Sally Helm: History This Week. August 27th, 1900. I'm Sally helm.

Dr. Jesse Lazear is walking around this morning. Toting his little brood of mosquitoes. Each buzzing around in their own glass vial. Before lunch, he takes them to Las Animas Hospital in Havana, Cuba. There, he pulls the vials out, and, one by one, he lets the mosquito’s feed.

These patients have agreed to be bitten by mosquitoes. This is all part of a plan. Dr. Lazear is stationed in Cuba as a US army doctor. Because disease has been killing soldiers left and right: yellow fever. And no one knows what causes it.

These patients at Las Animas Hospital have yellow fever. And Dr. Lazear wants his mosquitoes full of their blood so that he can later test a theory. It's a minor theory. For a long time, no one has taken it at all seriously, but the idea is that yellow fever might be spread by mosquitoes. Though Dr. Lazear has good reason to think this isn't true. A little over two weeks ago, he himself was bitten by one of his mosquitoes and he didn't get sick.

In the yellow fever ward. He has the system down. Remove the cotton stopper that keeps the mosquito penned in, turn the glass vial over, seal it against an infected patient's skin. Then Lazear just watches as the insect’s flutter lazily down to have their meal of blood.

All except one. This morning, a single female mosquito refuses to feed. She's stubborn or just not hungry. After his own lunch, Dr. Lazear goes back to his lab to check on her. When he gets there. He sees one of his colleagues, Dr. James Carol. They're talking about how this whole mosquito theory of yellow fever doesn't seem to be panning out. And Dr. Lazear mentions this one, stubborn mosquito. So, Carol takes the vial, turns it over, and places it against his own arm. Presumably, just to give the hungry mosquito another chance to eat.

And it works, but a few days later, James Carol feels an odd chill. A few days after that he is sweating through a severe case of yellow fever fighting for his life.

Today: chasing the source of yellow fever. Scientists try to understand this deadly plague by running a high stakes medical experiment on human subjects, including themselves. Why even after a high-profile death, did people willingly, knowingly, consent to take part in this study? And when we look back, should we be horrified or impressed?
Sally Helm: The yellow fever virus probably emerged thousands of years ago in West Africa. But it didn't arrive in the Americas until the 1600s. It came by sea on the ships that carried stolen and enslaved people during the transatlantic slave trade. The virus was a quiet stowaway, but it soon made itself known.

Molly Crosby: An epidemic struck a city or a region, very much like a natural disaster and it shut it down completely. Devastated economies. Not to mention the death tolls.

Sally Helm: Molly Caldwell Crosby is a journalist who has written a book about the toll of yellow fever, which was very high. In these outbreaks, thousands of people would die.

Molly Crosby: Even today, if you've been to New York to Washington Square Park, there's 20,000 bodies beneath it. Most of them were yellow fever victims.

Sally Helm: It was worst in urban areas, especially in the American South.

Molly Crosby: I remember reading descriptions of Memphis, in particular, felt like a ghost town. You couldn't get fruits, vegetables, milk. All the stores were closed.

Sally Helm: When a person died of yellow fever, terrified relatives would sometimes burn their belongings or their bedding to try and get the disease out of the house.

Molly Crosby: So, there were these fires going up all of the time. And, it was said that for three miles outside of the city, you could smell death just because there were not enough wagons to collect the dead, not enough people to bury them. And so, they began just piling up in places. Some of the nuns who were going door-to-door to try to offer help, would find children living with their dead parents. Because it was just, it struck so quickly. In such an overwhelming way. It just sounded almost apocalyptic.

Sally Helm: The disease itself was terrifying. Dr. Kathryn Olivarius teaches history at Stanford. She's just written a book about yellow fever, which for those who know her probably makes sense.

Kathryn Olivarius: My parents have actually always called me sort of like a historical hypochondriac. Since I was a little kid. I was always obsessed with disease.

Sally Helm: She told us about what yellow fever does to the body.

Kathryn Olivarius: Nausea, muscle aches, very severe back pains. And then chills.

