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**0:00:05.7 Sarah Crespi:** This is the science podcast for November 20th, 2023. Happy almost Chinese New Year live. I'm Sarah Crespi. Please take a moment to fill out our podcast survey, you can see it as a pop-up at science.org/podcast, or as a link in our show notes. First up this week, accusations of medical murder.

**0:00:26.8 SC:** Contributing correspondent Cathleen O'Grady joins me to discuss her story of how statisticians are weighing in on cases where nurses and doctors are convicted of murdering patients based on bad statistics. After that, allergies are on the rise, and it's linked with climate change. I spoke with researcher Kari Nadeau about her review in Science Translational Medicine on the status of allergy science, including how recommendations and treatments have changed.

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**0:00:55.0 SC:** This segment is going to sound a little different, I'm very excited about it, there is music, and of course we get to hear from the writer, Cathleen O'Grady about her story on the misuse of statistics and how that's led to false convictions in medical murder cases. After her reporting, we actually went back to the sources, people who are interested in seeing statistics used in a just way, and we're bringing their voices to you too. So here's Cathleen.

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**0:01:24.2 Cathleen O'Grady:** In 2001, Dutch nurse Lucia de Berk was on trial for serial murder. An expert witness for the prosecution testified that the probability of her shifts lining up with so many unexplained incidents was one in 342 million.

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**0:01:55.6 SC:** Cathleen, it's 2023, and we're still talking about what happened with de Berk. Why are we still paying attention to this?

**0:02:01.1 CO:** A nurse called Lucy Letby is currently on trial in England for crimes that superficially seem similar to the crimes that Lucia de Berk was charged with. Concerns about the way that Lucia de Berk's trial was handled led the Royal Statistical Society to publish a report about the statistical mistakes Lucia de Berk's trial, because they were concerned that similar things might be happening in the case of Lucy Letby.

**0:02:26.7 SC:** Right, so de Berk ended up being convicted and then losing an appeal, but eventually her conviction was overturned by the Supreme Court in the Netherlands, and a lot of it is thanks to intervention from statisticians who really had problems with the way the case shook out. We should bring in some of the statisticians that were involved in at least the de Berk case...

**0:02:50.1 CO:** Yes, let's talk to Richard Gill.

**0:02:51.5 Richard Gill:** Okay, well that's a complicated story, I'm afraid most of my story is gonna be complicated stories, but you can stop me when they get too complicated. My name is Richard Gill, I'm emeritus professor at Leiden University in the Netherlands. Okay, the case started in 2001.

**0:03:11.7 CO:** Richard Gill got involved in Lucia de Berk's case after a statistician friend of his read the whistleblower's book about the case and sent it Richard's way. Now he had been aware of the case before that point because it was a very famous murder case in the Netherlands, but he had not thought that the statistics had been mis-used, he didn't know the details and had not thought that it was necessary to get involved.

**0:03:33.4 RG:** And at the time I was working very hard on very different things, I didn't even work in forensic statistics yet.

**0:03:40.4 CO:** He was working on statistical problems in quantum mechanics, and before that, he was working on something called survival analysis. So forensic statistics was absolutely not his main field of research.

**0:03:52.0 RG:** And my wife said to me, "Richard, you should get involved." Well, because I'm a statistician and there were statistics involved and she said, "Richard, do something useful, you know, forget about this quantum stuff, there's a which hunt going on in the Hague."

**0:04:04.1 CO:** The statistics in the original trial turned out to be controversial, so controversial that during the appeal the Dutch judicial system said that they were not relying on statistics in Lucia de Berk's upheld conviction, but after that appeal two whistleblowers wrote a book together. There were people with intimate knowledge of what had happened in the trial because they had a family connection.

**0:04:26.3 RG:** So I got hold of this book and I read it and I got extremely angry. Because we had been told that statistics had nothing to do with the conviction, and that she'd been convicted on the base of irrefutable scientific medical evidence, and we found out this was a lie. I call it a lie. It wasn't true. Statistics was still the core of the case, she was convicted on the basis of a probability calculation, a one in 342 million chance.

**0:05:00.6 CO:** And because he had status and a name as a statistician in the Netherlands, he realized he was in a position to possibly do something about this, and so he jumped in with both feet.

