



Yellow Fever - The Scourge Revealed

by *Stanton E. Cope, Ph.D.*

The following story is that of a prolific and savage killer, yellow fever, and the events by which the veil of this terrible scourge was lifted. Some of the heroes' names will be familiar but most will not. The story contains three parts: first, a brief history of yellow fever and its impact on society; second, the experiments done in Cuba which elucidated the mode of transmission of this disease; and finally, the lives of two young men and their heroic roles in one of the great medical discoveries of our time.

Brief History of Yellow Fever

We believe that yellow fever originated in Africa and made its first visit to the New World in the late 16th or early 17th century. For the next 300 years or so, "yellow jack" ravaged hundreds of cities in North America from Texas to Massachusetts as well as the Great Mississippi Valley. Each wave of pestilence was marked by economic shamble, human panic and fear, and widespread death.

From 1668 to 1893 there were 135 major epidemics in port cities of the U.S. In 1793, yellow fever claimed one of every ten Philadelphians, a total of 4,000 dead. New Orleans, a frequent victim of attack, suffered 29,000 cases and over 8,000 dead in 1853. During the summer of 1878, a huge epidemic shattered the U.S.: 132 towns affected; 75,000 cases; 16,000 deaths; and a cost of over \$100 million dollars!

Medical authorities of the day argued over the mode of transmission. Some, such as Dr. Benjamin Rush of Philadelphia, believed that yellow fever was spread by miasmatic (poisoned) air. Others felt the disease was spread by fomites; that is, articles such as bedding or clothing that were believed to be contaminated. Preventive measures included cigar smoking by women and children, and massive burning of suspect items.

The Situation in Cuba

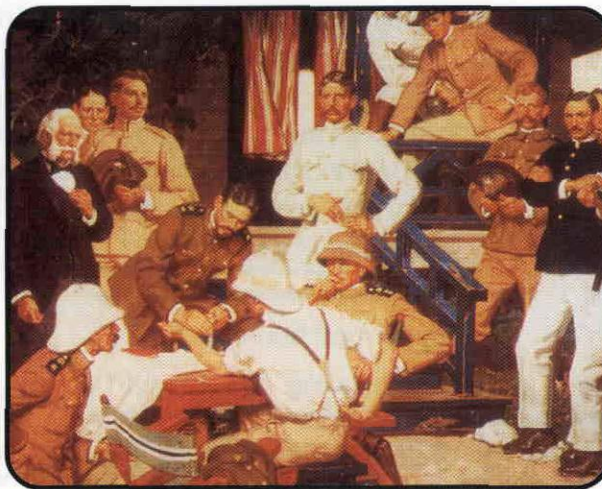
At the end of the Spanish-American War in 1898, Cuba was given to the United States by Spain. And what a deal it was! In Havana, dead animals were lying in the streets, typhoid fever was lurking everywhere, and yellow fever was always a

took her own life after her husband's unexpected demise.

The Surgeon General at the time was George Miller Sternberg who was considered the leading expert on yellow fever. Through his efforts and with his blessing, Special Order No. 122 from the Secretary of War was issued on May 24th, 1900. This order established a Board for the purpose of pursuing scientific investigations with reference to the acute infectious diseases on the island of Cuba, giving special attention to questions relating to the etiology and prevention of yellow fever."

Preliminary Work of the Board

The president of the Board was Major Walter Reed, an Army surgeon from Virginia. Reed had recently distinguished himself working on prevention of typhoid fever in Army camps and was a logical choice. An Englishman, Dr. James Carroll, was primarily responsible for the bacteriology work of the Board. He had been associated with Reed since 1893 and was highly trusted by him. Dr. Carroll would soon turn out to be the first experimental case of yellow fever.

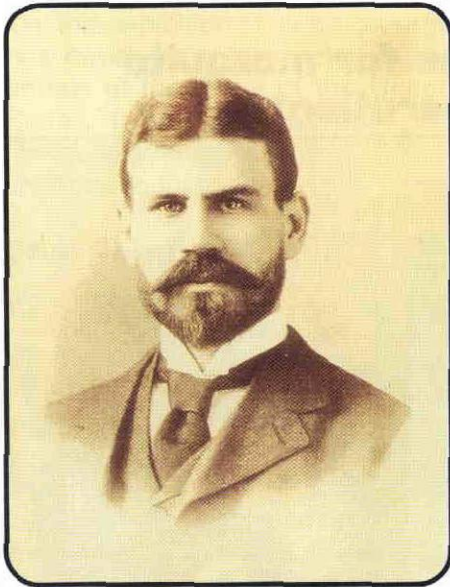


threat. During the war, 2,450 Americans had died in Cuba; 385 in battle and the rest from disease.

