernard and was President of the Commission. Quoting Dr. Matas—"To him more than to any other of my

teachers, next my parents, I owe the greatest inspiration in my professional life". Dr. George M. Sternberg, the most eminent bacteriologist of the day, subsequently Surgeon General of the U. S. Army during the Spanish American War. Colonel Hardie, distinguished Louisianian, and sanitarian engineer. Dr. John Guiteras, Cuban, former yellow fever expert, and sanitarian. He later became Professor of Pathology at the University of Pennsylvania. Dr. Rudolph Matas, then a medical student and intern at Charity Hospital of Louisiana. He worked as clerk, laboratory technician and interpreter. And Mr. Henry Mancel, photographer.

The Commission began working in 1879. Dr. Finlay was selected by the then Spanish Government of Cuba to assist the American Commission. Dr. Finlay felt that the high incidence of yellow fever in Habana was related to the high atmospheric alkalinity, which he had studied.

The results of the Commission were not too positive, but Dr. Finlay gained a great deal of experience by his personal contact with these men. He kept photomicrographs of Dr. Sternberg's slides and changed his point of view about the mode of transmission of the disease. He observed that the red blood cells were discharged intact in the hemorrhages of yellow fever, and stated "that as these hemorrhages take place, at times with no apparent rupture of the blood vessels. We came necessarily to the conclusion that this symptom, hemorrhage, being the most salient clinical feature of the malady in question, surely pointed to the vascular endothelium as the site of its principal lesion". Continuing quoting part of Finlay's theory of August 14, 1881, "in order that this disease might be inoculated, the inoculable material would have to be searched for in the blood vessels of the yellow fever patient from where it could be carried to the interior of a healthy individual's blood vessels, who would be in a favorable condition for the reception of the infesting material. All the requisite conditions for the successful transportation of the inoculating virus, are admirably combined in the mosquito, the sting of which would be almost impossible for us to imitate with the comparatively crude and coarse instruments which could be manufactured by our most dextrous artezans."

In 1881 Dr. Carlos J. Finlay was selected by the Spanish Government to represent Cuba and Puerto Rico at the International Sanitary Conference in Washington, D. C. At the conference he stated:

First—"For the Yellow Fever to exist a previous case in a definite stage of the disease is needed."

Second—"The presence of a susceptible individual."

Third—"The presence of an independent agent to both the disease and the patient is needed for transmitting the disease from the sick to the healthy."

Dr. Finlay did not mention the mosquito as being the vector on that occasion, because he wanted first to finish the experiments on which he was working.

Six months later, on August 14, 1881, Dr. Carlos J. Finlay at the Academy of Medical, Physical and Natural Sciences of Habana presented

his paper, "The Mosquito Hypothetically Considered as an Agent in the Transmission of Yellow Fever Poison."

In this session of the Academy the great Cuban scientist gave one of the bases for modern tropical medicine. He with Dr. Patrick Manson, who in 1881 published his experiments about the indirect transmission of filaria by the mosquito, could certainly be considered the fathers of modern tropical medicine.

Dr. Finlay stated in his presentation of August 14, that the Culex mosquito, today Aedes Aegypti, was the vector of this disease. He gave the origin of the mosquito, with a description of the way this mosquito implants its sting.

The precursors to Finlay's theory were men such as Beauperthuy 1853, Nott 1848, Wood, Beyrenheydt and Bennet Dowler, in New Orleans and also Barton in 1853, Rush 1797, Vaughan 1802, Crawford 1805, and others who suggested some relation between mosquitoes and yellow fever, although all of them were long before Finlay's discovery.

In his paper Dr. Finlay presented the original experiments he made to prove his theory. He stated that he inoculated five different individuals, all recent arrivals to the island, and considered susceptible, with Culex mosquito that had stung affected patients. Dr. Finlay showed: First: one case of benign yellow fever characterized by icterus and albuminuria. Second: two cases of abortive yellow fever. And third: two light ephemeral fevers without any definite character.

He then stated that further experiments were needed to confirm his theory, and that by just one mosquito bite a severe case could not be produced.

Dr. Finlay suggested that this disease could be prevented by applying measures to prevent the development of the Culex mosquito.