Sally Helm: They'd get a high fever, but the lucky ones, would pull through.
**Kathryn Olivarius:** The only protection the person could have against yellow fever was literally to survive it. So, you had to fall sick with this disease and gain lifetime immunity.

**Sally Helm:** So, some people get better, but some people feel like they're getting better. Their fever breaks. Their pain subsides... and then they get worse. This is where things get really ugly.

**Kathryn Olivarius:** They become somewhat delirious, and most patients will start to ooze blood through their external orifices. Their eyes. Their ears. Their nose. Famously, at the end of the illness, the victim will experience, black vomit. They will regurgitate this thick congealed blood that looks, a lot like coffee grounds.

**Sally Helm:** So understandably when yellow fever shows up in town, people are terrified. Not least because they have no idea how it spreads.

**Kathryn Olivarius:** There are a lot of different competing theories. The prevailing orthodoxies about disease, were to do with contagiousness. And so, a disease was contagious or non-contagious. So, a contagious disease was typically spread through human-to-human contact or through fomites.

**Sally Helm:** Fomites: anything likely to carry disease. Dirty utensils or soiled clothing. So that's why people in Memphis were burning, bedding in their front yards. But doctors aren't sure that yellow fever actually is contagious.

**Kathryn Olivarius:** It didn't seem to meet these kind of disease, transmission patterns.

**Sally Helm:** Like if you're in a family, you won't necessarily get it. treating someone who's sick or that kind of thing?

**Kathryn Olivarius:** Precisely. Sort of, you can't map it in the way that you can map other diseases.

**Sally Helm:** God, that must have made it scarier cause it seems sort of random.

**Kathryn Olivarius:** Yes, precisely. There was no real way to determine why somebody, what might remain healthy, why another person would die. There's so many unknowns.

**Sally Helm:** So, maybe it's not fomites. Maybe it's something else.

**Kathryn Olivarius:** So, there's also this notion of the miasma theory of disease. This is the idea, essentially, that foul airs cause ill health.

**Sally Helm:** So, like smells.
**Kathryn Olivarius:** Smells. Exactly. This was what probably most, doctors and physicians around the Atlantic world would adhere to.

**Sally Helm:** It made a certain sense. Yellow fever seemed to spread in crowded, smelly places like cities or army barracks. So, people who believed this theory would try to clean up the smells. Throw away the garbage. Hose down the city streets.

But it didn't seem to work. Maybe, because when you hose down the city streets, you might inadvertently create the perfect home for a little bug that loves to lay its eggs in puddles: the mosquito.

Molly Caldwell Crosby told us that by the 1880s, there was one person who had a totally different, outlandish, idea about how yellow fever spread.

**Molly Crosby:** A Cuban doctor for 20 years had been saying that a mosquito could be carrying it. His name was Carlos Finlay.

**Sally Helm:** On August 14th, 1881. Dr. Finlay arrives at the Havana Royal Academy of Sciences and takes the stage. He has wire rim glasses, a firm mouth set between his lambchop sideburns. And he announces, to his assembled medical peers, a theory about how yellow fever spreads.

**Molly Crosby:** He believed mosquitoes were the vector. They were transmitting the virus.

**Sally Helm:** The other doctors are taken aback. Yellow fever is a vicious disease, they think. The cause can't possibly be the tiny mosquito. Finlay is basically laughed off the stage. And abroad, in the U.S.?

**Molly Crosby:** He was just ridiculed in the US. Called 'mosquito man'.

**Sally Helm:** But Finlay is persistent. Everyone's calling him a crank, but he's not the kind of guy who will let that derail him. He's very motivated to help end yellow fever. You can't live in Cuba at this time without knowing someone who's died of the disease. So, he retreats to a farm outside Havana to experiment. Try to prove that the source of this terrible hemorrhagic fever really is the tiny mosquito.

Years pass. And then the medical establishment comes knocking at Dr. Finlay's door. It happens because the United States has just fought a war in Cuba, the Spanish American war.

