

**A JAUNDICED SOUL: THE WALTER
REED-GEORGE MILLER STERNBERG YELLOW
FEVER CONTROVERSY**

by

Vincent J. Cirillo, Ph.D.

Jealousie, the jaundice of the soul.

John Dryden (1687)¹

*A dark shadow in the scientific life is often thrown by a spirit of
jealousy.*

William Osler²

Jealousy, one of the oldest elements in humanity's arsenal of sins, stresses a coveting of something that belongs to another, because one believes that he/she is more deserving of it. The history of science and medicine is replete with stories of jealousy and its pernicious effects on the lives of those involved. The fault lies in the institution of science itself, which reserves its highest rewards for originality and makes recognition of priority uppermost. "In short, property rights in science become whittled down to just this one: the recognition by others of the scientist's distinctive part in having brought the result into being."³

One of the most egregious priority disputes in modern times involved Albert Schatz (1920-2005), a graduate student at Rutgers University's College of Agriculture,

and his dissertation adviser Selman Waksman (1888-1973) over their respective contributions to the discovery of streptomycin. The historiography of the last two decades resounds with pro-Schatz arguments which are then hotly contested by Waksman's supporters.^{4,5} Schatz's original laboratory notebook, recently unearthed at the Rutgers University Archives, has tipped the scales in Schatz's favor.⁶

Waksman alone was awarded the Nobel Prize in Physiology or Medicine in 1952 for the discovery of streptomycin, the first antibiotic effective against tuberculosis.⁷ It is a textbook example of the Matthew effect, which "consists in the accruing of greater increments of recognition for particular scientific contributions to scientists of considerable repute and the withholding of such recognition from scientists who have not yet made their mark."⁸

Schatz, who spent the rest of his life fighting for recognition, was finally vindicated on 28 April 1994 when Rutgers University conferred upon him the Rutgers Medal, its highest award for conspicuous scholarly achievement, thereby publicly acknowledging him as the co-discoverer of streptomycin.⁹

It is tempting to think that if Waksman had only exhibited some of Frederick Banting's (1891-1941) beneficence, this protracted and poisonous affair could have been avoided. Banting publicly shared the credit and his 1923 Nobel Prize purse equally with Charles Best (1899-1978), a medical student who was his coworker in the experiments that led to the discovery of insulin, because he was furious that the Stockholm trustees had unjustly ignored Best's contributions.¹⁰

While the contested discovery of streptomycin continues to receive serious attention in the literature, scholarly discussion of another controversy – also rooted in jealousy -- surrounding credit for the equally monumental discovery of the mosquito transmission of yellow fever is almost nonexistent. This essay attempts to rectify this situation by examining the historical evidence to provide fresh insight into the validity of the issues that formed the basis of this dispute.

REED-STERNBERG RELATIONSHIP

George Miller Sternberg (1838-1915), an internationally renowned bacteriologist and photomicroscopist, was America's leading expert on yellow fever. In 1893 he published a colossal volume titled *Manual of Bacteriology*, the first textbook on bacteriology in the United States. Because of his extraordinary scientific credentials, he was appointed Surgeon General of the U.S. Army on 30 May 1893, and promoted to the rank of brigadier general.

Walter Reed (1851-1902) wrote to Sternberg, "When I think that it places at the head of the Corps the one man who preeminently stands forth as the representative of progressive scientific medicine and that it means that the fossil age has passed, I have an irresistible desire to toss my very hat into the air."¹¹ Sternberg's success would later benefit Reed's career.

