Devic's Disease (Neuromyelitis Optica)

Dean M. Wingerchuk, MD, FRCPC

Department of Neurology

Mayo Clinic, Scottsdale, AZ

Neuromyelitis optica (NMO; also known as Devic's syndrome or Devic's disease) is an inflammatory disorder with a striking predilection for the optic nerves and spinal cord. Acute transverse myelitis is often its initial manifestation. The cardinal features of NMO (optic neuritis and myelitis) and tendency to recurrence led to its classification as a subtype of multiple sclerosis (MS), but it has several unique features. Herein, I describe the clinical, radiological, and pathological features of NMO, its pathogenesis, and its relationship to other forms of central nervous system demyelinating disease.

I. Clinical Features and Diagnostic Criteria

Devic's syndrome consists of one or more clinical episodes of optic neuritis in combination with myelitis. These clinical events also occur commonly in typical MS, however, in NMO they are usually more acute (sometimes fulminant) and severe; these characteristics may raise initial diagnostic suspicion of NMO. Paraclinical measures, such as magnetic resonance imaging (MRI) of the brain and spinal cord and cerebrospinal fluid (CSF) examination, also frequently reveal findings that differ from those in prototypic MS. In retrospective and small prospective series, most patients with NMO have no or few nonspecific white matter lesions on brain MR imaging. Spinal cord MR imaging also shows distinctive findings: a majority of patients have longitudinally extensive lesions extending over three or more vertebral segments. Furthermore, NMO patients frequently have a CSF pleocytosis of more than 50 leukocytes, with or without the presence of neutrophils. Recently, three groups have proposed diagnostic criteria that employ some or all of these features (Table 1).[1-3] With the development of these criteria the following key findings have become accepted: 1) the interval between the initial events of ON and myelitis is quite variable (several years, in some instances); 2) some patients experience unilateral rather than bilateral optic neuritis; and 3) the course may be monophasic or relapsing.

Neuromyelitis optica may follow either a monophasic or relapsing course.[3] In monophasic NMO, patients experience either unilateral or bilateral ON and a single episode of myelitis, typically but not always, within a very short time of one another, but do not have further attacks. In contrast, patients with a relapsing

course continue to have discrete exacerbations of ON and/or myelitis after they meet NMO diagnostic criteria. There are several important differences between the two disease courses that will be detailed further.

II. Epidemiology

Neuromyelitis optica affects young adults, much like MS, but has been reported in infancy through the ninth decade. The reported mean age of onset, especially for the relapsing type, may be greater than for typical MS. The mean onset ages were 35 and 47years in two series of relapsing NMO.[1, 2] Wingerchuk et al reported a mean age of onset of 29 years (range 1-54 y) for monophasic patients and 39 years (range 6-72 y) for relapsing patients.[3]

The ratio of women to men may also differ according to disease course. Most reports suggest a ratio of approximately 1.4 to 1.8; the rate increases to 83-100% women in recent case series that consist predominantly of patients with a relapsing course.

The incidence and prevalence of NMO are unknown. In Western nations, it has generally been considered a rare disorder but is almost certainly under-recognized, in part due to the lack of clear diagnostic criteria and confusion with MS. NMO appears to be more common in non-Caucasians such as African-Americans, Japanese, and other Pacific Islanders. Demyelinating disease in Asia and India is often restricted to the optic nerves and spinal cord; 7.6% of Japanese MS patients had NMO,[4] however, this rate may be declining with a concomitant increase in the frequency of "Western MS".[5] Up to 6% of demyelinating disease cases in India are NMO.[6] Reports exist of identical twins or siblings with NMO.

Despite these clues, the role of genetic factors in NMO is not known. Certain human leukocyte antigen (HLA) alleles are also associated with opticospinal forms of MS. The HLA-DPB1*0501 allele was present in a higher frequency of patients with opticospinal MS than prototypic MS in Japanese patients, whereas the DPB1*0301 allele may be underrepresented.[7] These HLA associations differ from those described in patients with "Western" MS, which is most consistently associated with HLA-DRB1*1501.

III. Onset and Concomitant Illnesses

A viral prodrome precedes the onset of the disease in 30-50% of cases. The prodrome most often consists of headache, pyrexia, fatigue, myalgias, and respiratory or gastrointestinal complaints. This suggests that infectious agents may cause or trigger NMO. Many diseases have been associated with NMO, including most viral infections, tuberculosis, hypothyroidism, lupus, Sjögren's syndrome and other connective tissue disorders.

