

anti-MAG ELISA

Diagnosis and Treatment Follow-up of
anti-MAG Neuropathies

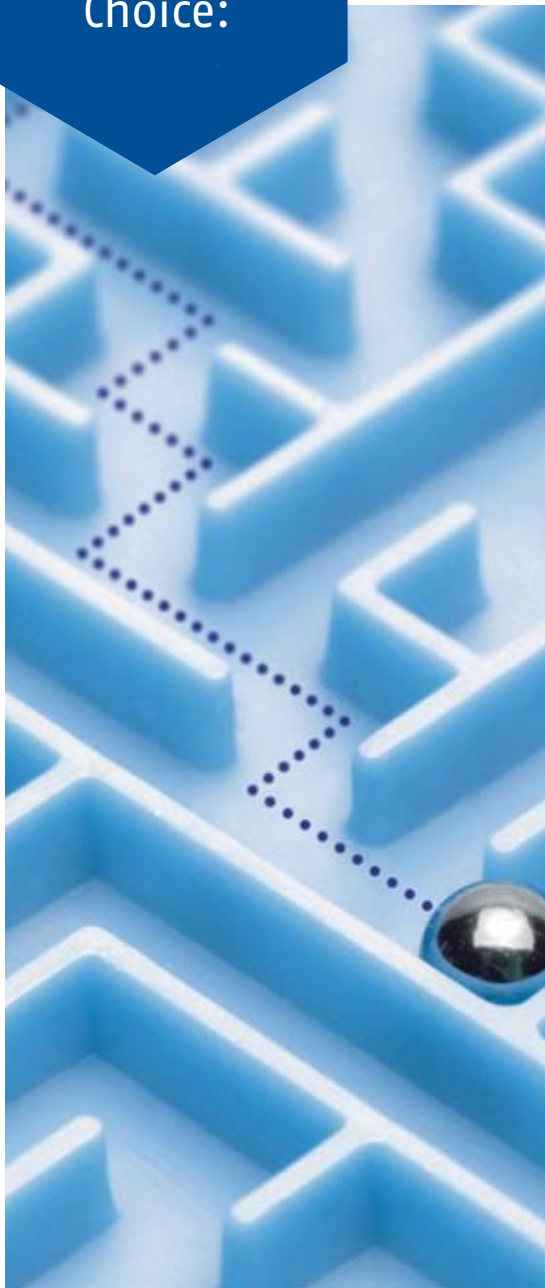
The
Expert's
Choice:

The Gold standard for anti-MAG-
Testing:

Specific: Based on human brain
MAG antigen

Sensitive: Even low titers of IgM
antibodies can be detected

Quantitative: Allows surveillance of
treatment efficacy



anti-MAG Associated Neuropathies

MAG and anti-MAG Antibodies

The myelin-associated glycoprotein (MAG) is a transmembrane glycoprotein which is localized in periaxonal Schwann cells and oligodendroglial membranes of myelin sheaths. The IgM antibodies in most of the patients with neuropathy react with the oligosaccharides (HNK-1 epitope) of glycolipids and glycoproteins that are concentrated in the peripheral nerves. This epitope is shared by a number of other neuropathy target antigens (eg gangliosides). Anti-MAG antibodies are associated with IgM gammopathy.

Paraproteinemic Demyelinating Neuropathy [PDN]

The anti-MAG Neuropathy is an antibody mediated demyelinating neuropathy. The clinical picture is characterized by a distal and symmetric, mostly sensory neuropathy. Monoclonal immunoglobulin M anti-MAG antibodies are uniquely found in this condition and are believed to be pathogenic. In patients who underwent neurological evaluation the prevalence of neuropathy with IgM has been reported to be 31%.

High titers of anti-MAG IgM antibodies occur in almost 50% of patients with a IgM paraproteinemic demyelinating neuropathy (PDN). Therefore, testing for antibodies to MAG should be considered in patients with an IgM PDN. Patients with sensory neuropathy may have MAG antibodies at low titers.