Reed's enthusiasm, intellect, inquisitiveness, and aptitude for the new tools and techniques of scientific medicine caught Sternberg's attention. As a result, Sternberg sent Reed to pursue advanced studies in pathology and bacteriology under Professor William Henry Welch (1850-1934) at Johns Hopkins University Hospital in Baltimore.¹²

After finishing his studies at Johns Hopkins, Captain Reed was appointed professor of clinical and sanitary microscopy and director of the pathology laboratory at the new Army Medical School in Washington, D.C.¹³

Their relationship started with Sternberg as Reed's mentor, and evolved into one of close colleagues. Reed, who was promoted to major in December 1893, was to become Sternberg's "right arm in disease outbreak investigation in the field."¹⁴

When a typhoid fever epidemic swept through the national encampments during the Spanish-American War in 1898, Sternberg turned to his trusted associate, Major Reed, to head the Typhoid Board he created on 18 August 1898 to investigate the cause of the epidemic. The other members were medical officers Maj. Victor C. Vaughan and Maj. Edward O. Shakespeare. The Board completed its work in twenty-one months in June 1900. The Board concluded that the typhoid bacillus was spread by human contact and flies. *The Report on the Origin and Spread of Typhoid Fever in the U.S. Military Camps During the Spanish War of 1898* is still the most complete study of the epidemiology of typhoid fever ever published.¹⁵

Because of Reed's impressive accomplishments Sternberg turned to him again to head the postwar Yellow Fever Board created on 23 May 1900 to investigate the "infectious diseases prevalent on the Island of Cuba and especially yellow fever." Also named to the Board were contract surgeons James Carroll, Jesse W. Lazear, and Aristides Agramonte. In a remarkably short time the Board discredited *Bacillus icteroides* and fomites as factors in the propagation of yellow fever, and demonstrated that the disease was transmitted solely by means of the bites of infected female *Aedes aegypti* mosquitoes.¹⁶

In summary, Reed and Sternberg admired and respected each other, which makes the surgeon-general's attempt to grab some of the credit for the discovery of the mosquito transmission of yellow fever all the more egregious.

YELLOW FEVER CONTROVERSY

By 1900 yellow fever became a significant problem for the victorious U. S. troops occupying Cuba after the Spanish-American War (1898). It was clear that something had to be done to avoid disaster. On 23 May 1900, U. S. Army Surg. Gen. George Miller Sternberg (1838-1915), a world-renowned authority on yellow fever, appointed a board of medical officers chaired by Maj. Walter Reed (1851-1902) to investigate the “infectious diseases prevalent on the Island of Cuba and especially yellow fever.” In a follow-up letter to Reed, Sternberg wrote: “You will naturally give special attention to questions relating to the etiology and prevention of yellow fever.”¹⁷

Others have argued that the Yellow Fever Board was created to remove the danger the disease posed for the southern United States, not to protect occupation forces.¹⁸ The influence of disease on U.S. foreign policy, however, is beyond the scope of this paper. The fact that the board was convened is the relevant point.

Also named to the U. S. Army Yellow Fever Board were contract surgeons James Carroll (1854-1907), Jesse W. Lazear (1866-1900), and Aristide Agramonte (1869-1931). U. S. Army surgeon Reed, professor of bacteriology and clinical microscopy at the Army Medical School, directed the whole operation; Carroll was in charge of the bacteriological investigations; Lazear, who had received special training in entomology at the University of Rome under famed malariologist Giovanni Battista Grassi (1854-1925),

was responsible for the mosquito experiments; and Agramonte did the autopsies and pathological work.¹⁹

In a remarkably short time, Reed and his colleagues discredited *Bacillus icteroides* (Sanarelli) and fomites as factors in the propagation of yellow fever and demonstrated that the disease was transmitted solely by means of the bites of infected female *Culex fasciatus* Fabr. (later *Stegomyia fasciata*; now *Aedes aegypti*) mosquitoes.²⁰ In a series of elegant, foolproof experiments the Board confirmed Cuban physician Carlos Findlay's (1833-1915) revolutionary concept of a bloodsucking insect transmitting yellow fever.²¹ Despite more than a hundred experiments conducted over a twenty-year period, Findlay failed to provide conclusive proof of his hypothesis. In fairness, Findlay did his work years before the publication of Henry R. Carter's (1852-1925) key epidemiological discovery of a two-week *extrinsic incubation* period necessary for infectivity. This incubation period represents the time needed between a mosquito ingesting the blood of a yellow fever patient and that insect becoming capable of transmitting the infection.²² Incubation encompasses virus multiplication in the insect's gut followed by migration to the salivary glands. Thus, at the time the Board began their work Findlay had few supporters, in great measure as a result of his own failures. In 1915, Agramonte wrote in *The Scientific Monthly*: "The best-known experts considered [Findlay's theory] as an ingenious, but wholly fanciful one."²³ It was, in fact, British medical officer Surg.-Maj Ronald Ross's (1857-1932) discovery of the anopheline mosquito as the vector of malaria that resurrected Findlay's hypothesis, and provided the Board with its working hypothesis.²⁴