IV. Disease Onset: "Index Events"

Textbook definitions of NMO generally require bilateral ON occurring in close conjunction with transverse myelitis. It is now well established, however, that patients with unilateral ON pursue a course indistinguishable from those with bilateral ON.[3] When bilateral ON and myelitis occur simultaneously or in rapid succession, it usually predicts a monophasic course. The index events (those that herald the onset of NMO) also include unilateral ON, myelitis, bilateral ON, or a combination of unilateral ON and myelitis. In one series, the initial presentation was an isolated event of either ON or myelitis in 90% of patients destined for a relapsing course compared with only 48% of those who had a monophasic illness.[3]

Acute transverse myelitis, defined as severe, bilateral inflammatory spinal cord injury with neurological dysfunction worsening over several hours to days and involving motor, sensory, and sphincter function, is a typical presentation of NMO. Deep or radicular pain, lower extremity paresthesias, or weakness may herald its onset. Weakness rapidly evolves to paraplegia or quadriplegia, often causing complete sensory loss caudal to the lesion and a flaccid bladder. The acute lesion usually traverses at least three contiguous vertebral segments of the spinal cord and may result in "spinal shock" with flaccid weakness, absent deep tendon reflexes, and mute plantar responses. A minority of patients experience less complete lesions that may present as Brown-Sequard or central cord syndromes. Lhermitte's symptom, paroxysmal tonic spasms, and radicular pain may occur, usually in those patients with relapsing disease.

Partial recovery is common following the initial myelitis event. Seventy-eight to 88% of patients improved by one or more levels on a seven-point ordinal scale of motor function regardless of eventual

disease course.[3] Recurrent episodes of myelitis increase the risk for permanent and severe morbidity from thromboembolic disease, urinary tract infections, decubitus ulcerations, and pneumonia.. Acute cervical myelitis is associated with respiratory failure and death, especially in relapsing NMO.[3]

Optic neuritis in NMO may be unilateral or bilateral. It is almost always acute, usually severe, and may or may not be associated with retro-orbital pain. Field defects are variable and include central and paracentral scotomata as well as altitudinal and chiasmatic defects. During the first episode of ON in NMO, nearly 40% of affected eyes become completely blind (no light perception) at the nadir of the event; however, some cases involve only minor visual deficits. Most patients experience some improvement in vision, especially if their disease course is monophasic; accumulation of visual impairment occurs with successive recurrences of ON in relapsing cases.

V. Other Clinical Manifestations

Symptoms outside of the optic nerves and spinal cord are very uncommon. They are usually minor or subjective, tend to occur later in the disease course, and are plausibly due to other causes than NMO. This includes symptoms such as vertigo, facial numbness, nystagmus, headache, and postural tremor. These features may be related to the brain MRI evidence that some patients have lesions that occur in the parenchyma or brain stem late in the disease course.

VI. Diagnostic Evaluation

Several diagnostic tests can serve to support a diagnosis of NMO. Brain and spinal cord MRI features and CSF findings have been incorporated into diagnostic criteria for NMO due to their ability to discriminate from typical MS.

A. Serological Tests. One or more autoantibodies, including anti-nuclear antibody, anti-double-stranded DNA antibody, extractable nuclear antigen, and anti-thyroid antibodies are commonly present at the time of diagnosis.[2, 3] The true incidence is not known, but may approach 50%.

B. Neurophysiological Tests. Visual evoked potentials may occasionally detect subclinical optic nerve lesions when the clinical history and examination confirm only unilateral deficits. Current clinical diagnostic

criteria do not allow subclinical optic neuropathy manifest as abnormalities on visual evoked potential to substitute for a history of optic neuritis, but this may have to be readdressed pending further study. Electrophysiological studies otherwise have little diagnostic role.

C. Brain and Spinal Cord MRI. The diagnosis of NMO is strongly supported by the absence of brain parenchymal lesions (i.e. excluding the optic nerves), or the presence of nonspecific white matter lesions that do not meet radiological criteria for MS.[1, 2, 8] Some patients with relapsing disease accumulate white matter lesions over time, but these lesions tend to be nonspecific punctate foci that fail to meet radiological criteria for MS.[3]

During acute ON, brain MR imaging may demonstrate swelling and/or gadolinium enhancement of an affected optic nerve or the chiasm. While occasionally more severe and extensive than encountered in MS (e.g. involve the entire chiasm), these nonspecific findings in the optic nerve do not distinguish NMO from isolated ON or typical MS.

