

Reed, Walter

**a
history
of
medicine
in
pictures**

by George A. Bender

painting by Robert A. Thom

The Conquest of Yellow Fever

"I THANK GOD that I did not accept anybody's opinion on this subject, but determined to put it to a thorough test with human beings in order to see what would happen...actual trial has proven that I was right..."

Thus wrote Dr. Walter Reed, 49-year-old surgeon with rank of Major, United States Army, stationed at Columbia Barracks, Quemados, Cuba, on December 9, 1900, in a letter to his wife. Dr. Reed had been sent to Cuba by the Army's Surgeon General to head a commission to study yellow fever, and he was on the threshold of discoveries that would unlock secrets of propagation of that dread disease.

Not far away, in Havana, undoubtedly another prayer of thanksgiving was in the mind of 67-year-old Dr. Carlos Juan Finlay, who at long last was witnessing men of science accepting and proving, beyond doubt, that his theories regarding transmission of yellow fever were correct.

The story of yellow fever is one of many men, as Dr. Joseph E. Smadel has pointed out. Dr. Reed and his associates gave the facts to the world. Surgeon Major William Gorgas transformed facts to action, freeing Havana of a scourge it had known for almost 400 years. It would be another forty years before Max Theiler would develop vaccines against yellow fever. But Carlos Finlay was first to have given the Reed commission the idea that mosquitoes transmitted the disease.



Where yellow fever originated is still a controversial question. Some authorities trace it back in Mexico to the fifteenth century; others believe it to have been reported in Africa as early as 1585. It has been said that no European writer mentioned the disease before Columbus' day; but older records are not easily interpreted—and yellow fever has borne at least 152 names during the course of history. A most dramatic record of its devastation is to be found in the writings of Dr. Benjamin Rush and others concerning the epidemic of yellow fever in Philadelphia in 1793; this was but one of the fever's visits to United States ports. In the eighteenth century, yellow fever is reported to have caused 41,000 deaths in New Orleans, 10,000 in Philadelphia, and 3,400 in New York; and the United States losses in the nineteenth century approached 100,000. Epidemics periodically devastated cities in the Caribbean islands, Central and South America, and frequently visited the shores of Spain, Portugal, and France. It helped shape the future of the new republic of the United States: Napoleon was forced to sell Louisiana after yellow fever had destroyed nine-tenths of his expeditionary force in San Domingo in 1802. Yellow fever, or "black vomit," as it was known, defeated more Spanish, French, and English expeditions in the New World than did military action.

Dr. Rush believed the Philadelphia epidemic of 1793 to have arisen from the fumes of a shipment of coffee spoiling on the docks. He noted that mosquitoes were numerous that summer, but failed to realize the significance. In 1797, he recorded the observation that one patient developed the fever after smoking a cigar; and that wind direction seemed to have some influence on the number of persons becoming ill of the disease.

The idea that insects might have a part in spreading disease came to acceptance only with great difficulty. Bishop Knud of Denmark alluded to it in 1498 in *De Regimine Pestilentico*. Ambroise Paré, at St. Quentin in 1557, said of battlefield flies: "Where they settled, they infected the air, and brought the plague with them." First scientific establishment of insects as carriers of disease was published by Dr. Patrick Manson, in 1880, concerning the mosquito as intermediary host in filariasis. In 1894, Manson communicated his theories concerning mosquitoes to Major Ronald Ross of the British Army. Two and a half years later, in India, Dr. Ross was able to pinpoint responsibility upon female mosquitoes of the genus *Anopheles* for a part in the life cycle of the parasites causing malaria.

First persons to suggest that insects play a part as carriers of yellow fever were Dr. J. Crawford of Baltimore, in 1807; Dr. J. C. Nott of Mobile, Alabama, in 1848; and Dr. L. Beauperthuy, in 1854. The mosquito was not specifically accused until Dr. Finlay's paper, "The Mosquito Hypothetically Considered as the Agent of Transmission of Yellow Fever," was read before the Royal Academy in Havana, Cuba, August 11, 1881. But for two decades no one paid attention to Dr. Finlay's claims.