The American Medical Association voiced its displeasure that the Nobel Prize Committee bypassed Reed whose achievements “though uncrowned by prizes and honors always will remain one of the chief glories of American medicine.”²⁵ In defense of the Nobel Committee, they did not award a prize for the yellow-fever work because it was seen as too analogous to Ross’s earlier Nobel Prize-winning malaria studies. Since the Nobel Prize is never awarded posthumously, Reed’s death in November 1902 sealed his fate.²⁶ Horatio Lord Nelson’s (1758-1805) motto *palmas qui meruit ferat* [let him bear the palm who has deserved it] notwithstanding, one realizes that prizes do not necessarily go to the most deserving. Sometimes duty and virtue are their only rewards.

REED’S GRIEVANCE AGAINST STERNBERG

In July 1901 Sternberg published an article in *Popular Science Monthly*, in which he appeared to take credit for the discovery by the Board of the mosquito transmission of yellow fever:

Having for years given much thought to this subject, I became sometime since impressed with the view that probably in yellow fever, as in the malarial fevers, there is an ‘intermediate host.’ I therefore suggested to Dr. Reed, president of the [Yellow Fever Board] appointed upon my recommendation for the study of this disease in the Island of Cuba, that he should give special attention to the possibility of transmission by some insect, *although the experiments of Findlay seemed to show that this insect was not a mosquito of the genus Culex, such as he had used in his inoculation experiments* [italics mine].²⁷

Clearly, Sternberg's statement indicates that he most likely would have discouraged Reed from challenging the validity of Findlay's hypothesis. Instead, he would have prompted his subordinate to look in the direction of a mechanical vector such as the common house fly.

Reed was incensed by these comments, and immediately wrote to his friend Maj. William C. Gorgas (1854-1920), the chief sanitary officer in Havana:

You might tell Dr. Findlay . . . he had better look to his laurels as the proposer of the Mosquito Theory, since Dr. Sternberg . . . puts forward his name very conspicuously for the credit for our work in Cuba. . . . The ungodly ___. What can our chief be thinking of to deliberately and grossly misrepresent the facts! . . . He . . . only mentioned Findlay's theory to condemn it! And now, after the work has been done, he not only is willing to rob the living, but even the dead of their just reward!²⁸

Reed had been worried for some time before this that Sternberg had increasingly embellished his role in the work the Board accomplished in Cuba: "George gives utterance to such sentiments as this: 'I have never doubted that mosquitoes might be the means of spreading yellow fever.' Proceedings Assoc. Amer. Physicians, Washington May 1-4, 1901. Exact words! . . . which compartment of Heaven contains those who have been S.Gs? I only want to avoid it."²⁹

Two months prior to the publication of Sternberg's *Popular Science Monthly* article, Reed delivered an address in Baltimore in which he staked out his claim for originating the shift in the Board's research from *B. icteroides* to the

mosquito-transmission theory. After attending a fatal case of yellow fever at the Pinar del Rio Barracks on 31 July 1900, Reed became convinced that the disease was not propagated by fomites, but appeared to be airborne, as if carried by some winged insect.

