

Dr. Donald Weaver 0:02

[Your Complex Brain theme music] It was actually a eureka moment. It really was. I've been involved in Alzheimer's research for 30 years and this new theory—Alzheimer's as an autoimmune disease—this is the most exciting time of my life.

Heather 0:21

This is Your Complex Brain, a podcast all about the brain, the diseases that impact it, and the path to finding cures. I'm your host, Heather Sherman, and I have the great pleasure of working alongside the team at the Krembil Brain Institute in Toronto, Canada, a leader in brain research and patient care. In each episode, we'll take you behind the scenes into our clinics and research labs to meet the game-changers of the future. We'll also empower you with the latest research to help you take charge of your own health. You'll hear directly from people who are living with brain disease, as well as their loved ones and the care teams who support them. Join us on a journey to unravel the mystery of your complex brain. [theme music fades out]

[steam train whistles then chugs] Imagine Alzheimer's as a speeding train that's coming for all of us one day. Whether as a patient, a caregiver, a neighbour, or a friend, we'll all be touched by this disease if we live long enough. [steam train whistles] [light, bubbly, electronic music] Alzheimer's steals our memories, and so cruelly robs us of our loved ones, often when we need them the most. But, there is hope and momentum in the world of Alzheimer's and dementia. In the past two years alone, we've seen the development of new drugs, and even a blood test to diagnose the disease. Researchers are also starting to think differently about the origins of Alzheimer's; in fact, a new theory suggests that it could even be an autoimmune disease. We'll talk about that and more advances in Alzheimer's research in today's episode. First and foremost, though, Alzheimer's is about families. Here's Lindsay Bongard-Batori about her mother, Barbara, a shining light who was taken from her loving family far too soon. [light, bubbly electronic music fades out]

Lindsay Bongard-Batori 2:35

[rhythmic electronic music] My mom was my person. Nothing explains it better than that. I mean, I remember faking sick in grade one just because I wanted to be home with my mom. I just always knew she was there for me. She was definitely my best friend. My mom's name was Barbara. She was an avid reader, and I think she passed that down to me. She loved going for walks and just appreciating the little things in life. She was a stay-at-home mom and just, I mean, her kids were her life. [rhythmic electronic music fades out]

We started to notice her repeating herself a lot. I don't even think it was forgetting things; it was more repeating what she had just said, and we started to get annoyed with that – my dad, my brothers and I. Like, "We depend on you. Why? What do you mean? You just said that." And then, I remember feeling this sense of guilt, like, "Why am I getting mad at her?" [gentle electronic music] I noticed her slowly drawing back from us. It was odd for her. Then, she started forgetting things. I remember one day she called me, crying. She went to Loblaws, and she couldn't find her car and the parking lot wasn't even that big, but she was hysterical, and she was scared, and I had to talk her down and had to talk her through it. Another thing that came up was, one year at a Passover dinner, somebody said the prayers and about two minutes later, she said, "Okay, let's say the prayers," and we all kind of looked at each other like, "We just... What? We just did that."

It was then that we decided as a family, with her involved, that it was time to talk to your doctor about this memory issue, and she was assessed with something called MCI, which is mild cognitive

impairment, and we knew. We knew. We'd been down this road before with my dad's parents and my mom's father. That's when it sort of became real and it started to have an effect on my entire nuclear family – [gentle electronic music fades out] my brother, my dad, my mom, and myself of, like, "What's to come?" and it was scary. [somber, delicate music] I could see in her when we would go to social events, she was quieter, and I remember saying to her one day, "Mom, you were so quiet," and she said, "I don't have anything to offer," and that hit me because I felt really sad for her, because I knew she was uncomfortable, and she started to not want to go out a lot, and then eventually, her license got taken away and that was a very hard blow. So, she was just staying home more and more, and we weren't letting her do so much, like take care of my kids, or, you know, go out by herself, and that's when we started to have the conversation of, "What's her next step? Like, what do we do? How long do we watch her decline before something really bad happens?"

We started looking into homes for one day, because I said to my dad, "I don't want it to get to the point where it's time to put her in a home because we can't care for her and there's nowhere for her to go, or we don't know, or it's an emergency," and my dad, he really tried. He retired. He thought he was going to devote everything to her. That was his plan, and it just came to the point where her speech pretty much declined completely and I remember her lying in bed one day, and I whispered to her, and I said, "Mom, get it together because if you don't, you're going to be going into a home and I know you don't want that, so please." Like, I was like begging her, "Don't do this," but obviously, you know, that was more my issue than her issue. She couldn't help it.