Episodes of myelitis in NMO are accompanied by striking spinal cord MR imaging abnormalities. During acute myelitis, the affected region of the cord is usually expanded and swollen[9] and may enhance with gadolinium. Heterogeneous T2 signal within the lesion may suggest cavitation and necrosis. The most distinct aspect of NMO cord lesions is that they usually extend over three or more vertebral segments of the cord.[2, 3] Over time the swelling and enhancement give way to persistent intramedullary T2 signal abnormality and/or cord atrophy. Typically, the lesions are in the central part of the cord, rather than in the periphery of the cord as generally occurs in patients with prototypic MS.

D. Cerebrospinal Fluid. CSF analysis may support the diagnosis of NMO. Occasional patients have a pleocytosis of more than 50 WBC/mm^3 around the time of an acute myelitis exacerbation[3]; this degree of CSF cellularity is very rare in typical MS.[10] The CSF leukocyte differential may also reveal the presence of neutrophils, another finding rarely seen in MS. These abnormalities may reflect the severity of myelitis, which often results in necrosis.

Approximately 85% of patients with MS have detectable oligoclonal bands on CSF electrophoresis.[11] Oligoclonal bands are far less common in NMO, occurring in 15-35% of patients in contemporary series.[1-3] Other immunoglobulin abnormalities, such as increased rate of IgG synthesis, are also much less common in NMO than in MS.

VII. Natural History of NMO: Monophasic and Relapsing Disease Courses

Most patients, perhaps 70% or more, with NMO develop a relapsing course with recurrent events of ON and myelitis. There are several differences in the demographics and outcomes of patients with the monophasic and relapsing forms of NMO (Table 2).

By definition, those who follow a monophasic course experience either unilateral or bilateral ON and a single episode of myelitis without any further exacerbations. Several factors are associated with a monophasic disease course. The index events of ON and myelitis are typically more severe, with over half of patients experiencing complete loss of light perception with index ON compared with about 28% of relapsing patients. Similarly, paraplegia occurs at the nadir of the index myelitis in 70% of monophasic patients compared with 31% of those who eventually relapse.[3]

The tempo of NMO onset also has prognostic value. Patients who present with a combination of ON and myelitis simultaneously or in rapid succession (over a few days) are much more likely have a monophasic course. In the largest contemporary series, the median interval between the first clinical event and the development of bilateral ON and myelitis (traditional definition of NMO) was 5 days (range 0 to 151 days) in the monophasic group versus 166 days (range 2 to 730 days) for the relapsing group.[3] To illustrate, a patient who presents with ON having had severe myelitis six months earlier is much more likely to follow a relapsing disease course than the patient presenting with simultaneous ON and myelitis. This prognostic information may be useful when considering preventative immunotherapies.

Most patients with monophasic NMO experience some recovery from the index events of ON and myelitis and, because no further relapses occur, subsequently remain stable. Although the index events that define the illness are more severe in this group than for relapsing patients, recovery and long-term function

are better, in part because permanent remission spares the patient cumulative deficits. About 80% of ON events improve by a clinically important degree (e.g., from no light perception to 20/200 vision) over the first six months. Wingerchuk et al found that most patients with monophasic NMO recovered to 20/30 vision or better, however, 22% remained functionally blind (20/200 vision or worse) in at least one eye.[3] The brunt of disability in those with a monophasic course occurs as a result of spinal cord injury; most patients experience at least moderate weakness of one or more limbs and moderate sphincter dysfunction with occasional urinary incontinence. Permanent monoplegia or paraplegia occurred in 31%. Five-year survival of this group is approximately 90%.

While the prognosis for most monophasic patients is to maintain some degree of independence (despite moderate visual and motor deficits), patients who have relapsing disease face the prospect of incremental accumulation of much more disability. The first events of ON and myelitis in this group are less severe, and the recovery better, than those of the monophasic group, but recurrent severe episodes of ON and myelitis abolish any apparent advantages of a relapsing course.

Most relapsing patients declare their disease course early. After meeting NMO diagnostic criteria, 55% have their first optic nerve or spinal cord relapse within one year.[3] The proportion increases to 78% at three years and 90% at five years. As in typical MS, relapse frequency is as extremely variable in NMO. Several attacks may strike over a few months or remissions lasting a more than a decade may occur. Over a median follow-up of 16.9 years, the median number of relapses was five (range 1 to 18). As in monophasic NMO, a progressive phase of neurological deterioration is uncommon, although there are many patients who seem to have rapid, sometimes stepwise, deterioration when they attempt to taper and discontinue corticosteroid therapy (see Therapy section).

Severe cervical myelitis causing respiratory failure is more common in relapsing NMO, possibly affecting as many as one-third of patients. In the largest contemporary series, the five-year survival of relapsing patients evaluated between 1950 to 1955 was 68%. Respiratory failure was the sole cause of death.[3] This was a frequent cause of death of NMO patients, but improvements in supportive care over the last two

decades have likely reduced these figures. For example, a recent patient under our care made an excellent recovery from NMO after being ventilator dependent for several days following plasma exchange treatment.

VIII. Etiology and Pathology

The cause of NMO is not known. Its clinical and pathological features have led most to consider it an autoimmune variant of MS. The fact that multiple infectious and systemic autoimmune diseases have been associated with NMO suggests that a single cause of the disorder is unlikely. A high prevalence of serum autoantibodies suggests that NMO may be driven primarily by B cell dysfunction. Although there are some similarities between the distribution of lesions in NMO and in myelin oligodendrocyte glycoprotein (MOG)-induced experimental allergic encephalomyelitis (EAE), the target (auto)antigen in NMO is not known.

The pathology and immunology of NMO will be discussed in detail by Dr. Lucchinetti. Briefly, optic nerve specimens typically reveal near-complete demyelination with modest inflammatory infiltrates.[12, 13] Brain parenchyma is usually normal or reveals only scattered small perivascular infiltrates. Spinal cord lesions are more distinctive but their characteristics depend on the stage of the disease. Macroscopic cord expansion with softening and cavitation is often noted acutely; in chronic cases atrophy is present. Changes ranging from modest perivascular inflammation and demyelination to complete necrotic destruction of both gray and white matter have been described.[13-16] In acute lesions, necrosis, hemorrhage, and an intense inflammatory infiltrate with a predominance of polymorphonuclear cells are often present; this may include large numbers of eosinophils.[17] Some groups have described a hyalinized appearance of medium-sized spinal cord arteries as a hallmark of NMO.[1, 17-19] The cause and significance of this vessel pathology is not known. Lucchinetti et al demonstrated prominent deposition of IgG and C9 neoantigen (a marker of complement activation) at regions of active myelin destruction and vessel walls, where there was vascular proliferation and fibrosis, suggesting that humoral mechanisms may be of some importance.

IX. Treatment

All therapeutic recommendations in the literature represent anecdotal experience from small uncontrolled case series. In the monophasic form of NMO and for index events and relapses of relapsing

NMO, the mainstay of therapy is treatment of acute attacks, prevention of medical complications, and rehabilitation. Specific measures aimed at preventing future attacks are considered for patients who have demonstrated a propensity to relapse.

Most patients who present with NMO exacerbations receive intravenous corticosteroid treatment, for example, 1000 mg methylprednisolone per day for five consecutive days. A recent double-blind crossover study of plasmapheresis versus sham exchanges documented that plasmapheresis (seven exchanges of approximately 55 ml/kg administered every other day) is beneficial treating exacerbations of demyelinating disease (including NMO) that are not responsive to methylprednisolone; this is used as second-line therapy.[20] In a recent series, 6/10 patients treated with plasma exchange for severe, steroid-refractory NMO attacks experienced moderate or marked improvement in close temporal proximity to the initiation of treatment.[21] Intravenous immune globulin has also been used anecdotally.

Prevention of medical complications is critically important. Acute cervical cord attacks may cause respiratory failure. Patients at risk for this complication by virtue of the location and severity of their acute myelitis require close intensive care unit observation with frequent evaluation of respiratory and bulbar status. Ventilatory assistance often becomes necessary. Medical measures to prevent thromboembolic complications, aspiration pneumonia, decubiti, and urinary tract infections are also required.

