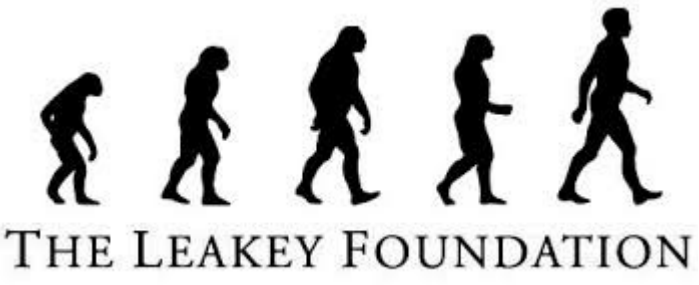

Origin Stories Episode 12: The Origins of Tuberculosis

Meredith Johnson
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This is Origin Stories, The Leakey Foundation podcast. I'm Meredith Johnson.

Meredith Johnson
Tuberculosis has been part of the human story for a very long time. You might know it as consumption, a turn-of-the-century disease that conjures up images of pale, delicate women coughing into lace handkerchiefs. In the 1800s tuberculosis was causing death and suffering on an incredible scale. In Europe and America, it caused one out of every seven deaths, but people didn't know what caused it. They thought that consumption maybe ran in families. The only treatments were rest, fresh air, and sunshine and then on March 24, 1882, a scientist named Robert Koch astounded scientific community when he announced he had discovered the cause of tuberculosis. It was a bacteria called *Mycobacterium tuberculosis* and this announcement was a turning point in our battle against TB. Koch's discovery gave us an enemy we could fight. It earned him the Nobel Prize and led to advances in hygiene and eventually to the development of antibiotics that worked against the TB pathogen. Now every year on March 24th organizations involved in the fight against TB observe World Tuberculosis Day to raise awareness about this deadly disease. On this episode of Origin Stories, we're marking World Tuberculosis Day with the first episode in a two-part series about how infectious disease has shaped human evolution. We'll take a look at our deep history with tuberculosis and hear a surprising story about the origin and evolution of one of the world's deadliest killers and unfortunately, TB isn't only a disease of the past. According to the World Health Organization, it's the leading cause of death by infectious disease today.

Anne Stone
The WHO estimates that about nine million people get TB each year. About 1.5 million people die from TB annually.

Meredith Johnson
This is Anne Stone. She is a molecular anthropologist at Arizona State University where she runs the Stone Lab.

Anne Stone
My laboratory works on questions about the population history— the evolutionary history of humans and other primates as well as our disease history. So we work on a range of projects from the population history of chimpanzees, to how people adapt to their environments and part of that is how they adapt to disease I'm very much interested in diseases as a selective force because we know that it's probably been the strongest selective force for humans over our evolutionary history. I have focused on tuberculosis.

Meredith Johnson
Our long history with TB is one of the things that makes it so fascinating. TB was known to the ancient Greeks. Hippocrates wrote that it was the most common cause of illness and always fatal. It's written about in the ancient Indian Vedas, and classic Chinese medical texts. Modern scientists had two main hunches about TB's origins. They thought either it originated very early on in human evolution; maybe as early as three million years ago or they thought we picked it up from cows at the dawn of agriculture when we started to live more closely with cattle. So there's been this debate about how long we've had it and where we got it, but we know it's been causing human suffering and death on a large scale for a very long time.

Anne Stone
So tuberculosis has affected human populations for centuries and we know from the London Bills of Mortality that in the 1600s it may have been the cause of death for about twenty percent of the deaths. So we know that it's had a long-term impact and probably with the increased urban density and people living in "close quarters" it became a greater problem.

Meredith Johnson
The way TB usually spreads when people breathe in infected droplets like from the cough of another person who is sick with TB and that will either start to make you sick or as is the case with the overwhelming majority of people, your immune system deals with it.

Anne Stone
There are many people walking around in the world who have latent TB and they don't know it.