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**0:05:10.4 CO:** Now, what had happened was that when a death was flagged as suspicious on Lucia's shift, the hospital and police started investigating other so-called unexplained incidents at Lucia de Berk had been present at, but they didn't compare this to unexplained incidents found at other hospitals with other nurses. They just looked at Lucia's incidents. And then they contacted other hospitals where Lucia had worked and asked them to re-investigate deaths that maybe weren't entirely explained.

**0:05:41.9 CO:** And so what happened was this whole investigation developed tunnel vision and looked only at this very, very biased sample of cases. Now, we don't know how many unexplained incidents the average nurse might deal with over say a year, and so looking just at the unexplained incidents of one nurse really can't tell us very much, other than that people find it improbable.

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**0:06:03.4 SC:** Another thing they did in the de Berk trial was they miscalculated by multiply the chances from one hospital to another hospital.

**0:06:15.9 CO:** One mistake in the Lucia de Berk trial was the way that the probability figure had been calculated, and what the statistician had done was multiply the improbability by each new hospital. This would mean that any nurse would start to see a growing improbability if they just change jobs.

**0:06:32.0 CO:** If the number of deaths that occurred on a certain nurse's shifts had a one in 10 probability of occurring, and then they go to another hospital and also have a one in 10 probability of that number of deaths, combining the two gives you a probability of one in 100. So of course the probability has not decreased by the nurse changing drops from one hospital to another, but this is the way that the statistic of one in 342 million was calculated in the Lucia de Berk trial.

**0:07:00.8 SC:** This is really a combination of problems that seemed to have made her look so guilty.

**0:07:07.5 CO:** Yeah. And also the statistics influenced the medical evidence, because what happened was that the cases were re-examined and deaths that had previously not been considered suspicious were now re-classified as suspicious purely because Lucia de Berk was present. So you have a correlation between Lucia de Berk and suspicious deaths, but the causation is not running from Lucia de Berk to suspicious death in the way that people thought it might be.

**0:07:33.7 SC:** Wow. So I think you're summarizing very nicely why this one person their conviction was overturned, but this problem is obviously not solved. Because this is something that kind of comes up at hospitals, they see a cluster and start an investigation and you already have the tunnel vision.

**0:07:55.0 CO:** The reason that Royal Statistical Society published this report is because Lucia de Berk is sadly not an isolated case, there have been other cases of overturned convictions and miscarriages of justice when statistics have being misused in murder trials.

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**0:08:13.6 CO:** When we're told a big number like one in 342 million, what does that mean? If you're told there's a one in 342 million chance that Lucia de Berk was present at this many deaths by pure coincidence, people may interpret that as a one in 342 million probability that the Lucia de

Berk is innocent, and statisticians will tell you that those are not the same thing. But we struggle to interpret these numbers in a way that makes sense.

**0:08:52.0 SC:** This Royal Society report that came out, it's actually a set of case studies. Does it also make recommendations for how to avoid these statistical errors and other problems ending up convicting people who might not be guilty?

**0:09:04.8 CO:** The Royal Statistical Society report covers a number of cases of medical murder. Some of them are cases where the conviction has been overturned because of misuse of statistics, among other evidence. Some of them are cases where statisticians are concerned that the defendant did not get a fair trial.

**0:09:23.8 CO:** And in one case, the case of Harold Shipman, there is no doubt really about Shipman's guilt. In fact, he may be the most prolific serial killer ever to have operated in the UK. He may have killed more than 200 of his patients. But statistics do crop up in this case because there have been questions about whether it would be possible to build systems to catch somebody like a doctor with a very high rate of deaths like Harold Shipman.

**0:09:47.0 CO:** So the report covers all of these cases talking about how statistics have been used and misused in these trials, and it also give some recommendations for how everybody involved in the process could make sure that trials for cases like these are fair from start to finish.

**0:10:04.0 SC:** Okay Cathleen, let's move over here into some of the specifics of how this could be fixed. What are some of the ways that this tunnel vision or bias could be prevented?

**0:10:14.3 CO:** The report makes a number of recommendations, and probably the most important recommendation is for investigators to be blinded to what they are looking at when they re-examine cases. So a pathologist studying a case report of a death that may be considered unexplained should not know whether or not that case happened under the watch of a nurse who is under suspicion. That's probably the most immediate and crucial step that can be taken.

**0:10:41.3 Adele Quigley-McBride:** One of the best ways to reduce the possibility that those decisions are going to be swayed by other information is to just remove that information.