A few weeks after we had seen the home and gone into the home and decided, my dad was in the other room and he heard her fall, and he ran into the hall and she had fallen and he was hysterical, finding her like that, and that's when we knew that this can't go on any more at home. [up-tempo electronic music] I went over. I packed her up, my brother and my dad and I, and I unpacked her, made her room as nice as possible, and she never even said goodbye. She didn't say, "Where am I?" She didn't say, "Take me out of here," nothing that you would expect a healthy person to say when you're being dropped off. They say with Alzheimer's, you mourn twice, and I understood what that meant.

My parents were married just over 50 years. I think they had plans. When she was to retire, they were going to travel and, you know, my dad depended on my mom for so much stuff. Like, he wasn't the easiest person to be married to, and my mother deserved a medal – that was the joke, and everybody would laugh about it. And, you know, she would plan these vacations and he would say, "I don't want to go. We're not going," and of course, he went and came back and had the best time of his life, and he needed her to push him and do that stuff, like we all needed her. We all kind of got that gene from my father. "If I'm nervous, I don't want to go, I don't want to do this," and it was her who would always sort of push and say, "You're going to be fine. You're going to be okay. It's going to be amazing." It was very hard for him to watch this. My mom was young to be in a home. Like, she was 72 when she went in, and that's considered young. You know, I would go to the home and visit and see people my age visiting their grandparents, so I think for my dad, too, like, this was opening up a whole new chapter that he was not prepared for, and I think he's still battles that today.

[pensive electronic music] This disease really affects more than just the person. It really affects the entire family. I have these rocks that I keep by the computer, and I have these acrylic markers and I just paint them. [lid clicks off marker] Like, I just, you know, make these rocks and then, when I go to the cemetery, I leave these painted rocks for her, or my kids will, and it's something I feel like she would have appreciated. She liked doing little crafts and stuff. [pensive electronic music fades out]

What life is like without her, I just wish she could see it because it's hard. It's hard without your mom, especially when you have a relationship the way I did. We all depended on her for so much, and we are still trying to figure out how to continue on without her. [hopeful electronic music] I do teach a program; it's called Project Give Back. We teach kids about charity and giving back to the community, and it's a passion project, and we teach kids to find a charity out there that touches their heart, and they have to research it and talk about it and why it's important to them, and I always do my own presentation for them to see what it's like. And, every year, I do a presentation on Alzheimer's, but I choose a different Alzheimer's charity, and these are kids who are 11, 12 years old. All the questions that these kids have is, "Why haven't they found the cure yet?" I don't know. We're not sure yet. We hope it's coming. And, yeah, it makes me angry, and yeah, that's life. But, I hope in my lifetime, I get to see some progression. [hopeful electronic music fades out]

Heather 11:35

[gentle electronic music] Today on the podcast, I'm speaking with two of the most widely respected and inspiring thought leaders in Alzheimer's and dementia. Dr. Donald Weaver is a neurologist, a medicinal chemist, and a senior scientist with the Krembil Brain Institute at UHN. Also joining us is Dr. Saskia Sivananthan, a neuroscientist and the Chief Science and Knowledge Translation Officer at the Alzheimer's Society of Canada. Both are sought-after speakers and are often called upon to provide much-needed context in the media on this topic. Thanks so much to both of you for joining me today.

Dr. Donald Weaver 12:15

Wonderful to be here.

Dr. Saskia Sivananthan 12:16

Thanks for inviting me.

Heather 12:20

Dr. Sivananthan, I'm going to start with you. The Alzheimer's Society of Canada released an incredibly comprehensive report last fall, navigating the path forward for dementia in Canada. One of the most eye-opening findings for me was just looking at the significant rise in the number of Canadians who are going to be living with dementia going forward. So, what more can you tell us?

Dr. Saskia Sivananthan 12:40

So, that report is actually one of a series of three reports that we plan to be releasing over the next two years, and we call it the Landmark Study Series, and the reason for that is because it's been over 10 years since there's been a comprehensive look at the dementia landscape, specific to Canada. We were looking at, if we stay on the trend that we are expecting, what are the projected number of people who will be living with this disease over the next 30 years? And, we're expecting a tripling, so by 2050, there'll be over 1.7 million people living with dementia, and there are a variety of reasons for why that trajectory is happening. But, the piece that really stood out for me is the number of care partners who would also be supporting that rise. We're estimating over a million care partners for that increased number of people, but dementia rarely touches one person. It's a family affair, if not broader than that. Then, when we did a bit of a breakdown and looked at those care partners, the majority are adult children of people living with dementia, followed by spouses, and then by other family, neighbours, etc. who are supporting them. When we looked at the number of hours, on average, for a care partner who is providing care to someone with dementia, they're providing about 26 hours of care, and so when you total that up, that's 1.4 billion hours of care, unpaid, being provided by these care partners. When we try to put that into statistics you can actually wrap your head around, that's 690,000 full-time jobs.

