Great leaps in multiple sclerosis treatment but the holy grail is still ahead

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<u>CEO of MS Australia</u> Rohan Greenland highlights the breakthroughs in treating attacks on the brain and spinal cord in multiple sclerosis (MS). But his sights are set firmly on the great unmet needs: to repair damaged nerves, reverse disability, and ultimately, prevent MS

What is MS?

MS is an autoimmune disease of the central nervous system (CNS), affecting the brain, optic nerve and spinal cord. In MS, the immune system mistakenly attacks the myelin sheath around the nerves, disrupting the conduction of nerve signals to other parts of the body. There are <u>many symptoms that can be variable and unpredictable</u> depending on which part of the CNS is damaged. They can be a one-off occurrence, come and go or change in severity over time, contributing to the uncertainty that MS brings.

What is the impact of MS?

MS is the most common chronic disease of the CNS among young Australians. It affects nearly 26,000 people in Australia and 2.8 million people worldwide and is three times more common in women than men. Prevalence is expected to increase steadily in the years ahead.

With onset most common between ages 20 and 40, a diagnosis of MS can be devastating. This is a highly productive time of life, when study, career-building, relationship development and/or family-making are often the focus, and the unpredictability of MS can disrupt plans and sabotage goals. MS can rob quality of life in diverse ways: mobility, energy, cognition, sight, speech, mental health, sexual health, bladder control, social inclusion or the myriad of other functions that can be suddenly or slowly taken.

Our 2017 <u>Health Economic Impact of Multiple Sclerosis Report</u> also highlights the significant economic implications: the societal costs of MS were \$30,561 Australian dollars (AUD) per person per year for a person with no disability, compared to AUD \$114, 813 for a person with severe disability.

How is MS diagnosed?

Multiple sclerosis means multiple lesions or scars on the brain, spinal cord and optic nerves. To clinically diagnose MS, there must be evidence of attacks on different parts of the central nervous system, but also that these occurred at different times. While this

might sound easy to determine, there is still no single clinical test to provide a definitive diagnosis. Instead, a careful combination of clinical examinations, magnetic resonance imaging (MRI) scans and lumbar punctures are required. If there has only been one clinical attack (physical symptoms), then MRI evidence of older scars or lesions in the brain can help make the complete diagnosis.

Significant advances in MS treatment

The past two decades have seen monumental advances in the treatment of MS, based on dampening inflammatory immune responses, or preventing immune cells from entering the brain. From the first "disease-modifying therapy" approved in 1996 in Australia, in 2022 we now have 16 therapies and a range of others coming through the industry pipeline, with new treatments expected shortly.

These therapies have had a huge impact. Some of the best evidence comes from <u>MSBase</u>, a global clinical registry born in Australia, recently showing that <u>immunotherapies reduced</u> <u>MS relapses by 40% and significantly improved disability outcomes</u> over 15 years in 15,000 people with the most common form of MS.

Genetics & environment reveal complex biology of MS

Both genetic and environmental factors increase the risk of developing MS, but none cause MS in isolation. Over 200 genes contribute a small amount to MS risk, and most of these genes control immune system function, making it more prone to mistakenly attacking the person's own body.

Australian work has been critical in understanding environmental factors increasing MS risk. <u>The "latitude gradient" in the risk of MS</u> is perfectly illustrated along Australia's vast east coast. People living in the far south of the continent have a 7-fold greater risk of MS than those living in the far north, closer to the Equator. This is likely due to the effects of vitamin D and UV exposure in dampening inflammatory processes. Smoking and obesity are also risk factors for MS.

2022 unveiled the most compelling evidence yet that <u>Epstein Barr virus infection (EBV;</u> <u>which causes infectious mononucleosis) is necessary for the development of MS,</u> <u>increasing MS</u> risk by 36-fold. Over 20 years in more than 10 million military personnel, EBV infection always preceded early signs of nerve damage in the blood, years before the clinical onset of MS. This may have significant implications for MS prevention.

Towards MS prevention

MS Australia has invested over \$55 million in Australian and international MS research since inception, towards prevention, better treatments and ultimately, cures. Our <u>Roadmap to Defeat MS In Australia</u> is focused on these goals and aligns with the global <u>Pathways to Cures MS Research Roadmap</u>.

MS prevention will involve reducing environmental risk factors, especially in people who have a strong family history or have already experienced one episode of myelin loss, or "demyelination". MS Australia is funding research into modifiable risk factors such as <u>diet</u>, and a world-first clinical trial of vitamin D to prevent MS in people who have had one demyelinating episode. *Preventing EBV infection may have the potential to prevent MS and <u>new generation EBV vaccines</u> are currently in clinical trials.

The holy grail: repairing nerves and reversing disability

A detailed understanding of immune attacks on the nerves has driven significant therapeutic advances in MS. However, progressive degeneration of the nerves is poorly understood and probably drives the accumulation of disability. For people with MS<u>time</u> is brain, and we are urgently seeking to understand this phenomenon and develop drugs to target it.

MS Australia is a managing member of a <u>unique global collaboration called the</u> <u>International Progressive MS Alliance</u>, seeking to bring together the world's best minds from MS medicine, allied health, science, industry, MS organisations, donors and regulatory authorities, to solve MS progression. Among the initiatives is fast-tracking drug development to protect nerve cells and regrow myelin, including harnessing the brain's own immune system for neuroprotection. We are also working with government and industry to fast-track the entire drug development pipeline, especially by rethinking MS clinical trial design and finding more sensitive blood markers of early drug effectiveness.

These advances represent real progress, and in 2022 our 50th year and beyond, give us great hope for a world without MS.

*More about the world-first clinical trial hyperlinks to our PrevANZ can be found at the following links: