NMOSD AUSTRALIA

DIAGNOSIS

Within this information sheet are quotes from patients previously diagnosed with NMOSD.

Clinical characteristics

The core clinical characteristics of NMOSD are[1]:

Optic neuritis[1]

This is swelling or inflammation that causes damage to the optic nerve. The optic nerve is a bundle of nerve fibers that transmits visual information from your eye to your brain. Optic neuritis can cause pain with eye movement and temporary vision loss or blurred vision, usually in one eye only.

I was resting at home, I had a nap in the afternoon and then after I woke up from the nap, the TV was on and when I looked at the TV, it was blurry. Then I tried to get up from my couch and then I started to lose balance. I didn't know what it was. I went to hospital. Participant NMO_001

I started to get sore eyes and I thought it must have been windy or something the day before and then it just got worse so I went off to see the eye doctor and they referred me on to a specialist. Participant NMO_007

Myelitis[1]

Myelitis means inflammation of the spinal cord and can cause paralysis and sensory loss. There are different categories of myelitis and this depends on the area affected (also described as a lesion). The impact and severity of myelitis often depends on which part of the spinal cord is affected.

After my arm first went then my whole left side, so my face and left leg went numb, but I still had full mobility and everything else. Participant NMO_014

I was totally healthy. It came on in well…I woke up about three in the morning and I couldn't feel my right-hand side. Participant NMO_009

[1] Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology* 2015; **85**(2): 177-89.

Brainstem syndrome[2,3,4]

Some people with NMOSD have brainstem symptoms when this part of the brain (the medulla) is affected. People affected in this way often have nausea and vomiting or hiccups (sometimes intractable). This occurs in 16 to 43% of people with NMOSD.

Anti-phospholipid syndrome[5]

Antiphospholipid syndrome (APS) is a disorder of the immune system that causes an increased risk of blood clots. It is also known as Hughes syndrome.

People with APS have a higher risk of developing conditions such as deep vein thrombosis (DVT) (a blood clot that usually develops in the leg), arterial thrombosis (a clot in an artery which can cause a stroke or heart attack) or blood clots in the brain (leading to problems with balance, mobility, vision, speech and memory).

Symptomatic narcolepsy[6]

Narcolepsy is a chronic sleep disorder characterised by overwhelming daytime drowsiness and sudden attacks of sleep.

Symptomatic cerebral syndrome with NMOSD-typical brain lesions[7]

The presence of brain lesions is helpful in the diagnosis of NMOSD and there are seven documented characteristic locations and configurations.

Aquaporin-4 (AQP4)

AQP4 is a protein that has a role in transporting water within the body and also has a role in maintaining balance within the central nervous system[8].

Patients that are seropositive for AQP4 require at least one core clinical characteristic for diagnosis[1]. Patients that are seronegative or unknown status for AQP4 require two core clinical characteristics with at least one of optic neuritis, longitudinally extensive transverse myelitis, or anti-phospholipid syndrome[1].

NMOSD is classified into AQP4 antibody positive and AQP4 antibody negative diseases[9]. NMOSD includes cases of MOG-antibody-positive disease with its unique clinical spectrum that is different from AQP4-antibody positive disease[9]. NMOSD patients with MOG antibodies have fewer attacks and better recovery from relapses than those with AQP4 antibodies, or those that are negative for both MOG and AQP4[10,11].

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[2] Misu T, Fujihara K, Nakashima I, Sato S, Itoyama Y. Intractable hiccup and nausea with periaqueductal lesions in neuromyelitis optica. Neurology. 2005 Nov;65(9):1479-82.

[3] Apiwattanakul M, Popescu BF, Matiello M, Weinshenker BG, Lucchinetti CF, Lennon VA, McKeon A, Carpenter AF, Miller GM, Pittock SJ. Intractable vomiting as the initial presentation of neuromyelitis optica. Ann Neurol. 2010;68(5):757.

[4] Wingerchuk DM, Banwell B, Bennett JL, Cabre P, Carroll W, Chitnis T, de Seze J, Fujihara K, Greenberg B, Jacob A, Jarius S, Lana-Peixoto M, Levy M, Simon JH, Tenembaum S, Traboulsee AL, Waters P, Wellik KE, Weinshenker BG. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015 Jul;85(2):177-89. Epub 2015 Jun 19.

