

Erin Welsh

Hi, I'm Erin Welsh and this is This Podcast Will Kill You. You are listening to the latest Book Club episode of the season, a series where we get to interview authors about their books covering fascinating and important topics in science and medicine. If this is your first time tuning in this season, welcome, thanks for joining us and also be prepared to make room on your bookshelf and to read list. Last time we did this series, we just sort of released the episodes without giving you an opportunity to read beforehand. And this season, we decided in the spirit of real life book clubs to give those of you who want it a sneak peek of the books that we'll be chatting about this season. So if you are one of those wanting to read along with us, head over to our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com) where you can find a link under EXTRAS to our bookshop.org affiliate page which has our reading lists including our book club list featuring all of the books we covered last season as well as the ones we'll be covering this season. It's a pretty incredible list if I do say so myself and I really can't wait to share all of these interviews with you all.

I'm especially thrilled for today's conversation with Dr. Sara Manning Peskin who is an Assistant Professor of Clinical Neurology at the University of Pennsylvania and author of 'A Molecule Away From Madness: Tales of the Hijacked Brain'. In this captivating and heartrending book, Dr. Peskin takes readers through stories of the brain gone awry, exploring the histories behind some of these neurological illnesses and deftly explaining some incredibly complex concepts that frame our limited understanding of how the brain actually works.

I want to ask you all to take a second to consider the human brain. What are you doing in this very moment? Besides listening to the podcast. Maybe you're cooking dinner, maybe you're out walking your dog, maybe you're crocheting, maybe you're driving home from work, or maybe you're just chilling on the couch. What did you do today? Took a shower and got ready for work, scrolled through Instagram memes for probably longer than you should have, guilty, wrote endless emails, watched some reality TV, also guilty. How do you feel? Exhausted, content, anxious, excited, curious, depressed. We are capable of doing so much and doing it all at the same time; of feeling so much of creative and imagining; of thinking and overthinking; of holding a million different emotions and to do lists and memories inside of ourselves all while doing something as mundane as cooking dinner. And it's our brains of course that allow us to do this miraculous multitasking.

I think it's easy for many of us to take our brains for granted. And maybe some of that comes from the expectation that every morning when we wake up, we assume our brains will be there just as they were yesterday, maybe a bit groggy, maybe in need of some caffeine but ready to help us take on the day. But what happens when our brains don't function in the capacity we expect them to? What happens when our brains betray us? I don't think we always appreciate just how close our brains are to the edge, how something so small and seemingly insignificant as a stray protein, for instance, can profoundly disrupt everything about how our brain works.

In 'A Molecule Away From Madness', Dr. Peskin shares stories that reveal the vulnerabilities in our brains, using each story to teach readers what we know about the inner workings of our brains to remind us how many mysteries remain and to convey that with every story told, with every molecule or protein examined people remain at the center. I really loved 'A Molecule Away From Madness' not just for the fascinating histories or thoughtful examinations of complex neurological concepts but also for the way that Dr. Peskin centers patients in the narratives of these illnesses, bringing so much compassion and empathy to a field where it can be too easy to lose sight of the whole person when your focus is on an individual protein. I am really excited to share my conversation with Dr. Peskin with you all. So let's just get right into it.

TPWKY

(transition theme)

Erin Welsh

Sara, thank you so very much for joining me today. I absolutely loved your book 'A Molecule Away From Madness: Tales of the Hijacked Brain' and I thought you beautifully blended clear and accessible medical information with such a strong sense of humanity and empathy. And it was such a great piece of scientific storytelling. And I know that you've often been compared to Oliver Sacks but hopefully you won't mind hearing that comparison one more time because I really, yeah, I just thought it was so amazing and I've been telling everyone I know about it.

Sara Manning Peskin

Oh thank you so much. I was so excited to be on.

Erin Welsh

So I wanted to start with asking you how you got this idea to write this book. When did you decide I want to write a book? And when did you decide I want to write this book? And what was your process like?

Sara Manning Peskin

So I started, I came to writing pretty late. Initially I was going to become a scientist and I wanted to like have a lab. And then I actually started an MD/PhD combined program, I did like a year and a half of the PhD and was like oh no, this is not right. This isn't the right fit. And so I quit the PhD program and I finished medical school and I was an intern and we had to do two months of night shift. And there were some nights that were wild and some nights where it's like nothing much happens and it's a little bit lonely. And so I started writing some memoir stuff. And then I essentially realized like my life is not that interesting, no one really wants to read about my life that much. But my work is fascinating and the patients I see are amazing and the family dynamics that you witness are incredibly intricate and emotionally moving and that stuff is interesting.

And so then I sort of started to think about what are the most interesting stories? And the way that someone actually put it to me in terms of how you think about what you want to do in medicine is when you open the clinic door, like who do you want to see on the exam table? And that's how I sort of started to shape the book itself. And I initially wrote, initially the idea was to do sort of the traditional thing of like oh this patient shows up and they have these curious symptoms and then aha, this is the diagnosis and here's how the disease works and that's your package. But the more I wrote about it, I realized that actually the more important thing is actually the history of the disease. Because learning about a disease itself and the mechanics is so dry but learning about how we discovered the disease and what kinds of sort of wacky and outlandish characters were involved, that's actually exciting. The narrative part is what's exciting.

