



VEIN HOPE

Patients are clamouring for a new, unproven vascular treatment for multiple sclerosis.

BY STEPHEN PINCOCK

THE first time Kerri Cassidy heard the name Paolo Zamboni was in November 2009, when a friend in America sent her an email. “Check this out,” the message said. “It could be really promising.”

Both Cassidy and her American friend had multiple sclerosis. Dr Zamboni, a vascular surgeon from Ferrara in northern Italy, had just published a paper showing that people with MS were 43 times more likely than controls to have specific abnormalities in the jugular and vertebral veins.

Dr Zamboni’s study of 65 MS patients and 235 controls raised the possibility that these abnormalities — dubbed chronic cerebrospinal venous insufficiency (CCSVI) — could be a cause of MS.¹

News of this controversial hypothesis soon spread among MS patients around the world, many of whom had become connected online, using websites like YouTube and Facebook to share stories, news and ideas.

In this tight-knit and highly motivated community, CCSVI suddenly became top of the conversation list.

Cassidy, a Melbourne mother of two, had been involved in that online community for some time, with her own YouTube channel that she used to talk about her life with MS. But the Zamboni paper initially left her cold. “I came out on

YouTube and said, ‘You know what? I don’t know about it and I don’t have the energy to think about it,’” she says.

However, a few days later Cassidy shot off an email about the report to another friend with MS, one who took a pretty conservative view of any new theory about the disease. That friend was characteristically cautious, but reminded Cassidy that many of the symptoms they experienced — like painfully cold feet or dizziness after hot baths — did seem like they could be linked to circulation problems.

“After that email, some of these things started to bump around in my head,” Cassidy says. A few weeks later she suffered a relapse that left her unable to drive and housebound for the school holidays. In January, a second relapse left her without proper bladder function.

“By the end of January, I was in a pretty bad place. I just thought, I can’t live like this. I’m 34 years old with two kids, but I feel like I’m 84. It was a catalyst.”

Meanwhile, the chatter about the Zamboni theory among the world’s MS patients had grown louder with the news that he had performed venoplasty to unblock the jugular veins of MS patients with CCSVI, and they had experienced improvements in their symptoms.

Cassidy talked to her neurologist about the Zamboni studies. The first

‘I am confident that this could be a revolution for the research and diagnosis of multiple sclerosis.’

— Dr Paolo Zamboni
Vascular surgeon

time she raised the topic he was interested; the second time he was antagonistic.

“He said, ‘This is not proven and I wouldn’t be putting my patients through this until it is,’” she says. When she asked him to order tests that would identify venous insufficiency, he said she should wait until her next scheduled MRI, in October.

Cassidy, perhaps unsurprisingly, wasn’t willing to wait.

In late January 2010, just two months after the first publication by Dr Zamboni, she discovered there was a radiologist in Melbourne who was willing to check for insufficiency in the jugular veins of MS patients. She asked her GP for a referral, called the clinic, and got an appointment the same day. By that afternoon, she had the news: there was evidence of bilateral jugular vein stenosis.

Paolo Zamboni reportedly began hunting for a cure for multiple sclerosis in 1995, when his wife Elena developed the condition. (He did not return an email request for an interview.) An apparently healthy 37-year-old, she began to experience classic signs of the disease: attacks of vertigo, numbness, temporary vision loss and devastating fatigue.

Remarkably perhaps, he found a potential cure not in the central nervous system, but on his profes-

sional home turf — the vasculature.

His first major paper on the topic, the one Cassidy read in November last year, said only that the link between CCSVI and MS “seems to be plausible”.

He found evidence for malformations or blockages in the veins draining blood from the brain in more than 90% of the MS patients in that study, including his wife.

And although Dr Zamboni and his co-authors pointed out that longitudinal studies were needed to confirm the hypothesis, he offered explanations for a link between venous abnormalities and autoimmune inflammatory disease.