**0:10:50.5 CO:** Adele Quigley-McBride is a cognitive bias researcher at Duke University, who does training on a technique called sequential unmasking, which allows analysts to gradually increase their access to information and note any changes in opinion that arise from information that they had previously considered might bias them.

**0:11:08.8 AQ:** So it's like, okay, now you have this other information from the case. Does it change your decision? If so, why? Now you have other information from the police officer, you have information from the defense, all of these things. It might be that at some point they receive information that is justifiably gonna change their mind, but they should explain it and you will know when it happened.

**0:11:32.2 CO:** If you talk to forensic scientists, they will tell you that blinding is not as simple as it sounds from the outside. There are a lot of resource difficulties in blinding forensic analysts to information about the case that they should not be privy to. It requires more staffing because you have to have case managers rather than having information go immediately to analysts.

**0:11:54.6 CO:** Even having software that allows for blinding is not necessarily a given, depending on where the forensics lab is and the kinds of resources it has access to.

**0:12:04.1 AQ:** One of the things that I've really tried to do in my work is go that extra step and try and be like, "Okay, here's how you would do this." So even if you just have one person working in a police station, they could implement this worksheet that I created where it steps them through this unmasking protocol.

**0:12:22.5 AQ:** It's just making people think through each piece of information they have and what impact that might have on their ultimate conclusion. So it's very simple and it looks very simple, but sometimes that's the kind of thing that works really well.

**0:12:39.9 CO:** Going further than that, it's also necessary to understand broader patterns in deaths.

**0:12:45.0 SC:** Yeah, I was really intrigued by some of these other examples of unlikely events that are not agent-based, there's not a person doing this, but a cluster of deaths due to something completely unexpected.

**0:13:00.1 CO:** Yeah. Well this is the difficult thing is that, first of all, humans can perceive a cluster of death, whether it isn't necessarily something statistically anomalous. But then even if there is an actual statistically anomalous cluster of deaths, our minds jump almost immediately to the idea that there must be a person behind it, there must be an agent behind it. And that isn't necessarily the case.

**0:13:23.6 Jane Hutton:** The human eye is very good at recognizing patterns, but what we're not necessarily good at is saying, "Is this pattern unusual?"

**0:13:32.0 CO:** I talked to Jane Hutton at the University of Warwick about how techniques from epidemiology could be adapted to use in these cases.

**0:13:40.4 JH:** What is critical in that is, is it unusual with respect to what? So for example, a cluster of deaths in January in the Northern Hemisphere. Well, in general you get more deaths in winter than summer, so you get things like that. There's a tendency for people to die in the morning.

**0:14:03.8 CO:** And so a nurse who is more of an on-shift in the mornings may be present at more deaths than the nurse who works a different shift pattern. So just the fact that there is a cluster of deaths doesn't automatically mean that there's a person behind it, but that's where our minds go immediately.

**0:14:16.6 CO:** Now, there are already techniques that are used in epidemiology to understand an

unexplained cluster of deaths, and what that entails is for each case of an unexplained death, finding a matched case control, which is a death that has many similar characteristics.

**0:14:31.7 JH:** And what you're trying to do is create the equivalent of a randomized comparison.

**0:14:38.9 SC:** What are some of the biases that are built into us as people that kind of make it hard for us to understand what's happening in these trials that's incorrect, that are kind of fighting against the facts here?

**0:14:52.3 CO:** You've gotta also understand the rarity of these cases. So like the really famous case of this was Sally Clark in the UK who had two infants die of possible Sudden Infant Death Syndrome and a pediatrician testified at her trial that the probability of this happening was I think one in 73 million.

**0:15:12.2 CO:** And statisticians pointed out that you also had to look at the rarity of a double infanticide within a family and compare those two very low probabilities to each other.

**0:15:23.2 JH:** What you're really interested in is given that there have been two deaths, what are the explanations we can consider? And we can consider two cot deaths, which is roughly speaking, "Oh dear, we don't know why they died." Or two deaths from natural causes. Or one death of either kind. Or that the mother has murdered the children.

**0:15:48.8 CO:** It wasn't the probability of double SIDS versus normality, it was the probability of double SIDS versus the probability of double infanticide, and compare those two very lower probabilities to each other.

**0:16:00.7 JH:** So really what you're wanting to say is, given that we know two boys died, what evidence do we have to separate out these possible explanations? Cot deaths are rare, but actually, mothers killing their babies is also rare. So to focus simply on the rarity isn't enough, you have to focus on the comparative rarity, and obviously both things like how common are cot deaths and how common are mothers smothering their babies, are quite difficult to find out, but at least you're beginning to ask the right question.

