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**00:06 Sarah Crespi:** Welcome to the Science Podcast for September 13, 2019. I'm Sarah Crespi. On this week's show, international news editor, Martin Enserink talks about the health of gold miners living at five kilometers above sea level and his visit to the site. I also talk with Annika Stefanie Reinhold about why her team plays hide and seek with rats.

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**00:29 SC:** Now we have Martin Enserink, he's our international news editor. He wrote about research being done at 5100 meters above sea level for our Mountains special issue. Hi Martin.

**00:41 Martin Enserink:** Hi.

**00:41 SC:** What's the name of the place that you visited?

**00:43 ME:** It's a town called La Rinconada, it's in south-eastern Peru, very high in the mountains, 5100 meters.

**00:50 SC:** And you were there visiting a group of researchers looking into chronic mountain sickness. How is this different than acute mountain sickness? You know, something that might happen to me if I went on a day trip to the mountains.

**01:03 ME:** Yeah, and it happened to me, actually, when I went to Peru. Acute mountain sickness is when lowlanders, people living at below 2500 meters or even at sea level go up into the mountains then you have a lack of oxygen, which you get acute symptoms like headaches, sometimes vomiting, that kind of thing, dizziness, but that goes away after a few days when you adapt and your body starts making more haemoglobin, more red blood cells which help you transport the oxygen throughout the body. Chronic mountain sickness is something that happens to people who live at high altitude for a very long time. Basically, the permanent lack of oxygen causes the body to make much more hemoglobin, it's almost like a runaway process, some people get very high numbers of red blood cells and what happens then is that the blood becomes very viscous almost, a bit syrupy. So it makes it more difficult for the blood to circulate which puts pressure on the heart...

**02:00 SC:** Right.

**02:00 ME:** And then you get symptoms like dizziness, permanent fatigue, red eyes, purple lips...

**02:05 SC:** Wow.

**02:06 ME:** Ringing ears, sleep problems, a whole range of symptoms.

**02:10 SC:** I was amazed to learn that oxygen levels where you... Were at about 4... About 50% what you see at sea level.

**02:16 ME:** It's pretty amazing and...

**02:17 SC:** Could you feel it right away?

**02:18 ME:** You feel it right away. Actually, I spent some time at a lower lying city at around 3800 meters to adapt. But even then, when you go up to 5100 meters, it's... The shock... Has very little oxygen, so you're panting all the time, you're out of breath. Quite a few people, including me, slept really badly. You wake up 10... 15 times a night gasping for air.

**02:41 SC:** Oh my goodness.

**02:42 ME:** That's very common because your... The oxygen level in your blood drops too low and then you... All of a sudden you wake up.

**02:48 SC:** This was also kind of a shock to me. This place you visited for your story, La Rinconada, it's extremely high and it has a huge population. It's 50,000-70,000 people. What are they all doing there?

**03:02 ME:** Now until a couple of years ago, people thought that humans couldn't really live at that altitude. It was believed that above 4500 meters it's almost impossible to live permanently. But yeah, there's 50,000-70,000 people here and that's because it's an area that's very rich in gold. There is a number of gold mines there and people are poor and they come to this town to work in the mines because they need the money.

**03:25 SC:** And then the conditions are rough. It's not just very high up, it's also cold and there's not a lot of comforts, creature comforts.

**03:33 ME:** You know, there's no running water, there's no sanitation so there's a lot of waste everywhere, there's no garbage removal. The food is terrible though, everything is pretty awful there. And yet all these people live there and they have to get by.

**03:47 SC:** The researchers were looking specifically at chronic mountain sickness. What kinds of questions were they asking?

**03:53 ME:** Yeah, so they had set up a study in which they enrolled about 55 people. Two-thirds of those had chronic mountain sickness and the rest did not. So what they wanted to do was compare these two groups. They were all miners, they were all male, they did a whole battery of tests. Physiological tests, looking at blood flow, at the heart, at blood vessels, at the brain, they did a sleep study, a whole series of tests that they had to go through. And it took them several days for each of the miners to complete all these tests.

**04:25 SC:** Not only did the researchers look at people with and without CMS, chronic mountain

sickness, they had other categories in mind too. Groups such as highlanders and lowlanders. What do those terms mean exactly?