Preventative therapy is required for patients with relapsing disease. Many North American NMO patients receive parenteral beta-interferon treatment but some clinicians have felt that this treatment may be ineffective based on their uncontrolled experience. A recent Japanese study, however, found that interferon beta-1b seemed to benefit the both the opticospinal form and Western-type MS.[22] Some clinicians have noted that long-term oral corticosteroid monotherapy may significantly reduce relapse frequency or severity. It is not uncommon for patients to become steroid-dependent such that they are unable to taper their dose below a certain level because of perceived worsening of lower extremity function; documentation of a new exacerbation in this setting may or may not be possible.

In the only published prospective treatment study, Mandler et al found that seven newly diagnosed NMO patients seemed to stabilize for at least 18 months on a regimen of azathioprine and oral prednisone.[23] Following an intravenous course of methylprednisolone, oral prednisone (1 mg/kg/d) was started. Three weeks later, patients received azathioprine (2 mg/kg/d). At two months, the prednisone dose was gradually tapered (by 10 mg every three weeks to 20 mg/d, then an even slower reduction to a maintenance dose of 10 mg/d). Most patients were maintained on prednisone 10 mg/d and azathioprine 75 to 100 mg/d. The authors noted that no exacerbations occurred and Expanded Disability Status Scale scores improved somewhat during the 18-month treatment period. Various other immunosuppressive drugs have been used but in limited numbers and outside the realm of a structured study. For patients who "fail" the azathioprine and prednisone combination, intravenous mitoxantrone, which is approved for use in rapidly worsening secondary progressive or relapsing-remitting MS, might be tried. There are no data concerning the use of mitoxantrone in NMO.

X. Summary

There is increasing evidence that NMO is a distinct entity. It differs from MS with respect to lesional topography, exacerbation severity, MR imaging findings, CSF abnormalities, and immunopathology. Early diagnosis and referral to tertiary care centers provides the best chance for complete case ascertainment and may make multicenter efforts at studying this disease possible. At Mayo Clinic, we have initiated an internet-based registry to allow prospective study of incident and prevalent cases of NMO and provide an infrastructure for initiation and management of controlled therapeutic trials.

References

1. Mandler RN, Davis LE, Jeffery DR, Kornfeld M. Devic's neuromyelitis optica: a clinicopathological study of 8 patients. Ann Neurol 1993; 34:162-8.
2. O'Riordan JI, Gallagher HL, Thompson AJ, et al. Clinical, CSF, and MRI findings in Devic's neuromyelitis optica. J Neurol Neurosurg Psychiatr 1996; 60:382-7.
3. Wingerchuk DM, Hogancamp WF, O'Brien PC, Weinshenker BG. The clinical course of neuromyelitis optica (Devic's syndrome). Neurology 1999; 53:1107-14.
4. Kuroiwa Y, Igata A, Itahara K, Koshijima S, Tsubaki T. Nationwide survey of multiple sclerosis in Japan. Clinical analysis of 1,084 cases. Neurology 1975; 25:845-51.
5. Kira J, Yamasaki K, Horiuchi I, Ohyagi Y, Taniwaki T, Kawano Y. Changes in the phenotypes of multiple sclerosis over the last 50 years in Japan. J Neurol Sci 1999; 166:53-57.
6. Singhal BS. Multiple sclerosis--Indian experience. Annals of the Academy of Medicine, Singapore 1985; 14:32-6.
7. Fukazawa T, Yamasaki K, Ito H, et al. Both the HLA-CPB1 and -DRB1 alleles correlate with risk for multiple sclerosis in Japanese: clinical phenotypes and gender as important factors. Tissue Antigens 2000; 55:199-205.
8. Fazekas F, Offenbacher H, Schmidt R, Strasser-Fuchs S. MRI of neuromyelitis optica: evidence for a distinct entity [letter]. J Neurol Neurosurg Psychiatr 1994; 57:1140-2.
9. Tashiro K, Ito K, Maruo Y, et al. MR imaging of spinal cord in Devic disease. J Comp Assist Tomogr 1987; 11:516-7.
10. Tourtellotte WW, Staugaitis SM, Walsh MJ, et al. The basis of intra-blood-brain-barrier IgG synthesis. Ann Neurol 1985; 17:21-27.
11. Paty DW, Oger JF, Kastrukoff LF, al e. MRI in the diagnosis of multiple sclerosis: prospective comparison of clinical evaluation, EPs, oligoclonal banding, and CT. Neurology 1988; 38:180-185.
12. Achard C, Guinon L. Sur un cas de myelite aigue diffuse avec double nevrite optique. Arch de Med Exper er d'Anat Path 1889; 1:696-710.
13. Stansbury FC. Neuromyelitis optica (Devic's disease). Presentation of five cases with pathological study and review of the literature. Arch Ophthalmol 1949; 42:292-335;465-501.
14. Goulden C. Optic neuritis and myelitis. Trans Ophthal Soc UK 1914; 34:229-252.
15. Beck GM. A case of diffuse myelitis associated with optic neuritis. Brain 1927; 50:687-703.
16. Kuroiwa Y. Neuromyelitis optica. In: Koetsler JC, ed. Handbook of Clinical Neurology. Vol. 47. New York: Elsevier Science, 1985:397-408.
17. Lucchinetti C, Mandler R, Weinshenker B, Wingerchuk D, Parisi J, Lassmann H. Humoral mechanisms in the pathogenesis of Devic's neuromyelitis optica. Neurology 2000; 54(Suppl 3):A259-260.
18. Ortiz de Zarate JC, Tamaroff L, Sica RE, Rodriguez JA. Neuromyelitis optica versus subacute necrotic myelitis. II. Anatomical study of two cases. J Neurol Neurosurg Psychiatr 1968; 31:641-5.
19. Lefkowitz D, Angelo JN. Neuromyelitis optica with unusual vascular changes. Arch Neurol 1984; 41:1103-5.
20. Weinshenker BG, O'Brien PC, Petterson TM, al e. A randomized trial of plasma exchange in acute central nervous system inflammatory demyelinating disease. Ann Neurol 1999; 46:878-886.
21. Keegan BM, Pineda A, Rodriguez M, Weinshenker B. Predictive factors for response to plasma exchange in the treatment of acute, severe attacks of central nervous system demyelinating disease. Ann Neurol 2000; 48:451.
22. Itoyama Y, Saida T, Tashiro K, Sato T, Ohashi Y, Japan TI-bMSCRGi. Japanese multicenter, randomized, double-blind trial of interferon beta-1b in relapsing-remitting multiple sclerosis: two year results. Ann Neurol 2000; 48:487.
23. Mandler RN, Ahmed W, Dencoff JE. Devic's neuromyelitis optica: a prospective study of seven patients treated with prednisone and azathioprine. Neurology 1998; 51:1219-20.