Heather 14:23

Yeah, I was going to say it sounds like a full-time job. I mean, it is a full-time job for anyone who's experienced it themselves but, you know, how can anyone possibly balance that type of lifestyle? And, people do every day.

Dr. Saskia Sivananthan 14:34

They do every day, and I think what I'm really excited about talking about is the need for multiple care pathways to really support dementia in the health system which, again, we really don't have, and we do quite poorly.

Heather 14:45

Absolutely. Dr. Weaver, this is what you're always saying, that dementia and Alzheimer's is a disease of the family. So, what's your reaction when you hear some of these numbers and some of these projections?

Dr. Donald Weaver 14:56

Well, I certainly believe them. They're quite accurate, and it's a wake-up call for our system that we can't keep going the way we are. Things have to change. This is a major, major personal health, family health, socio-economic problem that's coming at us. This is something where, at all levels of government, we really do need buy in. We need people to become passionate about this, to accept it as big a problem that it really is.

Heather 15:23

One of the other recommendations that came out was this whole idea of the underfunding of research, and so I wanted to talk for a moment about some of the momentum that we are seeing in research, especially in the area of new drugs, including two that have come out in the last couple of years: Aducanumab and Lecanemab. Dr. Weaver, what can you tell us about these drugs and their efficacy? What do we know?

Dr. Donald Weaver 15:45

Well, this is an area where there's a lot of controversy, and certainly I have my opinions, and you can hear people with other opinions, but from my perspective, Aducanumab was the first one that was approved in United States—not in Canada, I will say. Probably, it doesn't have that much to offer, and one's assuming that it will be quickly replaced with Lecanemab, which is the next logical one in this series. And, I get a lot of questions about this. I tell people, "It's a step in the right direction, but it's not a big enough step." So, this is wonderful, in that it's probably the first agent that's ever been demonstrated to have what we call disease-modifying effects, to actually really influence the course of the disease so, from that point of view, wow, we have an agent that does that, but it doesn't do it well enough. As I said, we're going in the right direction, but we need to go a whole lot further. So, I think that it brings optimism to the field, and optimism that we can, and will, do better in the near future.

Heather 16:52

Dr. Sivananthan, I can see you nodding along, so tell us why.

Dr. Saskia Sivananthan 16:55

[sparse electronic music] I absolutely agree with the way Don framed it. I think we, of course, also get a lot of those questions from clients, people living with dementia, and families who are worried that they

might develop dementia too, and the way I try to talk about it is it's sort of like an inflection point in research because, exactly as Don said, it's been something like two decades since a drug came to the market – period. But then, there's not been anything that's been attempting to be a disease modifier, to get at the underlying reason for why dementia might be developing.

Now, that being said, both of these drugs are sort of a class of drugs. They're the first out the gate but should not and will not be the last. I certainly hope not. They don't have the same level of efficacy that we would hope they would. They come with many, many side effects, they're extremely costly, they require infusions, and all these other infrastructure things that we haven't talked about or thought about, but all the same, it, to me, points to the need to continue to really fund more dementia research because it was those early investments in dementia that even resulted in these drugs. Imagine what more we could do if we invested more in dementia research. There was a report that was published that looked at the success rate of Alzheimer's disease trials, and it's low. We're looking at something like 0.4% of the likelihood of any drug being brought to market, and the next closest comparison is 15.3%, when you look at other therapies in other diseases, and that means that investment and that early investment in research continues to be so crucial to being able to bring any drugs to market.

Heather 18:43

Well, this obviously begs the question as to why. Dr. Weaver, do you want to weigh in?

Dr. Donald Weaver 18:48

I certainly do. Alzheimer's and dementia aren't like any other disease. The brain is probably the most complicated structure in the universe and, arguably, Alzheimer's disease is the most complicated disease of the brain. This is not a trivial undertaking. This is something that takes a whole lot of focus and a whole lot of attention. I always like to draw a comparison with high blood pressure. If you have high blood pressure and you go to see your family physician, they don't say, "Here is the high blood pressure pill. Take it." They have a whole range of different medications available to them and, you know, they try to pick the one that's best for you. [sparse electronic music fades out] They may give you multiple ones that complement each other, so why do we think there's going to be a single magic bullet—a single drug—that's going to work for Alzheimer's? It's not going to be the case. It's going to take multiple medications and who knows? Maybe person A with Alzheimer's and person B with Alzheimer's are two very different people and may require very different therapeutic approaches. So, just as it took many, many years of research to come up with Lecanemab—and it's, as I said, a step in the right direction but not far enough— for the other approaches, it's going to take time, lots of time, to get the drugs that are going to work on other different targets, other different approaches, and so lots of research and lots of patients are going to be absolutely necessary as we go forward.

