

[Sarah Alger] Welcome to Proto, a podcast that explores the frontiers of medicine. And welcome to Diagnosis, a series about the past, present, and future of a medical cornerstone. I'm Sarah Alger.

[Eric S. Rosenberg] And I'm Dr. Eric Rosenberg. The pioneering physician William Osler once wrote that in medicine, diagnosis, not drugging, is our chief weapon of offense. While the public spotlight tends to focus on treatments and cures, some of our most important advances are in how we come to recognize disease in the first place.

[SA] Our upcoming series will look at all aspects of diagnosis, how it happens, how it can be shaped by history or human bias, and how a diagnosis can itself affect a patient's health.

[ER] Today we'll be talking about the Case Records of the Massachusetts General Hospital, one of the oldest and most notable efforts to make public the process of diagnosis in all its blind alleys and surprising turns.

[SA] Diagnosis, case by case, coming up on this episode of the Proto podcast, brought to you by Massachusetts General Hospital.

Walter B. Cannon was a Harvard Medical School student in 1898. His lessons about the human body consisted of four-hour daily lectures that he found "dreary and benumbing." Cannon envied his roommate, a student at Harvard Law School, whose classes were taught through real legal cases provided by his teachers. At Cannon's urging one professor at the medical school, Dr. Richard C. Cabot, adopted what came to be known as the case method, in which students did discuss "actual cases of disease". The practice soon broadened beyond the school and before long Cabot and his colleagues were mailing four so-called case records per week to more than 800 subscribers. These records of patients would eventually become a fixture of the New England Journal of Medicine, where they have appeared consistently since 1923.

A main feature of the case records then and now is their focus on the act of diagnosis and the curious turns it can take. Each of these articles begins with a patient and their symptoms. Step by step the records tease out information in the manner of a mystery novel, challenging the reader to piece together the disease at the root of the problem. Dr. Eric Rosenberg has been the editor of the Case Records since 2014. He's also an infectious disease physician at Mass General Hospital and the director of the Clinical Microbiology lab there. We are honored to have him here today. Dr. Rosenberg, welcome.

[ER] Thank you, Sarah.

[SA] About a decade ago there was a well-publicized competition called the Tri-Corder Challenge. The organizers would give \$10 million to anyone who could recreate this fictional tool from *Star Trek*, which could be zapped at a patient for an instant diagnosis. Are we anywhere close to that kind of digital analysis with current diagnostic technology? Can you foresee a time when a physician's diagnostic skills will no longer be needed?

[ER] Sarah, over the course of my medical career, which dates back to the 1980s, I've seen dramatic changes in the technology that we use to make diagnoses. With that said, it also presents a different kind of challenge to a physician's ability to make a diagnosis because now all of a sudden we have so much more information that we have to sort through and contend with. So even though our diagnostic abilities and technology associated with them are so much better than ever before, it is a new challenge to us because now we just have way more data points that we then have to synthesize in the human brain to make sense of what's actually going on with the patient.

[SA] And so your feeling is that, say artificial intelligence or any other tool like that has a long way to go to do some of that synthesis?

[ER] Artificial intelligence has come a really long way and I think that it will play an increasingly major role in our ability to provide better diagnostic abilities. But we're still not there yet. And you know, if we really think about it, the most complex machine known on the planet is the human brain. And so any artificial intelligence has a long way to go to compete with the human brain.

[SA] Can you tell us the core mission of Case Records?

[ER] The core mission of the case records is education. And so our challenge is to present real clinical cases and teach our readers through a discussion how to clinically reason your way to solving a very complex problem and eventually establish a diagnosis. So whenever we're considering which cases are appropriate to present as a Case Records of the Massachusetts General Hospital, the first question that we always ask is, what are the teaching points that we want to convey through the use of this type of case?

[SA] In one sense, the Case Records show the art of diagnosis, twisting journeys to understand what's ailing a patient. Can you tell us about a few favorite examples or two from your tenure?

[ER] That is a really tough question because these cases that we use are really the best of the best and oftentimes the most challenging, interesting and captivating of all the cases that we see. So in a sense, we cherry pick these cases to present to others to convey an educational message. I'm a bit biased as an infectious disease physician and as a clinical microbiologist. My favorite always tend to be those that involve an infectious disease. Although we do present cases throughout all disciplines of medicine, from pediatrics to psychiatry, surgery, obstetrics/gynecology, medicine, et cetera, and all the specialties of them. But if I really had to pick my favorite cases, I think the first one that I'll always remember was a case that we published in 2009 when a young woman who happened to be a college student at a university in New England presented in transfer from a smaller hospital, critically ill, really on her deathbed from what appeared to be an overwhelming infection involving the gastrointestinal tract. And after a long, convoluted story, lots of twist and turns, we made a diagnosis of gastrointestinal anthrax.

[SA] Wow.