**Molly Crosby:** The war was won fairly quickly, but the soldiers remained occupying the island and for about everyone, soldier that had died of a bullet seven died of disease and yellow fever was the most feared disease around.
Sally Helm: So now the United States Army has a vested interest in tracking down the source of this plague.

Molly Crosby: And the Surgeon General of the United States sends a group of four doctors to study the outbreaks of the disease and he really sends them down there to find the bacteria. To find the germ that's causing yellow fever.

So, they go down there with their microscopes and they're gonna study the blood samples and autopsy samples.

Sally Helm: Their leader is major Walter Reed. A strait-laced army doctor. Molly Crosby says in her book that he was a man who throughout his life wrote the word "duty" with a capital D. He'd grown up in Virginia during the Civil War. The son of a Methodist minister.

Molly Crosby: For him, being a minister's son, but also being around such a devastating war in Virginia, he just seemed to have some drive in him to do something for humanity.

Sally Helm: Reed recruits doctors, James Carroll, Aristides Agramonte, and Jesse W. Lazear to help him track down the cause of yellow fever. So that they can eventually stamp it out. Agramonte later writes that when they first meet on the officer's veranda at the army barracks, at a place called camp Columbia, there is "a feeling akin to reverence. "They know how important this work is.

They start tracking outbreaks and studying yellow fever patients at Las Animas Hospital. They're conducting autopsies, looking at tissue under microscopes, trying to trace how the disease moves. They can tell, for example, that one outbreak started in Havana and then moved to a nearby town. But Dr. Agramonte later writes that knowledge wasn't much use as to the actual cause of the disease, "we were still entirely at sea."

And then Dr. Lazier says, what if we go talk to Carlos Finlay?

Molly Crosby: Jesse Lazear had been living down in Cuba for a while and working some with Finlay using some of his mosquitoes and he was really the visionary in the group who believed that was definitely the cause, and how it was spreading.

Sally Helm: And so, in the summer of 1900, these doctors visit the house of a man that many in the scientific world still view as a crank.

Kathryn Olivarius: They went to visit Finlay at his house, and they asked him, “what evidence do you have about this?”

Sally Helm: The Cuban doctor is now in his sixties.
Kathryn Olivarius: He probably would've admitted this himself, that fundamentally he didn't have enough data at that point to really prove beyond, any kind of reasonable doubt that this was how the disease was transmitted. He's incredibly excited about the prospect of sharing his ideas.

Sally Helm: The other doctor's pepper Finlay with questions. He walks them through the life cycle of the mosquito, telling them things he's learned from years of study.

Before the men leave. He walks them to his personal library towards an unassuming bowl of water inside are unhatched, larva of a particular mosquito. The Aedes Aegypti. The eggs are black. Shaped like cigars, and he gives them a few.

Kathryn Olivarius: A little porcelain dish of mosquito larvae.

Sally Helm: But sorry, but they leave the house with these larva, which is like, kind of scary. It's like, okay, nice host gift...

Kathryn Olivarius: Yeah. Like exactly. The host gift from hell.

Sally Helm: They take the mosquito eggs back to camp Columbia and wait for them to hatch. But then almost right away, Major Reed is called back to Washington DC. Dr. James Carroll has been the second in command and while Reed was sympathetic to Finlay's ideas:

Kathryn Olivarius: Carol, firmly did not believe that the mosquito theory was worth anyone's time.

Sally Helm: But Lazear is still intrigued. So, they keep breeding Finlay's mosquitoes and letting them feed on yellow fever patients so that they'll potentially become infected with the virus. And then:

Kathryn Olivarius: In August of 1900 they start experiments on live human beings.

Sally Helm: These are to be clear, willing volunteers, mostly American soldiers at camp Columbia, along with some Spaniards. And... they don't necessarily think that these mosquito experiments are gonna come to anything. Which might be why they sign up. Agramonte writes that the volunteers who agreed to be bitten by mosquitoes seem to just be "in a sporting mood."

He and the other doctors take the chance to test Finlay's theory:

Kathryn Olivarius: They would put a soldier in a tent with an infected mosquito who would bite the soldier. They would record what happened next.