**0:16:37.1 SC:** Okay, so what's the probability of double infanticide? I have to assume that it's less likely than double SIDS. Double sudden infant death.

**0:16:47.4 CO:** Exactly, yeah. It was less like even a double SIDS. And the point is there may be other explanations as well to put in the mix, but in the case of a serial killer nurse you're not just looking at the improbability of a number of deaths on a nurse's shifts, you're also looking at the improbability of a serial killer nurse.

**0:17:06.7 SC:** Listening to all these different cases, these stories, it's so clear that we want everybody to conduct these investigations in the right way and to think about statistics in the right way. Yes this is super rare, but it's also important because we're talking about people's lives.

**0:17:21.4 CO:** One of the things that's really hit me with the story is it's horrible. It's really horrible. There are points where I've been reporting it where I've been in tears. You're looking at just these case studies, and they're not case studies, they're real people. Lucia lost years of her life in jail, she had a stroke in jail.

**0:17:39.3 CO:** Sally Clark had a failed appeal, and then on the second appeal her conviction was overturned partly because of the problems with statistics, and party because it was discovered that there had been exculpatory evidence withheld from her defense. And she died of alcohol poisoning a couple of years later.

**0:18:06.1 CO:** Her psychiatrist said that she had never recovered from the experience, which had separated her from a third baby. So the miscarriage of justice in that case, partly down to misuse in statistics, was a indescribable tragedy.

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**0:18:28.3 CO:** Lucia de Berk was eventually exonerated, but it took multiple appeals and more than six years of her life in prison. Richard Gill has repeatedly refined his analysis over the years, building in complexity around the different mortality rates nurses might have, based on their own skill choices and work patterns, refining the original flawed statistic of one in 342 million. In a paper published in Chance in 2018, he and his colleagues calculated a probability of one in 49.

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**0:19:04.6 SC:** Thank you so much, Cathleen.

**0:19:08.4 CO:** Thank you.

**0:19:08.5 SC:** Cathleen O'Grady is a contributing correspondent for Science. You can find a link to the story we discussed at science.org/podcast. Stay tuned for my interview with Kari Nadeau. She's the Naddisy Professor of Medicine and Pediatrics at Stanford University. We talk about her Science Translational Medicine review of the current state of allergy science.

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**0:19:32.7 SC:** Allergies are on the rise. Around the world something like 25% to 30% of people are affected. In recent decades we've learned a lot about how our bodies react to allergens, and improvements in diagnosis and treatment are happening, but there's still a lot of challenges in the field. This week in Science Translational Medicine, Kari Nadeau and colleagues summarize the state of allergy science, and boy, is there a lot in here. I'm so excited to talk about it. Hi Kari.

**0:20:05.6 Kari Nadeau:** Hi. How are you?

**0:20:06.3 SC:** Good, I'm good. This number, 25% of people having some kind of allergy, this seems so huge. What are we including in this category?

**0:20:17.3 KN:** Well, it's interesting to know is that at any point in someone's lifetime around the world, this is for the entire global population, that 25% of the globe will have an allergy during their life, and that is a lot. And when we talk about allergy, that can be anywhere from an allergy to a grass pollen, to an allergy to a drug, to an allergy to a venom or a sea urchin sting. So that's what compromises all of allergies. They are quite broad.

**0:20:50.2 SC:** I was really surprised to learn that there are big implications for climate change. On allergy. This is... I was just completely... This is unexpected direction for this to go. Can you talk about some of the ways that our changing climate may be influencing changing rates in allergies.

**0:21:07.0 KN:** So we're talking about allergies, we're talking about allergies and asthma, the first thing that people should know, and this might be of interest to scientists but also their families and the public, is that because of climate changes and plant growth, CO2 increases proliferation of plants, especially grasses and ragweed.

**0:21:25.1 KN:** For example, in New Jersey, where there's a lot of ragweed, there'll be more replant per unit surface area compared to before and that's already happening. People have already published on that, and we talk about that in the article. In addition, because of the increasing temperature around the globe, now there's for example, ragweed plants in places where there never was before because it's warmer. Now we're following the rapid spread of some of these temperate climate type plants that now are inducing more pollen-related allergies around the planet.