**04:39 ME:** I think they define highlanders as people who had lived in that area all of their lives, who were born there and whose parents were also from a high altitude. And the reason is that we know that people in the Andes have evolved certain adaptations that make it easier for them to live at high altitude. They're adapted to low oxygen. And that's also true for people in Tibet for instance and people in the highlands of East Africa. These people have... Are known to have certain genetic mutations that make it easier to survive at higher altitudes. But even then, among those people, chronic mountain sickness does occur especially in the Andes and especially when people move so high up, as they do in La Rinconada. So I followed one of these miners throughout the study. His name was Emilio Sucasera. He was born in the region, in the town at about 3800 meters. His family had lived there, he was believed to have the adaptations that would help him survive at the higher altitude but not at this extreme altitude. Because, like I said, almost nobody lives at elevations over 4500 meters. And so he had CMS himself.

**05:49 SC:** A lot of people around the world, I think you say in your story, about 140 million actually live at high altitudes. So how common is chronic mountain sickness among people who have traditionally lived in these places, this is where they grew up, where their parents grew up. How common is the CMS?

**06:07 ME:** Well it's... In some areas, surprisingly common. For instance, in La Paz, the capital of Bolivia, which is at around 3600 meters, between 6% and 8% of the population has CMS. There are certain towns in Peru where it's more like 20%...

**06:23 SC:** Wow.

**06:24 ME:** And even higher in the older population because the risk goes up with age. In Tibet, on the other hand, among native Tibetans it's much lower, probably only around 1% and that may be because the other patients that people evolve, are different in the Tibetan plateau, than they are in Amids. There are few studies done in Ethiopia where I didn't find CMS at all.

**06:47 SC:** Wow. There are some preliminary results already available from the research that was done while you were visiting this gold mining town. What did the researchers find so far?

**06:57 ME:** They presented some of the results at a meeting in June and what they found was actually really striking. For one thing they found that yes people in La Rinconada have an astonishing amount of hemoglobin in their blood up to two kilos in some people. Whereas they also did measurements in Lima the capital of Peru, which is just above sea level, there the average was 747 grams. So more than twice as much, in some people almost three as much haemoglobin. So that was a very striking finding. They find very high blood pressure in the lungs, not healthy. They found that people have a large heart just to keep all of that CRP blood circulating and they know that chronic heart failure is one thing that can result from having CMS for a long time.

**07:47 SC:** I wanna turn now back to the town to talk about conditions again and this does connect

back to the research results. So you visited a gold mine, what was that like?

**07:58 ME:** Yeah so the miner I followed for a few days, Emilio, he showed me around, he also took me to his house. And we went to the mine. I wasn't allowed in, but the mines there are very not well-organized, they're not really regulated it. It's what I call informal or some people say illegal mining. So, from what I hear, they're very few safety precautions, it's dangerous work, there are accidents, there are explosions. And so hear stories about people who've died in the mine, it's currently not a safe situation.

**08:29 SC:** And nobody gets paid a regular paycheck?

**08:32 ME:** The workers don't get paid checks, they basically work for free, and then once a month for a day or maybe two days, they're allowed to go in and take all the gold ore, that they can carry out and keep it for themselves and they can sell the gold that's in it, and that's how they make a living. That's a very strange system. I talked to one environmental lawyer, who compared it to slavery, because he said it turns to your life into a lottery, you may earn almost nothing for months, and your hope is that one day you'll strike it rich. And some people do. The majority of course does not.

**09:06 SC:** One thing I was wondering about is that mercury is really important for separating gold from the ore. And that ends up contaminating all the environment around it and I assume there's a lot of contamination there. Is there a concern that that is also having effects on the health and it might be confused for parts of CMS.

**09:25 ME:** Yeah, that's a great question, because you're right. In this type of informal mining, Mercury is used to separate the gold from rocks and dirt basically, and the Mercury binds the gold it forms an alloy, and then the mercury is burned off with a torch. The Mercury then goes through little chimneys in these shops all around town, and it just goes up in the air. Of course it comes down again and there is a lot of Mercury contamination. People assume that that's a huge health risk. There's been no research at all, but we know Mercury is toxic and is dangerous. Nobody has really looked at the effects of that. And yeah, you're right, that could be a confounding factor in this study. What they hope to do, is by comparing people who are healthy and people who have chronic mountain sickness, is presumably they both have the same or a similar exposure to Mercury, and so perhaps that would cancel out but it's definitely something that people should be looking at as well.

**10:23 SC:** Yeah. It's one thing to study this in a preliminary trial, to go there and measure things with 55 people, but is there gonna be an opportunity to go back to this community with the results of this work and say, "This will help you, this will make your lives better."