Sally Helm: At least they would've recorded what happened next? If... anything happened at all.
**Kathryn Olivarius:** A lot of their initial experiments just didn't go very well.

**Sally Helm:** These volunteers, aren't getting yellow fever. Finlay insists that it must just be some kind of flaw in the technique or the experimental design.

But the other doctors start to think... maybe this theory is just bunk. Lazear even lets a mosquito bite him on August 16th and nothing comes of it.

And then one day at the end of the month, August 27th, Lazear brings home that mosquito from Las Animas Hospital. The one who refused to feed. She'd bitten an infected patient 12 days before... but not on that very morning. Lazear brings that mosquito to the lab. And Dr. Carol thinking, nothing of it rolls up his sleeve to give her a meal of blood.

A few days later, he feels a chill.

**Kathryn Olivarius:** He developed a very serious case of yellow fever.

**Sally Helm:** Carol still thinks he might have caught yellow fever in the autopsy room. Not from that mosquito bite, his condition gets worse and worse. Soon enough, he's confined to his bed. His wife waits for the daily cablegram update on her husband's condition. At first, it's bad news. He's delirious on the verge of collapse, but then...

**Kathryn Olivarius:** But he pulls through in the end and he survives.

**Sally Helm:** Carol's wife gets a cable, "Carol out of danger." The doctors all breathe, sigh relief. But then, on September 18th, 1900, Dr. Lazear turns to his colleagues and says, he's feeling a "bit out of sorts."

Soon, the doctor is fighting for his life.

**Sally Helm:** Just like his colleague, James Carroll. Dr. Jesse Lazear is sick.

**Molly Crosby:** He does come down with just a horrific case of yellow fever. He was delirious, and they were having to restrain him on the bed.

**Sally Helm:** Molly Crosby says Lazear tells his colleagues that a mosquito bit him by accident. It's plausible enough. He spends a lot of time around mosquitoes, but his notebooks seem to tell a different story.
Molly Crosby: When I was doing the research on this book, and I went to the New York Academy of Medicine and found his original notebook. The last entry in the book in his handwriting is: guinea pig number one.

Sally Helm: Guinea pig number one seems to be Dr. Lazear.

Molly Crosby: His notes certainly implied that he was testing the theory on himself.

Sally Helm: Perhaps he was moved by pure scientific interest. He wanted to prove or disprove the mosquito theory once and for all. Or maybe it was guilt. He'd watched his colleague be bitten by a mosquito and then watched his colleague fall ill. And Dr. Lazear soon follows, but his case is much worse.

Molly Crosby: He's just 34. He's got a pregnant wife. She had just had the baby when she got the news, he had died.

Sally Helm: One week after falling ill, Dr. Lazear dies of yellow fever. The news hits the remaining doctors hard.

Molly Crosby: He was a very well liked. Everyone described him as lovable.

Sally Helm: Major Walter Reed has been receiving reports on the experiment. And when he learns the news of Carol's illness and ER's death. You can't believe how far things have spiraled out of control. He races back to Cuba, deeply shaken and curious. The tragic sequence of events does seem to suggest that mosquitoes are responsible for yellow fever infections.

Reed wants the remainder of this experiment to be conducted by the book.

Molly Crosby: So, he begins to set up this elaborate experiment. Walter Reed goes on and asks for volunteers. 20, in total end up doing his experiments. They're all young, healthy soldiers and they knew the risk.

Sally Helm: They volunteer, knowing full well, there is no cure for yellow fever. There's no cure today either.

Molly Crosby: Reed said he couldn't in good conscience, do it without having people know what they were getting into and volunteers.

Sally Helm: So, he does something totally novel.

Molly Crosby: Walter Reed created the first consent form for human experimentation and medicine. He did a bilingual consent form. Prior to that, they just did not even ask.
Sally Helm: The medical community had often performed human experiments on orphans and the mentally ill. But this experiment is different. Reed explains the risk in English and in Spanish, he lays out the stakes. And the amazing thing is people still sign up.