[A]t this stage of our investigation it seemed to me, and I so expressed the opinion to my colleagues, that the time had arrived when the plan of our work should be radically changed; that the search for the specific agent of yellow fever, while not abandoned, should be given secondary consideration, until we had first definitely learned something about the way or ways in which the disease was propagated from the sick to the well. . . . [I]n view of the splendid work of Ross, Bignami and others with regard to the propagation of malarial fever . . . it was of the highest importance that the agency of an intermediate host, such as the mosquito, should either be proven or disproven.³⁰

Perhaps Reed's desire for the surgeon generalcy when Sternberg reached mandatory retirement age in June 1902 prevented his airing his feelings in public. Reed's aspirations were revealed in a letter to his wife describing his latest experimental results: "Four cases and no deaths, but my [sweet] wifie said that they would all die and that the country would turn against me and that I would be everlastingly disgraced! He! He! Miss Gouty, you will change your mind when you are 'Mrs. Surgeon General' and holding big receptions on K St.!"³¹ The surgeon generalcy went instead to Col. William H. Forwood (1838-1915) who served for only three months, when he too retired after a career spanning forty-one years.³² There is no evidence of malevolent intent against Reed on the part of Sternberg. Rather, Sternberg campaigned for Forwood, because he wanted to

assure that his old friend would retire with a brigadier general's pension. Sternberg may also have reasoned that Reed, who was fifty-two at the time, would be a future candidate for the job. Unfortunately, by the time Forwood left office on 7 September 1902, Reed was too sick to handle the administrative duties of the surgeon general's office. He may have contracted an amoebic infection of the cecum from infected fruits and vegetables he ate in Cuba.³³ Reed died at 2:02 am on Sunday, 23 November 1902 from post-appendectomy peritonitis.³⁴

Was Reed justified in his suspicions, or was he paranoid? Did Sternberg distort the facts in an attempt to grab some of the glory of the discovery that Maj. Jefferson R. Kean (1860-1950) claimed was "worth more than the cost of the Spanish war including lives lost & money expended"?³⁵ The circumstantial evidence presented below, when viewed as a whole, supports Reed's viewpoint. The historical record is clear: Sternberg never issued an official directive to Reed to investigate the possibility of insect transmission of yellow fever. Although the surgeon general later stated -- in an article published posthumously -- that he had "talked freely with Major Reed . . . and gave him my views as to the most promising lines of experiments . . ." ³⁶, what transpired during these private conversations is irretrievably lost to history. In any event, "Sternberg never intimated publicly -- before or after the yellow fever board's investigations -- that he had seriously considered the mosquito or its bite to be a possible -- or even likely -- method of transmission."³⁷

THE EVIDENCE

Yellow Fever Board's Research Timeline

Delaporte contends that the Board gave top priority to bacteriological investigations when they started their work in June 1900. Findlay's mosquito transmission theory was not pursued until August 1900 following discussions with Herbert E. Durham (1866-1945) and Walter Myers (1872-1901) of the Liverpool School of Tropical Medicine's Yellow Fever Expedition.³⁸ From 18-27 July, these British physicians met separately with Reed and his colleagues, Findlay, and Henry Carter of the U. S. Marine Hospital Service (forerunner of the U. S. Public Health Service) during their stopover in Havana on their way to Pará (now Belém), Brazil to study what Bean (1982) has called "the single most dreaded disease in the Americas."³⁹ Was the Board's change in the direction of their research related to the visit of Durham and Myers or was it simply coincidental? A report Durham and Myers published in the *British Medical Journal* a month after they left Cuba suggests a connection. Herein the Britons noted: "Dr. Findlay's hypothesis is able to account for several curious points which obtain with yellow fever. . . . [S]ome means of transmission by the aid of an intermediate host -- a town-loving host for this town-loving disease -- is to some extent more plausible than might be anticipated."⁴⁰ Interestingly, *Ae. aegypti* was later dubbed the "town mosquito," because it breeds in stagnant water around human habitations.⁴¹

Durham and Myers must have talked at length about the possibility of mosquito transmission of the yellow fever germ. Otherwise, why would Reed be so worried that the Englishmen might have stolen a march on him that he sent his driver to Findlay's home to get the copy of the 8 September issue of the journal as soon as it arrived in Cuba.