Erin Welsh

Oh yeah, absolutely. I mean that's our bread and butter here on the podcast. Mine especially, I love medical history and sort of getting into that step one, step two. How do all the pieces fit together? So of course that's another reason why I loved your book. So who did you want to see on the exam table? Like how did you end up choosing neurology as your specialty?

Sara Manning Peskin

I ended up realizing that I thought the most interesting diseases were ones that change people's identities. And I think we all sort of think about like look, if I broke my leg, I would still be the same person. Or I may go through this bad relationship but I'll come out and I'm still me and I'm learning things and I'm evolving. And yet there are these select diseases where there's a molecular problem and it actually sort of overhauls your identity and it actually makes you realize that the essence of what you think is yourself is actually not as protected as you think. And those are diseases that I found to be sort of most fascinating, both in terms of the science of them but also in terms of the social environment. So what do you do when your partner suddenly is incredibly disinhibited and going up to strangers and having affairs? And it's not sort of a moral failing, it's a molecular problem.

Erin Welsh

Let's take a quick break. And when we get back there's still so much to discuss.

TPWKY

(transition theme)

Erin Welsh

Welcome back, everyone. I've been chatting with Dr. Sara Manning Peskin about her book 'A Molecule Away From Madness: Tales of the Hijacked Brain'. Let's get back into things. And you get into a lot of this in your book, right? And there are so many different ways that the brain can change suddenly and change who you are or there can be just like the tiniest little switch that flips. And so how did you decide which diseases and also which personal stories that you wanted to include in your book?

Sara Manning Peskin

I tried to think of a structure of like what are the types of diseases that actually cause this type of thing? And there's not that many different categories, I basically described as sort of divided it into mutants, which are DNA mutations or DNA changes; rebels, which are problems with proteins, so if you think about DNA is like the biggest molecule that we have in our body, proteins are pretty big and proteins basically carry out, they're kind of the workhorses, that's what really keeps ourselves alive. DNA is really for the most part just a sort of instruction book, it's proteins that really do the work. And then there are small molecules, so there's things that are smaller than DNA, smaller than proteins, and they either cause a problem by being present, I called those invaders, or they cause a problem by being absent or not being there in enough quantities and I called those evaders. And a lot of the diseases that have a single molecular problem and most of them fit into one of those categories.

Erin Welsh

In terms of the personal stories, like are these all patients that you personally have treated? Or yeah, how did that aspect come into play?

Sara Manning Peskin

So there's only two of the patients are people that I treated and when I interviewed them they weren't under my care anymore, which also makes it easier. So to think about being confident that asking them if I could interview them isn't causing them to worry that their care might suffer if they say no. But no, I essentially wrote down the different diseases and then I reached out to specialists in different fields and said do you happen to have patients who you think might be interested? And it actually turned out when I went to interview patients, it was I think actually more meaningful for people to be interviewed than I realized. Because when we develop diseases and you go to a doctor and you say like look, I've been feeling XYZ. And the doctor says why don't we get some tests? And then you come back and you get a little more information and then maybe your symptoms change or you get more tests and there's sort of an evolution of getting a diagnosis and then the disease itself can evolve over time.

And it's really uncommon for people to be able to sit down and say what has this entire road been like? What's the last six years of my life been like from the beginning changes to where I am now? And it's actually fulfilling for people to be able to actually walk through that with someone sort of in slow motion. And so I was actually sort of surprised that after interviews people would be like oh that was actually a really wonderful experience. And I was sort of thinking oh my gosh, thank you so much for giving me so many hours of your time. Yeah. But actually it was nice, it was sort of a mutually beneficial thing.

Erin Welsh

Yeah, I can imagine it would be really sort of like cathartic and difficult. But also I think that the personal stories just add so much because it kind of places it in a human context, it grounds these diseases, these things. And you're like these are people who are experiencing them, this is their story. It's not just lab charts, it's not just these results, it's not just this list of symptoms. And so yeah, I felt like that was really impactful. Were there any stories that you didn't end up including or any diseases that you initially thought that you were going to include as part of the book but didn't end up making the final cut?

Sara Manning Peskin

There were some that got cut. I wanted to include a chapter on manganese poisoning because it can cause parkinsonism, so it can cause people to have movement changes. But it turned out it's really mired in legal issues because a lot of it was workplace exposure. And so I ended up, I was like reaching out to lawyers saying like are your clients interested in talking? And then it was sort of like I think I'm entering into a realm that I shouldn't go into. Yeah. And so that one got cut even though it's a fascinating story. And then there were some people, there was two people who I interviewed who were wonderful people and wonderful stories. And ultimately when I finished with the structure of the book, they sort of felt kind of extraneous in terms of the stories themselves. But the people were wonderful and so in the back of my head I'm always like oh well I have to write up those stories.

Erin Welsh

Yeah, next book. So when you're not writing, what are you doing on the day to day? I mean I know you're probably still writing. But yeah, what do you do besides being an author?

