

## HIV dementia

[00:00] [background music]

**Leigh Hatcher:** [00:06] Hello, and welcome to another "Nerve" podcast, "Hope Beyond Brain Disease." I'm Leigh Hatcher. With our aging population, there's an increase and an understandable focus on dementia, including a recognition that there are many and varied forms of the disease.

[00:21] In this podcast, maybe a surprise to many, HIV-related dementia. Of course, there've been huge strides in the treatment of HIV/AIDS over the past generation, and one of the consequences of that is that those with the disease are living longer and showing the distinctive signs of dementia.

[00:41] Professor Bruce Brew is one of Australia's leading authorities in neurology and HIV/AIDS. He's conjoined professor of medicine at the University of New South Wales and adjunct professor of medicine at the University of Notre Dame.

[00:57] I'm so pleased that he's joining us for this Nerve conversation on HIV-related dementia, beginning with how far we've come since those confronting early days of HIV/AIDS.

**Professor Bruce Brew:** [01:09] Back in the early '80s, patients were presenting with very advanced disease by and large, because the disease had only just been described.

[01:20] During the really early '80s, there was no definitive tests. That came shortly after. They were presenting in desperate straights, most commonly with severe pneumonia, sometimes with meningitis, and sometimes with a dementing illness.

[01:37] Their prospects, if they had pneumonia, weren't so bad. They could respond to treatment, but the underlying HIV disease was still a huge problem. Their prospects were not good until the mid-'80s when AZT, or zidovudine, came on to the scene, and that certainly turned things around to an extent.

**Leigh:** [02:00] Substantial amounts of money pretty soon flowed into this health issue. Can you briefly take us through beyond that? How did this progress for people and their prospects?

**Professor Brew:** [02:11] In the absence of definitive HIV treatment, there is inevitable progression to death within months. Then in the mid-'80s, zidovudine, or AZT, came along. That showed that there could be some response, and in some patients, quite dramatic response.

[02:27] When I was working in New York, one of the other neurologists on staff had HIV disease, and he described it as a light bulb moment when he started taking zidovudine. It turned things completely around for him.

[02:47] As time went on, more definitive treatments for HIV came around. In the early '90s, there was combination therapy, usually with two drugs, and then of course, the big three drug breakthrough came in the mid-'90s.

**Leigh:** [02:59] For those diagnosed with HIV/AIDS today, what are their prospects compared to those days?

**Professor Brew:** [03:05] It's essentially a modifiable disease. It's not a curable disease, clearly, and it's certainly very treatable. Their prospects are very good. They can live, in general, an almost normal life span.

[03:17] However, they're still not normal in general. There are some patients who do extremely well, but there is a reasonably-sized minority who don't do so well, and have ongoing chronic inflammation both systemically -- those in the blood, as well as in the spinal fluid.

[03:34] Those patients either have or are at risk of other comorbidities, and also at risk of the virus still affecting the brain, there's a mistake to think that with antiviral therapy, even though the drugs are extremely good, that if you are below detection that you are free from any risk of the virus affecting the brain. You're not.

[03:56] However, there's a sizable majority who are fine, but a significant minority who are not.

**Leigh:** [04:03] One of the consequences of living longer and being in better health comparatively is the emergence of HIV-associated dementia. How does that differ from other dementias?

**Professor Brew:** [04:15] It is unusual in this day and age to develop HIV dementia per se, and so that's using the term in a stricter sense, that is, severe cognitive impairment, enough to interfere with activities of daily living.

[04:29] The milder forms of impairment are much more common now, like mild cognitive impairment that patients have frequently diagnosed, who then go on to develop Alzheimer's later on.

[04:40] How is HIV-associated neurocognitive disorder or mild cognitive impairment different from other dementias? It's more a psycho-motor slowing, the content of what people say who have this disorder is often not too bad.

[04:57] You'd pass it for normal, but they're slower by and large. They often complain of forgetfulness and can't concentrate. They lose track of the conversation.

[05:07] These are relatively subtle deficits, but they can be impactful in the particular patient's life, and sometimes can lead to demotions at their particular job or even cessation of their job, because of inability to cope.

**Leigh:** [05:22] When you say slower, in what way? Give us some practical examples.

**Professor Brew:** [05:26] They're a little bit like a Parkinson's patient in that they are slower to respond in a motor sense, in terms of articulation, but also in just getting around. Their gate is a little slower, as well, in contradistinction to Alzheimer's patients, where they're not slow, they're just very forgetful, by and large.

**Leigh:** [05:49] Is it possible to determine of cause of this form of dementia, and how it develops?

**Professor Brew:** [05:54] That's an ongoing controversy. The big paradox is that you have these really powerful antiviral drugs that essentially have revolutionized HIV disease in general, and yet, you still have the mild form of cognitive impairment.

[06:10] You would think that the severe form of cognitive impairment would be harder for the antiviral drugs to treat, and the mild form should be really easy for the drugs to treat. In fact, the converse is true. The situation, I've termed it as a therapeutic paradox.

**Leigh:** [06:26] It is tough to diagnose?

**Professor Brew:** [06:28] It can be tough to diagnose, simply because there's no diagnostic test. It's not like cryptococcal meningitis, for example, where you have a test where if you find the bug, you've got the answer.