Havana, Cuba, historically had been a focus of yellow fever. After its occupation in 1898 in the course of the Spanish-American War, losses among United States troops became so great that Surgeon General Sternberg named a commission to go to Cuba to study the mystery concerning the cause and transmission of yellow fever. Thus, in the year 1900, were persons most responsible for conquest of yellow fever brought together upon that tropical Caribbean isle.

Chairman of the commission was one of Sternberg's most trusted officers, Major Walter Reed. Born the son of a minister, in Virginia, September 13, 1851, Reed had graduated in New York from Bellevue Hospital Medical College in 1870; he interned and practiced in New York for a time, then entered the Army with a commission as Assistant Surgeon and rank of First Lieutenant, in 1875. In 1876, he was assigned to his first post at Fort Lowell, Arizona. There his new bride joined him at the first of fifteen posts he was to hold in the "Old West." Returning East in 1889, he was assigned to be Attending Surgeon and Examiner of Recruits in Baltimore, with permission to pursue professional work at The Johns Hopkins Hospital. This brought him under the influence of Professor William H. Welch, and he received special training in pathology and bacteriology.

Dr. Reed was ordered to another two-year field assignment in the Dakotas; then, in 1893, he returned to Washington, D. C., to become curator of the Army Medical Museum and professor of bacteriology and clinical microscopy at the United States Army Medical School, with the rank of major. He published a significant work on the contagiousness of erysipelas in 1892; and, in 1898, headed a commission to study typhoid fever in army camps, reporting the importance of flies as probable carriers. With Dr. James Carroll, another of the Surgeon General's staff, he studied *Bacillus icteroides*, claimed by its Italian discoverer, Guiseppe Sanarelli, to be the cause of yellow fever. Reed and Carroll's findings were negative.

The yellow fever commission which Dr. Reed was appointed to head included Dr. Carroll, in charge of bacteriologic work; Dr. Jesse W. Lazear, specialist in insect work; and as pathologist, Dr. Aristides Agramonte, a native of Cuba serving in the U. S. Army. Drs. Agramonte and Lazear already were in Cuba; Drs. Reed and Carroll joined them at Havana in June, 1900. First work of the commission was directed toward determining whether *Bacillus icteroides* had a part in yellow fever. It soon was decisively ruled out.

At this time, Dr. Reed and his commission members met Dr. Finlay, who was to point them toward another important aspect of the yellow fever puzzle—the mosquito.

Dr. Finlay had been born in Cumaguey, Cuba, in 1833, the son of a Scotch physician and a French mother. Following early education in Cuba, he enrolled in Jefferson Medical College in Philadelphia, receiving his doctorate in 1855, entering medical practice in Havana in 1864. He became expert in epidemiology, and made contributions in the fields of leprosy, beriberi, filariasis, trichinosis, relapsing fever, cholera, and tuberculosis; but yellow fever held his greatest interest. Dr. Finlay began his long series of papers on yellow fever in 1872. In 1881,

he first pointed out necessity for consideration of an intermediate agent to explain transmission of yellow fever; and later that year, declared the vector to be a mosquito, then known as *Culex fasciatus*. He supported his claims with reports of experiments in humans. Though firm in his convictions, Dr. Finlay failed to gain support of medical men. When the Spanish-American War broke out, Dr. Finlay, then 65 years old, went to Washington, offered his services to the United States Army, and served in the Santiago campaign. In 1899, the provisional government of Cuba appointed him chairman of its Yellow Fever Board. It was in this capacity that he received Dr. Reed courteously, and patiently reiterated his theories regarding transmission of yellow fever by mosquitoes. Dr. Finlay's proofs failed to convince Dr. Reed; but nevertheless Dr. Finlay and his Cuban commission offered full cooperation with the United States commission.

