The Evolution of Yellow Fever

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Introduction

Yellow fever (YF) is a disease that has plagued our world for centuries. Through this presentation, we aim to bring light to how historical context intertwines with the evolution of medical understanding of the disease and public health measures as well as the spread of misinformation and disinformation. This background will provide insight into the socioeconomic effects of YF and how it impacted people's welfare.

Origins of Yellow Fever

Etiology of YF (Atishi)

YF originated in Africa and was brought to the western hemisphere during the slave trade era, primarily to the Americas (Carter). It quickly began to spread and by 1648, the first epidemic was reported in the Yucatan Peninsula (which is a part of current-day Mexico) (Carter). By the 19th century, it became common knowledge that YF didn't transmit from person-to-person, but was instead incorrectly thought to be communicable through atmospheric miasmata (Staples). In 1881, Cuban physician Carlos Finlay suggested the *Aedes aegypti* (AA) mosquito as the insect responsible for transmitting YF (Bryan). This significantly advanced the field by providing a basis for future American physician Walter Reed's research. Reed's work eventually proved that the AA mosquitoes were the most prominent form of transmission for YF and that the disease was caused by a filterable agent found in the blood of infected patients (Reed). After this discovery, attempts were made to eliminate YF by launching campaigns and establishing foundations dedicated to the elimination. "While these early activities were initially successful against urban (*Aedes aegypti*–borne) yellow fever, the goal of eradication was dispelled with the discovery that yellow fever was a zoonosis, maintained by sylvatic mosquito

species and nonhuman primates in the Amazon jungle," (Soper). It is now known that there are three types of the YF disease, stated as the following ("All Timelines Overview"):

1. "Sylvatic yellow fever occurs when the disease is passed from monkeys infected by wild mosquitoes to humans."
2. "Intermediate yellow fever—the most common type of outbreak in modern Africa—results when semi-domestic mosquitoes (which can infect both monkeys and humans) are present in an area where they commonly come into contact with humans."
3. "Urban yellow fever occurs when the *Aedes aegypti* species of domestic mosquito transmits the virus between humans, without transmission via other primates."

Chronological History (Atishi)

YF has been present throughout contemporary human history for hundreds of years. For reading convenience, the major events related to YF will be broken down into points separated by the year they happened to in order provide historical context. All information has been pulled from Brink's NPR article on the timeline of YF's history and Sowards' article on the origins of YF unless otherwise stated.

Pre-1600s

- 1000 B.C.E.: This is around the time YF originated in Africa. It started in local villages before quickly spreading to large cities.

1600s

- Early 1600s: As global trade and slavery increased due to the Columbian exchange, mosquitos came along for the ride in ships. The water kegs residing in these vessels were

the perfect breeding grounds for mosquito larva to be sustained for the long journeys. African slaves were also unknowing hosts who carried the disease. As a result of these overseas voyages, YF reached the Americas.

- 1648: The first recorded epidemic is recorded in the Yucatan peninsula according to Mayan manuscripts.
- Very late 1600s into early 1700s: YF rapidly grew in range and major cities throughout the Americas were affected. The US in particular saw an increase in YF cases during the summer. Some examples of American cities that were deeply affected are NYC, Boston, and Charleston, all of which were on the eastern coast (America was still a British colony at this time).

1700s

- 1737: The summer of this year kickstarts a seven consecutive years of YF epidemics on the eastern American seaports.
- 1730: YF hit Europe, with an epidemic breaking out in Cadiz, Spain (2300 deaths) followed by outbreaks in Britain and France. However, YF didn't Europe much because they didn't have the same slave trade industry, and ships would usually go from Africa to the Americas and then to Europe.

1800s

- 1848: American physician Josiah Clark Nott suggested mosquitos were the source of YF transmission.
- 1881: Cuban physician Carlos Finlay independently suggested the same theory as Nott and conducted an experiment to prove it.