Dr. Saskia Sivananthan 20:17

It, for me, links so crucially to the fact that dementia is an umbrella term, just like we would say, cancer, right? It's not one disease; it's a whole host and collection of diseases.

Dr. Donald Weaver 20:30

We don't even know if Alzheimer's is one disease.

Dr. Saskia Sivananthan 20:33

This is exactly true, and we know now that there's more of a rise in terms of mixed dementias, you know, so the types of treatments that we're going to need, we're just going to have to be much more outside of the box and how we think about this collection of diseases and the therapies for them.

Heather 20:48

I guess you could say this is a perfect pivot point to talk, Dr. Weaver, about your new theory of Alzheimer's as an autoimmune disease, and I just want to mention that you actually received an Oskar Fischer award for this new theory, and that's awarded to the world's top scientists who are looking at these new approaches and Alzheimer's research. So, congratulations on that, and can you tell us a little bit more about the theory?

Dr. Donald Weaver 21:09

Thank you very much. Yes, we have a theory and, of course, in my own perfectly unbiased way, I think it's wonderful, but I am sure there are people who, you know, would debate it. I'll defend their right to be wrong. [Heather laughs] So, you know, there are so many camps and so many different approaches, and one thing that I find unfortunate is almost the competitive nature with people going, "The amyloid hypothesis is wrong. We should abandon it." No, no. All ideas are open, all ideas should be on the table, and who knows? Maybe drugs from all of these ideas will eventually go into the therapeutic cocktail that is needed. We've tried to look at many other different approaches and try to bring them together into one concept, so the point I want to make about our theory is that, number one, there's this notion that amyloid is bad, amyloid is pathological, it shouldn't be there, its production is somehow wrong, and what we're arguing is that amyloid is, in fact, a normal part of your brain. It's part of the immune system in your brain. It's supposed to be there.

The second notion, then, that our theory is based on is that, unfortunately, the immune system in your brain cannot differentiate between a neuron, which is a brain cell, and a bacteria, which is an invading pathogen, an invading micro-organism in your brain. And so, what our thinking is, is as follows: an attack on the body happens. [percussive electronic music] It could be you have a dental infection and bacteria are wandering through your brain. It could be that you had head trauma repeatedly, you know, because of the nature of your employment as a professional athlete. It could be excessive exposure to air pollution. But, these factors turn on the immune system in your brain. When the immune system in your brain is turned on, beta amyloid, a peptide in your brain, is released as part of your immune system, and it goes out on its search-and-destroy mission. "I'm looking for bacteria. I'm going to kill bacteria in the brain." When it's on this mission, it gets confused and it can't tell the difference between a bacteria and a brain cell or a neuron, and unfortunately, oops, it starts to attack our own brain cells.

Heather 23:40

Wow. So, it's essentially a case of mistaken identity?

Dr. Donald Weaver 23:44

[gentle electronic music] Yeah, like the worst type of mistaken identity, [Heather chuckles] having your brain cells identified as bacteria, and so it starts to kill brain cells and, as those brain cells are killed and they release their products as they fall apart, that turns on more inflammation and this becomes a vicious cycle that goes on for decades and decades, meaning events that happen way in your youth could have consequences, and this brings into sharp focus all of these issues around risk factors. You know, you really should be doing your best to protect your brain. The brain is just so crucial. It's so essential to you. It's so complicated, and that's why you know, an autoimmune disease of the brain—which is what we are proposing—is so devastating.

Heather 24:33

If, indeed, this theory is proven as we hope, down the line, it will be, if it's an autoimmune disease, then can it not be treated as an autoimmune disorder? Can you explain that?

Dr. Donald Weaver 24:43

Yeah. It certainly opens avenues for new therapeutic directions. Now, there are lots of autoimmune diseases out there [gentle electronic music fades out] and, you know, and we think of like rheumatoid arthritis, or another disease called systemic lupus erythematosus. There's just lots of other things out there that we recognize this autoimmune disease, but once again, I'm going back to, "The brain's the most complicated thing. It's unique." You know, it should come as no surprise that an autoimmune disease of the brain is going to be different from an autoimmune disease anywhere else. And so, the normal drugs that are used to treat autoimmune disease—typically, steroids and things of this nature that the rheumatologist and others would use—won't work in this case because this is a completely different type of autoimmune disease, and so we're going to have to develop new agents and new approaches. But, there's optimism here because, if it's an autoimmune disease, just as we have drugs that treat rheumatoid arthritis, we can get drugs that are going to treat Alzheimer's disease.

Heather 25:44

And, when did you come up with this idea about a new theory?

Dr. Donald Weaver 25:47

So, we started to think about this probably about eight years ago and have been working away at it. And, I will point out that we got initial funding from the Alzheimer Society of Canada, and so I am grateful for their support over the years. You have to have people who are willing to take a risk, willing to take a chance that we need new thinking out there, and it's those individuals, it's those funding organizations that are going to be so crucial as we go forward in this continuing battle against Alzheimer's and dementia.

