



Your questions answered

STATEMENT BY MS AUSTRALIA
22 September 2010

There has been a lot of attention and hype surrounding CCSVI as a possible cause, with a subsequent treatment (or cure), for MS. This statement reveals the latest facts about CCSVI and MS.

What is CCSVI?

CCSVI stands for 'chronic cerebrospinal venous insufficiency'. It describes a situation where there is an apparent reduced blood flow from the brain and spinal cord over a prolonged period of time.

Why is it relevant to MS?

In 2009, a novel hypothesis for MS pathogenesis and a new treatment were proposed by Zamboni *et al.*, who suggested that cerebral venous outflow obstruction triggers central nervous system inflammation, and that such obstruction can be treated with angioplasty.

While some data suggests that there may be a relationship between CCSVI and MS, there is not enough information to understand what the relationship is, or what it means for treating MS. Further research needs to be undertaken before establishing the need for treatment.

Zamboni *et al.* coined the term "chronic cerebrospinal venous insufficiency" (CCSVI) to explain the changes they noted by ultrasound in the cerebral venous system of PwMS. The investigators examined cerebral venous drainage (blood flow from the brain and spinal cord) in 65 PwMS, compared with 235 people who were healthy or who had other neurological disorders.

The results showed a strong correlation between having MS and signs of venous insufficiency (reduced blood flow). A further study from the same group of 65 PwMS (who had all presented

with 'blockages' in the initial study) underwent angioplasty – an invasive technique that widens obstructed or narrow blood vessels using a small balloon at the end of a catheter. Following the surgery, the group reported some positive results, including a reduction in new lesions. However, in 47% of participants, the internal jugular veins returned to having restricted blood flow.

The University of Buffalo Medical Center (New York) described preliminary results by Dr Robert Zivadinov into the prevalence of venous obstruction in PwMS. Dr Zivadinov presented data on the first 500 participants, 289 of whom had MS. Results were less dramatic, with ultrasounds revealing blockages in 62% of PwMS, 26% of healthy participants, and 45% of people with other neurological disorders.

Doepf *et al* – a group that has published on the use of ultrasound to evaluate cerebral venous system integrity – tested the CCSVI hypothesis. These researchers studied 56 PwMS and 20 control individuals by ultrasound to characterize cerebral veins. This study found no difference between patients and controls with regard to flow velocities. Moreover, no abnormal changes

were noted in the MS group in jugular vein flow. From their findings, Doepp *et al*, concluded that there was no indication of venous congestion in PwMS and, thus, no support was forthcoming for the hypothesis that CCSVI is linked to MS.

In a coordinated response, the US National MS Society and the Canadian MS Society

Can treatment for CCSVI cure MS?

The research to date has had many limitations and is not yet complete. The concepts surrounding CCSVI (including the criteria and technology used to diagnose CCSVI and the effectiveness of treatments) are still relatively new and need to be validated by large-scale clinical trials before any results and their implications for patients can be understood.

To date, two treatments have been used for PwMS with CCSVI. The first was angioplasty (the insertion of a small tube to open the vein) and more recently by stenting (the insertion of a small valve into the blocked area of the vein).

While both of these surgical techniques are commonly used in heart surgery, the effectiveness and level of benefit versus the risk is unknown for treating MS. For example, while the people treated by Dr Zamboni's team did experience some improvement in their MS, there are a number of factors which make it difficult to know what this means.

It is known that in almost half of the people treated, the blockage re-formed. We also only know the effects after 18 months of participants having the treatment (i.e. we do not know the long-term effects).

announced plans to fund \$2.4 million in independent studies beginning in July 2010. These studies, as well as others from investigators worldwide, will, in time, resolve the controversy.

How can the MS community interpret the highly contradictory results surrounding the CCSV?

More information is needed to understand the full implications of the research. Diagnostic testing of the cerebral venous system is inherently imprecise. The use of ultrasound to measure venous physiology hasn't been validated. Chance, bias from various sources, design flaws, lack of objectivity, or some combination of these factors might also have influenced the results of one or all of these studies.

There are also well documented patterns among PwMS, such as the reduction of inflammatory activity in people over 50 or the geographic distribution of MS, which does not appear to fit with CCSVI as the primary cause of MS. If it is to be scientifically established that CCSVI causes MS, these and other well documented factors would need to be explained in a way that is consistent with Dr Zamboni's theory.

If the treatment for CCSVI cannot cure MS, can it treat MS?

Treating CCSVI may lead to improvements for PwMS, but the information to date is inconclusive. The study reported by Dr Zamboni and his team only included 65 people with MS. While it is documented that on average the group treated for CCSVI experienced improvement in physical and psychological measures of their health, the treatment was more effective for the people with relapsing/remitting MS.

It's also worth noting that all people with relapsing/remitting MS who were treated for CCSVI continued to take their immunotherapy medications, which are well documented as producing the types of improvement seen in this study. Before it can be established that treatment for CCSVI is an effective treatment for MS, there needs to be more extensive research demonstrating more significant results. ▶

If there is a chance that treatment for CCSVI could help, why not give it a try?

In addition to knowing whether a treatment is effective, it is also important to know whether it is safe. Because of the large number of people who experienced re-blockage after being treated by catheterization. Other treatments for CCSVI have included stents.

However, there are several uncommon but potentially fatal outcomes from inserting stents into veins. To date, one person with MS treated for CCSVI using this method has died, and one other needed emergency heart surgery. Treatments being performed were not part of a clinical trial and have since been halted.

The risk of serious negative outcomes does not necessarily mean that treatment should not be considered, but it is essential that the decision is looked at more carefully. In order to make an informed decision about treating CCSVI to improve MS, it is recommended that treatment should not be considered until properly conducted clinical trials have established the need.

Decisions about any treatment should also be done in careful consultation with your neurologist and healthcare team .

What is MS Australia's position on CCSVI?

With a complex disease like MS, it is important to consider all possibilities when searching for causes and treatments. Dr Zamboni's theory about CCSVI and MS is taking a new approach to MS research.

While existing data suggests that there may be a relationship between CCSVI and MS, so far there is insufficient information to understand what the relationship is, or what it means for treating MS. Again, further research needs to be undertaken before establishing the need for treatment.

MS Australia, through its research arm MS Research Australia (MSRA), is contributing to the worldwide effort to gather this information. MSRA is funding a CCSVI study at the Austin Hospital (Melbourne) to identify and measure the frequency of narrowed veins in People with MS and controls. MSRA is also in dialogue with MS Societies around the world to keep abreast and inform the Australian MS community of advances made in this area.

MS Australia recommends that PwMS only seek surgical treatment for CCSVI within controlled clinical trials.

Further information and reading on CCSVI and other MS research

- **If you want to know more about the implications of CCSVI for your MS**, the best person to talk to is your neurologist.
- **MS Research Australia website:** www.msra.org.au
- **The National MS Society (USA) website**, research section: www.nationalmssociety.org/research
- **The MS Society (UK) website**, news and events section: www.mssociety.org.uk/
- **The MS Trust (UK)**, research news section: www.mstrust.org.uk/research/news
- **For all media enquiries**, please call Sara Irvine on 0402 982 002

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