

Yellow Fever – The Scourge Revealed

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Slide 1 – Title

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 to you but most will not.

My presentation contains three parts: first, I will present a brief history of yellow fever and its impact on society; second, I will outline the experiments done in Cuba which elucidated the mode of transmission of this disease (C); and finally I will tell you about two young men and their heroic roles in one of the great medical discoveries of our time.

Slide 2 – Cartoon of YF in the Americas

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, the disease 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 widespread death.

From 1668 to 1893, there were 135 major epidemics in U.S. port cities. In 1793, yellow fever claimed 1 of every 10 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.

Slide 3 – Benjamin Rush

Medical Authorities argued over the mode of transmission. Some, such as this gentleman, Dr. Benjamin Rush (a physician in Philadelphia and a signer of our Declaration of Independence), believed that yellow fever was spread by miasmatic, or 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.

Slide 4 – Map of 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 lurking everywhere, and yellow fever was always a threat. During the war, 2,450 Americans had died in Cuba; 385 in battle, and the rest from disease.

Slide 5 – Sternberg

In early 1900, yellow fever killed many of the U.S. Army officers posted in Havana. The wife of one officer committed suicide after her husband's unexpected demise. Pictured here is the Surgeon General at the time, George Miller Sternberg. He was considered

the leading expert on yellow fever. Through his efforts, special order No. 122 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”*.

Slide 6 – Walter Reed

The President of the Board was Major Walter Reed, an Army surgeon from Virginia. Reed had recently distinguished himself working on typhoid fever in Army camps and was a logical choice.

Slide 7 – James Carroll

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. He would soon turn out to be the first experimental case of yellow fever.

Slide 8 – Agramonte

Dr. Aristides Agramonte handled pathology and autopsies. A Cuban physician, he was picked primarily because he was believed to be immune to yellow fever due to prior infection.

Slide 9 – Lazear

The fourth and final Member of the Board was Dr. Jesse W. Lazear. He had been a classmate of Agramonte's at Columbia 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.

Slide 10 – Goals of the Board

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;
- 3) Explore the *theory* of insect transmission.

Slide 11 – Carlos Finlay

The insect theory had been promoted in Cuba since 1881 by Dr. Carlos Juan Finlay. Finlay claimed that the mosquito *Culex fasciatus*, now known as *Aedes aegypti*, transmitted yellow fever virus but he had been unable to convince the scientific community during 20 years of experiments. Finlay's assistance, as pointed out in later writings by Major Reed, proved invaluable to the Board.

Slide 12 – Reed's Lab

The Board began work on June 25th, 1900 and spent June and July on bacteriology studies. The small building in this photo served as Walter Reed's laboratory.

Slide 13 – Table II

Cultures made from samples of 11 yellow fever victims were all negative for *Bacillus icteroides*, as shown in the right-hand column of this slide. The Board could not produce a single shred of evidence supporting a bacterial aetiology for yellow fever.

At about this time, Reed became extremely influenced by three pieces of information: 1) a prisoner in Cuba had died from yellow fever on June 18th. None of the 8 other prisoners in the cell got sick, including one who slept in the dead man's bed;

Slide 14 – Ronald Ross

2) Just 3 years before, Sir Ronald Ross had proved that mosquitoes were the vectors of avian malaria;

Slide 15 – Henry Rose Carter

And 3) Henry Rose Carter, pictured on the far right here, had recently worked out the Extrinsic Incubation Period concept for yellow fever and was now serving as a quarantine officer in Cuba. His presence greatly influenced the work of the Board.

Slide 16 – Officers' Quarters

On August 1st, the Board met on the porch of the Officers' Quarters seen here. Major Reed's quarters are marked by the "X". 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.

Slide 17 – Method of Feeding Mosquitoes

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. This slide demonstrates one method used to feed the mosquitoes.

(C) On August 30th, Carroll was taken seriously ill with yellow fever from the bite of one of Lazear's mosquitoes. On September 4th, a second experimental case was produced and Major Reed was notified in Washington.

(C) Under mysterious circumstances, Lazear himself was bitten on September 13th, became ill on the 18th, and died on the 25th.

Slide 18 – Lazear Death Notice

Pictured here is a facsimile of Lazear's death notice. 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 felt that Lazear was a victim of self-experimentation and, as his death could have been ruled a suicide, the hospital 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.

Slide 19 – Preliminary Note

On October 3rd, Reed returned to Cuba and immediately read Lazear's notebook. Although he understood that none of these first three cases of yellow fever 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. 2) **The mosquito serves as the intermediate host for the parasite of yellow fever.**

Slide 20 – Camp Lazear

Now, the challenge was to conclusively prove that mosquitoes were the primary mode of transmission. To do this, and to disprove the fomite theory, controlled experiments, using human volunteers, were necessary. On November 20th, 1900, Camp Lazear was established. As seen in this slide, it consisted of 7 Army tents and would serve as a quarantine station for the volunteers.

Slide 21 – 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! This photo includes six of the volunteers, including Private John Kissinger.

Slide 22 – Kissinger

Kissinger, seen here, 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.**”

After being quarantined in Camp Lazear for over 30 days, Private Kissinger was experimentally infected by mosquito bite, became ill

on December 8th, and suffered through a moderately severe case of yellow fever. 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.”**

Slide 23 – Reed Letter to Truby

In this letter, written on December 10th, Reed mentions Kissinger’s case and proudly exclaims that (POINT OUT) **“the theory is alright!”** In a few brief days, the mosquito theory had been changed to fact.

Slide 24 – Fomite House Floor Plan

Although the Board had clearly demonstrated that mosquitoes **could** transmit yellow fever virus, 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. The floor plan of the building is seen in this slide. When the building was ready for occupation, three large boxes filled with sheets, pillow cases 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.