Sara Manning Peskin

Yes. So I mean I watch TV, I do the normal things. But no, I'm a cognitive neurologist. So two days a week I see patients and it's mostly patients who are coming in and saying do I have dementia? What's going to happen in the future? And most of what we see is sort of atypical cases, so often it's people who are younger or people who have unusual symptoms. So someone who comes in and says look, I've been seeing people at the end of my bed and I know they're not there but they really look clear to me. Or things like xxxmy partner is acting strangely, he's totally apathetic and he used to be so warm and he went out and bought a sports car and didn't tell me. Or people who say look, I'm having trouble using the right side of my body and it's gotten worse and worse over time. So these sort of really atypical cases. Or people have language problems and so they come in and they say I used to be a big gardener and someone mentioned the word mulch before and I couldn't really figure out what it meant.

And so it's a lot of these atypical sort of conditions that people walk around for years and they can tell something's up but they go to neurologists, they go to psychiatrists and they can't get a diagnosis. And so a lot of what we do is sort of seeing those cases and saying you're not alone, this is a real disease, it's sort of in your head but not in your head. And so that's what I do much of the time outside of writing.

Erin Welsh

So I am a huge fan of medical history, as I mentioned and as everyone who listens to the podcast knows, it's what I talk about. And so I really enjoyed all of the historical components that you put in your book, especially the story of Alzheimer and how Alzheimer's disease got its name which of course involves this instance of Alzheimer himself standing up and presenting what he found at a scientific meeting where he was met with like absolute silence. So can you place his findings in the context of dementia research at that time and maybe kind of speculate on why no one really seemed to care all that much about or recognize immediately the importance of his presentation?

Sara Manning Peskin

Yeah. So the story is sort of fascinating. So Alzheimer was sort of a very social guy, very smart and he'd gone to this top school. And then he did a PhD on the cellular life of ear wax and he'd gotten like a citation for disturbing the peace. So he was sort of a work hard, play hard kind of guy. And he goes into work one morning at the Asylum for the Insane and Epileptic it was called in Frankfurt and he meets this woman, Auguste Deter, who was a housewife and she's in her early 50s, she was 51 when he met her. But in her 40s even she started having difficulty. She would forget things in recipes, she was getting confused where she was going around the house, she became very suspicious that her husband was having an affair with a neighbor even though there was no evidence. And her husband had taken her to the doctor and the doctor basically said pack her clothes and drop her off at the asylum. And so that's what he did and she never got out. But he saw her the next day and he very quickly realized her case was unusual.

And he realizes that she had a very horrible short term memory. So he would come and he would show her a bunch of objects and she could name them, she could do math, she could describe things like the color of soot. But as soon as he would take the objects away, she would have no idea that he had ever shown them to her. Or if he asked her to write her name, she would write, she wrote Mrs and then she couldn't write the rest of her name. She sort of forgot the task or forgot how to do it. And he realizes the case is unusual and so he treats her for a little over a year. And then he actually, Alzheimer's own wife actually dies very young and he's left with three kids and he ends up moving to another city but he basically calls dibs on her brain, which was something you could do in that time. And so everyone knows that this asylum, that when this woman dies, her brain's gonna go to Alzheimer.

And sure enough a few years later she passes away and an intern from the hospital in Frankfurt calls him up and is like do you want the brain still? And he's like send it over. And so they fix the brain in formaldehyde and they send the whole brain and her entire medical record to Alzheimer at this other hospital. There's no consenting, it's a totally different time. And he looks at her brain under a microscope and he sees builds up of these two structures. One is what we call plaques, which basically look like a spot of spray paint in the brain that obviously is microscopic. And then the other we call them tangles now and they basically look like spaghetti inside of neurons. And people had seen the structures before but they had seen it essentially in older people where they thought the structures didn't really mean anything. And Alzheimer's big contribution was finding this woman and realizing she had an enormous, enormous burden of these plaques and tangles.

And so what he did that was so sort of... Partly he was so good at microscopy and he was such an expert in the field but also he was very quick to say is this a different disease? And that was the key, it's that he said have I actually discovered something new? And so he goes to this conference and he presents his data and just as you said, so he basically talks about the case, he shows pictures and slides and at the end there's like total silence. The moderator basically says well it seems there's no desire for discussion and please take a seat. And later in the day actually the talk that garnered the most interest is the talk about excessive masturbation. That was the highlight of the meeting.

Erin Welsh

Of course.

Sara Manning Peskin

And so yeah, you were sort of left with this thing of oh my gosh, this is one of the most, it's one of the deadliest diseases in the world, it's one of the top causes of death. And yet at its discovery nobody really sensed that it was important. And I think there's a few reasons but I think the big thing is that he presented a single case. And so there's thousands of case reports that come out every day and it's hard to sift through which ones are actually meaningful. And you can sort of think about what about the index case of COVID? People probably didn't realize that that was anything unusual, it's only when it becomes more widespread that you realize oh in retrospect that was a big deal.