Dr. Carlos Finlay continued his work on yellow fever, giving subsequent papers. On August 22, 1882 he presented one of the pathogenicity of yellow fever. Later, on the relation of yellow fever and the mosquito, and on the history of the disease. On February 29, 1884, Dr. Finlay stated the way in which the diagnosis of this disease was made by him in his paper on "Experimental Yellow Fever." The most important points were: 1) a febrile sickness of the continuous type, of several days duration, with or without a spike of high fever, and with no remission up to the period of defervescence. 2) albuminuria from the second or third day on to remission or death of the patient. 3) icteric discoloration of the skin and sclerae after the period of convalescence had started, 4) passive hemorrhages of the mucosal membranes, skin or deeper tissues, 5) hematemesis during the last period of the severe cases (some digested blood was found in the gastrointestinal tract after death) and 6) a course of seven days, if no complications as hepatitis, cerebral hemorrhages, etc. were present.

Dr. Finlay stated that the first, second and sixth points had to be present to make the diagnosis of the disease. He gave also a broad discussion on the clinical aspect of yellow fever.

Dr. J. Bauer, Director of the Rockefeller Institute, according to Dr. Matas, said in 1944 that the most important diagnostic signs in yellow fever were albuminuria and leukopenia, both outlined by Finlay. (Today we have a very valuable adjunct for its diagnosis with the intracerebral mouse protection test, developed by Dr. Max Thelier in 1929.)

Dr. Matas stated that Dr. Faget, former professor of our school, made a very important contribution to the clinical aspect of this disease pointing to the divergence of the pulse and temperature found in yellow fever, known as Faget's law.

In the cited paper Finlay also gave a discussion on the techniques of the mosquito inoculations done by him. He did his experiments on Jesuit Fathers, who voluntarily offered themselves, as subjects. Dr. Finlay stated that out of eleven inoculations by the mosquito with material from patients in the third, fourth, fifth, or sixth day of the disease, six were positive, one was doubtful and four were negative. Of seven done with material from patients in their second and seventh day of illness all were negative; thus pointing the significance of the day of the disease in which the mosquito made the infective bite.

Dr. Finlay stated that the duration and the intensity of the febrile episode produced by the mosquito inoculation was in close relation with the number of bites and the amount of material that the mosquito was carrying.

Subsequent papers were presented by Finlay, on the hematic picture of yellow fever, relation between etiologic factors and evolution of yellow fever, statistics of the inoculations by the mosquitoes infected from patients of yellow fever, new therapeutic approach to yellow fever, and among others in 1895 he published a paper on the tetragonococcus and yellow fever.

Dr. Finlay's theory was not accepted in general at that time.

In 1888 a second American Yellow Fever Commission went to Cuba with Dr. George M. Sternberg as head, and Dr. Emilio Martinez as his assistant. They did an extensive pathologic study. Dr. Sternberg, although a personal friend of Dr. Finlay, did not believe in his theory.

Dr. Finlay continued having all sorts of difficulties. Even in Cuba the people turned their backs to him, calling him "the man of the mosquitoes". He joined the American Army on July 22, 1898, as a field surgeon, during the Cuban-Spanish-American War.

Nothing was known concerning the etiologic factor of yellow fever. Almost every microbiologist had discovered his own organism. Among others: Dr. Joseph Richardson, Philadelphia, 1878; Drs. Charrin and Capitan, Paris, 1881; Dr. Lacerda, Rio de Janeiro, 1883; Dr. Carmona Valle, Mexico, 1884-85; Dr. Domingo Freire, Rio de Janeiro, 1885; and Dr. Sternberg who described the micrococcus tetragenus febris flavae or vegetalis studied by Finlay and Delgado in 1887-88. Later Giusseppe Sanarelli, Director of the Institute of Hygiene of Montevideo in 1897, and Havelberg, from Rio de Janeiro in 1897, independently described a similar organism.

This was called Sanarelli's Bacillus icteroides. He found it in the small capillaries of the liver in 58 per cent of his patients at autopsies. Sternberg in 1897 stated that this organism was similar to his Bacillus X. Sanarelli thought that his bacillus produced a toxin responsible for this disease.

In 1898 the U.S. Government sent a new Yellow Fever Commission to Cuba; this was the third and was formed by Drs. Wasdin and Gedding to study Sanarelli's Bacillus icteroides. This Commission did not believe in Dr. Finlay's theory and stated that; "First, bacillus icteroides was the cause of yellow fever; second, that it was only found in yellow fever; and third, the patients were infected through the respiratory route."