[5] Iyer A, Elsone L, Appleton R, Jacob A. A review of the current literature and a guide to the early diagnosis of autoimmune disorders associated with neuromyelitis optica. *Autoimmunity* (2014) 47:154–61.

[6] Yijun Song, MD, PhD, Liping Pan, MD,Ying Fu, MD, Na Sun, MD, Yu-Jing Li, MD, Hao Cai, MD, Lei Su, MD, Yi Shen, MD, Linyang Cui, MD, and Fu-Dong Shi. Sleep abnormality in neuromyelitis optica spectrum disorder. Neurol Neuroimmunol Neuroinflamm. 2015 Jun; 2(3): e94

[7] Woojun Kim, Jee Eun Lee, Su-Hyun Kim, So-Young Huh, Jae-Won Hyun, In Hye Jeong, Min-Su Park, Joong Yang Cho, Sang-Hyun Lee, Kwang Soo Lee, Ho Jin Kim. Cerebral Cortex Involvement in Neuromyelitis Optica Spectrum Disorder. J Clin Neurol. 2016 Apr; 12(2): 188–193

[8] Bonomini Francesca* and Rita Rezzani. Aquaporin and Blood Brain Barrier. Curr Neuropharmacol. 2010 Jun; 8(2): 92–96.

[9] Fujihara K. Neuromyelitis optica spectrum disorders: still evolving and broadening. *Curr Opin Neurol* 2019; 32(3): 385-94.

[10] Mutch K, Methley A, Moore P, Jacob A. Life on hold: the experience of living with neuromyelitis optica. *Disabil Rehabil* 2014; 36(13): 1100-7.

[11] Sato DK, Callegaro D, Lana-Peixoto MA, et al. Distinction between MOG antibody-positive and AQP4 antibody-positive NMO spectrum disorders. *Neurology* 2014; 82(6): 474-81.

Diagnostic tests

There is little documented information about standard diagnostic tests for NMOSD in Australia. The Neuromyelitis Optica Unite Kingdom Specialist Services lists the following tests used to diagnose NMOSD[12]:

- Medical history
- MRI of brain and spinal cord
- Lumbar puncture (small amount of fluid is drawn from the spinal cord with a needle)
- Blood tests (Aquaporin 4 antibody blood test)
- Ophthalmological examination
- Visual evoke potential (Electrodes measure the speed of nerve messages along the optic nerve)
- Visual field tests (Peripheral vision test)
- Low contrast test (testing a person's vision against increasingly faded images)
- Ishihara test (colour perception test for red-green colour deficiencies)
- Optical coherence tomography.

Documented trends in NMOSD diagnosis

Early diagnosis and treatment is important for people with NMOSD[1314]. A range of 29 to 43% of people with NMOSD will have had a misdiagnosis of multiple sclerosis, causing delays in preventative treatments[15,16]. In addition, some treatments for multiple sclerosis increases relapse severity and frequency, increasing disability[49,50]. Diagnostic delay has been reduced with the specificity of the AQP4 antibody, which reliably distinguishes NMOSD from multiple sclerosis [16,17,18]. In addition, the application of the International consensus diagnostic criteria for neuromyelitis optica spectrum disorders in 2015[1], has led to an increase in the diagnosis of NMOSD[19].

Participants in the 2020 Australian NMOSD PEEK study reported between seven and nine diagnostic tests, with a median of six tests. Nearly all participants had blood tests, MRI of brain, optic nerves, or spinal cord, and physical examination. Most participants also had a neurologic exam, lumbar puncture and ophthalmology studies. Very few recalled having a family history taken, or CT scans.

Few participants in the 2020 Australian NMOSD PEEK could remember having conversations about biomarker, genomic, or gene testing that might be relevant to treatment. Over 60% said they did not have these tests, yet half of the participants in the study knew their AQP4 status. This may indicate that patients need more information and discussion about biomarkers, the purpose of testing, and what the relevance of their antibody status is in terms of treatment and prognosis.

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[12] Nmouk.nhs.uk. 2021. Diagnosis | NMO NHS | NMO Advice & Support UK. [online] Available at: <http://www.nmouk.nhs.uk/what-is-nmo/diagnosis> [Accessed 9 February 2021]

[13] Huda S, Whittam D, Bhojak M, Chamberlain J, Noonan C, Jacob A. Neuromyelitis optica spectrum disorders. *Clin Med (Lond)* 2019; 19(2): 169-76.

