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Autoimmune Peripheral Neuropathies – Selected Literature

1. Reviews

Anti-Ganglioside and -MAG antibodies in autoimmune peripheral neuropathies: A wide range of IgG and IgM neural antibodies related to immune-mediated nerve disorders has been described. These neural antibodies target glycolipids, gangliosides in particular, and glycoproteins which are enriched in the peripheral nerves. For its determination ELISA remains the most widely available, reliable and convenient assay methodology. Some antibodies have a particularly robust and widely appreciated clinical significance. Thus, **anti-MAG IgM antibodies** that are found in IgM paraprotein related neuropathies define a relatively uniform clinical and prognostic phenotype. **IgG antibodies against gangliosides** GM1 and GD1a are strongly associated with motor axonal variants of **Guillain-Barré syndrome**, and anti-GQ1b with Miller Fisher syndrome. In other chronic neuropathies, **antibodies against di-sialylated gangliosides** (for example GD1b and GQ1b) are detected in ataxic neuropathies, usually associated with an IgM paraprotein. Antibodies against GM1 are frequently found in multifocal motor neuropathy (MMN). While absence of anti-ganglioside antibodies does not exclude the possibility for an autoimmune neuropathy, its presence is usually very specific and confirmatory.

Gwathmey K G and **Smith A G**, **2020**: Immune-Mediated Neuropathy. Neurol Clin **38(3)**:711-735.
DOI: 10.1016/j.ncl.2020.03.008. Epub 2020 Jun 11. PMID: **32959381**

Lehmann H C *et al.*, **2020**: Diagnosis of Peripheral Neuropathy. Neurological Research and Practice **2**(20)
DOI: 10.1186/s42466-020-00064-2

Dalakas M C, **2019**: Autoimmune Peripheral Neuropathies. Clinical Immunology (5th edition); 903-915.e1
https://doi.org/10.1016/B978-0-7020-6896-6.00067-3

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

Delmont E and **Willison H J**, **2015**: Diagnostic Utility of Auto Antibodies in Inflammatory Nerve Disorders.
J. of Neuromuscular Diseases **2**: 107-112
DOI: 10.3233/JND-150078 PMID: **27858733**

Bourque P R *et al.* **2015**: Autoimmune peripheral neuropathies. Clinica Chimica Acta, **449**: 37-42
DOI: 10.1016/j.cca.2015.02.039 PMID: **25748038**

Dalakas M C, **2015**: Pathogenesis of immune-mediated neuropathies. Biochim Biophys Acta **1852(4)**: 658-666
DOI: 10.1016/j.bbadis.2014.06.013 PMID: **24949885**

Steck A, **Yuki N** and **Graus F**, **2013**: Antibody Testing in Peripheral Nerve Disorders. Handb Clin Neurol **115**: 189-212
DOI: 10.1016/B978-0-444-52902-2.00011-4

Willison H J and **Yuki N**, **2002**: Peripheral neuropathies and anti-glycolipid antibodies. Brain **125**: 2591-2625
DOI: 10.1093/brain/awf272 PMID: **12429589**

2. Acute Neuropathies

2.1 Guillain-Barré Syndrome (GBS)

Synopsis: **GBS** and related variants suffer from an **acute** onset of autoimmune neuropathy. In approximately up to 10% of cases the disease is fatal, and up to 20% of patients are left with significant disability. GBS may begin subtly, and may be difficult to diagnose at the onset. Early diagnosis of GBS is important: prompt intervention (such as e g plasmapheresis or intravenous gamma globulins) can hold or even reverse the disease. **Anti-ganglioside antibodies** are reported in up to 50% of GBS patients. They can help to confirm diagnosis and justify an initiated immune-modulatory treatment.

Leonhard SE *et al.*, **2019**: Diagnosis and management of Guillain-Barré syndrome in ten steps.
Nat Rev Neurol **15(11)**: 671-683.
DOI: 10.1038/s41582-019-0250-9 PMID: **31541214** PMCID: PMC6821638

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Uncini A and **Kuwabara S**, **2018**: The elctrodiagnosis of Guilllain-Barré Syndrome subtypes: where do we stand? Clin Neurophysiol **129(12)**: 2586-2593
DOI: 10.1016/j.clinph.2018.09.025 PMID: **30419502**

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
DOI: 10.1016/S0140-6736(17)30055-7 PMID: **28118915**

Van den Berg B *et al.*, **2014**: Guillain-Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. Nature Rev Neurol, **10**: 469-479
DOI: 10.1038/nrneurol.2014.121 PMID: **25023340**

Kuwabara S and **Yuki N**, **2013**: Axonal Guillain-Barré syndrome: concepts and controversies. Lancet Neurol, **12**: 1180-1188
DOI: 10.1016/S1474-4422(13)70215-1 PMID: **24229616**

van Doorn P A, **2013**: Diagnosis, treatment and prognosis of Guillain-Barré syndrome (GBS). Presse Med, **42**: e191-e201
DOI: 10.1016/j.lpm.2013.02.328 PMID: **23628447**

3. Chronic Neuropathies

3.1 Multifocal Motor Neuropathy (MMN)

Synopsis: **MMN** is a rare, purely motor neuropathy which is treatable. It is associated with asymmetric deficits predominantly in the upper limbs. The clinical presentation of MMN can closely imitate several neurological conditions including those with more malignant prognoses such as motor neuron disease. Therefore, early and rapid recognition of MMN is critical. Serological evidence of **anti-GM1 antibodies** and electrodiagnostic findings of **conduction block** are helpful diagnostic clues for MMN.