Detection of anti-MAG Antibodies

The source of the antigen is pivotal and has a significant impact on the sensitivity of the assay. BÜHLMANN uses purified human MAG as an antigen which makes the anti-MAG ELISA the most sensitive commercially available assay.

In a study of 112 patients¹, 72% of the IgM were nerve specific: 52% of these were directed against MAG or its cross-reactive glycolipids SG[L]PG (sulfoglucuronyl [lactosaminy] paragloboside) and 22% reacted with gangliosides.

EFNS/PNS PDN Guidelines

A joint taskforce of the European Federation of Neurological Societies (EFNS) and Peripheral Nerve Society (PNS) constructed clinically useful guidelines for the diagnosis, investigation and treatment of patients with both a demyelinating neuropathy and a paraprotein (PDN)². The guidelines are most clear and recommend amongst others:

- testing for antibodies to MAG in patients with IgM PDN
- testing for IgM antibodies against neural antigens, such as GQ1b, GM1, GD1b in patients with IgM PDN without anti-MAG antibodies

Treatment of PDN

Therapy has been directed at reducing circulating IgM anti-MAG antibodies by removal [plasma exchange, inhibition (IVIg), or reduction of synthesis (corticosteroids, immunosuppressive agents, cytotoxic agents or interferon- α)]. Preliminary reports suggest that Rituximab, a chimeric antibody specifically binding to CD20 antigen on normal and malignant B lymphocytes, may be a promising therapy. There is laboratory evidence of reduction of B-cells, anti-MAG antibodies and total IgM. Anti-MAG antibodies fell to a median of 38% of the initial values one year after treatment³ (cf figure).

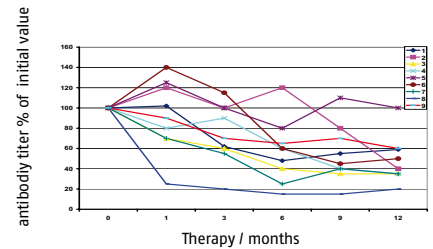


Figure 1: Anti-MAG antibody titers before (0) and after treatment.

A recent study⁴ performed at the Institute for Clinical and Experimental Pathology, Salt Lake City, UT, proves the BÜHLMANN anti-MAG ELISA to be the most sensitive method (sensitivity: 97.5% cf table) when compared to techniques such as Western blot or immunofluorescence. Anti-MAG ELISA was shown to detect very low anti-MAG antibody titers, which are discussed to describe a particular neurological picture. Detecting anti-MAG IgM antibodies by ELISA has some advantages over Western blot. The ELISA is objective, quantitative and is able to detect low titers of IgM that can be found in patients with an autoimmune neuropathy without demyelination. In conclusion, these data show significant variation for the different methods used to detect MAG IgM in serum.

Literature:

- (1) Caudie C et al. Monoclonal IgM autoantibody activity vis-a-vis glycoconjugates of peripheral nerves: a propos of 112 cases. Ann Biol Clin (Paris) 59, 567-577 (2001)
- (2) Guideline on management of paraproteinemic demyelinating neuropathies. Report of a joint task force of the EFNS and PNS. JPNS,11, 9-19 (2006)
- (3) Renaud S et al. Rituximab in the treatment of Polyneuropathy associated with anti-MAG antibodies. Muscle Nerve 27, 611-615 (2003)
- (4) Jaskowski, TD et al. Further comparisons of assays for detecting MAG IgM autoantibodies; Journal of Neuroimmunol, 187 (1-2), 175-78 (2007)

	MAG WB (monkey)		MAG ELISA (human)		Myelin IFA (monkey nerve)		
	+	-	+	-	+	-	
MAG WB (human)	+	29	11	39	1	37	3
	-	0	35	7	28	2	33
% Agreement	=	85.3		89.3		93.3	
% Sensitivity	=	72.5		97.5		92.5	
% Specificity	=	100.0		80.0		94.3	

Table 1: Comparison of MAG IgM assays to Western blot in 75 sera from patients suspected of having autoimmune neuropathy.



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