And so I think part of that was that it's a single case and part of it is also that in that time it's harder to disseminate scientific information. So you can imagine anyone who's not at that meeting is not going to hear that. So it's not the same as today where you publish a paper and then with a click of a button the entire world has access to it. So I think that's another part of it. And part of it also is that he wasn't as far in his career as he eventually would get. So the way that Alzheimer's disease, the way that term eventually gets coined is his mentor actually publishes a revision of a textbook and mentions the case and mentions Alzheimer's disease. And so it basically is a little bit of who you know. So I think that those were sort of I think some of the main reasons why it didn't really get recognition at the beginning.

Erin Welsh

Let's take a quick break here. We'll be back in just a few.

TPWKY

(transition theme)

Erin Welsh

Welcome back, everyone. I'm here chatting with Dr. Sara Manning Peskin about her book 'A Molecule Away From Madness'. Let's get into some more questions. It's such a fascinating story and another one that I found so interesting and I had no idea about was Abraham Lincoln and how he maybe was taking this medication that possibly was altering his personality. Can you share a bit about first of all how you came across that story and then what that story is?

Sara Manning Peskin

Yeah. So I was looking sort of at I wanted to do at least one chapter about toxins. And I mean people have written books about toxins. So yeah, I sort of thought how do you choose which one to write about? Either it's a really, really unusual toxin or it's a sort of unusually salient case. And I figured everyone's heard of Abraham Lincoln, it's an interesting case. And also sort of the idea of how do you speculate on the medical issue of historical figures who have died where you can never really prove it? So it brings up all sorts of questions.

And the guy who sort of unearthed or sort of created the theory is a fascinating guy who's an infectious disease doctor who actually essentially pioneered oral rehydration therapy. So he's credited with saving thousands and thousands of people. But he's also a medical historian on the side. And he was reading Gore Vidal's book 'Lincoln' and he saw that it mentioned something about Lincoln taking a substance called blue mass. And so he went back to the primary literature and realized there's all these references, there's no quote from Lincoln himself but there are quotes from his closest confidants basically saying Lincoln used to take blue mass. And then after he got elected, he realized it made him cross and so he stopped taking it. And it's kind of amazing to think about these incredible political figures having medication side effects. And sort of thinking about what if he hadn't realized? What would have happened then?

And then the guy who created the theory, Norbert Hirschhorn, he essentially went back and said look, there are actually these cases of Lincoln being really sort of actually sort of unhinged and not that... We think of Lincoln as basically his emotions are basically like the statue, he's sort of sitting and thinking. And like we think of it, that's what he was always like, he was calm and measured. And yet there are these cases of him attacking a judge in the middle of a court case, in one of the Lincoln-Douglas debates he almost strangled a guy on stage. And so the question is were those medication side effects? And the bottom line is we'll never be able to prove it. The thought is if he stopped using blue mass, which contains mercury I should have said, that was the main toxic component. But if he stopped using mercury right after he got elected, by the time he was assassinated there wouldn't be any traces of it in his body. So there's no way to figure it out.

Erin Welsh

On the podcast we are pretty used to dealing with the gross and the gory and the weird but even I was taken aback by the filth parties, the quote unquote "filth parties" held by Joseph Goldberger. So what was the deal with these parties?

Sara Manning Peskin

Yeah. So it was from a time when it was very common to test things on yourself and that's how scientists did their work. So there was this disease called pellagra which caused diarrhea, it caused people to have a rash in sun exposed areas, so your face, your hands, even the top of your neck. And it caused a dementia and cognitive symptoms. And for a long time people thought it just didn't exist in America. And then in the early 1900s it started cropping up in the Southeast and it basically became this epidemic. It became enormously common, people became extremely scared of it, it was often deadly. And it was affecting primarily impoverished people. So it was affecting orphans, it was affecting prisoners, it was affecting poor farmers. And so at the beginning it didn't get that much attention but then it started spreading and essentially you started getting national headlines saying that people are scared of this disease, people are scared of this killer.

And so the predominant theory at the time was that either it was caused by a toxin in spoiled corn or the theory that gained traction was that it was caused by an infection transmitted by flies. And the reason why that gained traction, there was literally zero evidence, so there was zero evidence to show. The guy who thought of the theory eventually went on to argue that cancer was caused by cockroaches. So there's zero proof that this is correct but everyone wants to believe it because then you can basically say the disease is their fault, it's the people who suffer from it, they're not clean and that's why they get this disease and so we don't have any responsibility. And so that theory starts taking hold but there's no proof and the disease is spreading so people are scared.

And so the Surgeon General calls on this guy Joseph Goldberger. And Goldberger was a public health officer who was no stranger to contracting the disease as he was studying. So he'd gotten typhus, he'd gotten typhoid, and he'd actually exposed himself to scabies to prove about, to try to like track the epidemic was coming through mattresses. And so he was very much this sort of roll your sleeves up and get into it kind of guy. And he very quickly realized like look, this is not caused by an infection, it's caused by something in the diet. But nobody would believe him because the optics are totally different. Now it's a dietary deficiency, it's not a toxin in the diet, it's that the diets of these people are missing a nutrient. And that's very problematic because now instead of saying you know what, these people are dirty and it's their fault, you're actually saying our country is literally starving its own people and now they're dying because of it. So the optics are totally different. And it's also more expensive to fix because now suddenly the solution is now you have to feed people.