1900s

- August 27, 1900: US Army physician James Carroll let an infected mosquito bite him and processed to come down with YF. His colleague, pathologist Walter Reed, thus showed evidence that YF spread from mosquitoes and that they were the source of transmission.
- 1905: The last US outbreak happens in New Orleans.
- 1906: Intense sanitation programs started in Panama & Havana, Cuba. They eradicated YF here and hence let the workers finish building the Panama Canal.
- 1930: 2 vaccines were developed: the 17D and the French Neurotropic.
- 1940s: Immunizations were used in mass campaigns in South America and certain African areas.
- 1982: The French neurotropic vaccine was stopped because high rates of postvaccinal encephalitis made it unsafe. Therefore, the 17D became the standard vaccine. It uses 2 substrains that have effective results.

2000s/Present Day

- There have been some outbreaks in Angola and the Democratic Republic of Congo, but WHO has vaccinated 16 million people already, and is planning to vaccinate 13 million more. The YF vaccine is running out as only 4 manufacturers make it, so instead of a larger dose for lifetime immunity, smaller doses are given instead which provides immunity for 1 year.

Before Finding Source of YF

Evolution of Medical Understanding (Deepti)

Before finding the source of the YF, medical understanding was at its primitive stages of evolution. Little was known about the disease and there were very few scientific methods to engage in any experiments or studies related to the epidemic. Therefore, countless numbers of theories, often ones that made little sense, were thrown about. Overall, no one knew the cause or prevention of the disease, setting a panicked frenzy amongst citizens all over the world.

Less Medical Understanding, More Discrimination

During this period of doubt, there was undeniable less medical, scientific understanding and more discrimination of those who were already held with low regard. For example, Scottish medical historian Charles Creighton stated that the fever was "a virulent filth-disease", accusing the African Americans of bringing the Yellow Fever to the Americas on trade ships (Britannica). Even an accredited scholar who specializes in medicine *and* history could not help but shift blame onto an already discriminated group of individuals due to a lack of knowledge. Throughout this period of uncertainty, African Americans were scapegoated because people were so desperate to settle on an explanation for why the Yellow Fever was spreading so rapidly and it presumably seemed easiest to blame the group of lower social status.

False Perceptions on Methods of Prevention

Additionally, just as fast as the disease was spreading, wrong assumptions on how to prevent the disease were propagating between the population. In 1793, Philadelphians believed that covering their faces with handkerchiefs dipped in vinegar or smoked tobacco would stop them from ingesting any contaminants (Pruitt). As silly or misinformed as this belief would seem

by today's standards and knowledge, people back then weren't receiving any medical advice on prevention because there was none to be given, so they had to take matters into their own hands. As a result, they created solutions based on their very limited knowledge of epidemiology and these solutions were disseminated. Even leading physician Benjamin Rush was unsure on how to prevent the disease; he was just as puzzled as any layman of the time (Pruitt). He imposed harsh treatment plans like bloodletting and forced vomiting, which did nothing to stop the spread, but just increased patient dissatisfaction. Overall, before finding the source of the Yellow Fever, regular citizens to top doctors alike were all just left in a state of bewilderment on how to battle this disease.

Information and Misinformation (Sanjana)

Very little was known about how the disease came about or what the transmission methods were. Prior to discovering the actual source of the yellow fever, there were many different theories that tried to offer an explanation to these unknowns, however, many of these theories just spread misinformation to the public. The two most popular theories were the contagion theory and the pollution theory.

Contagion Theory

The very first theory that came about was the contagion theory. It was widely held that the Yellow Fever came from the slave trade and through the excrements of African slaves on the boat (Britanica). For example, during the Philadelphia outbreak many thought that the disease came from a ship bearing French refugees from a slave rebellion in Santo Dominigo (Pruitt, 1). Many people falsely believed that the Yellow Fever could be spread from person to person through clothing, bed sheets, and other methods of direct contact. Because of this notion that

Yellow Fever was contagious, there were many people who quarantined themselves to their home as a way to avoid catching the Yellow Fever (Britannica). However, even though the Yellow Fever was thought to be caused by the slave trade and was also thought to be highly contagious, many doctors claimed that Africans had immunity to the disease and that they couldn't pass it on to others. As a result, while plantation owners tried to avoid contact with others, slaves were still forced to work (Donella, 1).