[06:42] You can certainly have impairment, and you have to make sure that there are no other causes for that impairment. It's more an exclusionary diagnosis, but at the same time, it's got to be within the clinical bounds of probability, it can be difficult to diagnose.

[06:58] It involves clinical assessment, ideally neuropsychological assessment -- although that can be a resource issue -- and then there should be imaging, preferably by MRI scan, often with spectroscopy, which can be helpful, and spinal fluid analysis, because it can be suppressed in the blood. The virus may be undetectable, but that may not be the case in the spinal fluid.

**Leigh:** [07:22] What should the patient themselves -- friends, family, partners -- be on the lookout for signs of HIV-associated dementia?

**Professor Brew:** [07:31] If we broaden it to HIV-associated neurocognitive disorders, not really at the severe end, because that's usually quite easy to pick up. In the milder forms of the disorder, I think family and friends should be alert to complaints of forgetfulness.

[07:48] At a superficial level, it may look like Alzheimer's, but at a deeper level, it's not. Patients complain that they're more forgetful, lose track of conversation. They may give up reading or find it longer to read. Their work performance can deteriorate because they can't organize themselves and multitask as well as they should.

**Leigh:** [08:10] Is there treatment available?

**Professor Brew:** [08:12] That's where it gets tricky. There is, in a broad sense. There are some patients who have this phenomenon called CSF viral escape. In other words, the antiviral drugs are working really well in the blood, but for whatever reason, the drugs don't get into the brain either at all, or as well as they should.

[08:34] In that case, the investigations won't show that, and you can modify the antiviral drug regime to optimize brain entry. There are some patients, as well, who seem to have inflammation in the spinal fluid and in the brain, but no detectable virus.

[08:52] That's where it gets a little tricky, and some people think that adding some other drug that gets into the brain to their existing regimen may be useful.

[09:02] Then, there's a cohort of people who don't have a detectable virus and not much in the way of inflammation. It's even less clear what the optimal treatment avenue is. There are some new drugs that are being looked at, very early stage of development, to try to target their particular Achilles' heel in the life cycle of HIV.

**Leigh:** [09:22] It's worth noting two things, I think, that not everyone with HIV develops cognitive impairment, and HIV today is also a disease experienced within the heterosexual community.

**Professor Brew:** [09:33] Absolutely, it's very important. Our figures would say that around 20 percent, maybe 30–40 percent at the very most, would experience some degree of cognitive impairment. It depends on how long they've had the virus, how long they've been suppressed. Did they go through a period where they weren't on therapy for a while? Did their T-cell count become very low?

[09:57] It is very true that heterosexuals are still at risk. It's important to realize that.

**Leigh:** [10:02] Are there risk factors, and are there measures that people can take with their health before this to reduce the risks?

**Professor Brew:** [10:09] There are risk factors over and above sexual practice. There are lifestyle factors that probably are important. There is some emerging evidence that physical fitness can be a significant, positive factor in terms of reducing the risk.

[10:26] The Mediterranean diet probably has benefits beyond just Alzheimer's disease, and probably has some role in HIV-associated neurocognitive disorder. And absolutely, stop smoking.

**Leigh:** [10:37] [laughs] Yes, for a whole lot of reasons. Is there, just as we wrap, one particular patient story you can relate to us to demonstrate, say, the benefits of early diagnosis, and therefore, treatment?

**Professor Brew:** [10:50] The person who comes to mind, I looked after about two years ago. He was a successful travel agent, and was on therapy, doing very well for some years. Then he got sick of taking medications, which is not uncommon, and decided he was doing fine, so he'll stop the medications.

[11:12] He was off medication for some two years, and unfortunately, presented after being found by friends in a disheveled state. He was unable to walk. He was completely cognitively impaired to the point where he didn't know where he was. He unequivocally had the severe end of impairment.

[11:34] We investigated him. He had a high viral load in the blood and spinal fluid. Treated him with a combination of antiviral drugs that we knew would get into the brain well, and after some months -- and that's the key issue, I think, in these sorts of brain disorders, recovery can take months. It's not like pneumonia, where you get better in a few days or weeks.

[11:58] In his case, it took about 6 months, and really not fully back on deck for about 12 months. He was a particularly successful case, because he regained the ability to walk. He can ambulate and run normally. He couldn't before. He was essentially bed-bound.

[12:13] His cognition has come back significantly to the point where he's thinking about returning to work. Hard to know whether he'll be able to do that to the same level.

[12:22] It's an instructive case, because one, it shows the importance of maintaining medication, two, that the disorder is reversible to a very significant degree in some people. There are plenty of people in whom there is damage, and you can't reverse the damage, but equally clearly, there are some people who respond very well.

[12:42] [background music]

**Leigh:** [12:42] Professor, it's been an important conversation, and I'm sure revealing for many in our audience. Thank you so indeed for your time.

**Professor Brew:** [12:50] It's a pleasure. Thank you.

**Leigh:** [12:50] We're so grateful to Professor Brew for generously giving us his time and expertise, and thank you for joining us on this Nerve podcast, Hope Beyond Brain Disease. I'm Leigh Hatcher. There's a whole host of information and resources at [www.sydcog.com.au](http://www.sydcog.com.au).