Sarah Alger: Welcome to Proto, a podcast that explores the frontiers of medicine. I'm Sarah Alger.

Dr. Paul Firth: And I'm Dr. Paul Firth. Not every patient we study is someone we can actually meet face-to-face. One subset of medical research looks at cases from history, and tries to puzzle out what happened.

Sarah Alger: This kind of sleuthing has led, for instance, to new insights in the death of writer Edgar Allen Poe. Dr. Ryan Boyd at Lancaster University has a new theory, despite working with the slimmest of medical records.

Dr. Ryan Boyd: There wasn't anything like an extensive autopsy or post-mortem, if there even was ever a death certificate, it certainly doesn't exist anymore.

Sarah Alger: One of the most notable discoveries this year concerns Sir Ernest Shackleton. A re-examination of the Antarctic explorer's life shows that we may need to rewrite current theories of his health and his untimely death.

Dr. Paul Firth: Delayed diagnosis, coming up on this episode of the Proto podcast, brought to you by Massachusetts General Hospital.

Sarah Alger: The age of Antarctic exploration has no more heroic figure than Sir Ernest Shackleton. The British adventurer was part of the first overland explorations of Antarctica in 1901, traveling nearly a thousand miles by foot and sled over three months. Shackleton set out again in 1907, to try to reach the South Pole, and came within 115 miles of his goal before he had to walk back to the coast, 800 miles away. He is perhaps best known, however, for his expedition in 1914. Off the coast of Antarctica, his ship, the Endurance, became trapped in the ice. For more than a year, Shackleton and his 28 crew members survived in that frozen landscape, eventually watching their ship be crushed. They made their way back to a nearby island in lifeboats, and Shackleton himself led a five man crew that sailed for 16 days over the open sea to find help. In the end, not a single one of his crew members was lost.

But for all of his stamina, Shackleton suffered from curiously poor health. During his initial 1901 mission, Shackleton was so short winded that the physicians noted, "The least exertion makes him breathless." During the next trip, he displayed a worrying "pulmonary systolic murmur." He died at the age of 47 from a heart attack. Several explanations have been advanced for these symptoms and for his untimely death. A recent paper in the Journal of Medical Biography advances a fascinating new theory. To discuss it, I'm here with lead author, Dr. Paul G. Firth, head of the Division of Community and Global Health in the Department of Anesthesia, Critical Care and Pain Medicine at Massachusetts General Hospital. Dr. Firth, welcome.

Dr. Paul Firth: Thank you, Sarah.

Sarah Alger: It sounds as if Antarctica was particularly punishing to Shackleton. Why do you think he kept going back?

Dr. Paul Firth: Well, there was probably a variety of reasons, but perhaps chief among them was the excitement of exploration. He went on his first expedition and he got a taste for exploring the unknown, for discovering new things. I think there was this excitement of finding new things that people have never been before, which kept him going back.

Sarah Alger: What was your particular interest in exploring his case?

Dr. Paul Firth: Well, I read some of his stories of his life, of course like many other people, was captivated, but what particularly interested me was these little aspects of medical history, and as a doctor and an academic researcher, of course, these intrigued me, and I set out on my own little journey of exploration to try and explore these parts of the story which were unknown.

Sarah Alger: As you started to look into Shackleton's health, what were the prevailing medical theories?

Dr. Paul Firth: Well, on his first expedition to the Antarctic in 1901, he developed a very severe shortness of breath, and what was thought to be a heart condition. And at the time, they had been eating preserved rations during the winter and on their trip towards the South Pole. And he and his companions developed early signs of scurvy. Now scurvy is a deficiency disease, a nutritional disorder due to a lack of vitamin C. And if you eat preserved food which contains no vitamins for a long period of time, you start with bleeding gums and loose joints and signs of vitamin C deficiency. And so this was what they thought was causing his heart problem, they thought his heart was suffering from whatever the underlying causes of scurvy were.

The second theory, which was at the time and also later, was the fact Shackleton also had an underlying heart condition, and so he was initially weakened, so when he started to get scurvy, his heart deteriorated. One theory of what was wrong with his heart was that he had a hole in his heart, he had a structural defect, he had an underlying atrial septal defect. And while he was in the Antarctic, this not only was present, but it basically triggered acute heart arrhythmias.

