

# YCBS1E1 - Alzheimer's\_V6\_mixdown

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## SUMMARY KEYWORDS

Alzheimer's, disease, drug, people, dementia, brain, patients, families, problem, risk factors, blood test, complex, future, individual, symptomatic, high blood pressure, symptoms

### **Dr. Weaver** 00:00

[electronic music plays] If we look at the last 20 years, tremendous progress has been made in the treatment of cancer, of heart disease, but we have completely failed at brain diseases, in general, and dementia, in particular. If we live long enough, whether we're a patient, a family member, or a caregiver, it is becoming that common that our lives will be touched by it.

### **Patty** 00:32

My mother is currently living with Alzheimer's disease. She continues to be strong, in a silent way, and she's happy on most days. I remind myself that this hurts so much because I love her so much. [music continues]

### **Heather** 00:52

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 our research labs to meet the game changers of the future, and we'll empower you with the latest research to help you take charge of your own health. You'll also hear directly from patients who are living with brain disease and the care teams who support them. Join us on a journey to unravel the mystery of your complex brain. [music continues]

### **Heather** 01:42

What's the first thing you feel when you hear the word Alzheimer's, or dementia? Maybe it's sadness, thinking of a loved one who's gone through it, or confusion about the latest headlines and what they really mean. But, more likely, it's fear - fear that it could happen to you or a family member, fear that, if it does, it could upend your life as you know it, or even fear that maybe you'll pass it on to your own children. What's clear is that Alzheimer's, which is the most common form of dementia, is a devastating diagnosis for an individual and a family. In fact, we'll hear a first-hand account from a woman whose mother is living with Alzheimer's later in this episode. There are currently more than 55 million people worldwide living with dementia, and that number is expected to nearly double every 20 years. Think about that for a moment. If it sounds like an emerging pandemic to you, you're not wrong, but it's not all doom and gloom because there are ways to reduce your risk of getting the disease and there are very smart people, like our next guest, who have made it their life's mission to try and stop Alzheimer's in its tracks or prevent it altogether.

**Dr. Weaver** 02:51

The chemical changes in the brain that happen before the person becomes symptomatic with Alzheimer's are happening 20, 30 years before their first symptom. Maybe the cure is already out there. Maybe the drug is out there, and we just can't recognize it, we can't see it.

**Heather** 03:13

Dr. Donald Weaver is Canada's only neurologist who is also a medicinal chemist. He is Co-Director of Krembil Brain Institute and a leading researcher in the field of Alzheimer's. Dr. Weaver, thank you so much for joining me on the podcast today.

**Patty** 03:27

And thank you for having me here.

**Heather** 03:29

It's a pleasure. So, let's dive right in and start with what everybody's talking about. There's an Alzheimer's drug on the market right now called aducanumab, and there's been a lot of controversy and confusion about the efficacy of this drug. So, what do people need to know?

**Dr. Weaver** 03:44

Aducanumab certainly is a source of controversy right now. It is approved in the United States, but nowhere else. Aducanumab is a biologic, so it's not a pill that you take; it's an injection that you receive. Families and patients with symptomatic Alzheimer's disease want to know, you know, "Can I take this particular drug?" and "Why is it approved?" It was approved because it targets the clumping and aggregation of this protein called amyloid and, for many, many years, amyloid clumping was thought to be the mechanism, the key to disease progression. I think that that is now heavily disputed and, even though we have a drug that supposedly deals with that, interrupting this is not going to be enough, and you'd have to get it so early in the course of the disease that, by the time you're symptomatic, it's too late.

**Heather** 04:53

So, what would you tell the patients and their families who are coming to you, asking for this drug?

**Dr. Weaver** 04:58

I can understand a patient's and families' desperation. This is an awful, awful disease and they will do anything to try to prevent it from progressing, and so, because of that, there's an interest in anything, and aducanumab certainly is an agent which has some justification for it. However, it's very expensive, it has a significant number of side effects, and it's not really been proven to truly reverse this disease. So, my duty as a physician, is to first do no harm, and I appreciate the desperation, but we have to balance risk versus benefits and, in that sort of scale, my personal opinion is that aducanumab is found wanting. You know, we always say that a voyage of 1,000 miles begins with a single step. Well, aducanumab is more than a single step. It's a whole lot of steps in the right direction, but it's not the end goal. It's not where we need to be. It's just a milestone on the way.

