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MEDICAL AFFAIRS

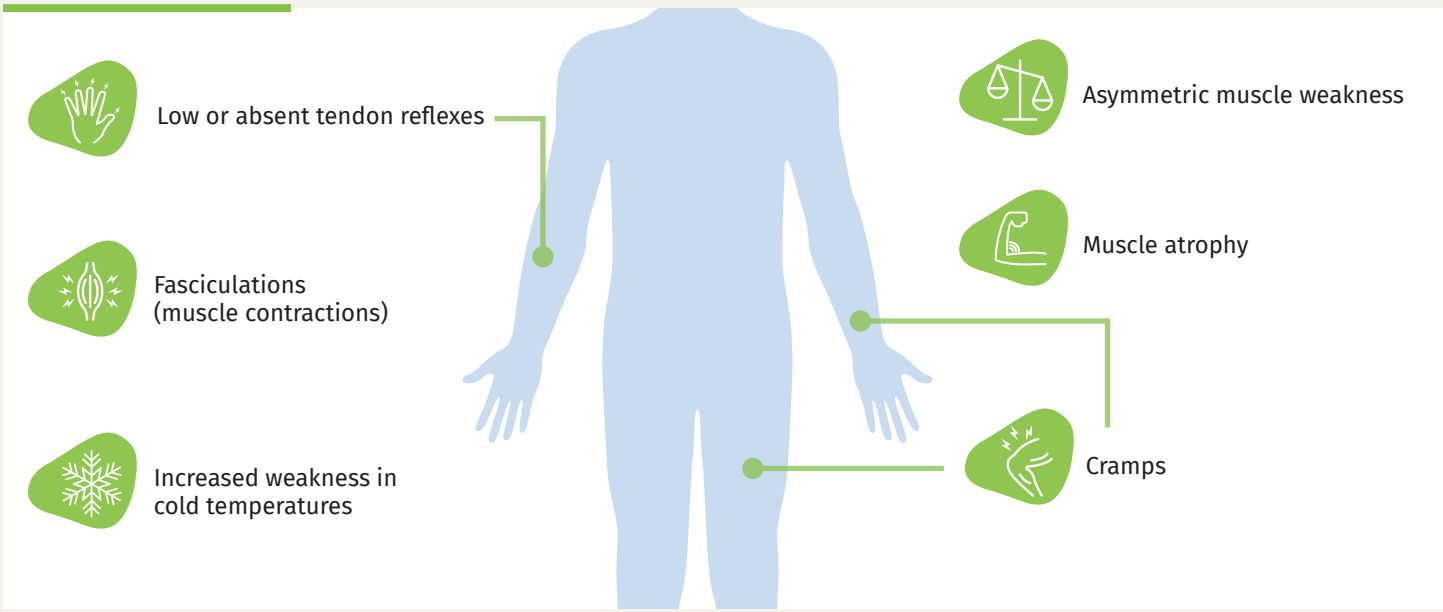
Scan to see argenx pipeline and enrolling trials

Multifocal Motor Neuropathy (MMN)

MMN is a rare, immune-mediated motor neuropathy characterized by nerve conduction block, often associated with complement activation[1]