Table 1: Diagnostic Criteria for Neuromyelitis Optica

Authors:	**Criteria:**
Mandler et al (1993)	*Clinical*: Acute involvement of spinal cord and ON, either coincidental or separated by months or years, independent of subsequent progression, but without other clinical features at any time during disease course *Imaging*: Normal-appearing brain MRI Enlargement and cavitation on spinal cord MRI *CSF*: Decreased serum/CSF albumin ratio with normal IgG synthesis rate and usually absence of oligoclonal bands
O'Riordan et al (1996)	1) Severe (more or less complete) transverse myelitis 2) An acute unilateral or bilateral optic neuropathy 3) No clinical involvement beyond the spinal cord and optic nerves 4) Illness may be monophasic or multiphasic
Wingerchuk et al (1999)	Diagnosis requires all absolute criteria AND: One major supportive criterion OR two minor supportive criteria *Absolute criteria:* 1) Optic neuritis 2) Acute myelitis 3) No clinical disease outside of the optic nerves and spinal cord *Major Supportive Criteria:* 1. Negative brain MRI at disease onset (normal or not meeting radiological diagnostic criteria for MS) 2. Spinal cord MRI with T2 signal abnormality extending over three or more vertebral segments 3. CSF pleocytosis (>50 WBC/mm^3) OR > 5 neutrophils/mm^3 *Minor Supportive Criteria:* 1. Bilateral optic neuritis 2. Severe ON with fixed visual acuity worse than 20/200 in at least one eye 3. Severe, fixed, attack-related weakness (MRC grade 2 or less) in one or more limbs

Table 2: Characteristics of Monophasic and Relapsing NMO

	Monophasic	Relapsing
Frequency	Less common	More common
Age of onset (median)	29 years	39 years
Sex ratio	About 50% female	80-90% female
History of autoimmune disease	Uncommon	About 50%
Index (presenting) events:		
ON or myelitis only	48%	90%
Bilateral ON	17%	8%
Simultaneous ON + myelitis	31%	0%
Severity at nadir	More severe	Less severe
Recovery	Good	Fair
Respiratory failure	Rare	About one-third
Mortality rate (5 years)	10%	32%