**0:22:00.1 KN:** In addition, there are issues like pollution and air potion. If we don't use renewable energy sources, we will increase the particulate matter due to diesel exhaust combustion and petroleum combustion. And both indoor and outdoor pollution has been shown, and this has been published, to exacerbate allergies and asthma.

**0:22:22.5 KN:** So there are many ways that on one component, the toxic chemicals associated with pollution, for which there are many, air pollution has about 200 plus different toxins in it, and that activates alarmin pathways on the skin, which then lead to isotope switching of B cells to make IgE.

**0:22:38.3 KN:** So that's one of the first mechanisms that people should know, that air pollution itself can induce newly allergies and asthma through now validated mechanisms in the immune system.

**0:22:49.8 SC:** And we should also include here changes in weather patterns.

**0:22:55.2 KN:** That's right.

**0:22:56.4 SC:** And forest fires. There's just all kinds of stuff going on with the air around us, which is going to impact our health.

**0:23:01.5 KN:** Yes. And that's so important to know, that it's air, it's soil, it's water, for example, more heavy metals as water becomes more scarce, then we will have to have more and more

recycled water, and that might increase heavy metals in detergents, and those also activate the allergic pathways.

**0:23:19.5 SC:** The point that you make in this piece about detergents and the exposure to surfactants, which can affect the fats and the different oils on the surface of our skin contributing to allergies, was also really interesting.

**0:23:34.0 KN:** With detergents, that's also increasing unfortunately. For example, in places like London where there's a lot of detergents that are used for babies and for adults and children, they're noticing now that 50% of infants born in and around the London area have something called eczema, which is dry skin.

**0:23:53.0 KN:** And when they have dry skin, that actually disrupts their barrier, and that also activates the alarmin pathway to activate allergies. So you see there's a bunch of concomitant issues going on with environmental exposures, detergents, air pollution, pollens increasing, and then finally, we have flooding. That's gonna increase mold, already we've seen mold, algal blooms are increasing inflammation pathways.

**0:24:18.6 KN:** So there are a lot of aspects around climate change, and we talk about them in these categories, but the other thing to know is that in any one day, people could be exposed to heat stress and a wild fire and air pollution all at the same time. So I think as scientists we need to get into the mode of thinking about multiple exposures and how that affects the immune system.

**0:24:38.4 SC:** Yeah, reading through this, I couldn't help thinking about this massive system that we've built around ourselves, the things that we use, what we put into the air, the changing climate, and it's interacting with this other massively complex thing, our immune system and our microbiome. It's really this clash of two universes, and then allergies are there in the middle telling us, reading out to us that something is going on.

**0:25:03.2 KN:** Yeah.

**0:25:04.2 SC:** What do we know about allergies and microbiome? How's our understanding of that changed in the past few decades?

**0:25:09.8 KN:** It's fascinating. There are mouse models showing that if you can change the microbiome in the gut, that can improve your immune system. And visa versa, if you improve your immune system to a more tolerant mouse model, for example, that changes your gut microbiome. So to me it's fascinating at the two are interconnected in some way and talking to each other and we don't know everything, I think there's a bit of neuroimmunology here too.

**0:25:33.8 KN:** But we did a identical twin study where we had identical twins where one was discordant for food allergy, for example. And we did fecal samples. And they were in the same home, same environment, ate the same foods, and what's really interesting is that the twin, they're identical twins, so again, genetics being taken out of this in controlled force and the same thing as sex.

**0:25:56.1 KN:** We found that the healthy twin that didn't have any allergies at all, and this is in children and adults, they had a more diverse microbiome and they had certain bacteria and certain products of those bacteria that seems to be actively enabling health, versus certain bacteria and certain products of those bacteria that seemed to be actively enabling allergy.

**0:26:16.2 SC:** I'm gonna change a little bit of a gear here. One thing that I think many listeners will have noticed in the past maybe few years, is that we are hearing different advice on peanut allergies. So when my daughter was born, we were still on the cusp, like avoid it 'til a certain age.

**0:26:38.3 SC:** Whereas nowadays, parents are kind of regularly exposing their kid to peanuts super early. What did we learn that caused that to happen? And is that advice going to generalize more broadly to other allergies that we see develop in children?

**0:26:52.4 KN:** Now, food allergy is a different subtype that can oftentimes be associated with severe reactions. But with food allergies, that is on the rise, and we think that that is in part due to the fact that more detergents are being used more, more dry skin is occurring for various reasons, less good microbiome is getting into the guts of babies early on.