Reed need not have feared a challenge to his priority, for the Liverpool Yellow Fever Expedition was aborted when both investigators contracted yellow fever in Brazil, and Myers's case proved fatal.⁴² The surviving member of the expedition subsequently reported that they initially searched for protozoa and bacteria in the organs of fatal cases of yellow fever. They had planned to look at mosquitoes as possible carriers, but were unable to initiate this work due to illness. “[N]o observations upon reared cleanly mosquitoes which had actually fed on yellow fever cases were made.”⁴³

Sternberg's Rejection of Findlay's Hypothesis

Sternberg rejected Findlay's hypothesis: “I have not considered the subject as demanding serious attention, for the reason that *the mosquito does not inject the blood drawn from a yellow fever patient into the inoculated individual, but it enters the insect's stomach, and whatever remains after its meal has been digested is passed per anum*” [Sternberg's italics].⁴⁴ In his 1882 paper, Findlay speculated that the yellow fever germ became encrusted on the mosquito's stylets, and was mechanically transferred from the sick to the healthy by the culicine in the same manner that a dirty needle conveys hepatitis today. Sternberg (1891) also addressed this idea, stating that the supposition “that a minute quantity of virus adhering to the surface of the proboscis . . . is sufficient to produce a mild attack of the disease in an unprotected person, does not appear very probable.”⁴⁵

Several years later, Sternberg was still opposed to Findlay's hypothesis, albeit now on the basis that the Cuban had failed to provide any experimental support to his hypothesis.⁴⁶ Indeed, one could argue that Findlay had, in fact, disproved his own theory. Sternberg was a widely respected medical scientist whose writings impacted American

medical thought. If he rejected Findlay's hypothesis so too would most of America's medical profession, including members of the Yellow Fever Board -- with the possible exception of Lazear.⁴⁷

Mechanical vs Biological Vectors

During the Spanish-American War Sternberg created the U. S. Army Typhoid Board to investigate the cause of the typhoid fever epidemics in the national encampments where 20,738 U. S. soldiers were stricken with the disease and 1,590 died (7.7% mortality). The Board chaired by Major Reed included medical officers Maj. Victor C. Vaughan (1851-1929), Division Surgeon, U. S. Volunteers, and Maj. Edward O. Shakespeare (1846-1900), Brigade Surgeon, U. S. Volunteers.⁴⁸

After an exhaustive analysis of the sick reports of 107,973 officers and enlisted men, the Typhoid Board concluded that, next to human contact, the common house fly, *Musca domestica*, Linn., was the most active agent in the spread of the disease. Further, they established that nonbiting house flies were mechanical vectors, transporting typhoid bacilli from the latrines to the kitchens and mess tents on their sponging mouthparts, hairy appendages, and within their digestive tracts. In contrast to the yellow fever virus, the typhoid pathogen does not multiply within the insect's gut or migrate to its mouthparts, but is spread via flyspecks and regurgitation of digestive juices.⁴⁹

Sternberg was of similar mindset when he wrote: "I am strongly inclined to believe that the ubiquitous house-fly [*sic*] is a factor of considerable importance in the propagation of yellow fever."⁵⁰ By focusing on a mechanical process, at the time he talked with Reed about the research protocol the Yellow Fever Board should follow, it is unreasonable to think that Sternberg would have promoted an intermediate host, which is

a biological process. In an intermediate host, the infective agent either completes some part of its life cycle within the insect's body (e.g., *Plasmodium falciparum*) or multiplies within the insect's stomach (e.g., arbovirus) before migrating to the salivary glands where it will be passed on through the insect's bite to a susceptible individual.