Heather 26:17

Dr. Weaver, you were on the podcast last year, and we talked about the need for new solutions in Alzheimer's and dementia. So, why did you decide to take this new approach in your research, and how does this new theory compare with your prior work?

Dr. Donald Weaver 26:30

You know, theories have strengths and weaknesses, and each one has to be weighed to see, "Does it really have what it takes to go forward? Does it really have what it takes to make a difference?" And, you know, I think that this autoimmune theory has that capacity. I think that the autoimmune theory really is innovative and insightful and, you know, perhaps could be a significant step forward in our thinking about this disease, and that's why we've certainly decided to focus all of our effort on this and, right now in our lab, it's all-in on this theory. We are passionate about it; we think it's the direction of the future.

Heather 27:11

And, what led you to this new theory?

Dr. Donald Weaver 27:13

What led us to this theory, actually, was a computer simulation. We were talking about, "What does beta amyloid do?" because this is this protein—this is this peptide—that's been implicated in Alzheimer's disease. And so, in a computer simulation, we put beta amyloid—this peptide—over a

model brain-cell membrane, and the peptide sort of sat and quivered on top of the brain cell membrane, and then it detached itself and started to worm its way through and destroy the brain cell, and we looked at it went, "That's the way the immune system takes out bacteria and other things it wants to, you know, get rid of anywhere in the body." And then, sort of like, "Bing", the light goes on. It's behaving just like it's part of the immune system. And, from that, it was dominoes – all the parts of the story felt in line, and we went, "This is really nice."

Heather 28:15

Isn't that amazing? So, it wasn't something that you had pre-planned?

Dr. Donald Weaver 28:19

It was actually a eureka moment. It really was. [Heather chuckles] I've been involved in Alzheimer's research for 30 years, and this new theory—Alzheimer's as an autoimmune disease—this is the most exciting time of my life. For years, we've been making drugs that try to address targets. This is an opportunity for us to make drugs that address a target that we've also discovered ourselves, and targets that we think really are the fundamental, underlying cause of Alzheimer's disease.

Heather 28:56

Dr. Sivananthan, how excited are you about this new theory and about other research coming out in Alzheimer's and dementia?

Dr. Saskia Sivananthan 29:04

[upbeat electronic music] The brain is this complex organ which requires different thinking about it, different funding for it, and I wear two hats here. I've got the hat from the Alzheimer's Society of Canada and as a funder. I'm excited that Don is exploring these new hypotheses, because that's exactly what we hope to do, to be able to support innovative research and researchers like Don who are looking to explore and find other avenues because, as scientists, you're naturally curious. That's the point. And so, how do we support that ongoing exploration? And, that's why we introduced the Proof of Concept Program. The intention is, is that you don't need to come to us with data. It's you've got a seed of an idea, and we'll give you the early funding to explore it and build the data, and not finding good evidence is still useful. It's important. You need to do that. And, it's equally important to publish that and to make that more well-known so that other researchers can build on those.

I really liked that interplay, but I actually do also want to link back to risk factors, which Don touched on a little bit earlier. We mentioned it in the first report that we've published, but it's also an area that I feel is going to be very important for the future of dementia and dementia research, because it takes a much broader public policy and public health perspective, so while researchers like Don are exploring the underlying causes of dementia, and trying to understand it better, trying to move through that pipeline that could eventually result in these cocktails of treatments, we can still take a public health approach to raising the awareness of dementia, and the field has moved forward there. [upbeat electronic music fades out] For a lot of folks, it might sound like, you know, news, new news. What's good for your heart is good for your head, and yes, but there are also risk factors that are specific to your brain and specific to dementia. Don mentioned head trauma being a very important one. Sleep, social isolation, hearing loss – these are really specific to the risk of dementia and not the risk of cardiac health. That's another area that I'm really excited about, moving forward – what it could mean for the changing landscape of dementia.

Heather 31:20



What could that look like, I wonder, this whole idea of a public health approach to risk reduction? You know, what's needed in that regard?

Dr. Saskia Sivananthan 31:28

When I worked at the World Health Organization, there was a lot of thinking about where does dementia fit? You know, when you think about the WHO, you don't think naturally about something like dementia. You think infectious disease maybe, maybe chronic disease, but they were pretty emphatic that dementia needs to be a public-health and an all-government approach, and that's also the approach that Canada has taken with the National Dementia Strategy when they published it. But, the reason is, dementia is a very promiscuous disease. It doesn't follow the rules. It's not just medical; it impacts your ability to drive, your ability to work, your ability to interact with other people, your ability to be you, and you can't approach that with just a clinical lens. It requires having to think about it in terms of how the communities need to be built, in the kinds of training and supports that others, outside of physicians—physicians definitely do need that support and training, but then, so does the bus driver because you're going to be interacting with them, as well as our family members—and I think that's why thinking about it from a public health perspective is important, but we've not done it before. And so, we're kind of lost. We're not really clear on how to do it, and dementia is almost the first experiment in terms of the disease in which we have to start really seriously thinking about and giving the numbers that we're expecting.