Dr. Sternberg, then Surgeon General of the U. S. Army, was not satisfied with the report of the Commission and sent Dr. Aristides Agramonte, later Professor of Microbiology of Habana University and Louisiana State University, to Habana to continue this work. Dr. Agramonte after his studies stated:

1)—"The yellow fever etiologic organism is not known.
2)—The Sanarelli's bacillus has the same relation as the colliform bacillus with yellow fever.
3)—The Sanarelli's bacillus is not found in the patients blood.
4)—The Sanarelli's bascillus is found in the tissues of patients of other diseases.
5) The Sanarelli's bacillus is not agglutinated by the serum from patients or the ones cured from a yellow fever attack."

At the same time, Major Gorgas, Chief of the Sanitary Corps of the U.S. Army in Cuba, was trying to improve the poor sanitary conditions of Habana, then under the United States dominion, and consequently little improvement was achieved in the yellow fever incidence.

Dr. Sternberg appointed a fourth Yellow Fever Commission. This one consisted of: Major Walter Reed, former professor of Microbiology at Columbia University, as President and military surgeon; Jesse W. Lazear, Aristides Agramonte, James Carroll, assistant surgeons. The major purpose of the Commission was again to study the bacillus of Sanarelli. They did not consider Finlay's theory when they started on their work.

Dr. Finlay and Dr. Guiteras, who went to Cuba interested in these experiments, worked closely with the Commission. Major Reed had no experience in yellow fever then. He believed in Sanarelli's theory. The fourth Commission began its work in 1900. In spite of all the sanitary improvements made by Dr. Gorgas, the yellow fever epidemic in Habana was worse than ever. The Commission, obtaining no positive results, again sought the help of Dr. Carlos J. Finlay. They inquired about his theory, his experiments, the way to conduct them, his statistics and requested some infected mosquitoes. Dr. Finlay gave them eggs of Aedes Aegypti, and all his personal support.

Dr. Lazear was placed in charge of the Finlay's theory investigation, working in the Columbia Army Camp. Dr. Agramonte stayed in the Laboratory of the Number One Hospital of Habana, and Dr. Carroll continued his investigations on the intestinal flora.

Dr. Walter Reed returned to the United States on August 2, 1900. Dr. Carroll, not believing in Dr. Finlay's theory, was bitten by an infected mosquito and contracted the disease after Reed had left. Dr. Lazear was also inoculated by an infected mosquito and contracted the disease. Dr. Carroll survived the attack, however, Dr. Lazear, who had always believed in the validity of the Finlay concept, died in September of 1900. His name will always be remembered by those in the field of experimental medicine.

Major Reed after hearing about Carroll's and Lazear's inoculations, returned to Habana, and changed his mind about the Finlay theory. The Reed Commission eventually made the important observation that in order for a fulminating case of yellow fever to be produced by the mosquito bite, more than ten to twelve days of incubation were needed in the mosquito.

A camp was established on the San Jose Farm in Marianao, on the outskirts of Habana, the place where Dr. Finlay had conducted his own experiments with the Jesuit Fathers. The camp was named after Dr. Lazear, the Lazear Camp, and here the experiments were conducted. At the same time Dr. John Guiteras was conducting his experiments at Las Animas Hospital in Habana.

Dr. Walter Reed returned to the United States immediately and on October 23, 1900 presented his "Preliminary Note" at the annual American Public Health Convention at Indianapolis. Here he said: "First—the bacillus icteroides has not been found in the blood taken from the venous circulation in subsequent days of the disease, in 18 cases of yellow fever. Second—negative results were found in cultures done from the blood and organs of 11 cases of yellow fever for the so called bacillus. Third—Sanarelli's bacillus has no casual relation with yellow fever and must be considered just as a secondary invader in this disease. And fourth—in this disease the mosquito is the intermediary host for the yellow fever parasite and it is very probable that the disease will only be propagated by this insect's bite."

The Third Pan-American Medical Convention took place in Habana on February 4, 5, 6, 7, 1901. At this convention Dr. Finlay gave his paper "Advances made during the XIX Century on the Yellow Fever Propagation." He mentioned that during 19 years 104 individuals had been inoculated by him in the confirmation of his theory although with a low incidence of positive results. And now quoting the words of the great Cuban scientist, "My mosquito theory, up to the point where my limited forces has been able to carry them through, was still in an evolutive phase and experimental demonstration of important details were remaining. During the last weeks of December, of the last year, the Fourth American Commission of Yellow Fever has made very important experimental work that has fulfilled my theory. These being of major interest for all of us interested in Tropical Medicine. The Commission will tell you exactly how it has been demonstrated that not only the Culex (fasciatus) Mosquito transmits yellow fever but besides that, the disease is not transmittible without the presence of this agent. If Drs. Reed, Carroll, and Agramonte are able to

convince every one about the two points I have just mentioned this will be the greatest advance in Tropical Medicine since Jenner demonstrated the validity of the Cow Pox vaccination for Small Pox."