So there was these two theories, one a vitamin C deficiency or scurvy, and secondarily, possibly was an underlying or coexisting heart condition.

Sarah Alger: But you have a different conclusion, can you explain it?

Dr. Paul Firth: Well, I looked at these two theories, the theory of scurvy and the theory of underlying structure defects, and neither of them really seem to fit all the picture of his condition. His condition first presented when they were trying to get to the South Pole, and they'd been out for a couple of months, and eating preserved food. And at this point, he and his two companions both developed slight symptoms of scurvy, but after a good point, he also started getting very, very short of breath and appeared to develop cardiac problems.

But I'm more astounded at all the other explorers, both on an expedition and others, you start to see other symptoms, and some of the people have very similar symptoms as well. So to attribute it to a heart condition would mean that all these other explorers had heart conditions as well, which seems very unlikely.

In fact, what one of the doctors considered was a disease called beriberi, which is a disease of thiamine deficiency. And so, when they were eating all this preserved food, without fresh food, on these long expeditions across Antarctica, they would have been short of a whole variety of vitamins. And so since his condition presented at a point where we know he had severe nutritional deficiency, perhaps it wasn't about a lack of vitamin C, in other words, scurvy, perhaps it was a lack of a different vitamin, vitamin B1, or thiamine deficiency. In other words, he may have been suffering from beriberi rather than scurvy.

Sarah Alger: And so why wouldn't physicians of the time have made that diagnosis?

Dr. Paul Firth: Well there was a number of reasons, for one, they didn't have an overlying unifying theory of nutritional disorders. They didn't know exactly what caused scurvy, and whether there were actually other things which could lead to nutritional deficiencies. They hadn't conceptualized the idea of the vitamins yet. Secondarily, of course, they were thinking scurvy. He had symptoms of scurvy, and so they were trying to attribute all of his symptoms to this one condition. And then the third reason was that beriberi thiamine deficiency wasn't really a condition which was associated with the Arctic or the Antarctic. It was something which presented in the Far East, in the Pacific, on long voyages there. And so really they weren't expecting to see this nutrition deficiency in the Antarctic.

Sarah Alger: So what kind of information did you have to go on? I can't help but think that this is a death on a remote island in the Southern Atlantic almost a hundred years ago.

Dr. Paul Firth: Yes, it was quite tricky to diagnose it. And so what I had to do is piece together lots of pieces of information. If one just looks at the accounts of Shackleton himself, there's not enough information there to tell you what was wrong with him. But if one looks at all the other accounts, the diaries of the other explorers, you start to see other symptoms and signs describing the other explorers. If you piece all of these signs and symptoms and presentations together, you can come up with a unified diagnosis of beriberi affecting all these explorers.

Sarah Alger: Can you tell us, on this work, who were your collaborators, and what the division of work was there?

Dr. Paul Firth: Well, I'm a pediatric anesthesiologist, so I teamed up with Oscar Benevidez, who's a pediatric cardiologist, and Lori Fichner, who's a pediatric nutritionist. And essentially, I had interest in the Antarctic and the history of it, so I had quite a detailed knowledge of it, but I'm not a cardiologist, and there was this question of this hole in the heart, this congenital heart defect. I'm also not a nutritionist, and I was chasing these theories of nutritional deficiency of beriberi and scurvy, and so while I assembled all the data, I then came up with these theories, but I put it to my cardiology and nutritional colleagues to see whether they agreed with it. And both of them came up with some good ideas and suggestions which strengthened our theory.

Sarah Alger: So I should mention that one of my other roles is at the Russell Museum of Medical History and Innovation at Mass General Hospital, and I would be remiss in not mentioning that our most popular lecture ever was actually delivered by you, about Shackleton. Can you pinpoint why people are just so fascinated with Shackleton?

Dr. Paul Firth: I think basically it's the human face to it, it's the human face of striving in the face of difficulty, of not giving up, of sticking together and overcoming things. He has stories which endure because of the strength of the individuals involved, of the characters and the people, and what they tell us about ourselves.

Sarah Alger: All right. Well, thank you, Dr. Firth. Coming up, the death of writer Edgar Allen Poe is as mysterious as any of his macabre short stories. Are we any closer to understanding it?

Dr. Paul Firth: That's next, on the Proto podcast, brought to you by Massachusetts General Hospital.