Meredith Johnson
And then later on if that person becomes immunocompromised TB can basically escape the cell that the immune system has built around it and cause active tuberculosis.

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Anne Stone
Typically it's a pulmonary disease. People lose weight, they cough, they become kind of emaciated, they may cough blood, they'll have fevers, they'll just be fatigued and for centuries it was known as consumption, right? The disease that you slowly died from.

Meredith Johnson
Tuberculosis has been really interesting to anthropologists because not only has it been so widespread it does something few other diseases do; it shows up in the archaeological record.

Anne Stone
So there are many diseases that kill very quickly and so when you find the skeleton of someone who died very quickly from one of these diseases they look healthy except they're dead, right? And so, but tuberculosis because it can be a very slow and chronic disease can cause lesions that are identifiable.

Female Speaker 1
What do these lesions look like?

Anne Stone
The lesions basically look like kind of holes, chewed up holes.

Female Speaker 1
So what's the earliest evidence of tuberculosis that's commonly agreed on?

Anne Stone
The oldest case that I think everyone would agree on it dates from about 4000 BC from Italy.

Meredith Johnson
Some of the puzzles that people who study ancient diseases are trying to solve are things like how old is it? Where did it start? How is it spread? And since you can see evidence of TB in the bones scientists can use the archaeological record along with DNA to track TB spread around the world and through time and across species.

Anne Stone
Because while TB typically spreads between humans it can also spread from humans to other animals or from other animals back to humans. So when we look at the phylogeny of modern tuberculosis complex strains these animal strains are nested within the human strains and so one of the things I'm really interested in is how have the tuberculosis strains spread around the world.

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Meredith Johnson
Stone is especially interested in how the way TB spread changed during the age of exploration.

Anne Stone
In particular, how has the age of exploration affected that patterning sort of pre- and post- age of exploration and when we look at the strains in animals, how did they, when did they get it from us, on what occasions have they sort of given it back to us. Those sorts of things have been of interest. They weren't actually— I was sort of dragged into that interest in a sense.

Meredith Johnson
Stone was dragged into it by a colleague named Jane Buikstra, an archaeologist who's also really interested in tuberculosis and a few years ago Buikstra came to Stone with a very strange discovery.

Anne Stone
Archaeologists and bio-archaeologists like my colleague Jane Buikstra started really identifying clear cases of tuberculosis in the Americas pre- contact.

Meredith Johnson
She had found telltale signs of TB in 1000 year old mummies in southern Peru from way before Europeans had ever been in the Americas.

Anne Stone
There are certain parts of the world where you may get mummies preserved and this is usually really dry places like Egypt or parts of Peru. Southern Peru is the northern extent of the Atacama Desert so it's very, very dry and the preservation is amazing. There'll be wooden bowls and these beautiful textiles in these burials that look as bright as when they were buried I think.

Meredith Johnson
The sixty-eight mummies were from a time and a place where there shouldn't have been TB. So Stone and her colleagues had a really big mystery to solve. How is it even possible for there to be TB in the Americas before Europeans and their cows got there?

Anne Stone
And so then the question became, all right, what kind of strains are these because today when you look in the Americas all the strains are European origin. So basically after European contact, there was a major replacement of tuberculosis strains.

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Meredith Johnson
And remember there was this very strong idea that humans first got TB from cows.

Anne Stone
This idea that that cows gave us TB was very strong and therefore it was assumed that there was no tuberculosis in the Americas pre- contact because there were no cows in the Americas pre-contact.

Meredith Johnson
But it was there, for sure. So where could it have come from? Using archaeology and information from ancient DNA they started to try to solve the mystery. So Stone and her colleagues carefully collected DNA samples from the sixty-eight mummies and working with ancient DNA is very tricky and difficult, but they were able to get enough from three of the mummies to reconstruct the entire genome of the bacteria in each of those three individuals.