And so nobody really wants to believe him. And so he basically says you know what? I'm gonna prove to you that this is not an infectious disease. And so he starts off with him and a colleague and they take a sample of blood from a patient with pellagra and they inject it into their own shoulders. And he talks about how like we had some sore shoulders but other than that it was okay. And then he has more colleagues who are confident in him and so they start getting a little bit more gruesome with the experiment. So they scrape the scales off of patients' rashes and they mix it in with their stool and their urine and they actually swallow the pills. And actually even his wife wants to participate. They had this sort of fraught marriage because he's always running off to these different states and other countries to expose himself to these deadly diseases. And she's sort of like stuck at home managing all the children.

But she decides she wants to participate. So she goes down to see him and he doesn't let her eat stool or the urine but he does the blood run and he makes sure to take it from a female patient, lest he should take blood from a male patient and give it to his wife. But so she does participate also where they take blood from a woman with pellagra and he injects it into his wife's abdomen. And at the end of it, they wait six months and he writes up this paper that basically says considering the amount of filth that we took in, it's pretty amazing that none of us got pellagra. And that's sort of the punchline is we tried as hard as we could to get the disease and we still couldn't catch it. Yeah.

And eventually he goes on actually to do this incredible work when he actually gets so close to getting to the answer of what nutrient is missing in pellagra and he figures out it's a B vitamin. And then he dies pretty quickly. And he was nominated for a Nobel Prize multiple times but he dies before he ever gets one. And then other researchers sort of finish it and end up figuring out that it's a deficiency in niacin which actually was available on the shelf the whole time in the office of the guy who coined the term vitamin but he just didn't realize that that was the solution. So it actually was an incredibly cheap disease to treat, they just didn't know. So all these people, thousands and thousands of people died in the meantime.

Erin Welsh

One of the themes that we frequently run into on the podcast is the shift that occurred in the late 1800s when medicine starts to become less personalized, focusing more on the disease, treating the disease rather than treating the patient. And it seems like that was largely due to things like germ theory being like well we can solve it this way or it's this that's making you sick, the problem is external, not internal, as well as technological advancements in like medical measuring devices where we can translate your disease, your symptoms into numbers essentially. But it seems like these close personal relationships between Auguste and Alzheimer and Anna and Pick that you talk about in your book kind of escaped that depersonalization. Do you think that they were unique at the time or did neurology as a field kind of overall escape the depersonalization that was happening so broadly in most of medicine?

Sara Manning Peskin

So I don't think they were that unique at the time, I think. So Auguste was sort of the first case of Alzheimer's disease that he witnessed. And then Anna Jirinec was this case that Arnold Pick, who was another researcher at the time and kind of a nemesis of Alzheimer, but that was a case that he wrote about. And they each wrote really extensively about these single patients. But I think the reason it's like that is just because they were the index patients of these new diseases. Jirinec, she was like one of the first 10 patients that he'd sort of seen like that. So I think it's more just that these are the seeds of new diseases. And at that level it is still personal because they're individual cases.

And even now case reports, you do still get sort of this personal sense of people even though we don't include people's names anymore, we don't include some of the offhand comments that people used that years ago. But the index cases I think are always still individual cases. And if anything, as you said, it's a little bit funny now but so many of the biggest papers, it's like written by people who have never met people with the disease that they're studying and they make these incredible contributions to the field. But there's actually no account of anyone with the disease, it basically starts off saying this is a meta analysis of X number of papers and X number of patients and this disease is characterized by a blah and here's the statistics. And you could get through the entire paper, you could learn groundbreaking material but literally have no idea what it's like to live with the disease.

Erin Welsh

Yeah. I think that it's an interesting disconnect. And do you feel like that's something that in medical school or medical training today kind of is, is a field that could be improved upon? Or like how do you integrate witnessing these firsthand experiences of what the disease is like? Is there a gap there that you think could or should be addressed?

Sara Manning Peskin

So there's a bit sort of emerging field of narrative medicine that's trying to address basically exactly that. If you look up most papers, it's all passive, it's sort of all passive language. It's essentially like you basically remove yourself from the experience. But the place where that's been sort of preserved or ideally is the first line place to preserve that sort of close intimate narrative relationship is actually in the patient interaction. Because really what you're doing when you sit down with a patient, what you're doing is actually you're trying to get a sense of their narrative. And when you write your note, what you're trying to do is basically say look, here's their story, here's how things evolved over time, here's how they feel, here's what it's like to be them.



And when you're telling your your attending or whoever else about the story, you're trying to lead them to a conclusion. So you actually do need a narrative arc. So it actually is a very useful tool in medicine. And so part of what narrative medicine is trying to do is to say can we treat these patient interviews as intimate personal experiences where you actually extract not numbers like lab results but actually you're extracting an experience and then you're trying to encapsulate that experience for someone else, you're actually using narrative to formulate what you've heard and to try to communicate to someone else what is this patient's life actually like? And that also allows you to create a more holistic plan. So for us it may be look, we'd like to start this medication but also they're bored during the day and they're not engaged and how can we find a way for them to be active during the day? So it allows you to think a lot more about a person's quality of life than just about whatever numbers get thrown up on the board.