**10:38 ME:** Not immediately, I think, but the goal of these researchers who went for the first time to this town and nobody had ever done studies there they were the first. And their goal is to go back and to do more work and they do also in the end want to help develop maybe a drug that might help these people. Because when you're talking about in the case of La Rinconada, you have a disease that affects a quarter of the population, you really have a big public health problem on your hand. And if one thing these people should probably do is move to a lower altitude but many are forced

stay because of economic conditions, some live there 10, 20 years or more. So maybe a therapy could help those people. That's the ultimate goal of this group and they have a few candidates that they would perhaps like to test.

**11:26 SC:** Alright, well thank you so much Martin.

**11:29 ME:** Thanks for having me.

**11:29 SC:** Martin Enserink, is the international news editor for Science, you can find a link to his story and the other pieces in the special issue on mountains at [sciencemag.org/podcast](http://sciencemag.org/podcast). Stay tuned for an interview with Annika Stefanie Reinhold about playing hide and seek with rats.

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**11:50 SC:** This week's episode is brought to in part by mova globes. Mova globes turn all on their own with or without a base in any setting with ambient lighting, no batteries needed and no sloppy cords to detract from your enjoyment. Instead hidden magnets provide the movement. With over 40 different designs including world maps, outer space, famous artworks, there's something for everyone. The outer space collection, even features graphics, provided by NASA and JPL complete with planets, moons, asteroids and constellation designs. It's a great gift for the person who has everything. Or pair it with your own home decor as a conversation starter. Not only do the globe show you the world as it is today, you can also get antique terrestrial maps, vintage maps from 1790, a red ecliptic line is also present showing the sun's position each day of the year. If you wanna go beyond the Earth, they also offer a Mars globe, this recreation presents a direct look at each crater along with multiple layers of red, brown and tan that makes up it's surface. All the graphics are satellite images taken by NASA, giving it a level of realism you won't find with other interpretations.

**13:01 SC:** So visit [movaglobes.com/sciencemag](http://movaglobes.com/sciencemag) and use the code [sciencemag](http://sciencemag) for 10% off your purchase, that's M-O-V-A [globes.com/sciencemag](http://globes.com/sciencemag). And use the code [sciencemag](http://sciencemag) for 10% off your purchase. This week's episode is also brought to you by Kroger Grocery Stores. Did you know that one in eight Americans struggle with hunger? Yeah, 40% of food produced in the US gets thrown away, and a lot of that food waste happens at home. I know I'm guilty of this, I buy a little bit too much, it goes bad in the fridge, I toss it, I don't always have a compost. And of course, I have a collection of very old bananas in my freezer, but when it does get thrown in the garbage, that food waste is sent to landfills. Greenhouse gases are released and it's a problem for our whole planet. Think about this, if we redirect it just one-third of the food we waste to people in need, we'd more than cover the unmet food needs across the country while helping to protect the planet. That's what Kroger is doing with their Zero Hunger|Zero Waste Foundation.

**14:03 SC:** Last year alone, Kroger donated 325 million meals to local food banks. And they've got some great tips to help reduce food waste at home too. It's all part of their goal to achieve zero hunger and zero waste by 2025. Check out [kroger.com/zhw](http://kroger.com/zhw) to learn more. That's [kroger.com/zhw](http://kroger.com/zhw).

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**14:30 SC:** Now we have Annika Reinhold, she's here to talk to us about her experience training rats to play hide-and-seek and what our team learned from that. Hi Annika.

**14:39 Annika Stefanie Reinhold:** Hi Sarah.

**14:40 SC:** Nice to meet you, what kind of questions did you think you could answer by training rats to play hide-and-seek?

**14:46 AR:** The pretty obvious question, can rats actually play hide-and-seek? I guess that was something that we all were pretty interested in on the science side. If they played, what kind of strategies do they use? Are they able to perform such complex task, playing different roles? Do they actually follow the rule? And in the end, we were also really interested in potential neuronal mechanisms of the social play.

**15:11 SC:** What is it like to play hide-and-seek with a rat, what does that exactly mean? No one's counting to 10, right?

**15:17 AR:** No, actually not, even though sometimes I was when I was the seeker. I think it didn't really have a great impact on how the rat performed, but in general, it was really fun. First of all, because rats are quite social and very friendly, and second because the game itself is fun, and you see that in the rat as well.

**15:39 SC:** So all the rats were able to do both, they look for the hider and the seeker in your study?

**15:44 AR:** Exactly, except one rat that we didn't train on hide actually, because that was still the very early part of the study.