[ER] We've known about anthrax, of course, for many, many, many years. But it really resurfaced in, you know, in public attention after 9/11, where anthrax was, you know, the big concern was that anthrax can be used as an agent of bioterrorism. So when this young woman had anthrax growing in her blood cultures, not only we were on one hand relieved to have an answer because then we knew how to treat her and make her better--and by the way, she did great--but on the other hand, we had to figure out where did it come from, because now this is not something that we haven't seen this at Mass General in many, many years and it's not something that we take lightly because of its connection with bioterrorism. Interestingly, she had naturally acquired anthrax, and anthrax is a bacterium that is present naturally in certain soils. And also there's an association between animal hides.

[SA] Oh.

[ER] And she was a bongo drum player and was in a bongo drumming circle at her university. And the hide that was covering her bongo drum had anthrax that was imported from somewhere else in the world. And that's how she got it. And so that was quite an incredible and memorable story. Although we have many equally captivating cases that we discuss.

[SA] If I may leap ahead to a more recent case, also related to infectious disease. I believe I have this right, the first U.S. case of monkeypox was identified at Mass General. Can you tell us about that case?

[ER] Absolutely. So that is correct. Um, whenever you have a potential outbreak or epidemic, there's always a first. And even though the patient whom we had the privilege of taking care of at MGH wasn't the first patient with monkeypox during this most recent outbreak, he was the first patient identified in the United States and he just happened to come to Mass General for care. And so he is a 31-year-old

man who two weeks prior to coming to Mass General, traveled to somewhere in southeastern Canada and that's where he was sexually exposed to the monkeypox virus, which causes the disease monkeypox. And he presented to us with genital ulcer, rectal pain and skin lesions. And because this was the first case, a lot of people were scratching their head about, Well what does this gentleman have? Because all the traditional tests that we do, things for herpes simplex virus and varicella virus, the virus that causes chickenpox, all of those tests as well as other sexually transmitted disease tests were negative.

And so one really astute, super smart clinician thought this lesion looks like monkey pox or a pox virus. And so she went ahead and contacted our state epidemiologist, who then in conjunction with the state Department of Public Health and the CDC performed a monkeypox test and it turned out he was patient number one. So that sort of a case and that sort of a story is a perfect not only diagnostic challenge, but a perfect case for our core mission at the Case Records, which is using a case like that to teach other physicians around the world about what we know about monkeypox.

[SA] Are there recurrent challenges to diagnosis that crop up in the case records? And has the nature of those diagnostic challenges changed over time?

[ER] Because every patient presents slightly differently from the person with the same disease who presented before them, making a diagnosis is often not straightforward. And we're used to getting curveballs thrown at us all the time. And that's, honestly, that's one of the fun parts of being a physician is you never really know what twist or turn your patient's gonna take you. And so the recurrent theme is that everybody presents a little bit differently. And one of the challenges, especially in the setting of the Case Records, is that traditionally the Case Records were always based on a hard diagnosis that was either made at autopsy or by a biopsy of a tissue. And the Case Records originally arose out of autopsies. So unfortunately to be the subject in a Case Records, you had to have died and have an autopsy. So the answer was established with 100% certainty. Now thank God we don't have to rely on our patients passing away in order to learn from them. But one of the challenges is we don't have that kind of hard information sometimes to make a diagnosis. So for example, somebody with a psychiatric illness really doesn't have a physical blood test or biopsy that we can look at. It's really using criteria that experts weave together in order to say you most likely have this particular diagnosis. So that's how things are sort of a moving target and, and have changed.

[SA] Part of the origin story of the Case Records came out of what were called clinicopathological conferences, which I gather are still held. So what I gather is that historically there could be sort of a right answer because of those results. But it sounds like today not necessarily so, is that right?

[ER] Not exactly. And in fact, one of our criteria to use a case is that we have to be very confident that we have the right answer because it would be a really bad thing to start teaching others about something when we haven't even nailed down the diagnosis ourselves. So one of the criteria is you have to have a right answer. The moving target is how you get to that right answer. Historically it was through autopsy; for many years it was through autopsy and the use of biopsy. But now it could be a blood test, it could be a genetic test, it could be a microbiological culture, or it could be published criteria in which somebody's symptoms match up to you, establishing a diagnosis. But the first question that we have to address is, is this diagnosis firm? Because we wouldn't move a case forward without knowing for sure what we're presenting.

[SA] Oh, that's interesting. Now the Case Records aren't just for new physicians. How might the same physician read the Case Records differently at different stages of their career?

[ER] That's a real challenge for us because in one manuscript, we have to put forward, you know, something for all readers. And so we need to make sure that we're incorporating teaching points for medical students, residents and fellows, young independent physicians as well as very seasoned

clinicians. And so we try to put a little bit of something for everybody. And the other really hard task that we have is to make the topic of a case and the teaching that we provide relevant, not just to somebody who is an infectious disease physician or is a cardiologist or a kidney doctor, but we try to make our cases appealing to all health care providers. So it's not uncommon for us to get comments from, you know, somebody who's an obstetrician commenting on a case about a teenager with lupus. And so our challenge is to appeal to all levels of students because we think of all physicians think of themselves as perpetual students because we're always learning.