Those earliest volunteers might not really have known what they were getting into. The mosquito theory seemed unlikely. Now it seems very likely. And Dr. Lazear is dead.

But these volunteers know that living in Cuba, they're likely to come down with yellow fever at some point anyways, maybe it makes sense to do it in the context of this experiment. When at least they'll be closely observed by army doctors.

If they survive, they'll gain lifelong immunity. They're also getting paid. There's a base rate. And if they end up getting yellow fever, they'll get a bonus and the volunteers might also feel some sense of duty or honor yellow fever is a scourge, a plague, and they can help stamp it out. Remember, many of them are soldiers.

Molly Crosby: I think in their minds, they really looked at it like they're more likely to die of an epidemic disease than they are in an actual battle. So, to them, this was a bigger enemy.

Sally Helm: Finally, after all these preparations, the experiment begins major Reed names, the testing area to honor his dead colleague. He calls it camp Lazear. He builds two shacks.

Molly Crosby: In one shack, he filled it with clothes from dying yellow fever patients that were covered and filth and vomit and sealed the whole place up and put the soldiers in there for 20 nights.

Sally Helm: It's not very pleasant, but it's a way to test the miasma. Because it certainly smells.

Agramonte says the stench is indescribable, but...

Molly Crosby: No soldier that ever came out of that shack, what was known as the infected building ever came down with yellow fever.

Sally Helm: So, the doctors scratch miasma theory from the list. Then in the other shack they test the mosquito vector theory.

Molly Crosby: He put a screen up in the middle and he put on one side, a couple of soldiers, with screening and cheesecloth all around. So that's, it's completely sealed off. I even saw the building it's all tongue and groove. There's no way anything can get in.

Sally Helm: They're group A. Group B comes in next.
**Molly Crosby:** On the other side of the screen were the volunteers that would come in with the mosquitoes.

**Sally Helm:** Group A. Insulated protected from mosquito bites, but otherwise in the same shock as group B breathing the same air smelling the same smells.

But group B is in with the mosquitoes, mosquitoes who have fed on yellow fever patients.

Now remember, they've tried this before and people weren't getting sick. But in a benevolent act from beyond the grave, Dr. Lazear has provided a final clue. In his scientific notebook, the same one where he recorded the experiment on Guinea pig number one, he kept detailed track of all the mosquito experiments he'd done.

**Molly Crosby:** You can see every soldier's name and date and the mosquito, which test tube the mosquito came from and when it bit them.

**Sally Helm:** Lazear was nothing. If not scrupulous. And when Reed looks over the pages, a pattern begins to emerge. If you take Carol's and Lazear's cases into account, it looks like a mosquito must bite a victim of yellow fever within the first three days of their infection.

The mosquito must then survive 12 days. During that time, the disease is incubating only after 12 days

Only after 12 days, is she capable of passing along the disease. This might have been why earlier experiments were so hit or miss. Some of those mosquitoes might not yet have been capable of passing on yellow fever, armed with this knowledge Reed and his colleagues returned to the shack.

**Molly Crosby:** No one on the side of the screen without mosquitoes, no one got sick. So, it's definitely not passing through the air, but everyone who came in contact with the mosquitoes got sick.

**Sally Helm:** They've finally proven the mosquito theory in a really detailed way

**Molly Crosby:** They're able to prove it is being carried by what's known as the Aedes Aegypti mosquito. Then it's being spread through the mosquito when it bites and draws blood.

**Sally Helm:** Case closed. At the 28th annual American Public Health Association meeting in October 1900 Major Walter Reed stands before an assembly of his peers.
He delivers the findings of the yellow fever commission experiments; mosquitoes are the culprit. Nearly two decades before Dr. Carlos Finlay had stood before a similar group of medical professionals and expound this exact theory, but now Reed and his team have proven it.

And they're not laughed off the stage. They're applauded US army Major Walter Reed goes down in history as the person who figured out yellow fever. To be fair. He was always personally careful to credit Finlay when he could the Cuban doctor's unshakable faith in the mosquito theory made possible the later experiments that finally proved it. In Cuba, people immediately take notice of the commission's report.