In early 1900, a severe outbreak of yellow fever in Havana killed many Army officers who were sent there after the war. The wife of one officer

Dr. Aristides Agramonte, a Cuban physician, handled pathology and autopsies. He was believed to be immune to yellow fever due to prior infection. The fourth and final member of the Board was Dr. Jesse W. Lazear. He had been a medical school classmate of Agramonte's at

Columbia University and was hired by the Army as a contract surgeon. In exactly four months, Lazear, who handled the mosquito colonies, would be dead from yellow fever at the age of 34.



Dr. Jesse W. Lazear

The goals of the Board were clear: 1) determine the nature of *Bacillus icteroides* which a famous Italian bacteriologist claimed was the cause of yellow fever, 2) perform bacteriological studies on patients and victims, and 3) explore the theory of insect transmission of yellow fever.

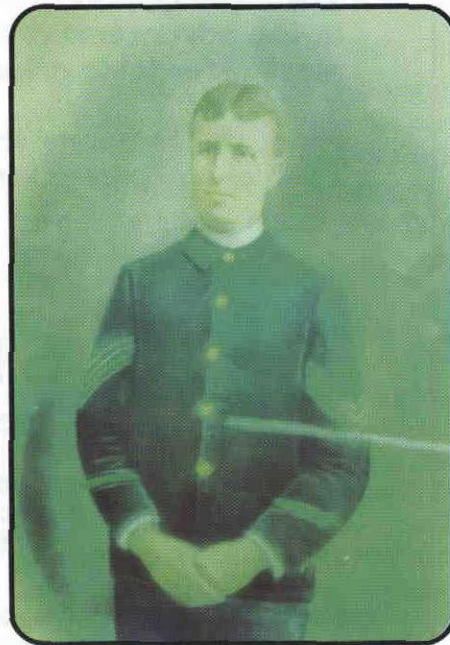
The insect theory had been promoted in Cuba since 1881 by Dr. Carlos J. Finlay. Finlay claimed that the mosquito *Culex fasciatus* (now known as *Aedes aegypti*) transmitted yellow fever but he had been unable to convince the scientific community during 20 years of experiments. Dr. Finlay's experience and assistance would prove invaluable to the success of the Board.

The Board began work on June 25th, 1900 and spent the rest of June and July on bacteriology. Cultures were made from the blood and tissues of 11 yellow fever victims. All results for *B. icteroides* were negative. The Board could not produce a

single shred of evidence to support a bacterial etiology for yellow fever.

At about this time, Reed became more and more influenced by three pieces of information. First, a prisoner in a guard house in Cuba died from yellow fever on June 18th. None of the eight other prisoners in the cell got sick, including one who slept in the dead man's bed! Second, just three years before in 1897, Sir Ronald Ross had proved that mosquitoes were the vectors of avian malaria. Finally, Dr. Henry Rose Carter had recently worked out the extrinsic incubation period concept (the time from when a mosquito picks up the virus to when it can transmit it) for yellow fever. Carter was a quarantine officer in Cuba and had a great influence on the work of the Board.

On August 1st, 1900 the Board and a few others met on the porch of the officers' quarters. They decided to test the mosquito theory. All members of the Board agreed that they must take the same risks which necessity would soon compel them to impose upon any volunteers. Shortly thereafter, fate played her hand.



John Kissinger

On the next day, August 2nd, Reed was ordered to Washington to finish a critical report on typhoid fever. During his absence, Lazear and Carroll began to test the mosquito theory. On August 30th, Carroll was taken seriously ill with yellow fever transmitted by the bite of one of Lazear's mosquitoes. On September 4th a second case was produced and Reed was notified in Washington.

Under mysterious circumstances, Lazear was bitten on September 13th, became ill with yellow fever on the 18th, and died on the 25th. There was considerable controversy surrounding his death. After realizing the gravity of his illness, Lazear claimed he was bitten by accident while working in the hospital. Others, possibly including Reed, felt that Lazear had experimented on himself and, as his death could have been ruled a suicide, the story was fabricated so that his family would not be denied insurance benefits. Unfortunately, Lazear's laboratory notebook, which may answer this question, was lost shortly after the experiments were concluded.

On October 3rd Reed returned to Cuba and immediately read Lazear's notebook. Although he understood that none of these three cases had been produced under controlled conditions, he still wrote the now classic paper in which the Board stated the following conclusions: 1) *Bacillus icteroides* stands in no causative relation to yellow fever, but when present should be considered a secondary invader in this disease, and 2) the mosquito serves as the intermediate host for the parasite of yellow fever.

Camp Lazear and the Controlled Experiments

Now, the challenge was to conclusively prove that mosquitoes were the primary mode of transmis-

sion. To do this, and to disprove the fomite theory, controlled experiments using human volunteers were necessary. On November 20th, 1900, Camp Lazear was established. It consisted of seven Army tents and would serve as a quarantine station for the volunteers.

Volunteers were drawn from Army soldiers and Spanish immigrants. Each volunteer signed an informed consent and was offered \$100 in gold for volunteering and another \$100 if he got yellow fever during the course of the experiments.

Army Private John R. Kissinger and a civilian clerk named John Moran were the first to volunteer their services to the Board. After Major Reed explained the inherent dangers and proposed payment, both men declined the money, making it their sole stipulation that they should receive no monetary reward. Upon hearing this, Reed touched his cap and said, "Gentlemen, I salute you."

John Kissinger

Allow me to digress for a few moments and tell you how John Kissinger got to Cuba. He was born on July 25th, 1877 on a farm in Henry County, Ohio. His family moved to Liberty Mills, Indiana when he was quite young. Being very patriotic, he joined the local militia when he was 19 years old. After the sinking of a U.S. ship in Havana harbor in 1898, Kissinger joined the Army to fight in Cuba but the war ended before he got that chance and he was discharged. Still determined to fight, he re-enlisted, hoping to see action in the Philippines but due to a foot deformity, he was transferred to the hospital corps and sent to Cuba.

After being quarantined in Camp Lazear for over 30 days, Kissinger was experimentally infected with yel-

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low fever by mosquito bite, became ill on December 8th, and suffered through a moderate case of the disease. Writing about Kissinger at a later date, Reed said, "In my opinion, this exhibition of moral courage has never been surpassed in the annals of the Army of the United States." In just a few brief days, the mosquito theory had been changed to fact.

The Fomite House

Although the Board had clearly demonstrated that mosquitoes could transmit yellow fever, it had not ruled out the fomite theory. Remember, this was the accepted mode of transmission of the day.

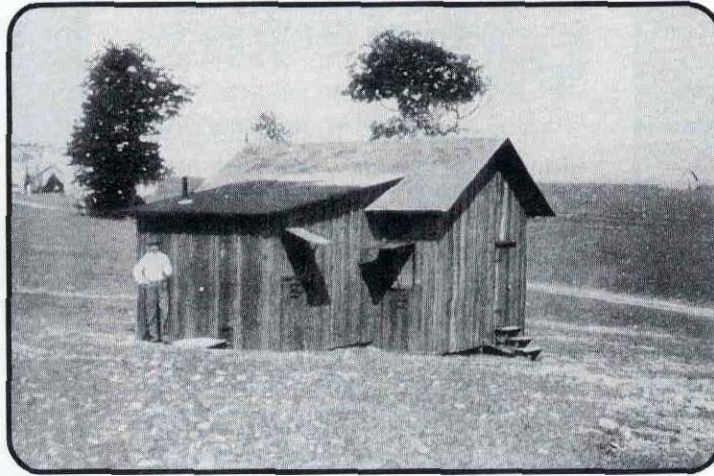
In order to address this question, a small building (14 by 20 feet in size) was constructed. When the building was ready for occupation, three large boxes filled with sheets, pillowcases and blankets were placed inside. This was no ordinary linen, however. Many of the articles had been purposely soiled with a liberal quantity of black vomit, urine and fecal matter from recent victims of yellow fever.

At 6 p.m., three American volunteers entered the building, gingerly unpacked the linen, thoroughly shook all items, used the linen to prepare their beds and settled in for a good night's sleep. One volunteer, overcome by the stench during unpacking, raced outside and vomited but returned to complete the experiment.

This scenario was followed for the next 20 days, although the men were allowed to spend the daytime hours in a tent. On December 19th they were placed in quarantine for five days; all remained in perfect health.

For good measure, the process was repeated from December 21st to January 10th, using different volunteers. This time, however, they actually slept in patients' soiled pajamas.

And finally, just to be sure, it was repeated again from January 11th to the 31st. As an added treat, this time the men covered their pillows with



The Fomite House

towels soaked with blood of yellow fever victims. Again, all remained well. At a later time, two of these volunteers were given yellow fever by blood injection which proved they were not immune while in the fomite house.

In a letter written on December 10th, Reed mentioned that the volunteers in the fomite house were relieved to hear about Kissinger's case. The fomite theory was now history.

