2018 Australasian MND Symposium

"It's a very exciting time to be involved in MND research. There's a lot of hope and positivity."
– *Prof Matthew Kiernan, Bushell Chair of Neurology, Sydney Medical School*

"I'm much more optimistic than I was 10 years ago. Researchers are intensely interested in MND."
– *Prof Kevin Talbot, Head of Clinical Neurology, Univeristy of Oxford UK*

"The rate of progress in recent years is very exciting." – *Lucie Brujin, Chief Scientist, ALS Association*

Biomedical research summary

- 4 to 5 million people now alive today will die from MND.
- MND is not one 'disease', it's a spectrum of things converging on one system – the cortico motor-neuronal system. There is *enormous* variety in how MND affects people.
- Because MND/ALS is not one disease, **it will not be solved by one treatment**.
- Riluzole prolongs the final stage of MND. It may also prolong the first stage but this effect is unknown.
- 18 clinical trials have failed in the last decade. For clinical trials to be more successful in future, they need to select more homogeneous groups of people with similar genetic factors, environmental factors, progression rate and pattern. Better disease modelling and better understanding of disease mechanisms will help.
- Diagnosis comes quite late in the progression of MND. People are enrolled in clinical trials well after their system begins dysfunctioning. Earlier diagnosis and studies of pre-symptomatic gene carriers are essential.
- Developing MND is now thought to be a **multistep process** where genetic risk & environmental factors accumulate over time until a threshold of disease is reached. About **6 steps** (triggers) are required for MND to develop. We have an incomplete understanding of these triggers and how they cascade.
- MND is extremely complex but there is **cause for optimism**.
- We now know of **25 risk genes for MND**. At this rate of discovery, in four years we will have found 50. (Each of these risk factors increase your risk of MND by 5-10%.)
- These genetic discoveries give us a better idea of the pathways that should be targeted by drugs, including common pathways between genetic and sporadic MND.
- It's much harder to identify environmental risk factors than to find genetic risks. Environmental risk factors that many (not all) studies have agreed on are: smoking, trauma (eg broken bone, surgery), diesel fumes, exercise, being a war veteran.
- There has been an **exponential increase in our knowledge of basic mechanisms of MND**. Knowledge Is increasing at an extraordinary rate, especially in the last 2 or 3 years. Professor Robert Henderson, University of Queensland, simply explained a theory of the mechanisms of MND: "Whatever causes MND results in misfolded proteins, which triggers an immune response, which causes inflammation, which causes damage to functional cells. This cell stress leads to motor neuron death, which leads to motor function loss."

Clinical research summary

"MDT clinics are the biggest advance in the treatment of MND. Patients in MDTs live on average a year longer."
– *Prof Jeremy Shefner, Barrow Neurological Institute, USA*

- Evidence suggests that patient survival and quality of life is improved by:
    - early intervention with non-invasive ventilation
    - maintenance of weight and nutritional status
    - the provision of coordinated care through multidisciplinary clinics (MDTs).
- Multidisciplinary clinics (MDTs) are the biggest advance – **patients in MDTs live on average a year longer**.
- There is increasing evidence that **palliative care**, integrated in a multidisciplinary approach to care, leads to improved symptoms and quality of life in people with MND and their families. These outcomes can *only* be achieved if palliative care knowledge and expertise is extended beyond the domain of palliative specialist services to include the full scope of health and community-based services.
- There is a strong connection between meaningful occupational engagement and a person with MND's self-perception as capable, engaged and having a sense of control and normalcy in their lives.

The next 5 to 15 years

"I'm really optimistic for the future for the next 5 to 15 years. It *will* lead to a cure."
– Prof Paul Talman, director, Australian MND Registry

- Those with familial (SOD1- and C9ORF72-related) MND are likely to be treated with therapies targeting DNA – eg CRISPR, antisense oligonucleotide therapies (ASOs). Researchers are **extremely optimistic** about the use of ASOs to treat familial MND within 5 to 10 years. Clinical trials for SOD1 ASOs have begun and C9 ASO trials will begin this year. ASOs could also be useful for lowering ataxin 2 in sporadic ALS.
- Sporadic MND will be redefined and separated into sub-types according to biomarkers (eg fast and slow progressors). This will allow those with sporadic MND to eventually be treated with personalised medicines, aka precision medicine. (Precision medicine is based on understanding the disease mechanisms, biomarkers, and individual responses to treatment.)
- Researchers are urgently working to identify biomarkers (eg in blood or urine) that reflect the underlying biology of MND, to guide more targeted clinical trials and better measure their effectiveness.
- Overall, there are more new therapeutic approaches to MND than ever before, increasing the likelihood that new therapies will become available that provide a meaningful impact on the lives of MND patients.
- Several other drug development avenues are being explored and any one could have a big impact. Immunotherapy may have great promise (people with fast progressing MND have higher inflammation).

Further information

What causes MND? Why me?

We highly recommend watching this presentation by Professor Ammar Al-Chalabi, one of the world's top researchers in MND:

- Part 1 https://youtu.be/Y30b8YLcmRQ
- Part 2 https://youtu.be/aNOm7fmL5V4

Why Haven't We Found a Cure Yet?

We highly recommend watching this presentation by Professor Kevin Talbot, Head of Clinical Neurology at the University of Oxford, UK: https://youtu.be/WzneGfPaoPQ

MND Research News

A more in-depth update about developments in research towards a cure and understanding the causes of MND. https://mnd.org.nz/wp-content/uploads/2018/05/AusMNDSym2018_1ResearchUpdate.pdf

Clinical Management

Advice for allied health professionals about new respiratory research, and developments in assistive communication technology. https://mnd.org.nz/wp-content/uploads/2018/05/AusMNDSym2018_6ClinicalManagement.pdf

Drug Development

This update discusses the early 2018 drug development pipeline and our current understanding of the disease mechanisms in MND. https://mnd.org.nz/wp-content/uploads/2018/05/AusMNDSym2018_2DrugDevelopment.pdf

Clinical Trials

Key global and Australian clinical trials in 2018, the current issues in clinical trial design, and new biomarkers being developed. https://mnd.org.nz/wp-content/uploads/2018/05/AusMNDSym2018_3ClinicalTrialsBiomarkers.pdf

Palliative Approach

The importance of quality palliative care throughout the course of MND from all health professionals involved. https://mnd.org.nz/wp-content/uploads/2018/05/AusMNDSym2018_5PalliativeApproachtoMND.pdf

Multidisciplinary Clinics

The life-extending importance of multidisciplinary teams in providing best practice care for people with MND. https://mnd.org.nz/wp-content/uploads/2018/05/AusMNDSym2018_4MulitdisciplinaryClinics.pdf