Dr. Donald Weaver 32:55

We need public awareness. People don't think of Alzheimer's disease and dementia. You know, if you stop a 30- or 40-year-old on the street and say, "You know what? What are your health concerns in the future?" they'll talk about cancer, they'll talk about heart attacks. They don't talk about dementia, and they should be. You know, if you look at the numbers, as has been presented, this is going to be a large component of their life, and maybe not them as an individual, but in their family. It's going to impact them in some way. The risk factors, they're hidden out there, too. I mentioned, you know, head trauma, and I deliberately use the old example of the athlete, but there's lots of hidden head trauma out there, and an area, you know, that I see alarmingly often is domestic violence. Domestic violence is a huge problem in our society. It's in 17%, or more of relationships, and here's a place where there's head trauma, and it's hidden, but it's there and it's a risk factor.

Dr. Saskia Sivananthan 33:55

What I was going to add on, it's also it's that life course approach, right? Like you've talked about, when you talk to the 30-year-old, they're not thinking about themselves 30 years from now and how dementia might impact them, maybe at that point, but, really, a lot of these risk factors are accumulating over a lifetime from the time that we're children, and there are very early changes that you could make. It's not about dementia; it's about your brain health. In the same way you think about your heart health, you're thinking about your brain health and raising that kind of awareness might be the better way in which folks who are younger can start thinking about what it could mean for them later on and reducing that overall risk of dementia.

The other thing I really loved that you talked about, is the hidden risk factors. The thing that I was thinking about is that not all risk factors are modifiable. So, we talk about eating healthy, and that is technically a modifiable risk factor, but there's all sorts of reasons for why some people can't eat healthy: groceries or expensive, organic food is expensive, access to that kind of food is expensive or difficult. And so, again, thinking about things a little more differently, that there might be nudge

approaches, and again, ways in which government might need to intervene to change how those factors become modified, because they're not always modifiable the way we think they are.

Dr. Donald Weaver 35:21

[light electronic music] You know, recently I had a patient who was sent to me with memory disorders. "Is this dementia?" It turned out, all it was, was malnutrition. This was an elderly woman, living in a city-centre sort of situation. All the grocery stores had moved out to the periphery. She didn't have access to them. She was actually, you know, living in a food desert. All she could get was convenience store food, you know, things of this sort, and when she actually started to get fed and was put on a normal diet, her memory completely normalized. There are a lot of societal factors in Canada, which we really do have to address.

Heather 36:03

Well, the whole idea and the whole issue of equity and accessibility, and especially looking at the diversity in the changing face of Alzheimer's is also a big part of the report as well. Can you talk a little bit about that, Dr. Sivananthan?

Dr. Saskia Sivananthan 36:16

Yes, absolutely. As I said, this is part of a series of reports, and so the next report—thank you for raising that, Heather—is to look at what we think of as the changing face of dementia. Traditionally, when you think of dementia, we think of it as a disease that primarily impacts the white population, middle to upper class, well-educated-ish, but we have to recognize that, in those rising numbers that I talked about, much of it is driven, yes, by an aging population in the baby boomer population, but also by the immigrant population. Canada is built on immigration. Our age and pyramid structures cannot sustain us if we don't have immigrants coming into our country and building it, but those immigrants are aging, and they speak multiple languages. They have different cultural needs. There's so much stigma that goes unaddressed in those communities as well, that we need to start recognizing. And, what the second report does is, again, put some numbers, but also some faces to those statistics because we're expecting a doubling and tripling of proportionate numbers in a much broader variety of communities than we've normally thought about.

Heather 37:29

Right. And, I guess that will also affect the way that we approach this from a research lens, as well.

Dr. Saskia Sivananthan 37:33

Absolutely. It's that need to really think about multiple hypotheses, and a broader range than just Alzheimer's disease and, as Don said, it might not even be that it's one disease that's Alzheimer's. There's mixed dementias, like up to 50 other types of diseases that have similar symptoms. For us, as a funder at least—this is me going back to wearing my ASC hat—it's important that we can support those kinds of research studies.

Heather 38:01

Well, as a researcher yourself, Dr. Sivananthan, I'm curious what else you're excited about in the research world when it comes to Alzheimer's and dementia?

Dr. Saskia Sivananthan 38:08

Can I say ChatGTP on here? [laughs]

Heather 38:12  
ChatGPT.