**15:53 SC:** How long did it take a rat to learn how to be a hider and a seeker?

**15:56 AR:** It took them five to 10 days to arbitrate, but afterwards actually learning the game was rather fast. So about two weeks I would say.

**16:05 SC:** It's really easy to see from the videos with your paper how this goes. I really encourage people to check those out, but can you give us the step by step of what a game with a rat would look like if you were the seeker?

**16:17 AR:** Yeah, sure. If I was the seeker, I would bring the rat into its starting box first, so the game would always start with a jump in from the rat, and then I would close the box because of course, I don't want the rat to see where I'm going to hide, therefore it's really important to not give them any visual or auditory cues. Then I would hide in one of the three optional hiding locations. Once I was hidden, I would open the box remotely and let the rat jump out. So whenever the rat decides to jump out basically, I had no influence in this obviously because I was hiding crouching silently behind this thing, trying not to breathe too loudly, it was really fun. And once the rat jumped out, it would start searching and sometimes naturally find me fast, sometimes not find me at

all, and very often check out one or two places before, and then find me still within time. So, we decided for a limit of 100-50 seconds. If it found me in time, I would play with the rats, do some social interaction like tickling and rough-and-tumble play with my hand, those kind of things.

**17:26 SC:** That was the reward for them.

**17:28 AR:** That was the social reward, exactly, and that would last for about 20 to 30 seconds, and then I would return it back to the stock box to start a new round.

**17:38 SC:** What about the role reversal where the rat is hiding?

**17:41 AR:** Rat is hiding, yeah, exactly. The game would start the same way, but the difference was... And that was actually the cue that I gave to the rat, that it was the hider because how can you tell a rat, "Oh, now it's your turn to hide." I would crouch immobile next to the box and leave the lid open so the rat could jump out any time, and then it had 90 seconds to look for a cover. We offered it seven hiding locations basically, then it would hide and I would go and find it a little faster than the rat finds me usually, also because I was cheating a little, I have to say, I have my eyes open because I wanted to have some little control at least, knowing in which direction the rat would go.

**18:23 SC:** Well, you weren't timing yourself I guess.

**18:26 AR:** Yeah, and also this, once I would find it, I would again start interacting with it for 20-30 seconds, and then return it back to the box.

**18:35 SC:** What were you measuring over the course of all these different trials with the rats as hidiers and seekers?

**18:41 AR:** First of all, we've been recording all those sessions on video, and we also recorded ultrasonic vocalizations. Many people don't know that rats actually emit vocalizations, we just don't hear them. Looking at the vocalizations, we saw very interesting patterns related to specific game events, we saw that rats preferentially call during interaction. So, the interaction with me return and darting. So this would also involve jumping in and jumping out of the box. More interestingly, we found some differences between hide-and-seek, indicating that they actually can differentiate between those two roles. The most interesting thing we saw was during finding, they actually increased the vocalization. So when they saw me, they called more and when I was finding them so they were found, they actually turned silent.

[chuckle]

**19:35 AR:** Even though... Which is really interesting. This is kind of how you would expect children to behave as well or maybe even adults, humans hiding, and then they're found of course, they don't want to be super loud and noisy when someone's approaching their hiding location, and this is what the rats did too. What they vocalize in is actually the ultrasonic range. So between 20-100 kHz usually, and you can infer from the vocalization if it is in a positive or a negative emotional state. So that was pretty interesting for us to know of course, we were really lucky,

because we've never seen a rat vocalizing in the 20khz range, which means they're afraid. We can tell they actually were habituated well, and they felt good in the room.

**20:23 SC:** Right. So they weren't hiding because they were scared, they were hiding because they were engaged in play.

**20:28 AR:** Exactly. And what we also saw was that they vocalized in the 50khz range which indicates positive emotions. They did this during many events in the game, not only during the interaction. We kind of expected that because it had been shown before that during tickling and so on, they actually vocalized with those positive emotional calls, but also during return and when they jumped out, when they jumped into the box, sometimes during darting towards a hidden location, so there were many events where they actually did those vocalizations.

**21:03 SC:** What about recording from neurons?

**21:06 AR:** We recorded neuronal data. And the neuronal data are of course, so far just correlates but they indicate that the media pre-frontal cortex which is the region we recorded from is highly engaged in this play behavior.

**21:24 SC:** What role does this region play in human brains?

**21:28 AR:** Well, it's actually involved in many things, but why we were interested in it, is because it's implicated in perspective taking, social cognition. It is associated with social proximity, it has been shown to include rules. So all those kind of things we thought are probably important during hidden seek, that's why we decided to record in that region.

