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00:06 Sarah Crespi: Welcome to the Science Podcast for September 25, 2020. I'm Sarah Crespi. Each week we feature the most interesting news and research published in Science and its sister journals. First up, we have contributing correspondent, Ann Gibbons. We talk about what might be the earliest human footprints found on the Arabian Peninsula. Continuing our history of humanity theme, I talk with Janet Kelso about the Y chromosomes of our close cousins, Neanderthals and Denisovans, and how the Neanderthal Y was mysteriously replaced with the Y chromosome from very early modern humans.

00:44 SC: Now we have contributing correspondent, Ann Gibbons. She wrote this week about the likely earliest human footprints on the Arabian Peninsula. Hi, Ann.

00:55 Ann Gibbons: Hi, Sarah.

00:56 SC: How old or how early are these footprints?

00:58 AG: Well, that's a good question. They threw a whole package of dating methods at them and came up with in the ball park of 121,000 to 110,000 years old. Now, the dates are not absolute, there's some questions about them, but that's a pretty good ball park.

01:16 SC: How does this age compare to previous hints or clues that humans... Modern humans, early modern humans were on the Arabian Peninsula?

01:26 AG: Here's the problem. We know that early hominins, members of the human family, have been migrating out of Africa for 2 million years because we find fossils of our ancestors in the Republic of Georgia, we find them in Asia, we find them in Eurasia, all over the place, but we don't know how they got out. And the most logical route is they had to walk through Arabia because they couldn't fly, they couldn't paddle boats, At that point, the one land mass in the way between Africa where humans arose originally, our ancestors arose and Eurasia is through Arabia. So we know they had to go through there. But there's a huge gap, there are no tools older than 300,000 to 500,000 years and what is there is not definitive. The only fossil we have of a member of the human family from Arabia is a finger bone that is about 88,000 years old. So the mystery is, where is the evidence of members of the human family marching through Arabia?

02:20 AG: And then the second part of that is, modern humans, specifically our ancestors, Homo sapiens, are most probably in Africa because we see fossils in the ball park of 180,000 to 300,000 years of proto early Homo sapiens arising in Africa. And then we find more of these sort of early Homo sapiens in Greece dating possibly back to as early as 210,000. So we know that they got out.

02:46 SC: Right.

02:47 AG: And now we're just trying to find evidence.

02:50 SC: Is there something going on in the Arabian Peninsula that either people didn't want to hang out there for very long or that erased a lot of evidence?

03:00 AG: The Arabian Peninsula has covered with deserts, it's very dry today. The Nefud desert where they found these fossils is parched and arid, but there were periods in the past where the climate was cooler and wetter, and during those times, some 125,000 years ago, was one of them, it was green. Arabia was covered with tens of thousands of lakes, there were grasslands between them. If you think about it, these early human ancestors, it's not a separate continent or a separate place for them to go to, it's Afro Arabia, right?

03:27 SC: Yeah.

03:28 AG: So it's an extension of Africa if the climate is good and they're following large game.

03:33 SC: How were they able to find these footprints? This is a very large area and it's a few remnants of a human passing through.

03:41 AG: Yeah, so this team led by Michael Petraglia, and it's an international team of Saudi Arabians and a number of people on it has been doing a search. They've been scouring the deserts of Arabia for the last decade. They start with satellite imagery, which helps them see parched ancient lake beds, which have sort of characteristic white paleosols, often these ancient sediments that stand out in the satellites. And then they go down to ground truths, what they see on the satellites and airplane shots. They go in on foot and in jeeps, and in this case, they saw this ancient lake bed eroding out as white sediment and it had just been recently exposed by erosion, and they found the footprints of the animals, which was amazing. And as they looked closer there were hundreds of footprints, almost 400, mostly animals, but they did identify this small number, I think it was seven, that seemed to be human footprints, and so they knew right away, they were very excited about that, that this was something that was important.

04:34 SC: How can you tell that they're human footprints and not some other upright walking relative?

04:40 AG: There's now a whole science of studying human footprints. Ever since the first ones were found in Laetoli, in Tanzania and Kenya, there have been a number of footprints that have been studied. People uses 3D morphometrics, this three-dimensional analysis with computational imaging where they can really look at the depth and they can model how much weight would have been needed to make that footprint, the length of the foot, the stride between the steps, and then they've done studies of living people and their footprints in Africa to test out those ideas. And lo and behold, when they do that to these footprints, they seem to come up with somebody kind of human that was taller and maybe a little lighter weight, more like a modern human, a Homo sapiens, than, say, a Neanderthal. And so based on that, they say, oh, these probably were made by Homo sapiens, although they cannot rule out that Neanderthals might have been there too.

