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Neuroimmunology - Key Literature

Reviews:

- **Goodfellow J.A.** and **Willison H.J., 2018:** Gangliosides and Autoimmune Peripheral Nerve Diseases. https://doi.org/10.1016/bs.pmbts.2017.12.010

  "… The review describes the immunological, pathological, and clinical features of autoimmune peripheral nerve diseases in the context of our broader knowledge of the ganglioside glycobiology of the peripheral nervous system."

- **Delmont E.** and **Willison H., 2015:** Diagnostic Utility of Auto Antibodies in Inflammatory Nerve Disorders. J. of Neuromuscular Diseases, **2**: 107-112

  "… Identification of autoantibodies that map onto a clinical phenotype not only allows for improved classification but also provides better understanding of the pathophysiology of inflammatory neuropathies and the potential for therapeutic interventions."

- **Bourque P. R.** et al., **2015:** Autoimmune peripheral neuropathies. Clinica Chimica Acta, **449**: 37-42

  "… Autoantibody testing helps to confirm a diagnosis and provides a framework for prognosis and may guide specific therapy."

- **Dalakas M. C., 2015:** Pathogenesis of immune-mediated neuropathies. Biochim Biophys Acta, **1852(4)**: 658-666

  "… in autoimmune peripheral neuropathies the autoimmunity is mediated by autoantibodies which are directed against myelin antigens ..."

- **Willison H. J.** and **Yuki N.**, **2002:** Peripheral neuropathies and anti-glycolipid antibodies. Brain; **125**: 2591-2625

  "… This review charts the progress of anti-glycolipid antibodies in neuropathy from their original discovery through to more recent discoveries mapping their relationship to subtypes of Guillain-Barré syndrome."

Guidelines:

- **Joint Task Force** of the **EFNS** and the **PNS**; **2010**: European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of **paraproteinemic demyelinating neuropathies**. Report of a Joint Task Force of the European Federation of Neurological Societies and the Peripheral Nerve Society – first revision. J Peripher Nerv Syst, **15(3)**: 185-195

  "… Screening for anti-**MAG** antibodies is recommended for all patients with a paraproteinemic demyelinating neuropathy."

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- **Joint Task Force** of the **EFNS** and the **PNS**; **2010**: European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of **multifocal motor neuropathy**. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society – first revision. J Peripher Nerv Syst **15(4)**: 295-301

  "… testing for anti-ganglioside **GM1** is recommended (level A recommendation) and a good practice point in patients with MMN."

Acute Neuropathies

1. GBS

Guillain-Barré syndrome

Out-line: Guillain-Barré syndrome (GBS) is the most common and severe acute paralytic neuropathy. Under the umbrella term of GBS are several recognizable variants with distinct clinical and pathological features. The optimal choice for treatment are intravenous immunoglobulin (IVIg) or plasma exchange. The presence of anti-ganglioside antibodies can define subsets within the large group of idiopathic neuropathies. Raised anti-ganglioside antibody titres therefore are an additional diagnostic measure.

- **Willison H. J.** and **Goodfellow J. A.**, **2016**: GBS100: Celebrating a century of progress in Guillain-Barré Syndrome (1916-2016). http://eprints.gla.ac.uk/136380/1/136380.pdf

- **Willison** H. J., Jacobs B.C. and van Doorn P. A., **2016**: Guillain-Barré Syndrome. Lancet; **29**: 1-11

- **Ishii J.** et al., **2016:** Recurrent Guillain-Barré syndrome, Miller Fisher syndrome and Bickerstaff brainstem encephalitis. J Neurol Sci, **364**: 59-64

- **Van den Berg B.** et al., **2014:** Guillain-Barré syndrome: pathogenesis, diagnosis, treatment and prognosis**.** Nature Rev Neurol, **10**: 469-479

- **Kuwabara S.** and **Yuki N**., **2013**: Axonal Guillain-Barré syndrome: concepts and controversies**.** Lancet Neurol**, 12:** 1180-1188

- **Winer J. B., 2014:** An Update in Guillain-Barré Syndrome, Autoimmune Dis., **2014**: Article ID 793024

- **van Doorn P. A**., **2013**: Diagnosis, treatment and prognosis of Guillain-Barré syndrome (GBS). Presse Med, **42**: e191-e201

- **Jacobs B. C.** et al., **1997**: Cytomegalovirus infections and anti-GM2 antibodies in Guillain-Barré syndrome. J Neurol Neurosurg Psychiatry **62**(6): 641-643

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Chronic Neuropathies

2. MMN

Multifocal Motor Neuropathy

> ***Out-line:*** MMN (Multifocal Motor Neuropathy) is an immune-mediated neuropathy and is frequently associated with anti-**GM1** IgM antibodies. Other antibodies such (*e g* **GD1b** and/or **GM2**) may cross-react with GM1 (Cats E et al., 2010). Elevated anti-GM1 antibodies is a level A recommendation of a supportive criterium for MMN (EFNS/PNS guidelines on the management of MMN, 2006)."