Air Pollution Theory

The second and more popular theory of how the Yellow Fever came to be was the miasma, air pollution, theory ("Historic Dispute"). Philadelphia's leading doctor, Benjamin Rush, stated that the Yellow Fever didn't spread through direct contact, but spread through the city's poor sanitary conditions. Rush and many others believed in this theory as the Yellow Fever was more prevalent in places with a lack of sanitation such as shipping docks (Pruitt, 1). In addition, it was found that the working class was more susceptible to the disease and they had a lack of proper drinking water, a poor sewage system, and they lived in cramped conditions ("Historic Dispute"). Because of this evidence, people thought that the Yellow Fever could be spread through the noxious vapors in the air (Pruitt, 1). There were different purification methods that arose due to this theory such as the burning of tar in order to clean the air. Even though these methods weren't effective, they still remained prevalent and the air pollution theory was the most accepted cause of the Yellow Fever until the emergence of the Mosquito Theory.

Public Health Measures (Navya)

Since the source of the virus was not yet discovered, many of the public health measures implemented across the globe failed to prevent outbreaks; the immense speculation and spread of

misinformation were some of the causes of this. Areas that enforced quarantine regulations, however, were the most successful. For instance, in Boston Massachusetts, in 1625, a strict quarantine was established in response to the epidemic in Barbados, forbidding all ships from entering from the West Indies. Due to this measure, a great number of cases were prevented. Similarly, in 1747, it is believed Philadelphia prevented a major outbreak through the quarantine of a particular vessel. A ship arriving from Barbados was carefully examined and quarantined; it was not permitted to unload cargo or passengers. It is believed that this ship carried yellow fever, so the measures the authorities took potentially prevented a major outbreak(Yellow Fever). Additionally, many Northern cities on the Atlantic coast were at an especially high risk due to their proximity to the ocean. Fortunately, however, they were able to prevent outbreak through instituting rigid quarantines as well as improving drainage and sewer facilities—a measure which would be widely implemented once the source of yellow fever was located.

Social Consequences (Judith)

Division Between People

Prior to the 20th century, people of higher social status were able to justify discrimination against minorities. For instance, the previously mentioned notion that African Americans were immune to Yellow fever was used to justify slavery and further exploitation African Americans for essential labor during the 1793 epidemic in the United States (Pruitt). Furthermore, the influx of immigrants in the 1850s supported the curtailing of immigration and xenophobia, as many of the immigrants were jobless and thus lived in insanitary conditions that promoted the spread of yellow fever (McKiven Jr., 3). The lack of knowledge about and preventative measures against

Yellow fever as well as widespread misinformation cultivated an even more inhumane attitude against social minorities.

Additionally, Yellow fever created more tensions between people of differing political ideologies. Since not much was known about the disease in the 19th century, people took advantage of Yellow fever to advance their political agendas, affecting which treatments people chose to take ("Politics of Yellow Fever in Alexander Hamilton's America"). There were no medical treatments proven to help Yellow fever, and so treatments and preventions were decided solely based on advice from their respective political parties. Conflicts between scientists also arose due to both colonialist and nationalist positions (Chippaux, 2). Because people lacked scientific knowledge to back personal opinions and suggestions, Yellow fever gave way to division between people.

Economic Standstill and Loss

The new outbreak of Yellow fever also led to economic downfall. In general, countries experiencing an outbreak had paralyzed industry and trade (Tomori), and due to the delay in the Panama Canal construction, Napoleon Bonaparte was dissuaded from achieving the conquest of the U.S. (Chippaux, 2). Since there were no effective preventative measures or treatments at the time, and there was a consequent economic downturn due to fear of contracting Yellow fever.