So we have to appeal to all students as well as all disciplines within medicine. And the one unifying place that I think most physicians go to since they're medical student on are the Case Records of the Massachusetts General Hospital because we were the first place to do this sort of teaching exercise, which is called the clinicopathological conference, or CPC. And this has been something that over the years has been mimicked in hospitals, academic medical centers, medical schools throughout the world. And in fact, I have, I receive letters on a fairly frequent basis from individuals trying to solve our cases in groups, in different medical schools, in different countries all over the world. And it's really quite rewarding to, to see the impact that we are potentially making on, on people learning alongside of us throughout, throughout the globe.

[SA] That's terrific. This might be a good segue to this sort of what seems to have become the popular appeal of trying to figure out a diagnosis. You know, there's the diagnosis column in the New York Times in which Lisa Sanders presents a case and invites readers to make their best guess about the cause. Why do you think even just the general public enjoys this format so much?

[ER] I think everybody loves a good whodunnit and a good mystery. Some of our very best cases are medical mysteries, and that's probably what put the hook in somebody like me as a medical student because I would read these cases that I had no chance of answering on my own as a student, but I got to participate in a paper version of a medical mystery. And it, it just made all the difference to me as a student when I was in training as a resident. The hospital, the academic medical center that I was at, had a conference that we called the COW, which was the Case of the Week. And that was essentially a mimic of the clinical pathological conference, which is originated here at Mass General.

[SA] I should add that under your watch the Case Records has added a quiz component, which also seems to be wildly popular.

[ER] It is surprisingly, but maybe not surprisingly very popular. One of the biggest challenges that we have is this is a hundred-year-old tradition that really hasn't changed much. I mean the, other than new technology and just a load of information that wasn't in existence a hundred years ago, that is every day medical speak now. Now the process of how you clinically reason your way to the right answer, that really hasn't changed. So the CPCs or the Case Records of the Massachusetts General Hospital really haven't changed much. But one of the key challenges to us is how do you take this 100-year-old tradition and make it relevant in a format that people use and learn from today. Because honestly it's not holding a paper journal anymore. Everything is pretty much moved to online learning, at least with younger students and trainees. So one of the things that we did to try to catch people and sort of pull them into reading these cases was to present the case online two weeks in advance and we would set up a poll asking people what they thought was the right answer.

And there's a blog site where people blog why they picked a given, you know, choice over another. And we give them six choices and ask them, pick which diagnosis you think is most likely. And then that's all done online. And then two weeks later the case is published officially in the New England Journal of Medicine and it appears also simultaneously online. What's been fascinating for me is, first of all, the number of people who participate is beyond, you know, my wildest dreams. On occasion we are the number one most popular section of the New England Journal online. It doesn't happen every week. It

happens when we have a particularly intriguing case that draws a lot of people. What's also really interesting and was a big revelation to me, is who's actually reading these cases?

Because when somebody takes our online challenge, you can actually see what country they're from, how they identify themselves in terms of their specialty and their level of training. And there are people who participate from almost every single country around the world. And it, it was shocking to me because this is sort of something that I do with a very close knit, you know, group of associate editors. And I never really thought, you know, what happens around my little office when we're planning all these cases and editing them, it's really hard to see the impact that you have and the ripples that you have across the, the world, but it happens.

[SA] That's very cool. Your immediate predecessor, Dr. Nancy Harris, said: "Medical school trains you to think like a researcher but the Case Records train you to think like a doctor." What did she mean by that?

[ER] I think what Dr. Harris meant is that in medical school there's a lot of information that is presented to students, but it's very compartmentalized. So you might spend weeks learning about the normal function of the lung and then you may spend more weeks learning about what happens to the lung and disease. And that's all taught in the context of a very discrete unit. And it's also seemingly unrelated to the rest of the body because you're being taught lung physiology and you learn about famous experiments that researchers have done to figure out how the lung functions and how the lung becomes abnormal in disease states.

The Case Records is really that on steroids because you're not just thinking about the lung, we're providing information that may be relevant to the diagnosis, may be a complete red herring. We're providing all the facts surrounding what happened to a particular patient. And you have to think like a doctor. You can't think about, well this is the lung compartmentalized in a separate little box. You have to think about the relationship of the lung to the heart, the lung to the kidney, the relationship of that person in their social setting, what their blood tests mean, what their x-rays show. And so that's what doctors do and I think that's how these Case Records are much more appealing to people who want to think like a doctor rather than the stuff that we're taught in medical school, which is really important and the building blocks, but they're just the building blocks and I think the CPCs are the whole house.

[SA] Dr. Rosenberg, thank you so much.

[ER] Thank you, Sarah.

[SA] And listeners, thank you for tuning in to the Proto podcast. Today's podcast was produced by Joshua Krisch, Bradley Klein, and Jason Anthony. Thanks also to our technical directors, Adam Keller and Nathan Marcus. Subscribe to the Proto podcast on iTunes and Stitcher and follow us on Facebook, Twitter, and Instagram. Stay safe and see you next time.