The Mosquito House

If fomites did not spread yellow fever, the logical question before the Board was how does a house become infected with the disease? To address this question, they built a second house, similar in construction to the first, was built. It consisted of two rooms separated only by a screen partition. It was very sanitary compared to the fomite house and

all articles entering the house were steamed.

On December 21st, 1900, with Reed watching from one side, 15 female *Aedes aegypti* were released on the other. These mosquitoes had all fed on patients' blood teeming with yellow fever virus and subsequently held for the appropriate extrinsic incubation period; their cargo was deadly.

At noon, our yellow fever susceptible friend, John Moran, clad only in a night shirt and fresh from a bath, entered the room and reclined on a cot. For the next 30 minutes he was bitten by seven mosquitoes while he held a hand lens and wrote a detailed account of what he saw. Later that day he re-entered and took five more bites and the next day, three more bites.

Most importantly, during each of Moran's visits, two volunteers that were also susceptible to yellow fever, remained on the other side of the partition at all times and slept there each night from December 21st to January 8th. They remained in good health. For John Moran, however, Christmas Day came with a bang. He awoke to find himself firmly in the grip of the case of yellow fever he seemed so intent on having.

Aftermath

The conclusions of the Board were published on February 16th, 1901 and presented at the Pan American Congress in Havana the same month. The first four conclusions dealt with mosquito transmission and the extrinsic incubation period for yellow fever.

Conclusions 5 through 8 discussed infection by blood injection, immunity, incubation period of the

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disease in humans, and the rejection of the fomite theory. Number 9 stated how a house became infected with yellow fever. Conclusion 10 was important as it proposed that the spread of yellow fever could be stopped using mosquito control

IN A NUT SHELL
WE ALL KNOW THE DANGER OF
YELLOW FEVER
but we become EARNEST ONLY
after it claims our own blood.
INFECTION BY MOSQUITOES
IS NO LONGER A THEORY
BUT A PROVEN FACT
GET RID OF THE MOSQUITO
BY BURNING
SULPHUR FOR FUMIGATION
UNDER THE DIRECTION OF THE
MARINE HOSPITAL SERVICE
START IN ON
SUNDAY AT 10 A.M.
AND KEEP AT IT UNTIL NOON

measures and patient isolation techniques. Finally, the Board stated that although the mode of transmission was now known, the specific cause of yellow fever remained a mystery.

The Board produced 22 cases of yellow fever under controlled conditions; 14 by mosquito bite, six by blood injection and two by injection of filtered serum. It is significant to note that, although yellow fever may have a case fatality rate of 50% or higher, the controlled experiments produced no deaths. It has been said that the Board had good nursing, good diet and good patient handling but most of all it had good luck. Any fatalities among the volunteers may have terminated the experiments immediately.

The Board Members

The events in Cuba left Walter Reed physically and mentally ex-

hausted. The ordeal of human experimentation had exacted a sizeable toll. In Washington, he was plagued by the daily routine of military life and his work on yellow fever was attacked by jealous friends and enemies. Finally, and most incredibly, he was charged with being absent without leave in connection with presenting the Board's findings in Indianapolis. Reed, who was thankful his life had not been lived in vain, understood none of this and was humiliated.

In November, he confided to friends that he was a very sick man. On November 17th he was operated on for a ruptured appendix. Five days later he developed peritonitis, became unconscious and died on November 23rd, 1902 at the age of 51 and at the zenith of his career.

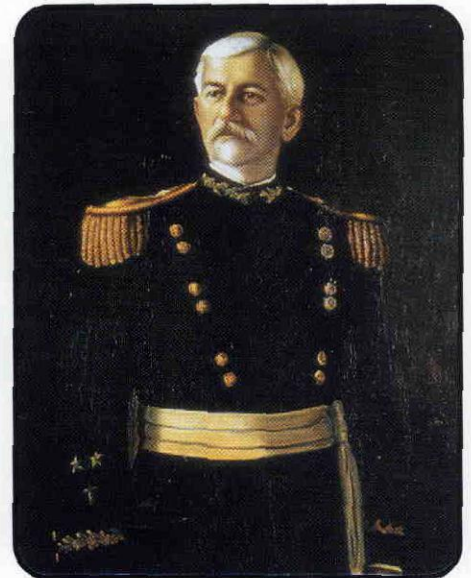
Major Reed is interred in Arlington National Cemetery where a granite headstone and bronze plaque commemorate his accomplishments. Among other items, the plaque states, "He gave to man control over that dreadful scourge, yellow fever."

Dr. James Carroll, Reed's trusted assistant, died in 1907 from heart disease which he blamed on his case of yellow fever. He left behind a wife and five children. Dr. Agramonte became a professor at the University of Havana and, as far as I know, lived a long and productive life. He never received any material reward for his share of the work on yellow fever.