Anne Stone
We thought what we were going to find was that some of these older East Asian strains of tuberculosis had come over the Bering Strait with the first Americans and that TB was old and it had gotten there when people walked to the Americas. That was not what we found and we were actually very surprised.

Meredith Johnson
What they found was that the TB strains they pulled from the Peruvian mummies were different than other known human-adapted strains.

Anne Stone
These strains are most closely related to strains found today in pinnipeds and pinnipeds are seals and sea lions.

Meredith Johnson
So what they think happened is this; TB emerged in humans in Africa, spread to other humans, but we also gave it to animals, including domesticated animals like cows and goats. Then seals came up onto the beaches in Africa to have their pups and picked up tuberculosis from either people or animals— they're not sure which— then those seals passed it on to other Southern Hemisphere seals and then they, those other seals brought it to the Americas where people like to eat seals.

Anne Stone

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And so probably in the process of butchering seals or eating meat that wasn't completely cooked they acquired tuberculosis from the seals. So this was not what we expected.

Meredith Johnson
Another surprise came when they looked at how old this TB was. Knowing that the mummies were a thousand years old they were able to establish a molecular clock. A way to date changes in the DNA of the TB.

Anne Stone
Normally when you're asking questions about the evolutionary history of a species— so let's say we're talking about primates. We can look at the archaeological record.

Meredith Johnson
And we know when certain events happened; say the separation of Old World monkeys and New World monkeys.

Anne Stone
And we can use that as a time point, a sort of a calibration point in our clock to then date parts of that family tree that maybe we don't know as well. With bacteria, we don't really have that because we don't really have bacterial fossils.

Meredith Johnson
And with ancient DNA they can take a sample from a bone that's clearly infected with TB, radiocarbon date it and sequence the genome of the bacteria in that infected bone or mummy.

Anne Stone
And use that as a way to calibrate the molecular clock. So how many changes have occurred given the amount of time from then till now.

Meredith Johnson
And with TB before Stone and her colleagues' work we only had a few points set on TB's molecular clock. We knew the earth's atmosphere became oxygenated about 2 1/2 billion years ago and a lot of bacteria that needs oxygen originated then.

Anne Stone
And then sixty years ago someone took a strain, a culture of TB and put it in the freezer so we have these really old calibration dates and this really young calibration date and depending on which you use or even if you use both, depending on your method it would really bias your

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estimate of how old TB was and make it really old or really young and so the previous estimates of the origin of TB in humans ranged from three million to twenty thousand years.

Meredith Johnson
So they added the information from the thousand year old mummy samples to calibrate the clock and find a more accurate date for when tuberculosis originated.

Anne Stone
And when we did that we found that the most recent common ancestor for all of these strains was roughly three thousand to six thousand years ago, which was much more recent than we'd expected. We assumed that either TB was older than agriculture or possibly acquired during domestication but I think most of us thought it was older and so we were quite surprised when it was quite a bit younger.

Meredith Johnson
From seals on the shores of Africa to ancient mummies in the Peruvian desert to the slums of 16th-century London and around the world today, TB has infected, sickened and killed us by the millions. But now with new investigative techniques for developing a deeper understanding that will help us fight it in the future.

Anne Stone
So it's sort of truth is stranger than fiction.

Meredith Johnson
The results of the study were published in the journal *Nature* in 2014 and they have given us an important new piece of the story about our long history with tuberculosis.

Thanks to Ann Stone for sharing her work with us. We'll have links to more about her work in the show notes.

Next time on Origin Stories, the evolutionary arms race between us and disease-causing microbes. We'll look at how the human story has been shaped by infectious disease and how understanding both human adaptation and disease adaptation can help us fight ancient pathogens like TB and emerging threats like Ebola.

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And visit stoptb.org to learn more about the World TB Day initiative.

This episode was produced by me, Meredith Johnson. Our editor is Audrey Quinn. We have music by Henry Nagel, Lee Rosevere, Podington Bear, and Black Ant.

Thanks for listening.

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