Dr. Saskia Sivananthan 38:13

I always get the acronym... ChatGPT – I get the acronym wrong, but I use it, and what's exciting about AI, outside of all of the scary aspects and potential risks associated with it, is how it can really support people living with dementia. We generally don't think about technology and embrace it very well, particularly for older adults, but my goodness, older adults are really early adopters in any way of technology, and it's--

Heather 38:44  
They're savvy.

Dr. Saskia Sivananthan 38:45

They are savvy. It was my mother-in-law who came and, like, introduced me to the concept and told me how she's using it.

Heather 38:54  
Wow.

Dr. Saskia Sivananthan 38:55

And, I went, "Wow, I need to look into this a bit more." But, the idea of being able to use AI to support decision-making, for family physicians, for example. We did a survey a couple of years ago where we talked to family physicians across the country, and we asked them, you know, "What do you struggle with? Where are the gaps?" and, outside of concerns with confidence in making a diagnosis—many family physicians aren't really trained for that—the other is, "What do I do post-diagnosis? I can make the diagnosis, maybe, but then I don't know how to support it. I don't know how to manage it, and it needs such a tailored approach that maybe AI and technology could play a role in supporting that decision-making."

Heather 39:39

That's fascinating. I hadn't even thought of that angle.

Dr. Donald Weaver 39:42

You know, just talking about exciting new directions, we've been talking a lot about Aducanumab and Lecanemab – therapeutics, but the other side of this coin is the diagnostics. You know, it's not like we can do a chest X ray. It's not like we can do a blood test to go, "Yeah, this is what you've got." We're not there yet and being able to diagnose the problem is just as important as being able to treat the problem, and so there is a lot of research going on in coming up with new blood tests, new ways of imaging the brain to try to help with the diagnosis, and they are coming along in parallel with the therapeutics, and I think this is also an exciting direction.

Dr. Saskia Sivananthan 40:24

Absolutely. Non-invasive ways, right? Like retinal scans and being able to get a blood test as opposed to what we currently do, you know, with MRIs and spinal taps.

Heather 40:34

I know that there's been other advances, too, into research into the gut microbiome. So, can you tell us a little bit more about that, Dr. Weaver?

Dr. Donald Weaver 40:41

[light, rhythmic electronic music] The gut microbiome – that's a very exciting area. You know, there's a whole lot of brain tissue, neural tissue, that sort of stuff, within the gut. Some of the chemicals produced by the microorganisms in your gut. They behave like neurotransmitters, like the messengers in your brain. There is a really, really close connection between your gut and your brain and, you know, I think that clever new therapies are going to be evolving therapeutic. Manipulation of the microbiome – that is going to be one of the really neat areas where we start to make advances in brain disease, and I think that, you know, there's a future here for the therapies of Alzheimer's disease. Certainly at the Krembil Brain Institute, this is an area of immense interest and importance to us, is appreciating the role of neuroinflammation and how we can creatively try to control it, and certainly, one of our recent hires, Dr. Rojas, she is very passionate about the therapeutic potential of the microbiome and how we can manipulate it for innovative treatments of neurodegenerative disease. [light, rhythmic electronic music fades out]

Heather 41:46

Dr. Weaver, what keeps you optimistic after so many years of treating patients, and also being in research?

Dr. Donald Weaver 41:54

You know, I've been seeing people with memory disorders for 30 years, and that's been a long 30 years. It's been a long 30 years of seeing people, seeing their families, and having difficult conversations with them. It's a disease that has even affected my own family, and so I know this from both sides of the desk and, you know, if you're in drug design, people frequently say you have to be pathologically optimistic. You have to get up every day and go, "Today is the day," and let's face it, it usually isn't. I've been at it for 30 years, and we haven't got the cure yet but, every day, you go at it, and you go, "Yeah, today's the day we're going to add some insight, something that makes a difference," and you think back on all the people that you have seen and their families, and that's the motivation that you need. You know, they need this. You know, as long as they need this, I hope that there's people like me, other people who are interested in the research, people who are interested in supporting the research, the full spectrum of activities, because we certainly need it.

Heather 43:01

Dr. Sivananthan, are you equally optimistic?

Dr. Saskia Sivananthan 43:04

I am. I think you have to be to be in the dementia space, quite frankly, because it's been tough. It's been very difficult, and the resilience that people living with this disease and that their care partners show, that absolutely keeps me going.

Heather 43:20

I know that you've also been fortunate to meet and interact with many of the patients, including as part of your Alzheimer's Society Research Program. So, is there one story that stands out that you can share with us today?