- **Martinez-Thompson J.M.** et al., **2018:** Composite Ganglioside Autoantibodies and Immune Treatment Response in MMN and MADSAM; DOI 10.1002/mus.26051

- **Leger J.-M.** et al**., 2015:** The pathogenesis of multifocal motor neuropathy and up-date on current management options. Ther Adv Neurol Disord; **8**(3); 109-122

  > "… Underlying mechanisms in MMN seem to be very specific, mainly because of the presence of IgM anti-GM1 serum antibodies and the dramatic response to intravenous immunoglobulins."

- **Lawson V. H.** and **Arnold W. D**., **2014**: Multifocal motor neuropathy: a review of pathogenesis, diagnosis, and treatment. Neuropsychiatric Dis Treat, **10**; 567-576

  > "… Serological evidence of anti-GM1 antibodies and electro-diagnostic findings of conduction block are helpful diagnostic clues for MMN."

- **Nobile-Orazio E.** and **Gallia F**., **2013**: Multifocal motor neuropathy: current therapies and novel strategies. Drugs, **73**(5):397-406

  > "Multifocal motor neuropathy (MMN) is a purely motor mononeuritis multiplex characterized by the presence of conduction block on motor but not on sensory nerves and by the presence of high titers of anti-GM1 antibodies."

- **Cats E**. et al., **2010**: Multifocal motor neuropathy: association of anti-GM1 with clinical features. Neurology **30**; 75(22): 1961-1967

  > " … anti-ganglioside IgM antibodies are associated with severity and clinical characteristics."

3. CANOMAD:

Chronic Ataxic Neuropathy Ophthalmoplegia Monoclonal M-protein cold Agglutinins Disialosyl-Antibodies

> ***Out-line:*** Willison H J et al. (2001) described the signs, symptoms, and laboratory findings of 18 people with CANOMAD syndrome. This is the largest case series reported to date. The CANOMAD phenotype is associated with anti-disialosyl antibodies (*e g* **GQ1b** and **GD1b**) IgM antibodies.

- **Krenn M** et al., **2014**: CANOMAD responding to weekly treatment with intravenous immunoglobulin (IVIg). BMJ Case Rep doi:101136

- **Leger J. M.** et al., **2009**: Polyneuropathy associated with monoclonal gammopathy: treatment perspectives. Bull Acad Natl Med 193(5): 1110-1111

- **Willison H. J.** et al., **2001**: The clinical and laboratory features of chronic sensory ataxic neuropathy with disialosyl IgM antibodies. Brain, **124**, 1968-1977

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4. Paraproteinemic Neuropathies and Neuropathies with anti-MAG Antibodies

Out-line: In a high percentage of patients (> 70%; Kuijf M et al., 2009) with IgM-PNP antibodies against MAG can be detected using the BÜHLMANN anti-MAG autoantibody ELISA which is the acknowledged gold standard (Pihan M et al., 2012). Moreover, the quantitation of anti-MAG autoantibodies is a relevant tool for the management of patients under Rituximab® therapy (Renaud S et al., 2003) and for the differentiation of patients with MAG Neuropathy from more CIDP-like neuropathies (Magy L et al., 2015).

- **Dalakas C. M., 2018:** Advances in the diagnosis, immunopathogenesis and therapies of IgM-anti-MAG antibody –mediated neuropathies. Ther Adv Neurol Disord, **11:** 1-2

- **Paludo J and Ansell S M, 2017:** Advances in the understanding of IgM monoclonal gammopathy of undetermined significance. **6** (F1000Faculty Rev):2142 (doi: 10.12688/f1000research.12880.1)

- **Pruppers M.H.J., 2017** et al.: 230th ENMC International Workshop. Neuromuscular Disorders, doi: 10.1016/j.nmd.2017.08.001

- **Lunn M. P. T.** and **Nobile-Orazio E. 2016:** Immunotherapy for IgM anti-myelin-associated glycoprotein paraprotein-associated peripheral neuropathies (Review): Cochrane Database of Systematic Reviews; 10: Art. No.: CD002827

- **Vallat J. M.** et al**., 2016:** Therapeutic options and management of polyneuropathy associated with anti-MAG antibodies. Expert Rev Neurother, **16(9)**: 1111-1119

- **Magy L.** et al., **2015**: Heterogeneity of Polyneuropathy Associated with anti-MAG Antibodies. J Immunol Res, 2015: 450391

- **Stork A. C.** et al**., 2014**: Prevalence, specificity and functionality of anti-ganglioside antibodies in neuropathy associated with IgM monoclonal gammopathy. J Neuroimmunol, **268**(1-2): 89-94

  "Anti-ganglioside antibodies were found in 19 (35%) patients with polyneuropathy and IgM monoclonal gammopathy (IgM-PNP) without anti-MAG antibodies."

- ***Nobile*-Orazio E**., **2013**: Neuropathy and Monoclonal Gammopathy. Handb. Clin. Neurol. **115**; 443-459

  "Monoclonal Gammopathy is present in 1-3% of the population above 50 years … and in at least 8% of patients is associated with a symptomatic neuropathy ..."

- **Nobile-Orazio E.,** et al., **2010:** Up-date on neuropathies associated with monoclonal gammopathies of undetermined significance (2008-2010). J Peripher Nerv Syst. **15**(4); 302-306

  "Anti-myelin-associated glycoprotein (MAG) antibodies were reduced in most treated patients ..."