05:28 SC: Is there anything else they can tell about these people by looking at these marks?

05:34 AG: I think if they get more, they can start to tell about their social structure. Footprint studies in Africa have got quite complicated where you could see the direction that they're going in the pace, different members of social groups, you can start to see what the packs of humans look like, what size are they, how many are in these groups, what are they doing along the way. In this case, they're not spending a lot of time there, they're just walking through. This is a meandering group. What is really, really cool, though, is that footprints like these are a snapshot of a single moment in time, a single day. Most of the time when you have an archeological site, in the layer of soil that you get the fossils or the tools and the dates, all that in one place, the span is usually hundreds, if not thousands or tens of thousands of years.

06:18 AG: So if you find an animal bone near a hominin bone or a early human bone or a tool, you don't necessarily know if they were there at the same time or they were years apart. With footprints like these, these were laid down in the same day, maybe a couple of days, and they dried out and then got covered up and preserved. So we know they were all there at the same time. So you get this really cool day in the life look at the hominins and the animals they were with, which is really cool in this case.

06:41 SC: And lots of animals.

06:44 AG: Yes, almost 400 footprints of animals, including, very interestingly, wild asses, which I don't think were carrying their burdens, but that's kind of neat, and there were elephants. And the thing that's interesting about the elephants is they're about to disappear from the Middle East and just in Africa, at that point, 300,000 years ago, and here they are at 120,000 in Arabia. And the camels, they also found camels. It's interesting that such large animals were there, and it begs the question, were these humans following them, were they tracking them?

07:14 SC: Going back to the date, we talked about it being about 120,000 years old, there's some question about the date. But if that were correct, is there anything particularly important about this time in human history about what we know about migrations that we could link these prints to?

07:30 AG: Yes. So what is really interesting is the genetic evidence says that everybody outside of Africa came from migrations that happened in the last 50,000 to 80,000 years. So this date predates that. We happen to know that early Homo sapiens were in the Middle East pretty quickly after this, or at the same time. There are fossils in caves at Skhul and Qafzeh that are early sort of proto-Homo sapiens. So we know humans are out, but it sort of suggests that because we don't have DNA that dates back this early, these were failed migrations, that these were members of the human family that went out, they weren't failed migrations for them, they lived, but they did not contribute to the gene pool of living people today.

08:09 AG: That's one hypothesis, but it also shows that there's a more complex story of groups of humans migrating out of Africa constantly whenever the weather and the climate is right, that it's green enough that they can get water, follow animals, hunt meat, and trek out of Africa, that they can cross the desert, that looks like humans were doing that whenever they could. And so how do they contribute to our ancestry today is a really interesting question, and how many different kinds of hominins were out there.

08:36 SC: Thank you so much, Ann.

08:38 AG: Thank you, Sarah.

08:39 SC: Ann Gibbons is a contributing correspondent for Science. You can find a link to her story at sciencemag.org/podcast. Stay tuned for an interview with Janet Kelso about what Y chromosomes and our close cousins, Neanderthals and Denisovans, tell us about ancient interbreeding.

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09:01 SC: We humans have 46 chromosomes, or you can say 23 pairs of chromosomes. Twenty-two of these pairs are called the autosomal chromosomes, and one pair is our sex chromosomes, think XY or XX usually. When we have kids, half the chromosomes come from mom, the other half from dad. Mom always donates an X, and dad sometimes donates an X, sometimes a Y. Because Y chromosomes can only be inherited from the father, they therefore travel a special path through our ancestry, kind of like the way last names only come from men in certain societies. They don't tell you the whole history of a family, but they do convey certain interesting things about the past. Until now, the path of the Y, the history of the Y chromosome in our ancient relatives, the Neanderthals and Denisovans, has not been accessible. Janet Kelso is here to talk about her work looking at these Ys, and what they can tell us about how these populations intermixed with us modern humans. Hi, Janet.

10:07 Janet Kelso: Hi.

10:08 SC: Why haven't we been able to take a look at the Y chromosomes from our ancient relatives before this point?

10:14 JK: Yeah. We have had autosomal genomes of Neanderthals and Denisovans for almost 10 years. And we've had mitochondrial genomes, that's the part of the genome that's inherited from the mother for even a bit longer than that. But funnily enough, all the fossils that we had that were well preserved enough to do high coverage genome sequencing were female, so we had no Y chromosomes. And it's not that there aren't any male Neanderthals or Denisovans, but the ones that we had were just very poor candidates for sequencing. Most of the DNA in the bones that we could get out of these bones and teeth, they didn't come from the owner of the bone, they came from microbes that colonize the bone, perhaps after the individual died. And so what we have is this huge sea of microbial sequence, which makes it really hard and really expensive for us to sequence the tiny amount of Neanderthal or Denisovan sequence that's hiding in there.