**Heather** 06:19

And can you clarify for us... Health Canada hasn't yet approved this drug, here in Canada. Correct?

**Dr. Weaver** 06:24

You are correct. Health Canada has not approved the use of aducanumab for distribution in Canada at this time. I mean, I always like to say, "Global diseases need global solutions," and aducanumab is not a global solution. [gentle electronic music]

**Heather** 06:44

You're a medicinal chemist. You've got a whole team working on an Alzheimer's drug in your lab at the Krembil Brain Institute. So, where does your research stand, currently? Have you made any progress on that?

**Dr. Weaver** 06:54

We're always making progress, of course. When I speak to the people in my lab, I like to draw a comparison between Alzheimer's disease and high blood pressure, and I like to point out that high blood pressure, mechanistically speaking, is a trivial disease compared to Alzheimer's, and yet, we have lots and lots of different medications that work by lots of different mechanisms, and many people on more than one medication that complement each other. And so, I think it's a bit naive to believe that we're going to have one pill that's going to cure Alzheimer's disease. I don't think there's a magic bullet here. I think that, you know, if we can't even get the magic one drug for high blood pressure, I don't think we're going to get the magic one drug for Alzheimer's disease and, ultimately, I think it's going to be, hopefully, multiple medications that work through multiple mechanisms, and that is the philosophy that my lab is pursuing, so we have various groups working on various approaches. So, the time-honored approach for developing drugs for Alzheimer's disease focuses on what's called protein misfolding, or clumping, so two proteins, amyloid, and tau, misfold and clump up, and that's bad for the brain, and so we are working on approaches to try to address that problem. But, more recently, it's being appreciated that there is a role for inflammation, neuroinflammation of the brain, which also contributes to Alzheimer's disease and, with this in mind, we also have multiple groups tackling different targets that may help in developing drugs to address neuroinflammation. So, we're not putting all of our eggs in one basket. We are looking at multiple different approaches and we are trying to develop a variety of different drugs that, hopefully, we'll be able to use in complementary fashion, in combination, to help people with this disease.

**Heather** 09:07

Amazing. Well, you and a whole lot of pharmaceutical companies have been at this for a long time, trying to come up with a new treatment for Alzheimer's and yet, there's still only one drug on the market. So why is it so challenging?

**Dr. Weaver** 09:20

I'll correct you. First of all, there's more than one drug on the market. There are symptomatic agents, so there are drugs like Donepezil and various other agents, which help, symptomatically, and then, of course, we've already spoken about the one agent which attempts to be curative or disease modifying, but isn't, and that is aducanumab. And so, I mean, if we look at the last 20, 30 years of drug design,

drug development, and clinical trials in the area of Alzheimer's and dementia, it really is a long track record of failure - failure after failure - and there's lots of reasons for this. I think, first and foremost, it's just the overwhelming complexity of the problem. The brain, as I've mentioned, is the most complicated entity in the universe and, arguably, Alzheimer's is the most complex disease of the brain. And then, if you add into this, trying to develop drugs for this, you have to develop drugs that can get into the brain and, given the patient population that we're targeting, older individuals, these have to be very safe drugs, so there's just a whole lot of complex issues that have to be dealt with, that really are quite formidable. So, first and foremost is the issue of complexity. The second major contributing issue, from my mind, is funding or, more importantly, lack thereof. Diseases like cancer get 10 times the amount of funding that dementia and Alzheimer's get. This is a complex problem, and we need as many brains as we can working on it, but scientists tend to go where the money is, [chuckling] much like Willie Sutton, the robber, and you go where the money is, and the money isn't in Alzheimer's disease. So, you know, I really think that society, as a whole, needs to appreciate the significance of this disorder, and put a bit more of its weight behind it.

**Heather** 11:32

So, what about diagnostics? You mention that, if we can actually diagnose the disease earlier, we may be more successful in the future with treatments down the road. There's a new blood test available in the US right now to diagnose Alzheimer's disease. How groundbreaking is this? And what does it mean for patients?