*Molly Crosby:* One of the men who's appointed down there in the army decides to use this knowledge about mosquitoes and clean up Havana.

*Sally Helm:* He forms inspection parties that go to nearly every home in Cuba.

*Molly Crosby:* If you have standing water on your property, they fine you. They stock ponds and lakes with fish that eat mosquito larvae. They slept with mosquito netting.

*Sally Helm:* Mosquito control measures that today seem simple, common sense, and they have a huge impact.

*Molly Crosby:* Cuba which had seen yearly epidemics for 150 years, yellow fever is wiped out there in 150 days.

*Sally Helm:* Other cities like New Orleans take similar measures and see similar results. This is an enormously consequential, finding. It paves the way for scientists to discover other mosquito borne illnesses and help eradicate them.

And it has some more surprising consequences. Like it helps make possible the building of the Panama Canal. Workers there had been dying of yellow fever in droves, but mosquito mitigation measures turned things around, saving many lives and making the canal possible. It links the Atlantic and Pacific oceans forever changing the face of global trade.

So, it is hard to overstate how important this experiment was. It saved untold lives. And it was an early example of medical consent practices that are now commonplace. Getting there certainly was not a straight line but Reed helped pave the way. And yet, despite all of that, it is easy to look back on this experiment and feel almost frustrated with scientists of the past.

Here's Kathryn Olivarius.

*Kathryn Olivarius:* I find myself having to catch myself sometimes thinking like, why don't they just notice that? Like, how do they not see it? You know, here are the mosquitoes
they're everywhere. How did somebody not come up with this theory earlier than that? But of course, we have the absolutely the benefit of hindsight here.

**Sally Helm:** She said back then, they'd only just figured out what germs are. And recently she has felt more and more able to relate during the early months of the COVID 19 pandemic in 2020 Olivarius said she kept thinking about letters. She'd read from the time of yellow fever, feeling a renewed empathy for the people who suffered through it.

**Kathryn Olivarius:** You know, you have people expressing extreme anxiety, fear, they're recounting, you know, are my eyes yellow yet? How do I feel? And then you have almost sort of like extreme boredom. That time itself seemed to kind of move by like molasses. And I really recognize that. I'm sure many people might as well.

**Sally Helm:** I guess another way that it makes me feel more empathy for people of the past is like, I think it is sort of easy to feel like scientists in the past were stupid. It's sort of like, oh, why didn't they see about mosquitoes or about germs? They were so much dumber than we are now. But you think about the beginning of COVID and you're right. We didn't know how it spread in the same way that they didn't know how yellow fever spread. And so, you know, people were wiping down their like apple skins with…

**Kathryn Olivarius:** Yeah, with Clorox, like…

**Sally Helm:** Yeah, exactly.

**Kathryn Olivarius:** Imagine those a three months stretched out over centuries. we were able to sequence COVID very quickly. We had a vaccine so quickly, you know, in large part because of their work that they did in the past. It's why we are here today in some sense, and why we had the ability to so quickly determine some really key things about COVID. Knowledge building takes time, and it takes experimentation, and it takes sometimes some somewhat controversial and sort of radical theories like the mosquito vector was. and then it requires people to be really dedicated to proving that theory correct.

[CREDITS]

**Sally Helm:** Thanks for listening to history this week. For other moments throughout history that are worth watching. Check your local TV listings to find out what's on the history channel today. If you want to get in touch, please send us an email at our email address history this week, history.com or you can leave us a voicemail: 212-351-0410. We are reading and listening, and we'd really love to hear from you. So please reach. Special. Thanks to our guests, journalists, Molly Caldwell, Crosby author of *American plague: The Untold Story of Yellow Fever, The Epidemic That Shaped Our History* and Dr. Catherine AVAs, author of *Necropolis: Disease, Power, and Capitalism in the Cotton Kingdom*. This episode was produced by Morgan Givens
sound designed by Dan Rosato and story edited by Jimmy Gutierrez. Our senior producer is Ben Dickstein. History This Week is also produced by Julia Press and me Sally Helm.

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