11:02 SC: So it was a combination of who got preserved, but also some limits on technology up until this point.

11:08 JK: Yeah. Here, what we've done is take a different approach. Instead of trying what people would call shotgun sequencing, so just sequencing all the DNA that's there, we use the modern human Y chromosome to design some probes, and then we use those probes to fish out Y chromosome sequences from this huge mass of microbial sequence. And that worked amazingly well, actually.

11:28 SC: Okay, so you enriched for Ys.

11:30 JK: Right.

11:31 SC: Where exactly did you go to find these Ys? Where did you go fishing?

11:34 JK: We had DNA libraries from three Neanderthals and two Denisovans that we thought might be suitable for getting Y chromosomes. We knew from some sequencing that we were able to do that they were male, and so we went fishing in those libraries and managed to hybridize out about 7 million bases of the Y chromosomes of those individuals.

11:55 SC: Did these Y chromosomes that you fished out, do they have a different story to tell from what we've seen in the autosome, the other genomes that have been sequenced before?

12:06 JK: Surprisingly, yes. We know that from analysis of our autosomal genomes and the autosomal genomes of Neanderthals and Denisovans, that the Neanderthals and Denisovans are rather closely related sister groups, more equally closely related to the both of them. And so we expected that the Y chromosomes should show the same pattern. And what we found instead was that the Denisovan Y chromosome forms a separate lineage. Neanderthal and modern human Y chromosomes are more similar to one another than either of them is to the Denisovan Y chromosomes.

12:35 SC: So Neanderthal humans were closer together. We made a little group.

12:39 JK: We did. And what we did to try and figure out what was going on there is we calculated the time of the most recent common ancestors. This is sort of the point at which the populations of modern humans, Neanderthals and Denisovans, would have shared common ancestral population, and we calculated that for modern humans and Denisovans, and for modern humans and Neanderthals. Normally, when we look at the autosomes, that time is the same and it's in the range of 500,000 to 700,000 years. But when we looked at the Y, we saw that for Denisovans, indeed, it's this approximately 700,000 years. But when we looked at this most recent common ancestor of Neanderthals and modern humans, what we saw is that it's much younger, this common ancestor. It's about 370,000 years ago.

13:22 SC: That's a different story than the genome tells you, from the autosomal chromosomes. But as we mentioned early on, there was also mitochondrial DNA. This is inherited from the mother, so this is kind of a parallel to the Y chromosome. When you look at that, does it support what you're seeing with the Y?

13:40 JK: Yeah, so fascinatingly, there was previous work with mitochondrial data that had provided hints that early modern humans and Neanderthals might be more closely related to one another than either was to Denisovans. And the evidence for that were the mitochondrial genomes from the very earliest Neanderthals that we have, the very earliest Neanderthals for which we have genetic data. And these are Neanderthals that are dated to around 400,000 years ago, from the Sima de los Huesos in Spain, and unlike all the other Neanderthals that we see, these very early Neanderthals from Spain carry mitochondrial genomes that look like Denisovans, like the mitochondrial genomes of Denisovans.

14:17 JK: That suggests to us that at some point between the time that those Neanderthals lived 400,000 years ago and the later Neanderthals that we have genomes from, sort of 100,000 years ago, the mitochondrial genomes, the mitochondrial DNA of Neanderthals was possibly replaced by interbreeding with very ancient, very early modern human population. So there were already hints about a strange inconsistency between the autosomes and the mitochondrial DNA, and it was thought perhaps that the mitochondrial was an exception. Now what we see is the Y looks just like the mitochondria.

14:50 SC: Who's replacing who in the Y chromosome world?

14:53 JK: What we see is that the Neanderthal Y chromosome, the original Neanderthal Y chromosome, must have been replaced by a Y chromosome that comes from a population of ancient modern humans. It's a bit tricky for us what to call these individuals, they're not modern humans as we know them. They were a population of very, very early modern humans, and we tried to estimate how long ago this could have been. There's been a few papers that have looked into this and tried to figure out could there have been earlier interbreeding. So we know, I think it's quite well-established by now that all modern humans living outside Africa today carry a little bit of Neanderthal DNA on their autosomes. What we see here is something different. What we see here is that all Neanderthals, somewhere after 400,000 years ago, carry modern human Y chromosomes.

15:40 SC: That means that all the male Neanderthals had basically a human Y.