Unable to find a bacterial cause for the fever, Reed and his associates determined to try to clear up two remaining questions: Dr. Finlay's controversial mosquito theory, and the ideas generally embraced by the medical profession that the disease was spread by personal contact and by fomites—a term applied to clothing, bedding, and personal effects of the sick.

Dr. Reed frequently was called away from work in Cuba for special assignments from the Surgeon General. However, three events soon emphasized the importance of checking the mosquito theory more fully: Dr. Carroll deliberately allowed an infected mosquito to bite him, developed yellow fever, and nearly lost his life; Dr. Lazear accidentally was bitten and died September 25, 1900, of fever; and, Dr. Reed observed, nonimmune nurses in attendance of very sick yellow fever patients seldom contracted the disease.

With the permission of Major General Leonard Wood, Military Governor of Cuba, Dr. Reed established a heavily quarantined experimental headquarters, named Camp Lazear, a mile outside Quemados. Dr. Reed and his associates determined to seek answers to the puzzling questions by daring use of human volunteers. Two wooden structures were built and heavily screened. In one, deliberately poorly ventilated, enlisted volunteers spent twenty nights in beds, bedclothes, and personal wear that were heavily saturated and stained with excrement and with "black vomit" of patients who had died of yellow fever. Revolting and uncomfortable as were their experiences, two groups of volunteers came through the tests healthy and unharmed.

The other experimental building at Camp Lazear was light and well ventilated. It was divided by a screen wall into two compartments. Equipped alike, one side was used by volunteers who allowed themselves to be bitten by mosquitoes; the other by control volunteers carefully protected from mosquitoes, but living under identical conditions and breathing the same atmosphere.

First man to be exposed to contaminated mosquitoes was Private John Kissinger. On December 8, 1900, Kissinger had the beginning of a well-defined attack of yellow fever. But Dr. Reed did not depend on diagnoses by his staff alone; the Havana commission, led by Dr. Finlay and including Drs. Juan Guiteras, W. C. Gorgas, and A. Diaz Albertini, was invited to examine Kissinger. All

agreed beyond doubt that he had yellow fever.

Reporting the experiments to the Medical and Chirurgical Faculty of the State of Maryland, in Baltimore, April 24, 1901, Dr. Reed said of Kissinger: "In my opinion this exhibition of moral courage has never been surpassed in the annals of the Army of the United States."

In addition to Kissinger, three other volunteers were bitten by mosquitoes which previously had fed on yellow fever victims. Each developed typical yellow fever, and diagnoses were verified by physicians of the combined commissions. Meanwhile, nonimmune controls, sleeping in the other half of the building and sharing a common atmosphere, suffered no ill effects. Results of the experiments at Camp Lazear were so clear cut that Dr. Reed, at the conclusion of his report, "The Etiology of Yellow Fever, an Additional Note," read before the Pan-American Medical Congress at Havana, in February, 1901, was able to make eleven statements, of which the most important were:

"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.

"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.

"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.

"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."

Two months later, in Baltimore, Dr. Reed also made this statement:

"To Dr. Carlos J. Finlay, of Havana, must be given...full credit for the theory of the propagation of yellow fever by means of the mosquito..."

Further experimental work of the United States Commission, carried out largely by Dr. Carroll in 1901, proved that the causative agent of yellow fever was not a bacterium, but a filterable virus which could be transmitted either by mosquito bite or by injection of blood from a sick patient into a nonimmune subject. The conclusive, courageous, rapid, and brilliant work of the commission added greatly to the prestige of medical science in the United States.