Yeh W Z, *et al.*, **2020:** Multifocal motor neuropathy: controversies and priorities. J Neurol Neurosurg Psychiatry **91**: 140-148.
DOI: 10.1136/jnnp-2019-321532 PMID: **31511307**

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
DOI: 10.1177/1756285615575269 PMID: **25941538 F**

Lawson V H and **Arnold W D**, **2014**: Multifocal motor neuropathy: a review of pathogenesis, diagnosis, and treatment. Neuropsychiatric Dis Treat, **10**: 567-576
DOI: 10.2147/NDT.S39592 PMID: **24741315**

Guimarães-Costa R *et al.*, **2013**: Multifocal Motor Neuropathy. Presse Med **42**: e271-e224
DOI: 10.1016/j.lpm.2013.01.057 PMID: **23623583**

Nobile-Orazio E and **Gallia F**, **2013**: Multifocal motor neuropathy: current therapies and novel strategies. Drugs, **73(5)**:397-406
DOI: 10.1007/s40265-013-0029-z PMID: **23516024**

Muley S A and **Parry G J**, **2012**: Multifocal motor neuropathy. J Clin Neurosci **19(9)**: 1201-1209
DOI: 10.1016/j.jocn.2012.02.011 PMID: **22743043**

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Cats E *et al.*, **2010**: Multifocal motor neuropathy: association of anti-GM1 with clinical features. Neurology 30; **75(22)**: 1961-1967
DOI: 10.1212/WNL.0b013e3181ff94c2 PMID: **20962291**

Meuth S G and **Kleinschnitz C**, **2010**: Multifocal Motor Neuropathy: Update on Clinical Characteristics, Pathophysiological Concepts and Therapeutic Options. Eur Neurol **63(4)**: 193-204
DOI: 10.1159/000282734 PMID: **20150737**

3.2 Chronic Ataxic Neuropathies (CANOMAD / CANDA)

(Chronic Ataxic Neuropathy, Ophthalmoplegia, IgM paraprotein, Cold Agglutinins, and Disialosyl antibodies / Chronic Ataxic Neuropathy with Disialosyl antibodies)

Synopsis: CANOMAD is a rare, debilitating syndrome characterized by the presence of ataxic neuropathy, ophthalmoplegia, monoclonal gammopathy, cold agglutinins and the presence of an IgM paraprotein typically reacting with gangliosides bearing two sialic acids (such as GD1b or GQ1b). IVIg and Rituximab are the most effective therapies.

Krenn M *et al.*, **2014**: CANOMAD responding to weekly treatment with intravenous immunoglobulin (IVIg). BMJ Case Rep
DOI: 10.1136/bcr-2013-202545 PMID: **24722712**

Willison H J *et al.*, **2001**: The clinical and laboratory features of chronic sensory ataxic neuropathy with disialosyl IgM antibodies. Brain, **124**, 1968-1977
DOI: 10.1093/brain/124.10.1968 PMID: **11571215**

3.3 Neuropathies with anti-MAG antibodies

Synopsis: Anti-MAG peripheral neuropathy is an autoimmune demyelinating neuropathy. Pathogenesis of MAG-Neuropathy is often associated with monoclonal IgM reacting with MAG glycoprotein. Anti-MAG IgM has also been identified in Waldenström's macroglobulinemia and IgM secreting lymphoma. IgM-reactivities against gangliosides may co-exist in anti-MAG antibody polyneuropathies.

Vallat J-M *et al.*, **2020**: The Wide Spectrum of Pathophysiological Mechanisms of Paraproteinemic Neuropathy. Neurology Publish Ahead of Print
DOI: 10.1212/WNL.0000000000011324

Dalakas M C, **2018**: Advances in the diagnosis, immunopathogenesis and therapies of IgM-anti-MAG antibody – mediated neuropathies. Ther Adv Neurol Disord, **11**: 1-2
DOI: 10.1177/1756285617746640 PMID: **29403542**

Franciotta D *et al.*, **2017**: Diagnostics of anti-MAG antibody polyneuropathy. Neurol Sci (2017) **38 (Suppl 2)**:S249–S252
DOI: 10.1007/s10072-017-3024-4

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 PMID: **29399323**

Pruppers M H J *et al.*, **2017**: 230th ENMC International Workshop: Improving future assessment and research in IgM anti-MAG peripheral neuropathy: A consensus collaborative effort, Naarden, The Netherlands, 24-26 February 2017. Neuromuscular Disorders, **27(11)**: 1065-1072
DOI: 10.1097/WCO.0000000000000236 PMID: **26263475**

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
DOI: 10.1002/14651858.CD002827.pub4 PMID: **27701752**

Vallat J-M *et al.*, **2016**: Therapeutic options and management of polyneuropathy associated with anti-MAG antibodies. Expert Rev Neurother, **16(9)**: 1111-1119
DOI: 10.1080/14737175.2016.1198257 PMID: **27267749**

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Nobile-Orazio E, **2013**: Neuropathy and Monoclonal Gammopathy. Handb. Clin. Neurol. **115**; 443-459
DOI: 10.1016/B978-0-444-52902-2.00025-4 PMID: **23931795**

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
DOI: 10.1111/j.1529-8027.2010.00283.x PMID: **21199101**

4. EFNS* Guidelines (*European Federation of Neurological Societies)

Joint Task Force of the **EFNS** and the **PNS**; **2010**: 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
DOI: 10.1111/j.1529-8027.2010.00278.x PMID: **21040140**

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
DOI: 10.1111/j.1529-8027.2010.00290.x PMID: **21199100**

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.
J Peripher Nerv Syst **15(1)**: 1-9
DOI: 10.1111/j.1529-8027.2010.00245.x PMID: **20433600**