After Finding Source of YF

Evolution of Medical Understanding (Deepti)

Finding the source of the Yellow Fever was a critical turning point during the battle with the epidemic. In 1881, Cuban epidemiologist Carlos Finlay made the crucial suggestion that the Yellow Fever was spread through the *Aedes aegypti* mosquito (Britannica). This theory was the

beginning of a new era of Yellow Fever, one that included a series of tests and experiments to prove that the disease was, in fact, spread by mosquitoes. If Finlay's claim was proven correct, researchers would have the source of the disease, and therefore would be able to combat it. So, in 1900, Army pathologist and bacteriologist Major Walter Reed demonstrated exactly how the yellow fever was transmitted between humans through the bite of the *Aedes aegypti* mosquito (Britannica). Major Reed's pivotal research was at the forefront of not only sourcing the epidemic, but also of starting studies to create a vaccine, an invaluable weapon against the Yellow fever.

Information and Misinformation (Sanjana)

The emergence of the mosquito changed the way the yellow fever was perceived and combatted. Army pathologist Walter Reed led the main experiment that disproved the contagion and air pollution theory and proved that the Yellow fever was caused by mosquitos. First, in order to disprove the contagion theory, Walter Reed had volunteer army soldiers wear soiled clothing from known patients of Yellow Fever (Feng, 1). Through many days of wearing this clothing, it was found that these soldiers did not display any symptoms of the Yellow Fever and therefore, Reed confidently ruled out direct contact as a cause ("Historic Dispute", 1)." Reed then conducted an experiment at Camp Lazear where he hatched many mosquito eggs and had them drink blood from Yellow Fever patients, and then had them bite several volunteers ("Camp Lazear", 1). These volunteers showed clear symptoms of Yellow Fever, and Reed's experiment proved that mosquitoes were the true cause ("Historic Dispute", 1). Based on this new information, many health measures were created.

Public Health Measures (Navya)

Aedes Aegypti Population Elimination

Once the source of the virus was located as originating from the Aedes Aegypti mosquito, most health measures revolved around controlling these mosquito populations. For instance, in Ecuador, mosquito squads were deployed to systemically spray mosquito-killing chemicals on rooftops, where the pests often gathered. Similarly, in New Orleans, seals and cheesecloths were added to water storage tanks. This was especially effective since mosquitoes often resided in unsanitary water systems (Yellow Fever).

William Gorgas

Columbia followed a similar principle, adding larvae-eating fish into storage systems in order to kill the mosquito at the start of the life cycle. William Gorgas, a chief sanitary officer, had implemented several health measures which completely eradicated yellow fever in Havana. He then went on to implement these same measures to eradicate yellow fever in Panama as well. These measures include screening windows and doors, fumigating houses and indoor spaces, destroying Aedes Aegypti breeding sites, and emptying out open water receptacles. These measures were successful because they were able to target several stages of the Aedes Aegypti life cycle (Control).

Social Consequences (Judith)

The discovery of the source of the disease motivated people to further research Yellow fever and develop a scientifically supported treatment. In 1915, the International Health Division prioritized research and eradication of Yellow fever and funneled money to Yellow fever programs (“Yellow Fever.”). This helped to develop emphasis on scientific careers and America

began to establish a network of research laboratories. Discovering the source of Yellow fever led to a step towards higher importance of scientific research and knowledge in society. In terms of the economy, the anti-mosquito methods developed by William Gorgas allowed for the completion of the Panama Canal ("Yellow Fever Timeline"). Because of the growth in medical knowledge, people were able to develop effective preventative measures, allowing for economic growth.