**0:27:17.9 KN:** And potentially a lack of diverse diet, when in our ancestors, children were oftentimes being given a lot of breast milk, but also a lot of things that either their parents were pre-chewing at the kitchen table and giving to their babies, or just basically mixing up a bunch of different foods and giving it to the baby.

**0:27:33.6 KN:** But now with the current way that a lot of commercial brands have this staged approach to feeding, even though there's no science behind it, that's decreasing the diversity of the diet and that's probably increasing the chances of food allergies. So they've done research around the world, and not just me, but also many other food allergy specialists, to know that those countries that diversified the diet, gave kids early and often different foods to taste, that those are the kids that have the less frequent food allergies, and those children that have the less ezcema also have the less frequent food allergies.

**0:28:09.0 KN:** So it's a great question. Unfortunately, it is on the rise, and it is a serious condition. It's very disabling, you hear about in the news, there are severe reactions that we are working on. But it's all a reflection of how potent the allergic pathways are. Within six minutes, muscles can get activated, histamine released, and someone can anaphylax in a near fatal or fatal reaction. And that's just not for foods, but for drugs, for snake bites. So we know that this is something that humbles scientists and we know to take it really seriously.

**0:28:42.4 SC:** Absolutely. So when I was a kid, I got allergy shots and I'd have to wait some amount of time so that I didn't have a reaction before I went home. And then it actually turned out that moving out of a 150-year-old house, moving to a different state all together, basically eliminated my dust allergy. [chuckle] But I think...

**0:29:00.3 KN:** Wow.

**0:29:00.4 SC:** Yeah, I just don't have it anymore. And it was all the way through high school that I had it. But once I left town it was really... Now, I guess this is more of a question about what the common practice is today, do people still get allergy shots? And what about sublingual treatment, which I started to hear about at the turn of the century, is that growing?

**0:29:20.4 KN:** People still get allergy shots. That is a rather draconian technique, but it is occurring and it is what has been considered by many efficacious. But we're still trying to do our best at doing something better, 'cause as you know, you had to wait in line and wait there. So SLIT is another sort of grade up from that, where it's potentially safer as well as...

**0:29:44.1 SC:** What does that stand for?

**0:29:46.4 KN:** SLIT, sublingual immunotherapy. And that's where you give the same allergens that you might in a shot, but you give them underneath the tongue and they are taken more easily that way. And you can do it at home, you don't have to be at the doctor's office, and that there are now products that are covered by the FDA for that use. So that's good.

**0:30:04.5 KN:** I think there is a lot of hope and promise that new therapies are coming up, Anti-IgE coming up, there's receptor alpha blockade agents to format and that's done really wonders. So I think there's a lot now, over the past 20 years that I've been in the field, to know that all of our discoveries of targeted pathways for allergy, as well as the alarmin pathway, anti-IL 33 for example, but that is resulting in some really I think efficacious and hopefully in the future, very impactful medicines for all allergy and asthma.

**0:30:35.8 SC:** Has there been an interaction between the coronavirus pandemic and allergies?

**0:30:41.5 KN:** Yeah, Sarah, great questions. So it was like an experiment of nature, right? We thought, "Awesome. There's gonna be less influenza, less RSV, less Rhino virus, so the kids would have less asthma and allergies." And that in general was true, that first year that we locked down, we did not have as many people coming into the clinic for asthma exacerbated issues, but who knows what was happening at home, that's the hard part.

**0:31:02.9 KN:** And a lot of pollution is indoor too, that's the other problem. So kids were getting exposed to more indoor air pollution when they were at home compared to the schools, which tend to have less indoor air pollution than home because there's not like stoves. And there's an article that just came out, that indoor air pollution increases asthma rates in children about 12%.

**0:31:22.7 KN:** So on the whole we were hoping that asthma, you would see a blip during COVID, but it didn't. And now, unfortunately, again, back to the immune system getting educated, we think that because a lot of kids didn't get exposed to typical... You know this story already. Then they didn't exposed to normal variance of RSV and Rhino virus and different viruses, now that they're coming back into school now it's more severe.