Practical consequences of the work of the Reed commission were tremendous. Dr. William Crawford Gorgas, Havana's chief sanitary officer, applying rigid, vigorous antimosquito measures, was able to rid the city of yellow fever within ninety days, in 1901, freeing its people of a centuries-old rule of terror. In 1903, Dr. Guiteras freed Laredo, Texas, of the scourge; New Orleans combated an epidemic in 1905; and other cities in North, Central and South America soon adopted measures that wiped out epidemics and controlled new cases as they arose. Drs. Licéjia, in Mexico, and Oswaldo Cruz, in Brazil, did outstanding work in ridding their countries of the fever. In 1904, Dr. Gorgas, now a General, applied his antimosquito measures to the Panama Canal Zone,

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the picture Methods of controlling and preventing yellow fever resulted from investigations conducted in 1900 at Camp Lazear, Cuba, by a United States Army Commission led by Major Walter Reed (1851-1902). This research proved conclusively that mosquitoes carry the yellow fever virus from person to person. First volunteer patient to be infected by mosquito bites was Private John Kissinger. Examining physicians were Major W. C. Gorgas, Havana sanitation officer; Dr. A. Agramonte, pathologist; Dr. Carlos J. Finlay, chairman of the cooperating Cuban Yellow Fever Commission and first man to point to the possible infective role of mosquitoes; Dr. James Carroll, bacteriologist; and Dr. Reed, commission chairman.

making possible completion of that monumental engineering project.

It was not Dr. Reed's fate to live long in the light of his triumph, or to add further to scientific knowledge of medicine. He died suddenly in Washington of appendicitis, November 22, 1902.

Of him, General Wood said, at a memorial service: "I know of no man who has done so much for humanity as Major 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 in each year than the cost of the entire Cuban war." Today, near Washington, D.C., a great research hospital bears Walter Reed's name.

Fate dealt more kindly with Dr. Finlay. In 1902, he became Chief Sanitary Officer of Cuba, a position from which he retired in 1909. Before his death in 1915, at 82 years of age, he had become an international hero, and several institutions have been named for him.

Romantically, the yellow fever story might end here. But the tiny virus that causes the death-dealing disease is not romantic; nor is it choosy about whom it attacks. The most common insect host in its man-mosquito-man cycle has been renamed—Dr. Finlay called it *Culex fasciatus*; later, it became known as *Stegomyia fasciata*; today, it is known world-wide as *Aedes aegypti*. This mosquito is definitely of domestic inclination, living near man and depositing its eggs in small bodies of water—in rain barrels, in tin cans, in hollows of roofs, in puddles, and in swamps. Sanitation experts succeeded in combating yellow fever by rigid inspections and measures to eliminate breeding places for mosquitoes, by adequate closure and screening of living quarters, and by preventing mosquitoes from biting yellow fever patients. Like measures applied to ships, plus health inspections of passengers at ports of arrival, minimized transportation of the disease to far-distant communities.

The Rockefeller Foundation, in New York, taking a cue from the work of Drs. Reed and Gorgas, appointed General Gorgas to head its Yellow Fever Commission, when his work in Panama was completed upon opening of the Canal in 1914. Between 1916 and 1949, the Foundation spent over \$14,000,000 on research and on grants to help various countries stamp out yellow fever. For a while, it seemed that the fever fighters were to be crowned with success. *Aedes aegypti* could be wiped out, or controlled. But from time to time, unaccountable new outbreaks occurred. Thus, yellow fever presented scientists with a new mystery. As in the first instance, the fever was not quick to give up its secrets. Hideyo Noguchi, a Rockefeller investigator, searching vainly for a spirochete as cause of yellow fever, was a victim of the fever in 1928. Researchers both in Africa and in South America discovered that yellow fever existed in the jungle, that monkeys and marsupials are susceptible to the disease, and that several species of forest-dwelling mosquitoes also serve as intermediaries. These forest-dwelling mosquitoes do not invade cities, as does *Aedes aegypti*; but jungle travelers, lumbermen, and others who have occasion to visit the forest may be bitten. If, during the incubation period, they are able to reach populated centers, they readily may serve as means of infecting domestic *Aedes* mosquitoes—and the epidemic chain will be reformed.