As mentioned earlier, Dr. Lazear died from yellow fever at the age of 34, leaving behind a wife and two young children, one of whom he had never seen. He is interred in Baltimore, Maryland where a battery in the harbor is named for him. The widows of Reed, Carroll and Lazear all received pensions of \$125 per month from the government.

Benefits of the Work

The benefits derived from the work in Cuba are truly inestimable. Without doubt, thousands of lives were spared and millions of dollars were saved. Dr. William Gorgas was a sanitary engineer for the



Dr. William Gorgas

Army in Cuba. Skillfully applying the recommendations of the Board, he coordinated an intensive mosquito control campaign. Within a few short months, yellow fever was literally eliminated from Havana.

General Gorgas then applied his methods in Panama where yellow fever had been a major obstacle to the completion of the Panama Canal. Within a short time, yellow fever was gone and the Canal a reality.

The United States continued to have outbreaks of yellow fever after 1900 but the fear and panic associated with prior epidemics was now replaced by determination and cooperation in the fight against mosquitoes.

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The Volunteers

And what ever happened to the brave volunteers without whom none of this would have been possible? Most were lost track of. After about ten years, however, it was decided that a Congressional Medal of Honor should be given to each of them. Curiously, medals were awarded only to those who got sick or who slept in the fomite house. There was no medal just for volunteering. On occasion, reunions were held which were generally well attended.

John Kissinger's fate after Cuba is an interesting tale. He survived his battle with yellow fever but not without some telling losses. He left the Army in 1901 and returned to Indiana to try his hand at farming but he was not physically strong enough for this labor. He then went to Seattle, Washington where he worked at various jobs, got married and operated a restaurant.

After returning to Indiana, Kissinger, while walking home one night, collapsed and lost the use of his legs for 12 years or so. An application to the government for pension, which Kissinger did reluctantly, was turned down as John could not prove his disability was caused by his bout with yellow fever.

To make ends meet, Mrs. Kissinger took in washing with John slowly and awkwardly assisting while propped in a chair. She also scrubbed post office floors. Finally in 1907, Congress reconsidered and Kissinger was awarded a pension of \$12 per month and a few favors such as free street car rides. Outraged at this action, many people wrote letters on Kissinger's behalf. As a result of this public outcry, Kissinger was given a pension of \$100 per month in 1911. Incredibly, the pension was later withdrawn and the Kissingers were

asked to return all the money. Fortunately, after a short time the pension was restored.

In the early 1920's, the Kissingers moved to a small town in Indiana called Huntington, which just happens to be my home town. So now you know how I got interested in this story. Eventually, the American Medical Association became aware of the Kissinger's plight and through it a fund was raised to purchase a house for them to live in.

Kissinger finally started to receive some of the accolades he so richly deserved. He was a modest man and rarely spoke about the events in Cuba unless asked. He was interviewed often by the media and despite all the attention, remained a humble soul. Even Hollywood got into the act; John and his wife Ida were the guests of honor for the 1938 premiere of the movie *Yellow Jack*, the story of the events in Cuba.

The Kissingers lived in Huntington until they thought it best to enter the Indiana Soldiers' Home in Lafayette. Hoping to relieve the pain in his joints, Kissinger moved to Florida where he died on July 16th, 1946 at the age of 68. His remains were returned to Huntington where he and his wife are buried. His gravestone reads, "A martyr to yellow fever in the interest of humanity and a hero of the Spanish-American War."

On the hospital grounds in Huntington is a plaque dedicated to Kissinger. As the plaque states, Kissinger, Moran and the other volunteers were, and still are, quiet heroes. Also in Huntington, one corner of the courthouse museum is dedicated to Kissinger. The display contains several of Kissinger's uniforms, documents pertaining to the yellow fever experiments, numerous awards and photographs.

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A painting by Dean Cornwell shows all the central figures in the fight against yellow fever in Cuba. Although this exact scene probably didn't take place, it is a fitting tribute to those involved. The two figures on the right clad in blue medic jackets are our two heroic young men, John Kissinger and John Moran.

In closing, I would like to paraphrase Dr. Howard Kelly from his book on Walter Reed: the inspiration of these men lies in the fact that, though men of war, they ravaged no distant lands, destroyed no tens of thousands to make their reputation, but, by quiet methods when there was no strife, saved countless lives and swept away a hideous plague which from time immemorial had periodically visited our shores, devastated our fair land, and too often snatched from the years of peace and plenty all their blessings.

Acknowledgments

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