15:44 JK: Right, so they have a Y chromosome that is from a very early population of modern humans, and just so that I'm really clear, this suggests a different interbreeding event. So we know about the one that contributes Neanderthal genes to present-day non-Africans. We think that interbreeding happened somewhere 50,000 to 70,000 years ago as modern humans come out of Africa. This one is much older than that.

16:06 SC: How much older?

16:07 JK: Our estimates are that it must have happened sometime between 100,000 years ago with an upper date of around 370,000 to 400,000 years ago.

16:15 SC: What could be happening where you get this very specific replacement of the Y? Are there any ideas about how that might have happened?

16:23 JK: I think we now have to explain two replacements. So this is not only the mitochondria, but the Y. Now, this is a priori really, really unlikely, that you would get complete replacement of two loci. We don't know why this happened. We did some simulations, some computer simulations, to try and determine scenarios under which this could happen. One explanation I think that is quite plausible is that we know from genetic data that the population size of Neanderthals is quite small, and we know that in small populations, deleterious mutations can accumulate and that they can't easily be removed by natural selection. And so we speculate that an accumulation of mutations on the Y chromosome could have reduced the fitness of the original Neanderthal Y chromosome such that when a slightly more fit modern human Y chromosome was on offer through interbreeding, it might have provided enough advantage that over time, that modern human Y was favored and took over, or increased in frequency among Neanderthals.

17:22 SC: So male Neanderthals' sperm, when they combined with the Neanderthal female egg, weren't doing a great job.

17:30 JK: That would be one potential scenario, yes, that they were perhaps not doing as great a job as they could.

17:36 SC: Either in fertilization into development into actually making the living offspring. But then, here comes an early modern human male and his sperm gets it done, and then you have a mixed offspring who then, what? Goes on with that Y chromosome to go back into the Neanderthal population and...

17:54 JK: And continues to breed with other Neanderthals. And then, of course, the obvious question is, what about the autosomes? If this happened, do we see it on the autosomes too? And the answer is we do, there were a couple of papers in the last year that have pointed to evidence for early gene flow from a modern human-related population into Neanderthals, contributing a very small part of the autosomes. I think the estimates are in the range of less than 10% of the autosomes of Neanderthals.

18:21 SC: There's possibility that this is, as you say, a deleterious mutation on the Y chromosome makes it not such a great thing to have in your genetic makeup. Could there be something else happening where these are early modern humans, these are Neanderthals, they have preferences, they might have some kind of culture. Could there have been some other kind of influence like that?

18:41 JK: I think it's always hard to rule out that there might be some other effect. However, the fact that we see... So we know that the Y is inherited from the father and the mitochondria from the mother, so we know that there must have also been a modern human female contributing if these later Neanderthals carry modern human mitochondrial DNA as well as Y. So it can't have been as simple as a very, very strong sex bias for that, but mate preference, that is of course very hard for us to rule out. It's possible that that was going on.

19:15 SC: But this does suggest that there were these interbreeding couples where the mother was human sometimes, and then other times where the father was human.

19:24 JK: Correct.

19:25 SC: What other questions would you want to take on with this method looking at somewhat degraded samples and pulling out Y chromosome?

19:32 JK: Yep. Not even specifically for the Y chromosome. In other fields, even in more recent ancient modern humans, this idea of capture using baits to capture particular regions of the genome has become quite widespread. We've never really done this for Neanderthals. We do it typically for early modern humans. We're developing this method further here where people are using more and more, using capture arrays to go after... There are large numbers of Neanderthals and Denisovans where we would never be able to shotgun sequence the genomes. The preservation is simply not good enough. But we could get enough DNA to analyze larger groups of Neanderthals if we used these capture type approaches. And so that's something that's in the pipeline here.

20:13 SC: Very cool. Alright, thank you so much, Janet.

20:16 JK: Thank you, it was a pleasure.

20:17 SC: Janet Kelso is the leader of the Minerva Research Group for bioinformatics at the Max Planck Institute for Evolutionary Anthropology. You can find a link to her article, her Science article, at sciencemag.org/podcast. And that concludes this edition of the Science Podcast. If you have any comments or suggestions for the show, write to us at sciencepodcast@aaas.org. You can listen to the show on the Science website at sciencemag.org/podcast. On the site, you'll find links to the research and news discussed in the episode. And of course, you can subscribe anywhere you get your podcasts.

20:54 SC: This show was edited and produced by Sarah Crespi with production help from Podigy, Meagan Cantwell, and Joel Goldberg. Jeffrey Cook composed the music. On behalf of Science Magazine and its publisher, AAAS, thanks for joining us.