In 1928, other Rockefeller researchers in Africa, Drs. A. F. Mahaffy and Adrian Stokes,

discovered that rhesus monkeys could be infected with yellow fever. Following up on this lead, Dr. Max Theiler and his associates in Rockefeller Foundation's Division of Biological and Medical Research in New York developed two strains of attenuated live yellow fever virus for possible use as vaccines. One, known as the French strain, propagated in mouse brains, is widely used today, especially in Africa. But, because this vaccine occasionally gives rise to serious reactions, Dr. Theiler set up a series of tests employing other tissue cultures. Virus, grown on chick embryos, resulted in a vaccine known as 17D. This vaccine was field-tested in Brazil from 1937 to 1940. From 1940 to 1947, the Rockefeller Foundation produced over 28,000,000 doses of 17D vaccine, which it furnished free of charge to health agencies in thirty-three countries, and to the United States military services. In 1951, Dr. Theiler was awarded the Nobel Prize in Medicine in recognition of the vaccines' benefit to mankind.

Thus was yellow fever, scourge of the centuries, conquered in a half century; that is, nearly conquered. It has virtually vanished from the world's major cities; but pools of the virus that defy eradication still lie deep in the world's tropical jungles, passing unnoticed from animal to mosquito to animal, back and forth. The infected mosquitoes will not hesitate to feed on humans that come within their range.

In this day of rapid, world-wide travel, of pushing back of jungle frontiers, of exploding populations, vaccination is the only method available for protection of persons likely to be exposed to the risk of jungle yellow fever, and for protection of people living in communities which may be visited by travelers who have been in the tropics.

REFERENCES

- Ackerknecht, E. H., unpublished monograph.
Burnet, F. M., *Viruses and Man*. London, Penguin Books Ltd., 1955.
Kelly, Howard A., *Walter Reed and Yellow Fever*. New York, McClure, Phillips & Co., 1906.
Peller, Sigismund, *Walter Reed, C. Finlay, and Their Predecessors Around 1800*. Bulletin of the History of Medicine, Vol. 33, No. 3, May-June, 1959.
Reed, Walter; Carroll, James; Agramonte, Aristides; and Lazear, Jesse W., *The Etiology of Yellow Fever, A Preliminary Note*. Philadelphia Medical Journal, Vol. 6, No. 17, Oct. 27, 1900.
Reed, Walter; Carroll, James; and Agramonte, Aristides, *The Etiology of Yellow Fever, an Additional Note*. Journal of The American Medical Association, Vol. 36, No. 7, Feb. 16, 1901.
Reed, Walter, *The Propagation of Yellow Fever; Observations Based on Recent Researches*. Medical Record, Vol. 60, No. 6, Aug. 10, 1901.
Reed, Walter, and Carroll, James, *The Etiology of Yellow Fever, A Supplemental Note*. American Medicine, Vol. 3, No. 8, Feb. 22, 1902.
Ross, Ronald, *Malaria and Mosquitoes*. Nature, Vol. 61, No. 1587, March 29, 1900.
Ruiz de Zarate, Serafin, *Dr. Carlos J. Finlay and the Hall of Fame of New York*. Havana, Ministry of Health and Hospital's Assistance, 1959.
Rush, Benjamin, *An Account of the Yellow Fever as It Appeared in Philadelphia in 1797*. Philadelphia, Thomas Dobson, 1798.
Theiler, Max, *Yellow Fever*. In Rivers, Thomas M., and Harsfall, Frank L., Jr., *Viral and Rickettsial Infections of Man*. Philadelphia, J. B. Lippincott Co., 1959.
Williams, Greer, *Virus Hunters*. New York, Alfred A. Knopf, 1959.
Yellow Fever. A Symposium in Commemoration of Carlos Juan Finlay. The Jefferson Medical College of Philadelphia, 1955.