Neuroimmunology - Key Literature

Reviews:

• **Wanleenuwat P et al. 2020:** Antiganglioside antibodies in neurological diseases. *J Neurol Sci, 408*: 116576

• **Dalakas M. 2019:** Autoimmune Peripheral Neuropathies. *Clinical Immunology (5th edition); 903-915.e1*

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

• **Delmont E and Willison H J, 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."

Quality Control/Routine:

  "... There is high variation between commercial assays and the ELISA which is supported by Key opinion leaders. BÜHLMANN GanglioCombi® is the most sensitive and in delivers very reproducible results in all thirteen participating laboratories."
EFNS* Guidelines (*European Federation of Neurological Societies):

  
  “... Screening for anti-MAG antibodies is recommended for all patients with a paraproteinemic demyelinating neuropathy.”

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

- **Joint Task Force** of the EFNS and the PNS; 2010: Guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the EFNS and the PNS – first revision.

### Acute Neuropathies

1. **GBS**  
   **Guillain-Barré syndrome**

   **Outline:** 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.


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Neuroimmunology Key Literature – 6/2020
**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; 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."


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

- **Guimarães-Costa R et al., 2013:** Multifocal Motor Neuropathy. Presse Med 42: e271-e224


  "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


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).


• 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)


• 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


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


> “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 ...”