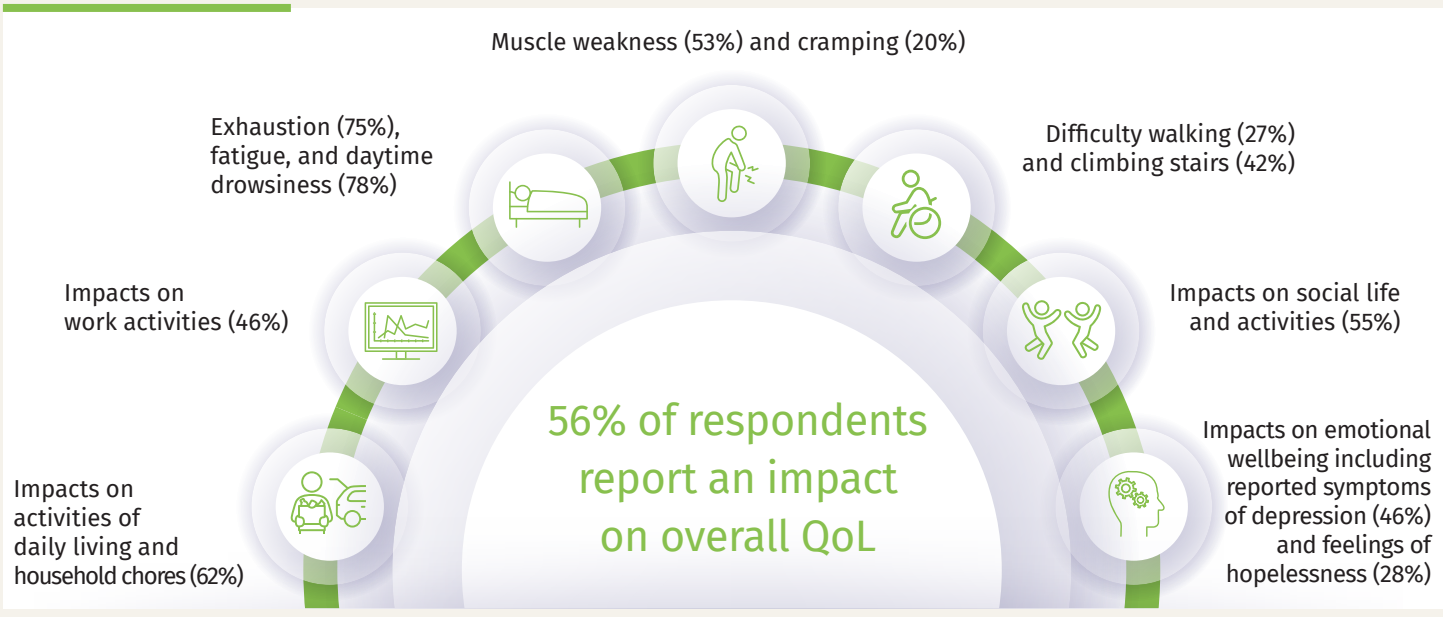
Patients with MMN may experience progressive asymmetrical weakness of the distal limbs, typically without sensory loss[1]

Symptoms[1,2]



Disease Burden[3]

Based on findings of the first global MMN QoL survey (N=211), MMN restricts daily activities and impacts emotional well-being and overall QoL[3,a]



[a]Completed by 211 individuals with MMN in 2016, 53% women, 89% white, >70% located in the United States[3,4]

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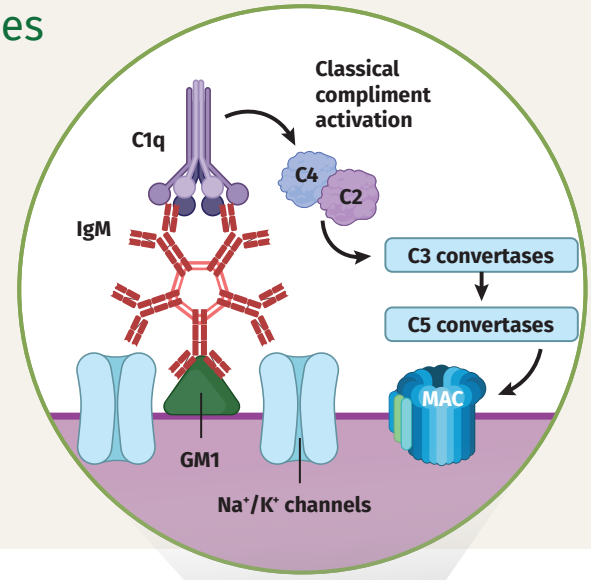
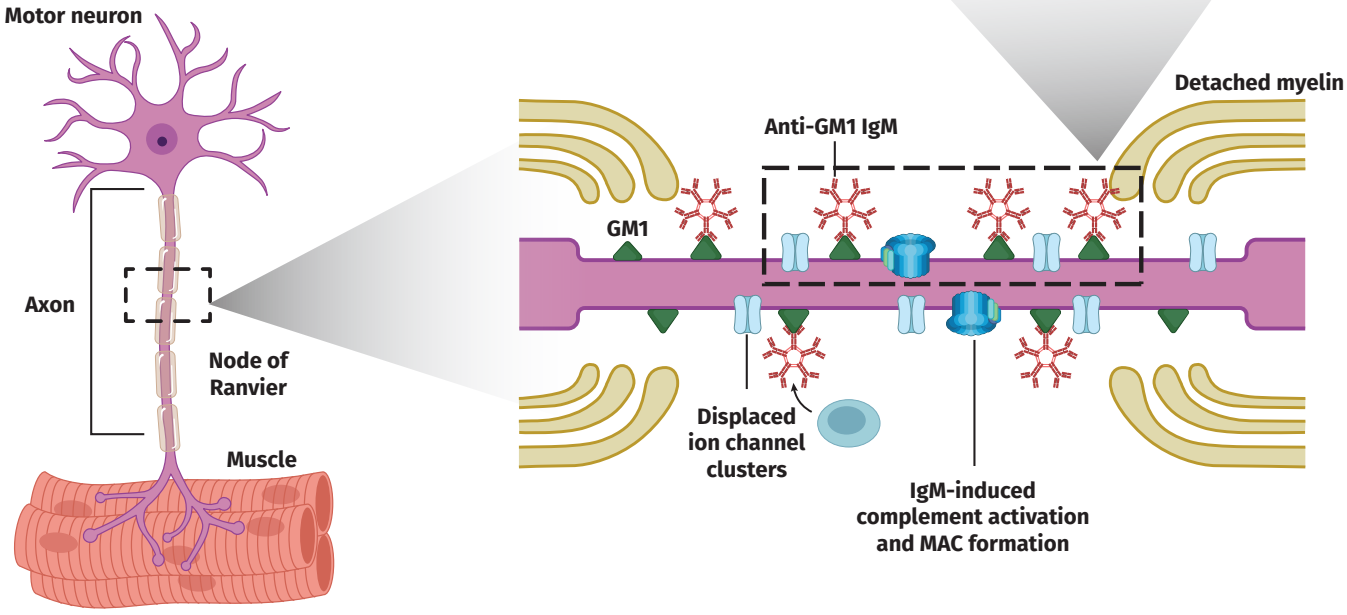
Proposed Involvement of IgM Autoantibodies and Complement Activation in MMN