Dr. Saskia Sivananthan 43:32

Yes, absolutely. When I first started at the Alzheimer's Society of Canada, our research program included people living with dementia, but not that many. Their voices weren't necessarily valued as much as we would like them to be, and over the years, we've really built a program that weights two things: the scientific merit, first and foremost of the applications that come through for research funding; but also, the value of that research, if it gets funded, and it becomes results that could impact the lives of people living with dementia. That's where we have who we call citizen reviewers, and these are people living with dementia, these are care partners, and then there are also those who support them – social workers, staff.

So, with our citizen reviewers, there's two quotes that I would love to read. The first is from a current citizen reviewer, Cory. [gentle electronic music] "I am compelled to help support finding a cure for dementia in my lifetime. My parents were taken by Alzheimer's disease, and more than 44 million people, worldwide, live with Alzheimer's and other related dementias, and we know these numbers are growing rapidly. I'd rather not be its next statistic." And the second quote is from a very, very close friend of mine, Roger Marple...

Heather 44:56

Yes, I remember Roger.

Dr. Saskia Sivananthan 44:56

..who was an amazing advocate for dementia and really helping people to speak about their journey, and to remove the stigma of what's often really seen as a mental health disease. And, Roger passed away a few months ago, but I'd love to honour his memory because of all of his amazing advocacy. And, this is what he had to say: "I'm a big believer that research equals progress. If we are going to realize meaningful advancement towards living with dementia, it will be done through research." [gentle electronic music fades out]

Heather 45:32

Mm-hmm, and the challenges they face, and yet they're still so motivated to help others.

Dr. Saskia Sivananthan 45:38

Absolutely, exactly.

Heather 45:41

Dr. Weaver, recently, the Globe and Mail feature to story about you writing poetry for your patients.

Why do you do it?

Dr. Donald Weaver 45:48

Because I think it helps both of us. I think it helps the patients, families, and me. Sorry for a trip into the past, but in September 1981, it was my first year after graduating from medical school and I was called in the middle of the night to see this patient. He was a World War I veteran who had gone through awful times in the trenches of the First World War and, unfortunately, as his dementia was taking hold, his ability to suppress all the bad memories that he had experienced in the war – he had lost the ability to suppress that, and it was all bubbling back up again, and he was actually hiding underneath his hospital bed, because he was living a nightmare of the First World War event. And, I remember being called to see him and I remember, like, getting down on the floor and peering underneath the hospital bed where he was cowering and hiding underneath the hospital bed. And, wow. I mean, it just tore at my heartstrings. Here was this elderly man, and just the hell that he was living through, you know? And, I

realized that I didn't have anything to offer him, and so, that night, I went back, and I wrote a poem for him. I came back the next day and gave it to him. It meant the world to him, and it meant the world to his wife. They realized that I couldn't do anything, but they realized that I cared, and that was therapeutic in its own right.

Heather 47:18

Would you be able to read some of the poem for us today?

Dr. Donald Weaver 47:23

[thoughtful music] Okay. "But every war is like the last / There are no wars to end all wars / Scorched souls and human shells remain / For those who fought, for all the souls / Their sacrifice and courage, great, we grieve / We must abhor war's carnage, strife / We must embrace each human life.

Heather 47:45

Oh, I got shivers. That was incredible. Well, I just want to thank you both for being here today and having this discussion—an important discussion—and I'm sure it's not going to be the last as there's so much more to talk about. Thank you so much.

Dr. Donald Weaver 47:59

Thank you.

Dr. Saskia Sivananthan 47:59

It was my pleasure. Thank you.

Lindsay Bongard-Batori 48:06

[gentle electronic music] I lost my mom, May 3, so almost three years ago, and I was lucky to be in the room with her when she passed, and I was able to whisper in her ear that she'd better send me signals. She'd better show me that she's with me. When I do find things, the red cardinals that visit me every day, I have to believe that that's my mom checking in on me. [cardinal sings]

Heather 48:53

[Your Complex Brain theme music] Thank you to Dr. Donald Weaver and Dr. Saskia Sivananthan for joining me on the podcast today. Thanks also to Lindsay Bongard-Batori for sharing her heartfelt story and memories of her mother, Barbara. If you'd like to hear more of Lindsay's interview, please go to our website [uhn.ca/krembil](http://uhn.ca/krembil).

This episode of Your Complex Brain was produced by Jessica Schmidt. Our executive producer is Carly McPherson. Thanks also to Dr. Amy Ma, Twayne Pereira, Suzanne Weiss, and Megan Andheri for their production assistance. [theme music continues]

For more information about the Krembil Brain Institute, please visit [uhn.ca/krembil](http://uhn.ca/krembil), and you can reach us by email at [krembil@uhnresearch.ca](mailto:krembil@uhnresearch.ca), but please note that due to privacy regulations, we cannot answer any personal health questions. Thanks for listening. We'll be back in two weeks with another exciting episode. Have a great day. [Your Complex Brain theme music continues then fades out]