They pointed out that in some situations, obstruction of the inferior vena cava and venous disease of the lower limbs can lead to insufficient drainage in the liver or cutaneous tissue, resulting in “inflammation, sclerosis and degenerative lesions”.

In subsequent interviews and publications Dr Zamboni went a lot further.

“I am confident that this could be a revolution for the research and diagnosis of multiple sclerosis,” he told a reporter for Canada’s *Globe and Mail*.

In a second paper, he reported the effects of treating the insufficiency in a group of 65 patients with MS — 35 relapsing–remitting, 20 second-

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According to that paper, among those who underwent surgery in Italy, the number of active lesions in the brain fell and MS symptoms improved significantly.² The effects were particularly notable in those with relapsing–remitting patients. His wife reportedly underwent the procedure, and has not had a relapse in the subsequent three years.

About a week after she received her test results, Kerri Cassidy had an appointment to see an interventional radiologist at the Alfred Hospital in Melbourne, Professor Ken Thomson.

Professor Thomson told her she was the third person who had come to see him about venoplasty for CCSVI, which patients were now calling the “liberation procedure”.

“He made no promises at



Dr Paolo Zamboni

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all,” Cassidy says. “He said, ‘I’m not a neurologist and I don’t know about multiple sclerosis, but I know about veins and you’ve got an abnormality.’”

If Cassidy was willing, Pro-

fessor Thomson was willing to do the procedure, which was covered by Medicare purely as a treatment for a vascular abnormality.

Professor Thomson declined to be interviewed for

this story, saying the hospital was currently evaluating a proposal for a clinical trial to study the procedure.

Cassidy remembers him saying there were risks, but that they were minimal. In

Cassidy’s mind, they couldn’t have been worse than the risk of the brain disorder — progressive multifocal leukoencephalopathy — that was being reported in patients who, like her, were taking the drug natalizumab (Tysabri). “I felt very comfortable,” she says.

Three weeks later, at eight in the morning, Cassidy was at the hospital, preparing for the operation. By midday, she was under the scalpel, so to speak, although the procedure — in which a venoplasty balloon was threaded up to her jugular veins from the groin — was not particularly invasive.

“I’ve had so many infusions and so on that a needle in my groin wasn’t much to worry about,” Cassidy says.

Cassidy’s husband shot a video of the procedure and posted it on YouTube.⁵ So far, some 5000 people have viewed it.

After three days of rest, Cassidy woke up one morning, looked out the window, and realised something was different.

“My vision was so sharp and everything was really bright, especially the greens.” A couple of days later she tried out having a really hot bath — the usual vertigo and confusion were utterly absent.

For someone who had never felt properly well during the previous three years, these feelings were remarkable.

“I just had this sense of clarity. As those few days went on, I just felt more connected to the world.”

Gradually, her bladder problems began to resolve, the leg spasticity she’d been struggling with loosened up and her fatigue faded. Before the surgery, she had been barely able to walk 100m without a cane. Four weeks after her venoplasty, she went for a 3km walk.

With stories like Cassidy’s spreading around the online world, people with MS began to clamour for “liberation”,

particularly in Canada. Some travelled to countries such as India and Poland to undergo treatment.

In Australia, Professor Thomson was not the only radiologist willing to perform the procedure. Associate Professor Lourens Bester, at Sydney’s St Vincent’s Hospital, was another.

However, Dr Bester told *Australian Doctor* that he did not take referrals from GPs for the procedure.

“We have decided, in conjunction with the Alfred in Melbourne, to do this procedure on a limited basis to gain some form of experience before we enter the proposed CCSVI trial in Australia,” he said.

But it had become apparent that restenosis was common within months of the procedure. In some cases — although not, it seems, in Australia — stents were placed in the jugular veins to keep them patent.

Meanwhile, the medical profession began to study Dr Zamboni’s hypothesis and found the evidence lacking. In the early months of this year, researchers in Sweden and Germany published studies that showed differences in jugular venous outflow in MS patients and controls.^{3,4}

In February, a panel of international experts published an article in *Annals of Neurology* that pointed out “conceptual and technical shortcomings that challenge the potential relationship of this phenomenon to MS”. Their advice was that “invasive and potentially dangerous endovascular procedures as therapy for patients with MS should be discouraged until such studies have been completed, analysed and debated in the scientific arena”.