Sarah Alger: On October 3rd, 1849, the writer Edgar Allen Poe was found delirious in a Baltimore gutter. He was hundreds of miles from home, and wearing another man's clothes. Poe never regained enough consciousness to explain what had happened, and four days later, he died. It remains a mystifying capstone to one of the greatest lives in American literature. Medical historians have come up with dozens of theories, a brain tumor, alcohol withdrawal, syphilis, and carbon monoxide poisoning from a leaky gas fixture. One idea that hasn't gotten a lot of attention, however, is the notion that Poe died as the result of trying to take his own life. A paper published last year in the Journal of Affective Disorders offers a fascinating new data point. Here with more is Proto editor Jason Anthony speaking with Dr. Ryan Boyd, Lecturer of Behavioral Analytics at Lancaster University in the United Kingdom.

Jason Anthony: Welcome to the podcast, Dr. Boyd.

Dr. Ryan Boyd: Hi, thanks for having me.

Jason Anthony: Now your team looked at more than 400 of Edgar Allen Poe's works, his poems, his short stories, personal letters. You were looking to see if there was "a pattern of linguistic clues consistent with depression and suicidal cognition." Can you tell us a little more of how that search worked?

Dr. Ryan Boyd: Sure. So, one of the things that we know from decades of research in psychology is that people's words, the way that they talk, the way that they write, provide a lot of really rich information about how they think, feel, and behave. Now what this means is that we can take a data set of a person's language and measure a lot of different parts of the person's psychology, especially if the data set is large enough. Now this isn't what we would say is a Freudian type of language analysis, where we would obsess over every little word that a person uses, or look for hidden meaning or anything like that. Instead, what we're doing is we're using computers to count psychologically meaningful words. So what we can do is we can measure a lot of really subtle statistical patterns in what people talk about, and this tells us a lot about how they think and experience the world.

Jason Anthony: And that can be used to look for patterns of mental illness?

Dr. Ryan Boyd: Absolutely, so this depends a lot on what it is that we're trying to study. So if we're trying to understand how socially enmeshed someone is, we might look for affiliation words. When we're looking at something like depression, there's this whole constellation of words that tell us about the psychological states that go along with depression. So, for example, we know that people who are suffering from depression tend to self reference at very high rates, some people have even described depression as a disease of self-focus. So what we can do is we can use a computer to look for how often a person is self-referencing. Or another type of language associated with depression is what we call cognitive processing words, so people who are depressed tend to use a lot of words that are indicative of mental efforts or cognitive load. So where it's like, think and maybe, and things like that, and essentially it takes people who are depressed more energy, more mental energy, to work through even basic thought processes, and this is something that spills over into language, and we can capture that computationally.

Jason Anthony: As I understand it, this isn't the first time this has been tried on historical figures. Teams have looked at other possible suicides, one team looked at the death of Marilyn Monroe, and by looking at her writings, they spotted a pattern of profound, psychological duress. What made Edgar Allen Poe a person that you would try this approach with?

Dr. Ryan Boyd: So I think, like most people, I knew that Edgar Allen Poe's death was something of a mystery, it's kind of a weird cocktail party trivia type of information. So he was found in another town, completely delirious, wearing someone else's clothes, it's just a really strange case, but I never thought about it too much more deeply than that. So one of the issues here is that there's really very little or practically no objective data on his death. So we have reports about what type of condition Poe was found in, but there wasn't anything like an extensive autopsy or post-mortem, if there even was ever a death certificate, it certainly doesn't exist anymore.

Now a former student of mine who did this work with me, Hannah Dean, she raised the question during a lab meeting as to whether it was possible to tell whether he committed suicide, and I had never even thought about it before, to be honest. And so we did some background work and we started digging into the details of Edgar Allen Poe's life, and we found that basically his entire life, his circumstances, the behaviors that he engaged in throughout his life, it was basically like a checklist of suicide risks. He was a male, he had a history of substance abuse, depression, and substance abuse ran in his family, and he even had at least one previous attempt at suicide.

And so it occurred to us that this was a hypothesis that we could actually test with data. So one of the big issues around his death was that there was no data that could be looked at objectively, everything was just speculation up to that point. But, given that we have ways of determining depression from language data, and we have this really rich history of language data from Poe, we could actually go and do an objective test of his mental state.