Diverse autoantibodies targeting gangliosides have been observed in MMN[5]

- IgM autoantibodies targeting GM1 found in the central and peripheral nervous system have been detected in 40%-60% of patients with MMN using current diagnostic tests[6,7]
- Patients seropositive for IgM autoantibodies targeting GM1 show greater weakness, disability, and axon loss than patients without these antibodies[5]
- IgM autoantibodies, including those targeting GM1, can activate the complement pathway in a titer-dependent manner, with greater complement activity correlated with more severe muscle weakness and axonal loss[8,9]





Proposed Pathophysiology[10,11]

In MMN, IgM antibodies may cause nerve dysfunction by targeting ganglioside GM1, leading to conduction block through direct and complement-driven indirect mechanisms[1]

- IgM autoantibodies may result in[1,11,12]:
  - Displacement of ion channel clusters
  - Demyelination
  - Activation of the complement pathway, resulting in deposition of MAC and additional membrane and axonal damage

All figures were created with BioRender.com

Abbreviations: C1q, complement factor C1q; GM1, monosialotetrahexosylganglioside; IgM, immunoglobulin M; MAC, membrane attack complex; MMN, multifocal motor neuropathy; QoL, quality of life.

References

1. Harschnitz O, et al. *J Clin Immunol*. 2014;34(suppl 1):S112-S119. **2.** Allen JA, et al. Mayo Clin Proc Innov Qual Outcomes. 2024;8(1):74-81. **3.** Katz J, et al. First global multifocal motor neuropathy (MMN) quality of life (QOL) patient survey identifies needs in education and treatment. Accessed Jun 27 2023. http://www.neuropathyaction.org/downloads/MMN_article%209-26-2016.pdf. **4.** Katz J, et a. First global multifocal motor neuropathy (MMN) quality of life (QOL) patient survey identifies needs in education and treatment (P2.061). *Neurology*. 2017;88(16_supplement):P2-061 **5.** Cats EA, et al. *Neurology*. 2010;75:1961-1967. **6.** Nobile-Orazio E, et al. *J Neurol Neurosurg Psychiatry*. 2014;85:754-758. **7.** Delmont E, et al. *J of Neuroimmunol*. 2015;278: 159-161. **8.** Yuki N, et al. *J Neurol Neurosurg Psychiatry*. 2011;82(1):87-91. **9.** Vlam L, et al. *Neurol Neuroimmunol Neuroinflamm*. 2015;2(4):e119. **10.** Sathe A, Cusick JK. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023. https://www.ncbi.nlm.nih.gov/books/NBK555995. **11.** Vlam L, et al. *Nat Rev Neurol*. 2011;8(1):48-58. **12.** Beadon K, et al. *Curr Opin Neurol*. 2018;31(5):559-564.