In June, the US National MS Society and the Multiple Sclerosis Society of Canada put out a press release simultaneously announcing \$2.4 million of support for grants to determine the role of CCSVI, while warning that the jury was still out.

“We don’t know yet whether CCSVI contributes to MS disease activity and there have been conflicting data as to the frequency of this condition in people with MS,” said Dr Aaron Miller, chief medical advisor to the US society.

In Australia, MS Research Australia took a similar line: “MSRA discourages patients with MS from any invasive procedures until there is more conclusive evidence to justify their benefit for treating MS,” the agency said in April.

MSRA has provided funding for a blinded study of the prevalence of CCSVI in people with early MS. The neurologist conducting that trial is Associate Professor

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NEWS REVIEW



Kerri Cassidy



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Brian Chambers, head of neurovascular ultrasound at the Austin Hospital in Melbourne.

Professor Chambers says he understands why MS patients are so keen to try anything that might improve their condition, but more evidence is needed.

"I think the evidence at the moment is pretty flimsy," he says. "I think it is unlikely that a scientific study of venoplasty will show a benefit. But it's possible, and I think it is important to keep an open mind."

Professor Bill Carroll, scientific chairman of MS Research Australia, echoes these sentiments. He says MS neurologists are between a rock and a hard place. While they feel sympathy for the patients clamouring for this treatment to be available, "you can't dispense with the idea that you need to gather the evidence", he says.

In the meantime, according to insiders familiar with the situation, the Alfred Hospital has also clamped down, saying that Professor Thomson can no longer treat CCSVI patients without a neurological referral.

"My friends and I in Melbourne can't find any neurologists to make that kind of referral," Cassidy says. The hospital's public relations staff declined to confirm or deny these claims.

Professor Thomson designed a protocol for a clinical trial of the procedure, which he put before the hospital's ethics committee for review.

Cassidy and her friends raised \$70,000 to help fund the trial. They also set up a popular Facebook page called CCSVI Australia.

By the beginning of June, Kerri Cassidy noticed a familiar pain behind her neck had returned. Her vision was also starting to fade.

She contacted Professor Thomson, and he ordered a magnetic resonance venogra-

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phy scan, confirming what she had suspected: there was evidence of restenosis.

In July, she underwent the procedure again, and again felt improvements in her vision. Her feet, which had gradually become colder again, also warmed once more.

The improvements weren't as dramatic as the first time around, but, then again, she hadn't yet deteriorated to the state she had been in last year.

Now, in September, Cassidy thinks her symptoms may be returning yet again.

"It's a weird place to be," she says. "Do I go and have it again?"

She has decided to hold

out and see what happens. In a way, she wonders if leaving her symptoms to get worse again — and once again going through a transformation — might be more convincing to others.

Not, it seems, that many of her fellow MS sufferers need much convincing.

"We don't necessarily think that CCSVI is the cause of MS, or that the venoplasty procedure is a cure," she says. "But I'm pretty convinced that it has helped me."

Cassidy says she heard that the Alfred Hospital's ethics committee had turned down Professor Thomson's application to conduct a clinical trial. The hospital's public relations office did not return calls to confirm whether this was the case, and an email to Professor Thomson bounced back with the message that he was on holiday until late October.

Talking to Kerri Cassidy, it's clear she can see things at least a little from the medical establishment's position. She understands that doctors can feel "ambushed" when patients arrive pre-armed with videos she has loaded onto YouTube, demanding the same procedure.

On the other hand, she is angry that others have so much control over what treatments she and her friends can access because they have MS.

"The reality is, if I did not have MS, I would have treatment and monitoring of my venous abnormalities. As patients, we're so much more educated about all this now," she says. "I feel we should have some control over these things." ●

References

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