Erin Welsh

Several of the conditions that you discuss in your book like Huntington's disease or Alzheimer's disease for instance are heritable at least in part. For the children of those diagnosed with these potentially heritable dementias, I feel like that can be doubly traumatic, right, where you're watching your parent lose themselves or your grandparent lose themselves and knowing that this likely awaits you. Can you talk about this experience and the complex ways that you've seen people deal with it?

Sara Manning Peskin

Yeah. So this is a big part of what we do partly because we see a lot of these atypical cases. So the woman who essentially pioneered the research that led to finding the gene that causes Huntington's disease, she was a woman who was highly educated, she'd done a Fulbright scholarship and then her dad called her home and said your mom has Huntington's disease and you have a 50% chance of getting the disease. And she basically overhauls her career, ends up focusing, she had taken I think either zero or one biology classes in her entire life. And she basically starts focusing on trying to find a cure and in order to find a cure, you have to find the cause.

And so eventually she actually pioneers this work that leads to our current ability to test people for the gene that causes Huntington's disease. So you can now tell people who are totally asymptomatic that look, you have this gene abnormality that will likely cause Huntington's disease if you live long enough. And even though they have no symptoms. She actually never took the test. She basically said look, I have a lot more to lose by taking the test than I have to gain. She never took the test. She eventually developed symptoms of the disease and now has sort of come out in public thing that she's developed the disease and her sister didn't.

And so it's sort of this fascinating story and so much of what we deal with our work actually is diseases where you find out there's actually a single gene mutation or a single gene change that's causing the disease. And you sort of think it's a little bit strange, you've had this DNA your whole life and why is it suddenly causing you a problem in your 60s, even your 70s? And some of these diseases you have the same gene change in one person and multiple family members and sometimes they all get the disease at the same time and sometimes they get it at vastly different ages or it doesn't even always cause the disease.

And so the issues that arise are are incredibly emotionally complex. So the biggest thing that people think of is do you wanna know? Do you want to know if you have a mutation that causes a neurodegenerative, a deadly progressive disease that we have no cure for? And we couldn't tell you exactly when you'll get it, we can tell you the chances of getting it but we can't tell you exactly when or that you'll definitely get it. And do you wanna know? And there's a few things to think about. So one is maybe you wanna know because you wanna enroll in a research study and and maybe you'll get a treatment, you'll never develop the disease. One of the big things is do you want to know so you can plan? So if you knew that you were gonna get a neurodegenerative disease and someone said look, it often starts in your 50s or 60s. Would you change your career? Would you change your decisions about having kids? Would you change how much you travel? Would you change how much you spend?

And the other really sort of the thing that I find most interesting is you also can have kids that don't have the mutation. So if you carry a mutation and you wanna have biological children that don't have it, you can do IVF. So essentially they take egg and sperm, they mix it together in a lab and then they take the cells, sort of grow and divide and grow and divide and after a certain amount of time they take away one cell or they take I think it's more like four or five cells. So they take away a few cells and they look at the gene in those cells and they can say okay, this is a normal version or not a normal version. And then they basically only use the embryos that have normal versions. They put it back in the uterus, you grow a kid and the kid does not have the disease. So it's actually we have the technology to literally root out the mutations from family lineages. But only if you know that you have it, only if you know to look. So it's really such a complex issue.

And ultimately there are normal people who decide to find out and there are normal people who decide not to find out. And even within families there'll be some siblings who do testing and some who don't. And it's one of the most fascinating issues that we deal with. The other big issue that comes up is basically if a grandparent had the disease, a parent decides not to find out but their child decides to get tested. If the child has the mutation, then the parent now knows. So actually your decisions affect other people in the family. So it's just sort of scientifically fascinating and emotionally so fraught but also actionable.

Erin Welsh

Like with so much else in the history of medicine, broad categories of diseases end up being broken down into smaller clinical units as we grow to understand more and more about their pathologies. Like fever became many different things, hysteria became endometriosis or MS or PCOS or so many other things. And dementia in some ways was split similarly. In what ways do you think that the diseases that you talk about in your book or that you encounter in your work are still undergoing this type of revision?

Sara Manning Peskin

So the diseases, I mean one of the big diseases that I see is frontotemporal dementia. And even the name for that is like a little over 20 years old. So it's very much still an active field and in that area in particular. So that's the disease where it has a few different variants, it's been in the press a lot because Bruce Willis has now come out saying that he has or his family has come out saying that he has frontotemporal dementia. So it's had a lot of coverage lately. And essentially sometimes it can cause people to have these sort of really sort of antisocial behaviors, going up to strangers, saying inappropriate things, hypersexuality, eating non-food things. Sometimes it can cause people to have language problems where they lose the connection between words and objects. So you were taught when you were a kid that an apple is a green or red thing that's crunchy in the middle. But there's nothing inherent about an apple that sounds like apple, it's just that sound was attached to the word. And you lose that connection.

Or some people start having trouble with the motor programming of speech. So when you want to say a word, your mouth and your tongue has to move in a certain way to say it and that's a message that goes from your brain to the muscles in your mouth. And that connection gets lost. So in that disease, it essentially had like 10 different names, each of which had like the names themselves were like six different words put together. And people thought it was like multiple diseases and then they finally figured out actually it's the same disease and it's sort of this aha moment. And then actually they go on and they realize when you look at people's brains under a microscope it's actually not the same disease. So it sort of had this full evolution of like is this one disease? Is it multiple diseases? And ultimately we're not very good at...