Jason Anthony: So you plotted his works chronologically, and you compared each one against a "depression metric." And as you looked across the span of his adult life, you found that some of those depressive episodes were strongest during the years of his greatest success. Why do you think that was?

Dr. Ryan Boyd: So there are a lot of reasons we can speculate why he seemed to be more acutely depressed during his years of greatest success. So there are a couple of things that are going on during these periods in his life. Now, one of the biggest clues that we have is that Poe had a really long and complicated relationship with money and success. So he spent a rather large portion of his life in really abject poverty. And this resulted in, I should say, Poe's poverty resulted largely from an especially strange relationship with his adoptive father. So money was a really hot point of tension between the two of them.

Now we suspect that Poe, when he did start to become really successful, that he experienced something of a disconnect. So he achieved fame on multiple occasions, so in 1845, The Raven was published and it basically granted him overnight success. But there really wasn't any major financial benefit that came with that fame. So he got the fame, but he didn't really get the fortune. So he can, in a way, be seen as a very early American example of someone who really struggled with the ups and downs of fame and success.

Now the second thing that was going on in Poe's life during this time period is that his success, his fame, overlaps with a period of time where his wife was also slowly dying from tuberculosis, and this really deeply bothered him. He found it particularly difficult to cope with her illness.

Jason Anthony: So does your data offer strong support of depression as a cause of death for Edgar Allen Poe?

Dr. Ryan Boyd: So when we look at the data we can definitely say that he was in, or at least at the beginning of, a rather major depressive episode in the final months of his life. Now we don't have super clear evidence that depression was the cause of death, but we do have evidence that it was almost certainly a contributing factor to his death. So we don't have a pattern in the data that is just waiving a huge flag that says Poe clearly committed suicide.

Instead, it's more likely that his major depressive episode motivated what we would say is a pattern or a constellation of behaviors that led to his death. For example, if he was experiencing a particularly strong depressive episode that could have led to an especially extreme binge drinking session, and it almost certainly would have impaired his reasoning and decision making skills, whether there was alcohol involved or not. So, if he was in fact experiencing a very pronounced episode of depression, this could have made him perhaps less wary or cautious of potentially dangerous or life-threatening situations that led to his death.

Jason Anthony: And are there plans to use this approach for other historical figures?

Dr. Ryan Boyd: There's always plans. Stay tuned.

Jason Anthony: Thank you much for joining us, Dr. Boyd.

Dr. Ryan Boyd: Thank you so much for having me.

Sarah Alger: I'm here with Dr. Paul Firth. Dr. Firth, I wonder if I could ask you a few final questions. The University of Maryland School of Medicine hosts an annual conference in which they look at cold cases like this. Presenters have recently offered new diagnoses for Charles Darwin, Vladimir Lenin, and the Roman Emperor Claudius. So can you tell us other benefits to medicine for this kind of work?

Dr. Paul Firth: Absolutely. I think they add life and excitement to dry medical practice. I think when we look at individuals, we identify with them, and when we see their struggles, we can see ourselves in them. I think it's a very invigorating part of medical science.

Sarah Alger: Edgar Allen Poe is also the inventor of the modern detective story. I imagine there's also a kind of satisfaction in solving a who done it like this?

Dr. Paul Firth: Oh, absolutely. When one's pouring through these old dry and ancient discussions of Antarctic exploration and suddenly you come across these clues, these bits of information, that's very exciting. And then when you start to assemble these little bits and suddenly the picture appears, the puzzle starts to show a recognizable pattern, it's very, very satisfying and very, very rewarding.

Sarah Alger: So do you think we've arrived at a final medical diagnosis for Shackleton?

Dr. Paul Firth: Well, personally, I think so, but I'm a little biased.

Sarah Alger: Dr. Firth, thank you so much.

Dr. Paul Firth: Thank you, Sarah.

Sarah Alger: And listeners, thank you for tuning in to the Proto podcast.

Dr. Paul Firth: Today's podcast was produced by Emily Silva, Bradley Kline, and Jason Anthony.

Sarah Alger: Thanks also to our technical directors, Adam Keller and Chelsea Andes. Subscribe to the Proto podcast on iTunes and Stitcher, and follow us on Facebook, Twitter, and Instagram. Stay safe and see you next time.