**0:31:46.9 SC:** It's a crash course. Yeah, crash course for the immune system.

**0:31:48.3 KN:** Yeah, it's a crash course. You got it.

**0:31:52.9 SC:** Sounds really interesting.

**0:31:54.4 KN:** So yeah, we were hoping, but that's not the case. They were still exposed. And now we're gonna do a study to see whether or not for asthma and allergies, this is a big group, I love collaborating on this because you need big data, big science, big cohort. So all of Europe is coming together, including me here in the United States, to work to see to what extent COVID changed the outcome long-term of allergies and asthma in children.

**0:32:17.3 SC:** We've talked a little bit about an increase in understanding, increase in medications that address this, what are some of the drivers of increasing allergies. What can be done to kind of slow this rise in allergies? Are there any kind of more structural approaches as opposed to use a different kind of detergent or feed your kid little different things when they're a baby? What more holistically can be done to kinda slow the rise in allergies?

**0:32:44.7 KN:** On a global level, think about the public health level, how do we really as a community also help each other, help vulnerable populations find out where there are certain vulnerabilities in the immune system of either certain groups of individuals, like older or younger individuals, but then think about it within the context of climate change, how do we mitigate and adapt to climate change?

**0:33:06.7 KN:** How do we make sure as scientists we have a very powerful voice and that we can speak with data in mind and say now, with a lot of valued literature that's already in existence, there's tons of science to say on the good side, that if we can put filters into buses or we can use electrified cars, if we can use better monitoring of water pollution, that those data now have become available, and they have shown that by having good policies there's co-benefits of health, co-benefits to your immune system and co-benefits to your mental capabilities, but also who co-benefits to the economy...

**0:33:44.0 SC:** Yeah, it'd be nice to deter climate change and also help people stay healthy.

**0:33:49.4 KN:** Yes, exactly.

**0:33:50.1 SC:** What are some of the challenges, the puzzles that people working in this field are still faced with?

**0:33:56.4 KN:** I think there are some big questions that we alluded to. For example, how do we find biomarkers that can serve as a signature for what cumulative exposures any one individual has been exposed to over their lifetime? Is there a way to look at the DNA and epigenetics of certain immune cells to know, "Ah, that person was exposed to arsenic when they were little." Or, "That person was exposed to a lot of air pollution."

**0:34:23.3 KN:** And the reason why those biomarkers are important is because if a policy does come

up, you could go back and say, "Alright, let's test the blood, let's test that biomarker." Because if a policy occurs that can help with climate change, then you wanna test if the person's health is better.

**0:34:37.0 KN:** And perhaps these biomarkers are one of the first ones to test, rather than waiting months to see if they worsen their asthma or have their asthma get better. So that we can look at biomarkers in the immune system as a bellwether, as a canary in the coal mine as it were, to see if what we're doing in terms of decreasing toxic exposures, if that's helping the immune system, and then eventually also looking at health outcomes. So I think that's gonna be a challenge, but I think it's doable.

**0:35:04.7 SC:** Super interesting. Actually finding out what exactly someone is allergic to is still a really big problem. Why is it so hard to figure out?

**0:35:12.0 KN:** Yes, that's another big challenge. We also need to get better diagnostics, diagnostics that can be faster. But on that regard, we are working on that. There are many diagnostic companies now moving forward in the area of allergies, especially severe allergy, so that you can have point-of care testing so that this can be available at your doctor's office with a mere prick to your finger, and then one drop of blood can be used to analyze quickly your allergies, but also the extent of your allergies, how severe they might be. So hope is on the way.

[chuckle]

**0:35:44.9 SC:** Thank you so much, Kari.

**0:35:48.5 KN:** Thank you so much. Really great to talk to you. Have a great day.

**0:35:50.0 SC:** Kari Nadeau is the Nadissy Professor of Medicine and Pediatrics at Stanford University. You can find a link to the Science Translational Medicine review we discussed at science.org/podcast.

[music]

**0:36:06.2 SC:** And that concludes this edition of the Science Podcast. If you have any comments or suggestions, write to us at sciencepodcast.aaas.org. Or better yet, take our audience survey at science.org/podcast. Again, that's science.org/podcast, there'll be a pop-up or you can click on a link in our episode description.

**0:36:25.5 SC:** You can listen to the show on the Science website or search for Science Magazine on any podcasting app. This show was edited produced by me, Sarah Crespi. Our amazing segment on medical murders was produced by Kevin McLean, with sound designed by James Roland. We also had production help from Podigy and Megan Cantwell. Jeffrey Cook composed the music.

**0:36:48.3 SC:** On behalf of Science and its publisher, AAAS, thanks for joining us.