For Alzheimer's disease we actually have tests that we can do in living people and we can say look, we're essentially almost sure that that's what it is. With frontotemporal dementia you can have two people who have exactly the same symptoms, their imaging looks similar and yet at under a microscope their brains look completely different. It's caused by a totally different protein in one person compared to another. And so a lot of these fields are still very much evolving. And part of the issue is that difficulty in making the link between symptoms and imaging and testing and what's going on under a microscope because you can't access the brain. It's not like the lungs where you can take a piece out and look at the molecules. The brain, it's like we're using all these proxies. And that's the big barrier.

Erin Welsh

Speaking of frontotemporal dementia, in your chapter where you focus on that particular condition, you talk about the stigma and you mentioned some of these symptoms that are commonly seen with frontotemporal dementia and how they're maybe not what we typically think of when we think of dementia. And maybe that's because that's the way that dementia is portrayed in popular media. So there can be more of like a stigma maybe with these atypical symptoms or symptoms that we perceive to be atypical even though they're not. So can you talk a little bit about this problem between the disconnect in how dementia is portrayed vs the actual wide variety of ways that it can actually look in reality?

Sara Manning Peskin

Yes. So actually this is probably maybe two years ago I actually gave a class about dementia in the media and there's some fascinating stuff out there. And it's also really a big topic of debate because one question is should you basically, if you were writing a movie about someone with dementia, should your goal be to write about the typical cases so that people could learn about the disease and see what it usually looks like? Or is your goal to write about whatever case is most interesting, whether it's rare or not? So if you think about the example of Still Alice, it's a woman with Alzheimer's disease so it's a very common disease but it's young onset. And I think it turns out to be a genetic cause. So it's really atypical, those are like less than 1% of cases. And so one question is is that a really useful movie? Because it was a big movie, it got lots of attention. So it got a lot of sort of light onto Alzheimer's disease.

Is that really helpful or is it actually like you're making people think that it's all caused by a single gene when actually that was a really unusual case? Or if you're portraying people with dementia getting diagnoses, should you portray a compassionate doctor or should you portray what often gets portrayed which is neurologist as being sort of aloof and sort of not emotionally engaged? And how do you portray that interaction? And I think the bottom line is that it's complex. And the most important thing from my perspective is really just portraying the humanity of the people with the diseases. The key is not talking about them when they're in the room. So portray them as real people. And then you can drop clues in of like this is unusual, so this is an atypical case or something like that. So you can get around that stuff. But the key really is to try to portray some sort of semblance of real life experience with these diseases.

Erin Welsh

I want to take that class. That sounds really interesting. In your book you also tell the story of a young woman who was diagnosed with a NMDA receptor encephalitis. And I love how her mom was so integral in like pushing for no, I think it's this and just advocating, advocating, advocating and how frustrating but also inspiring that part was. But one of the things that you point out is how different this person's experience might have been if she had gotten sick just a couple of decades ago when the disease was largely unknown or completely unknown. And I know there's been some speculation of like historical cases, might the people accused of witchcraft actually had an NMDA receptor encephalitis? So do you feel like there might be other fields in medicine or other conditions in medicine that might undergo a similar revolution in the future?

Sara Manning Peskin

NMDA receptor encephalitis is a wild disease that essentially works like PCP and now has been getting increasing attention. But it's still rare. And so the hope is that can we get there with the more common things like Alzheimer's disease? And so that's the goal. And then the other question which is to be honest beyond my field of expertise is all these psychiatric diseases that we think of, there's this schism in the late 1800s and psychiatry and neurology suddenly split and dementia is kind of at the seams because there may be a molecular cause but a lot of the symptoms are sort of psychiatric in nature. And it's sort of gone along at the scenes of psychiatry and neurology. And one question is are we gonna move that over more to psychiatry? So things like schizophrenia and other conditions that we think of as being really purely psychiatric, are those also gonna end up having molecular causes over time? But I don't know.

Erin Welsh

Even though dementia has been now sort of broken down into many different types where you can specify this vs that and maybe the medications might be different. But is non pharmaceutical therapy or just care, are there similarities in the way that all of these different types of dementias are treated?

Sara Manning Peskin

Yeah. So there's a lot of similarities and that sort of becomes of importance because in some cases we say look, I could put you through this invasive test to try to figure out what's actually going on at a molecular level in your brain but it's not worth it because we're gonna treat it the same. So that really comes to it's actually a clinically relevant question. And the bottom is there's a few rules of thumb that really are very helpful. Things like people come in all the time and say when someone makes a mistake, should I correct them or should I not correct them? And the bottom line for most of this stuff is essentially if it's not unsafe, you don't need to correct them. And that having dementia oftentimes people are not aware of it or if they're aware of it, it's painful for them to think about.