**21:48 SC:** Did you see different seeking or hiding strategies between rats or over time?

**21:53 AR:** Yes. We suddenly saw them using strategies which was very interesting and actually the part that convinced us that they actually do hide and seek. In seek they use certain cues to find me faster. We did another paradigm where they could see me hiding so they could use visual cues and they found me significantly earlier than when they didn't have those cues. And also they use memory cues, I had a paradigm where I was hiding in the same place over and over again, for five times in a row. And at some point pretty fast actually the rat realized that and then it resulted in faster search time, so it would find me faster than if I would hide randomly in the room. And for hide the other way around, they really frequently changed hiding locations. So they weren't always going to the same location, over and over again, but changing it kind of in order to make it more difficult for me. This is just an assumption of course because we can't look inside their head. But they didn't target the last hiding locations as often as in seek. And more stunning even is they preferred opaque hiding locations, over transparent hiding locations, even though I was giving them the same social reward for both of them.

**23:13 SC:** And why did you offer this social reinforcement? So a little bit of play, a little bit of petting or tickling rather than say a food reward?

**23:22 AR:** That is actually one of our key statements in the paper, which is that if you want to study such complex behaviors as play behavior, especially social play behavior, it often is not enough to use the paradigms that we are used to in neuroscience which are very often those food reward, operant conditioning tasks that the rats perform over and over again. We wanted them to engage in the game because of the fun, for the sake of it, so to say. And if we would have given them a food reward and of course, we could have never been sure if they do it just to eat or if they also do it for the fun.

**24:02 SC:** Why is it important to study play and play behavior in rats? What can we understand more broadly about animal behavior or even human behavior from these kinds of studies?

**24:12 AR:** Neuroscience traditionally relies on the strict experimental and well-controlled paradigms. Since this doesn't go well together with the characteristics of play, we need paradigms with a high degree of freedom and this paradigm hide and seek can also be used for many other complex cognitive tasks. It's not only something that we can look at to understand how do rats actually play hide and seek, but it's something that we could start studying perspective-taking theory of mind, those kind of things that so far only have been studied in primates and humans mostly. And on the other side, I also think studying play behavior in itself is also something really valid for us because it has been shown that play behavior is really important to developing social and cognitive skills. So as a child, it's very important that you engage in some of those social play behavior.

**25:09 SC:** So sometimes when you find a rat, it runs away and re-hides. What do you think is going on there?

**25:15 AR:** This would classify as some kind of cheating in the game. But we were really interested in this behavior because this re-hiding or also just running away, even though I would reward them like socially interact with them, shows us to a certain extent that they have fun playing the game, they are not just playing it for the reward, but they're prolonging it, because the game itself which also involves re-hiding and running away those kind of behaviors, it's more interesting for them.

**25:45 SC:** It does remind me. I have a kid and I actually have rats too.

[laughter]

**25:49 AR:** What a coincidence.

**25:50 SC:** I have some rats. They are really fun. But it does remind me that how important play is to learning, and that it makes sense that animals do this but I can see why it would be difficult to capture it in a laboratory setting.

**26:03 AR:** Totally, yes. Yeah I think learning is why it is really interesting to further study the role of play in animals as well as in humans, because most likely it plays a very important role in learning and we know already that in certain diseases, not playing, or lacking some of the social play is correlated with psychiatric diseases. So I guess, learning how to play again could be a very

interesting target also for those potential treatments in the far, far future.

**26:38 SC:** Alright, thank you so much Annika.

**26:40 AR:** Sure. It was fun talking to you.

**26:41 SC:** Annika Stefanie Reinhold worked on this project for her Masters at the Bernstein Center for computational neuroscience at Humboldt University, in Berlin. You can find a link to her paper at [sciencemag.org/podcast](http://sciencemag.org/podcast).

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**26:56 SC:** And that concludes this edition of the Science Podcast. If you have any comments or suggestions for the show, write to us at [sciencemag@aaas.org](mailto:sciencemag@aaas.org). You can also subscribe to the show on iTunes, Stitcher, many other places. Or you can listen on the Science website. At [sciencemag.org/podcast](http://sciencemag.org/podcast). There you'll also find links to the research and news discussed in the episode. To place an ad on the podcast, contact [mid-roll.com](http://mid-roll.com). The show was produced by Sarah Crespi and edited by Podigy. Jeffrey Cook composed the music. On behalf of Science magazine and it's publisher, AAAS, thanks for joining us.