**Dr. Weaver** 11:50

Excellent question, and I get this one a lot. If we look, traditionally, at trying to diagnose Alzheimer's disease, you know, traditionally, it's been-- spell the word "world" backwards. I've done that one so many times, I'm doing it in my sleep, and we've always said, "Oh, what we would give for a blood test." Well, a blood test has appeared, and it certainly is available in the United States, and this is a blood test that looks for the presence of this protein called amyloid in the blood. And does it diagnose Alzheimer's disease, 100%? No. What it does is it gives additional information to the clinician, and it helps that individual gather more and more information about the patient, and so it really enables us not to diagnose the disease so much as to assign a probability that the person has the disease or will get the disease. So, once again, just as I mentioned, aducanumab is a major step forward. This blood test is another major step forward, and, you know, it really speaks to the fact that we are so far ahead of where we were 30 years ago, with so many things happening, that, you know, I think that this is an area where there's a tremendous amount of optimism. The future's bright. [gentle, uplifting music]

**Heather** 13:27

Well, let's talk about the caregivers because you're meeting with these patients, you're meeting with their families. Caregivers are often the unsung heroes dealing with Alzheimer's and dementia head on. So, let's hear from Patty Kim, the daughter of one of your patients about her experience.

**Patty** 13:43

Caring for someone with Alzheimer's, it's, I would say it's phasic. I have, I guess, periods of chaos and then interludes of some stability. Juggling my roles as being a wife, a mom to two growing children, doing my best at work, and trying to find time to self-care, [chuckles] it's certainly not easy, and, you

know, you're out of control. But everybody goes through this, and I have to remind myself, I'm not the first, not the last. I remind myself that this hurts so much because I love her so much.

**Heather** 14:38

I've often heard you say that Alzheimer's is a diagnosis of a family, not just an individual. So how common is Patty's story?

**Dr. Weaver** 14:45

Patty's story is common, very common. Certainly, when I meet with patients and their families, the suffering is certainly spread throughout everyone. Their loved one, be it their mother, their father, whoever, is not the person that they remember. It's not the person who, you know, was their mom or their dad when they were growing up. This is a different person. This is a person who can't recognize friends, can't share fond memories, and, you know, it's painful - very painful - emotionally, to watch a family member go through this, and so, yeah, Alzheimer's is not a disease of individuals. It's a disease of families.

**Heather** 15:31

A lot of people want to know about prevention. Is there a way to prevent or delay the onset of the disease? So, what can the average person do to reduce their risk of getting it?

**Dr. Weaver** 15:41

Going back to earlier, when I talked about a comparison with high blood pressure, we recognize that sometimes subtle changes in lifestyle factors are a help, and, you know, people go, "Well, Alzheimer's is just so complex. That's, you know, that's wishful thinking." It is not wishful thinking. Since Alzheimer's is such a devastating disease, it's absolutely crucial that we do our utmost not to get it, and the sooner you start avoiding the risk factors, the better. It's never too late, but you should start as soon as you can. And, there was a very important paper in the summer of 2020, published in the prestigious medical journal called The Lancet, which listed 12 risk factors associated with Alzheimer's disease, and the statement is made that probably we could reduce Alzheimer's by about 40% if we could just deal effectively with these risk factors, and these risk factors include smoking, obesity, alcohol abuse, head trauma, exposure to air pollution, physical inactivity, hard of hearing or deafness, high blood pressure, social isolation, depression, diabetes, and a low education rate. We can do a lot about these. These are risk factors that can be addressed. I mean, the areas of smoking, obesity, alcohol abuse, head trauma, these are all things that, you know, are within our reach and that we can do, and I would really like to see the government buy into this and to do public education programs, and to make people aware that, you know, with some simple measures, you can substantially reduce your risk. [gentle electronic music]

**Heather** 17:44

What are the signs and symptoms to watch out for? When is it actually time to worry?