[14] Mealy MA, Mossburg SE, Kim SH, et al. Long-term disability in neuromyelitis optica spectrum disorder with a history of myelitis is associated with age at onset, delay in diagnosis/preventive treatment, MRI lesion length and presence of symptomatic brain lesions. *Mult Scler Relat Disord* 2019; 28: 64-8.

[15] Mealy MA, Wingerchuk DM, Greenberg BM, Levy M. Epidemiology of neuromyelitis optica in the United States: a multicenter analysis. *Arch Neurol* 2012; 69(9): 1176-80.

[16] Jarius S, Ruprecht K, Wildemann B, et al. Contrasting disease patterns in seropositive and seronegative neuromyelitis optica: A multicentre study of 175 patients. *J Neuroinflammation* 2012; 9: 14.

[17] Lennon VA, Wingerchuk DM, Kryzer TJ, et al. A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. *Lancet* 2004; 364(9451): 2106-12.

[18] Hyun JW, Jeong IH, Joung A, Kim SH, Kim HJ. Evaluation of the 2015 diagnostic criteria for neuromyelitis optica spectrum disorder. *Neurology* 2016; 86(19): 1772-9

[19] Hamid SH, Elsone L, Mutch K, Solomon T, Jacob A. The impact of 2015 neuromyelitis optica spectrum disorders criteria on diagnostic rates. *Mult Scler* 2017; 23(2): 228-33.

About a third of the participants in the 2020 Australian NMOSD PEEK study were diagnosed more than a year after first noticing symptoms, very few were diagnosed within a month of noticing symptoms. In addition, delays between testing and diagnosis were common. Over a quarter of participants with NMOSD in the 2020 Australian NMOSD PEEK study were misdiagnosed with multiple sclerosis, contributing to the delay with an NMOSD diagnosis.

Yes. I was actually diagnosed with multiple sclerosis for two and a half years or three years before I got my NMO diagnosis. Before, I was diagnosed with MS, I had numbness in my arm and on the back of my neck, lots of fatigue, and a lot of weakness that would come and go. NMO_003

I went and had an MRI and it showed some lesions in my brainstem and my spinal cord and I was referred to a neurologist. I was first admitted to a hospital and diagnosed with MS. It was about six months later when I was diagnosed with NMO. Participant NMO_010

Other studies in the NMOSD community reported average time between noticing symptoms and diagnosis between one and 3.3 years[20,21]. Most participants in a United Kingdom study described having difficulty with getting an NMOSD diagnosis. This was mostly due to misdiagnosis with multiple sclerosis[12].

[20] Eaneff S, Wang V, Hanger M, et al. Patient perspectives on neuromyelitis optica spectrum disorders: Data from the PatientsLikeMe online community. *Mult Scler Relat Disord* 2017; 17: 116-22.
[21] Beekman J, Keisler A, Pedraza O, et al. Neuromyelitis optica spectrum disorder: Patient experience and quality of life. *Neurol Neuroimmunol Neuroinflamm* 2019; 6(4): e580

Diagnostic tests question checklist

If you are currently going through the diagnostic process, this is a list of questions that may help you through the process.

- [ ] What kind of tests(s) will I have?
- [ ] Why do you think I need this test/these tests?
- [ ] Is there a cost for this test/these tests?
- [ ] What do I need to do to prepare for this test/these tests?
- [ ] Are there foods or supplements I need to avoid beforehand?
- [ ] How do I schedule these tests?
- [ ] When will I get the results?
- [ ] How will I get my results?
- [ ] What do you think it is (what are you testing for)? Can you explain the diagnosis?
- [ ] What else could it be?
- [ ] If the test/tests are inconclusive, what are the next steps?

Diagnosis question checklist

If you are diagnosed with NMOSD, this is a list of questions that may help you through understand your treatment and management options

- [ ] What does this diagnosis mean for me?
- [ ] What symptoms will NMOSD cause?
- [ ] What is the aim of the treatment? To cure, or to control it and manage symptoms?
- [ ] How likely is it that my symptoms will get worse or move to other parts of my body without any more treatment? **or** How likely is it that the treatment will improve my symptoms?
- [ ] What is the expected prognosis or outcome for people with my level of NMOSD?
- [ ] What allied health professionals should I be referred to? (e.g Physiotherapy, counselling/psychologist, occupational therapy, social work, speech pathology)