Slide 25 – Fomite House

At 6 PM, three American volunteers entered this building, gingerly unpacked the linen, thoroughly shook out all the items, used the linen to prepare their beds, and settled in for a good night's sleep.

This same 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 5 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 towels soaked with blood of cases. Again, all remained well. At a later time, two of these volunteers were given yellow fever by blood injection, which proved that they were non-immunes while in the fomite house.

Slide 26 – Reed Letter to Truby (2)

In this page of the letter mentioned earlier, Reed writes about the volunteers in the fomite house and how they were *relieved* to hear about Kissinger's case! The fomite theory was now history.

Slide 27 – Mosquito House

Now, the logical question before the Board was “**how does a house become infected with the disease?**” To address this issue, a second house, similar in construction to the first, was built. It consisted of 2 rooms separated only by a screen partition. It was

very sanitary compared to the fomite house, and all articles entering the house were steamed.

Slide 28 – Mosquito House Cartoon

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 during viremia and had been held in the laboratory for the appropriate time. Their cargo was deadly.

(C) At noon, our friend John Moran, clad 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 7 mosquitoes while he held a hand lens and wrote a detailed account of what he saw. Later that day, he re-entered and took 5 more bites, and the next day, 3 more bites.

(C) Most importantly, during each of Moran's visits, 2 non-immunes remained on the other side of the partition at all times and slept there each night from December 21st to January 8th.

Christmas Day, 1900, came with a bang for John Moran. He awoke to find himself firmly in the grip of the case of yellow fever he seemed so intent on having.

Slide 29 – Conclusions (1)

The conclusions of the Reed Board were published on February 16th, 1901 and presented at the Pan American Congress in Havana the same month.

Conclusions 1-4 dealt with mosquito transmission and the extrinsic incubation period for yellow fever.

Slide 30 – Conclusions (2)

Conclusions 5-8 discussed infection by blood injection, immunity, incubation period of the disease in humans, and the rejection of the fomite theory.

Slide 31 – Conclusions (3)

Number 9 stated how a house became infected with yellow fever. Conclusion 10 was most important, as it proposed that the spread of yellow fever could be **stopped** using vigorous mosquito control measures and patient isolation.

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

Slide 32 – Yellow Fever Title

The Reed Board produced 22 cases of yellow fever under controlled conditions: 14 by mosquito bite, 6 by blood injection, and 2 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, they had good luck. Any fatalities among the volunteers may have terminated the experiments immediately.

Slide 33 – Walter Reed

The events in Cuba left Walter Reed physically and mentally exhausted. 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 (AWOL) 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 of 1902, 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 at the age of 51, and at the zenith of his career.

Slide 34 – Reed Grave

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.”**

Slide 35 – Commission

Dr. James Carroll died in 1907 at age 53 from myocarditis that he blamed on his case of yellow fever. He left behind a wife and 5 children.

Dr. Agramonte became a university professor 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.

Slide 36 – Lazear Grave

As mentioned earlier, Dr. Lazear died from yellow fever at the age of 34, leaving behind a wife and 2 young children, one of whom he never saw. 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.

Slide 37 – Gorgas

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

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

Slide 38 – Yellow Fever Poster

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. This poster was used during the 1905 epidemic in New Orleans, the last major outbreak of yellow fever in the United States.

Slide 39 – Reunion Program

And what ever became of the brave volunteers without whom none of this would have been possible? Most were lost track of. After about 10 years, however, it was decided that gold medals of honor should be given to them but curiously, medals were awarded only to those who got sick or who slept in the fomite house. There was no medal just for volunteering.

(C) Occasionally, reunions were held. Pictured here is the program from one such event, held in 1933. Note the signatures of the volunteers on the left side.

Slide 40 – Kissinger

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, returning to Indiana to try his hand at farming but he was not physically strong enough.

After working at various odd jobs, Kissinger, while walking home one night, collapsed and lost the use of his legs. 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.

Slide 41 – Kissinger House

Outraged at this action, many people wrote letters on Kissinger's behalf. As a result of this public outcry, Kissinger was given a \$100 per month pension in 1911. Incredibly, the pension was withdrawn and demand made for return of past receipts. I am pleased to tell you that after a short time, the pension was restored.

In the early 1920's, the Kissingers moved to a small town called Huntington, Indiana, which just happens to be where I am from. Now you know how I got interested in this business. The American Medical Association became aware of John's plight and through it a fund was raised to purchase the house seen here for the Kissingers.

Slide 42 – Radio Interview

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 often interviewed by the media and, despite all the attention, he remained a humble soul.

Slide 43 – Hollywood Premiere

Even Hollywood got into the act. John and Ida Kissinger were the guests of honor for the 1938 premiere of the movie *Yellow Jack*, the somewhat inaccurate story of the events in Cuba.

Slide 44 – Grave

John and Ida lived in Huntington until they thought it best to enter the Indiana Soldiers' Home. Hoping to relieve the pain in his joints, Kissinger moved to Florida where he died in 1946 at the age of 68. He is interred in Huntington where his gravestone reads, **“A martyr to yellow fever in the interest of humanity and a hero of the Spanish-American War.”**

Slide 45 – Plaque at Hospital

The hospital in Huntington bears a plaque to Kissinger. As the plaque states, Kissinger, Moran and the other volunteers truly were, and still are, quiet heroes.

Slide 46 – Courthouse Museum

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, photographs and several of the items I have shared with you today.

Slide 47 – Cornwell Painting

This painting by Dean Cornwell shows all the central figures in this fight against yellow fever. Although this exact scene couldn't have taken place, it is a fitting tribute to those involved. The two standing figures at the right of the painting in blue medic jackets and white pants are John Kissinger and John Moran.

In closing, I would like to paraphrase 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, (C) 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.**