**Dr. Weaver** 17:49

That's another question that I get a lot, and, you know, let's face it, we all forget things, we all misplace things, and I don't want people to suddenly go out and go, "Oh, no! This is the first steps!" Forgetting things is normal. But what are the early signs? Well, first and foremost, it's problems with your short-

term memory, and of sufficient magnitude that it really has an effect on your day-to-day living, your day-to-day activities, and may involve misplacing objects, misplacing items, so this is a short-term memory problem that has an impact. Another symptom or sign that is quite relevant is difficulties with familiar tasks, something that the person has done every day, and they've done it for years, and now they're struggling to do it, and that's a change. Next, there's problems with planning or problem solving. An issue which they would normally be able to sort through or a task that has multiple stages, they just can't do it anymore. They stumble. Next are issues around language, so word substitution, or using the incorrect words. I frequently ask patients, you know, "Are you having problems stumbling with your words?" And then, I think a final area of early signs and symptoms relate to their ability to process time and space. Do they get lost in their own house? Do they get up to go to the washroom in the middle of the night and get lost on the way to the bathroom? Do they forget the day? You ask them, "What year is it?" and they smile, going, "Well, that's a silly question. Of course, I know what year it is," and they give you a year that was, say, 10 years past. So, all those sorts of things are, collectively, signs and symptoms that indicate that perhaps it's time to have a conversation with your health care provider.

**Heather 19:55**

Dr. Weaver, you have been studying Alzheimer's and treating patients for more than 30 years. Do you still feel hopeful, even optimistic about the future of Alzheimer's research, and for your patients?

**Patty 20:07**

I have more optimism now than I've ever had in my career. I think that the future is really bright, and I know people go, "Well, you know, 30 years ago, we didn't have anything, and we still don't really have anything, so, you know, what progress has been made?" Tremendous progress has been made. First of all, we realize now that Alzheimer's is a disease like any other disease. You don't have to say, "Dear old mom or dad, they're getting a little senile," and sort of hide them away. That's not the case. We also recognize that not all dementia is Alzheimer's disease, but certainly all Alzheimer's disease is dementia, and we have the ability to recognize certain subtypes. We have the ability now to recognize what frequently happens along with dementia, such as depression, and the ability to treat some of those so that we can improve an individual's quality of life and, as we've been talking about, hey, aducanumab means that we are moving in the right direction towards therapeutics that might be meaningful, and we have a blood test, a blood test that's also moving in the right direction. Didn't have any of this even three, four years ago, and so, I think, now is the time to be optimistic, and I think that we're going to see substantial changes in the next four to five years. People don't think that Alzheimer's is a sexy disease, and this has something to do with the funding of it, and they go, "Oh, you know, it's a disease that affects 90-year-olds so, like, why do I care?" I was actually reading The Economist magazine just this morning, and they had an article which stated, if we look at the last 20 years, tremendous progress has been made in the treatment of cancer, of heart disease, and the orthopedic surgeons have made huge advances in putting new joints in, but we have completely failed at brain diseases, in general, and dementia, in particular. What the future of healthcare is, is an overwhelming number of elderly people with functioning bodies and non-functioning minds. That's the future, and we have to do something about it now, because the socioeconomic impact of that is going to be huge. And, the other thing is, is that I think people need to appreciate that their lives will be affected by this, even if they don't get it, because, you know, if we live long enough, we'll all be touched by Alzheimer's disease or dementia.

Whether we're a patient, a family member, or a caregiver, it is becoming that common that our lives will be touched by it. [gentle electronic music]

**Patty 20:11**

My message to other families that might be going through living and caring for someone with Alzheimer's would be to just take it day by day. My mom is not as verbal as she used to be, but I can look into her eyes and I know she knows, and she'll eek out a smile, and then it turns into a big laugh, so then we're both laughing, and that's a real moment of connection and I'm very grateful for that. [gentle electronic music continues]

**Heather 23:56**

[Your Complex Brain theme music] Thank you to Dr. Donald Weaver and Patty Kim for being featured in today's episode of Your Complex Brain. You can learn more about Patty's story and about how to reduce your risk of getting Alzheimer's by checking out the links in today's show notes. This episode of Your Complex Brain was produced by Jessica Schmidt. Executive Producers are Tobin Dalrymple with Pilgrim Podcasting and Carley McPherson, with production assistance from Dr. Amy Ma, Twayne Pereira, and Suzanne Wice. 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 fades out]