In the next session of the Convention Dr. Walter Reed read his paper "Etiology of Yellow Fever" where his most important points were:

"First—The mosquito is the intermediary host for the yellow fever parasite.

Second—Yellow Fever is transmitted to susceptible individuals by means of the bite of the mosquito that has previously bitten a patient with this disease.

Third—More than ten to twelve days of incubation in the mosquito are needed for the transmission of the disease."

Among other points, it was demonstrated that yellow fever was not transmitted by means of the clothes, or any articles in contact with the patients of this disease and their disinfection was thus unnecessary. Most of these essentials had been already stated by Dr. Finlay, including the advice that the propagation of yellow fever could be restricted by destruction of mosquitoes and protection from their bite. Although the propagation of yellow fever had already been clearly defined, the specific cause of this disease remained unknown.

An unexplained rivalry arose between Dr. Finlay and Dr. Reed, that brought a world-wide controversy concerning the validity of the Finlay concept, today entirely accepted thanks to the persistent work of men such as Dr. Rudolph Matas, Dr. Dominguez Roldan, Cesar Rodriguez Exposito, Dr. Abascal, Dr. Carlos Finlay, Jr., and others. The 14th International Congress of History of Medicine, which took place in Rome and Salerno, Italy, in 1954, finally established the priority of the Finlay theory.

Dr. Moll, in 1944, stated: "Not only has it been proven for the first time that a human disease was transmitted by an insect but man had been provided with means to eradicate it, thus redeeming some of the wealthiest portions of the earth so far, the prey of this scourge."

Dr. Finlay had previously indicated in Chicago in 1893, in Budapest in 1894, and on several other occasions, the measures needed for the eradiction of the mosquito and Yellow Fever. Major William C. Gorgas was the one to put in practice what he called, "The Finlay Plan," that effectively redeemed the capital of the so called "Pearl of the Antilles," from the ailment that had been its greatest enemy through the centuries.

Dr. George M. Sternberg ordered the Finlay measures for the eradication of the mosquito in the Panama Canal Zone under Major Gorgas, making possible the construction of this important waterway of our hemisphere.

In 1905 New Orleans adopted the anti-mosquito measures when a full-blown epidemic had just begun. This course resulted in the eradication of the dreaded "Yellow Jack" from this previously highly affected area. Quoting Dr. Landry, "Although our fair city bears memorials to Jackson, Lee, Beauregard, and other military leaders it would be more than fitting to immortalize the names of those who were responsible for the greatest and most important victory that the city has ever achieved."

On Independence Day in Cuba, May 20, 1902, Dr. Finlay was appointed head of the Health Department of the country. He directed the Cuban Sanitary Code and made multiple epidemiologic campaigns.

At the age of 76, in 1909, he retired and spent the rest of his life with his wonderful family and his many friends, especially his valuable assistant and friend, Dr. Claudio Delgado, famous Spanish hematologist, who was close to him during his fight against yellow fever. Dr. Finlay expired on August 20, 1915, in his home in Vedado, Habana.

This is just a short sketch of the life of one of the great men in the field of medicine. Quoting our great Dr. Rudolph Matas, while in Habana for Dr. Finlay's 108th birthday celebration, "Little did he or I imagine that 62 years later (1879-1941) I was to return to Habana and represent the city of New Orleans at a great international celebration in commemoration of the 108th anniversary of his birth. To bring the homage of New Orleans, one of the first cities in America to benefit by his discovery, and one of the last to recognize its debt to his genius."

Mr. Sol Bloom in the House of Representatives of the United States on October 23, 1943 stated, "It is very appropriate that the name of Carlos Finlay should grace and identify an institution designed to promote research in Medicine throughout all the Americas."

"Finlay," quoting Dr. Matas, "symbolizes in my mind the teacher who deserves to be emulated by everyone having a vocation for the service of Science and Humanity."

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