After Developing Vaccine

Evolution of Medical Understanding (Deepti)

The first major era of the path to finding the vaccine was tied to Major Reed's demonstration of the source of Yellow Fever. The 2nd major era, which started in 1928, was the link between this sourcing and finding the vaccine. This era consisted of Adrian Stokes, Johannes H. Bauer, and N. Paul Hudson realizing that the Indian rhesus monkey, which was susceptible to Yellow Fever, could be used in laboratory experiments (Theiler). These three noted researchers then developed the first strain of the virus, Asibi strain, which was named after the person it was extracted from. The Asibi strain later became the parent strain from which the original 17D vaccine was produced, after years of conducted study, of course. Once the vaccine was developed, the medical understanding of the Yellow Fever escalated more than previously ever imagined. One study led to one realization, which in turn led to another study, and so on and so forth until a vaccine was able to be developed. Medical professionals went from forcing patients to vomit to administering vaccines, displaying a major stride in the field of medicine. Overall, just as the battle against Yellow Fever evolved over time, medical understanding

drastically advanced over the years, providing the medical field with vital research that will be remembered and cherished for years to come.

Information and Misinformation (Sanjana)

Even though the Yellow Fever vaccine is widely accepted by many world health leaders and doctors, there is still disinformation being spread during the recent outbreaks in Brazil. Social Media has a heavy role in contributing to the disinformation about the vaccine. For example, an audio message from a woman claiming to be a doctor at a well-known hospital began circulating on WhatsApp, warning that the vaccine is dangerous and not to use it (Molteni, 1). There have been other messages on Twitter stating that the vaccine is a scam that is meant to reduce the world population (Haelle, 1). Many other rumors have been circulating through social media damaging the reputation of the vaccine (Molteni, 1). Because of the disinformation, there has been an increased panic throughout Brazil and a resistance to vaccine campaigns that have sprung up (Haelle, 1). However, even though false information has been spreading, Brazil's government has taken precautions and is educating its citizens on how the vaccine is beneficial as it still remains as the most effective way to combat the Yellow Fever.

Public Health Measures (Navya)

Once the vaccine was invented, most of the public health measures were still oriented towards reducing the population of the Aedes Aegypti mosquito. The vaccines were simply an added benefit. In an attempt to prevent yellow fever in the United States, law required a vaccination certificate from travellers coming into the country from areas of infection, inspection of other primates coming in from areas of infection, and the disinsectization of airplanes and ships(Hughes). As previously stated, most public health measures continued to focus on the

elimination of Aedes Aegypti. Vector Disease Control International, a mosquito control company, recommends a 4-pronged plan to target all stages of Aedes Aegypti's life cycle, including educating the public, surveying populations, larval mosquito control, and adult mosquito control (Yellow Fever). The Eliminate Yellow Fever Epidemics (EYE) strategy in Africa, aims to protect populations that are at the most risk as well as prevent outbreaks, both at a local and international level (Yellow Fever). They intend on achieving this through making vaccines affordable for all, cultivating a sustained vaccine market, and forging strong political commitment to the cause.

Social Consequences (Judith)

The formation of the vaccine also gave more credit and importance to science in society. The success of Yellow fever research and the vaccination campaign had an immense impact on the reputation and direction of the IHD. It solidified IHD's record of producing high quality research and validated the IHD's decision to direct more funding towards research ("Yellow Fever.") This marked the transition to a more modern outlook towards research and science became a crucial part of society like it is today. As for the economy, cost per DALY (disability-adjusted life-year) averted in Colombia was $19,022 for payers and $12,114 from a societal perspective, both in USD (Kieffer et. al). From these statistics, the vaccine proved to be extremely cost effective, and there was no economic loss like in the past. This helped to boost the importance of medical understanding of such diseases that is crucial in modern society.

Conclusion

Through studying the world's long and gruesome battle with YF, we came to the conclusion that although there were hindrances to the quality of life due to disinformation along

with ineffective health measures, the standard of living overall improved significantly through locating the source of Yellow Fever and developing a vaccine.

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