And so the general approach really is if it's not unsafe, if they think that their dead father is coming for dinner, then by all means let them set the table. That's okay. I mean it's not gonna hurt if they are wearing their clothes inside out. Who cares? And in the same way in public. One thing that we sort of talk to caregivers about is if you're worried about them doing something socially inappropriate, carry business cards that just say look, my loved one has this condition, thanks for your understanding. And you just pass it to someone after it happens and that way you're not having to like yell at your loved one in public, you're not having to explain it to someone else, and it actually spreads awareness and people realize that there's more than what meets the eye.

So there's all sorts of things like that and things like we talk a lot about sort of empathic lying. And basically if you need something to get done, trying to frame it in a way that has nothing to do with the person's cognitive status. So if you need someone to move to a facility, how do you figure out some explanation for that that doesn't completely involve their cognitive status? Because if you can imagine or oftentimes the example we give is like tell the the cognitively normal care partner. Like if I was going to try to convince you to move to a nursing home, what would I have to say? And it's tough to think about because with all these conditions you're dealing with people who live in a different world in some ways. And so the tools, regardless of the type of dementia, a lot of the tools are the same from that perspective.

Erin Welsh

Has the process of writing this book changed the way you practice medicine or the way that you interact with your patients?

Sara Manning Peskin

It had. I didn't expect it to. I think I thought of it initially as like two separate things. But a lot of what I do is give diagnoses of untreatable neurodegenerative progressive diseases. And I talk now a lot in the diagnoses, I talk a lot about the history of the diseases because it made me realize like we all carry around these diagnoses and we have no clue where they came from. It's sort of as if like they were always around but none of these diseases were known from the beginning of time. And talking to people about how these diseases were discovered actually first of all it allows you to go back to the basics, so it allows you to communicate at a level that's actually more scientifically clear. And also it gives people a sense of look, this is an evolving field and our hope is to find cures for these things. And not that this is a static, it's not that Alzheimer's disease has always been around and we've never made any progress. It was discovered at a certain time and we've actually made a lot of progress. And there is a lot of hope even though it's true, we haven't found a cure. And so I try to couch the diagnoses and the sort of history of the diseases now. And I haven't gotten any negative feedback. So hopefully it works okay.

Erin Welsh

No, I love that. You cover so many different diseases in your book and they range from ones that are fairly well known like Alzheimer's to those that may not be on most people's radar like a NMDA receptor encephalitis, even though it has gotten more press recently. Do you find yourself more intrigued by one than the other or do you find them all equally interesting or are there aspects of these conditions that you find the most compelling?

Sara Manning Peskin

I think the cases that move me most are the ones where people have these atypical symptoms and they're walking around thinking that they're crazy. And so people who have speech problems, they say look, for the past two years I feel like people think I'm drunk every time I open my mouth because my words don't come out clearly. And it's very emotionally fulfilling to be able to say look, actually there's a name for this disease and you're not crazy and this is what's going on and if I had to put money down, this is the molecule that I think is going haywire in your brain. And this is where we are in terms of trying to find treatments and here are research opportunities. That's sort of the most fulfilling is these atypical cases where they've gone years without a diagnosis and you can say look, this is what's going on. I mean the typical ones are also interesting because even typical cases bring up interesting family dynamics. But for me I think it's one of the atypical ones that are the most fulfilling in clinic.

Erin Welsh

What is something you wish you had known before starting on your career journey?

Sara Manning Peskin

I guess this part I learned in the book, I guess. I think the biggest thing was that I wish I knew more about communicating with patients. So much of medical school is like trying to cram an enormous amount of information in your brain, much of which if you become a specialist or a subspecialist you're literally never gonna use. And so much of it is just this academic exercise and there's not as much emphasis on like how do you explain a disease to a patient who has no medical background and variable health literacy? And I think in writing a book for the lay public, I was in a writing group with lots of people, none of whom had any sort of medical background. And they were all very educated and I was like shocked, there were words that I would use and they would say like that doesn't make sense to me, I don't understand that explanation. And I realized that it was not them, it was my failing. And I think I wish it was emphasized in medical school more. And I mean there's so much to learn and there's more to learn every day. So you only have four years and how are you going to learn all this material? So I know that it's sort of tight to fit in new stuff. But it's really something that's not covered much in medicine.

TPWKY

(transition theme)

Erin Welsh

What a fascinating conversation. I had such a great time chatting with you, Dr. Peskin. Thanks so much for taking the time and for writing such a wonderful book. If you all enjoyed this as much as I did and want to learn more, check out our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com) where I'll post a link to where you can find 'A Molecule Away From Madness' as well as a link to Dr. Peskin's website. And don't forget you can check out our website for all sorts of other cool things including but not limited to transcripts, quarantini and placebo recipes, show notes and references for all of our episodes, links to merch, our [bookshop.org](http://bookshop.org) affiliate account, our Goodreads list, a firsthand account form, and music by Bloodmobile. Speaking of which, thank you to Bloodmobile for providing the music for this episode and all of our episodes. Thank you to Lianna Squillace and Tom Breyfogle for our audio mixing. And thanks to you, listeners, for listening. I hope you liked this bonus episode and are loving being part of the TPWKY Book Club. And a special thank you as always to our fantastic, generous patrons. We appreciate your support so very much. Well until next time, keep washing those hands.