On 24 August 1898 Ross sent a reprint of his work on bird malaria to Sternberg and, in an accompanying letter, emphasized that the infective stage of the *Proteosoma* (now *Plasmodium*) parasite is injected into the host when the mosquito releases saliva containing an anticoagulant into the wound prior to ingesting blood.⁵¹ In his treatise on malaria, Sternberg noted “that there is much evidence which appears strongly to sustain the view that malarial infection may occur as the result of the ingestion of ‘malarial waters.’”⁵² Despite Ross's data, Sternberg remained skeptical of the mosquito's role in transmitting malaria, and hung on to the outworn belief that the disease was waterborne.⁵³

Sternberg vs. Sanarelli Priority Debate

From the late 1870s onward, the medical literature abounded with reports of discoveries of bacteria purported to be *the* germ of yellow fever. All were eventually discredited. After several years in which no new candidates were proposed, Giuseppe Sanarelli (1864-1941) electrified the medical world with his announcement that he had discovered the hitherto elusive microbe of yellow fever. He named the pathogen *Bacillus icteroides* (Gk: *ikteros*, jaundice) after the old term for yellow fever, icteroid typhus.⁵⁴ A debate over priority rapidly ensued as Sternberg claimed he had found the identical organism -- his so-called *Bacillus x* -- a decade earlier in Havana.⁵⁵ The controversy soon became acrimonious with Sanarelli writing: “I cannot understand . . . [Sternberg's]

unwillingness to concede that another has succeeded in solving the problem which proved unsolvable to him.”⁵⁶

The surgeon general’s biographer writes of this episode that Sternberg “was determined to prevent Sanarelli from upstaging him.”⁵⁷ Warner’s assessment was much harsher: “Sternberg had a penchant for asserting his primacy in the race to tease out the etiology of yellow fever; *he was to exhibit this tendency later in jealously claiming credit for his role in Reed’s discoveries.*”[Italics mine]⁵⁸

This dispute became moot, however, when the Yellow Fever Board proved that *B. icteroides* bore no causal relationship to yellow fever and was, in fact, merely a secondary invader in this disease.⁵⁹ Further, *B. icteroides* was none other than *Bacillus cholera suis*, the hog cholera germ.⁶⁰ “Sanarelli’s discovery suffered almost as rapid a decline in scientific popularity as it had enjoyed in rising to medical attention.”⁶¹

RESULTS

The following evidence supports Reed’s suspicion that Sternberg was trying to grab some of the glory of the proof that yellow fever is transmitted from the sick to the healthy by the bite of a female *Ae. aegypti* mosquito:

(1) Sternberg never issued an official order for the Yellow Fever Board to investigate the validity of Findlay’s hypothesis.

(2) The Yellow Fever Board’s original assignment was to challenge Sanarelli’s claim that *B. icteroides* was the etiological agent of yellow fever. It was only after the visit of the Liverpool scientists that the research abruptly changed its course to pursue the

mosquito transmission hypothesis. There is no evidence that Sternberg, who was not in Cuba at the time, was involved in this decision.

(3) Sternberg rejected Findlay's work and, on several occasions, noted that he considered the hypothesis worthless.

(4) Sternberg envisioned insect transmission of pathogens as a mechanical process, not a biological one as it must be to satisfy the criteria for an intermediate host. Even Ross's Nobel-Prize-winning work failed to convince Sternberg otherwise. Sternberg never seriously considered the mosquito's bite as a possible means of disease transmission.

(5) Sternberg's controversy with Sanarelli over who first discovered the putative germ of yellow fever provides a precedent for Sternberg's seeking credit for an important discovery.

CODA

Who deserves the credit for a discovery? Is it the person who originated the idea or the one who brings it to fruition? Meyers contends "the credit goes to the man who convinces the world, not to the man to whom the idea first occurs."⁶² By this criterion, full credit belongs to Reed and his collaborators, not Sternberg, for proving to the world that yellow fever was spread by the bite of an infected mosquito. Professor Welch, who was friends with both men and intimate with their work, wrote: "I am in a position to know that the credit for the original ideas embodied in this work belongs wholly to Major Reed."⁶³

Despite media stereotypes, scientists are not disinterested souls whose search for the truth is untainted by the frailties common to the rest of humanity. Indeed, even though

he was one of nineteenth-century America's most celebrated medical scientists, Sternberg's jealousy shows that he was all too human and subject to the flaws that flesh is heir to. He had worked for much of his professional life on the etiology of yellow fever, but came up empty-handed. It is understandable that Sternberg might resent those to whom success came more easily, and to covet a share of their laurels.

FOOTNOTES

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