

Anti-MOG Abs in MS and NMO

Dr Thierry VINCENT
Department of Immunology
St ELOI Hospital – CHU de Montpellier (France)

Ann Neurol. 2000 Jun;47(6):707-17.

Heterogeneity of multiple sclerosis lesions: implications for the pathogenesis of demyelination.

Lucchinetti C, Brück W, Parisi J, Scheithauer B, Rodriguez M, Lassmann H.
Department of Neurology, Mayo Clinic, Rochester, MN, USA

→ 4 different pathological patterns of demyelinating lesions

**→ groupe II = Ig + C'
deposition**

**→ Response to plasmapheresis
→ Pathogenic role of Abs**

But... which is (are) the auto-antigene(s) ??

1- Anti-MOG auto-Abs in MS

- **MOG is expressed on the outer surface of CNS myelin sheaths**
- **Comprises about 0.05% of total myelin protein**

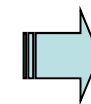
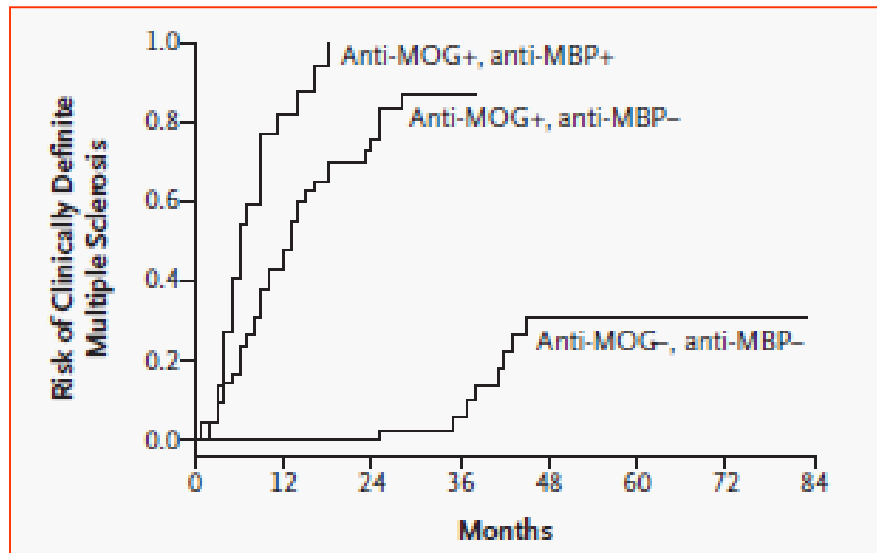
ORIGINAL ARTICLE

Antimyelin Antibodies as a Predictor of Clinically Definite Multiple Sclerosis after a First Demyelinating Event

Thomas Berger, M.D., Paul Rubner, M.D., Franz Schautzer, M.D., Robert Egg, M.D., Hanno Ulmer, Ph.D., Irmgard Mayringer, M.D., Erika Dilitz, M.D., Florian Deisenhammer, M.D., and Markus Reindl, Ph.D.

N Engl J Med. 2003; 349: 139-145

Fig 1. Risk of Clinically Definite MS, According to Ab Status.



Anti-MOG- / anti-MBP- → 23%
Anti-MOG+ / anti-MBP- → 83%
Anti-MOG+ / anti-MBP+ → 95%

Anti-MOG and anti-MBP IgM identification / western blot

Results not confirmed by subsequent studies

Similar low frequency of anti-MOG IgG and IgM in MS patients and healthy subjects.

Lampasona V, Franciotta D, Furlan R, Zanaboni S, Fazio R, Bonifacio E, Comi G, Martino G.
Neurology. 2004 Jun 8;62(11):2092-4.

Even from the same group...

Anti-myelin antibodies do not allow earlier diagnosis of multiple sclerosis.

Lim ET, Berger T, Reindl M, Dalton CM, Fernando K, Keir G, Thompson EJ, Miller DH, Giovannoni G.
Mult Scler. 2005 Aug;11(4):492-4.

Conformational epitopes

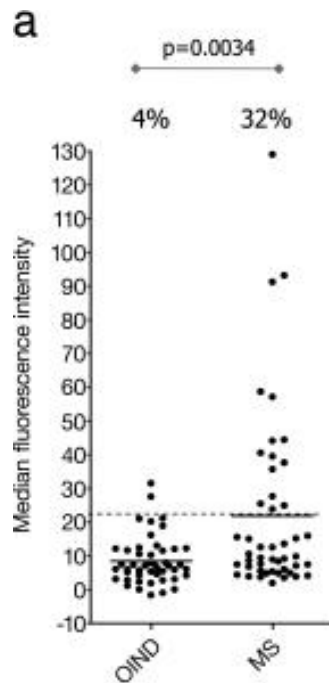
PNAS

Identification of a pathogenic antibody response to native myelin oligodendrocyte glycoprotein in multiple sclerosis

Dun Zhou*, Rajneesh Srivastava*, Stefan Nessler*, Verena Grummel*, Norbert Sommer¹, Wolfgang Brück*, Hans-Peter Hartung*, Christine Stadelmann², and Bernhard Hemmer*¹

¹Department of Neurology, Heinrich Heine University, 40225 Düsseldorf, Germany; ²Department of Neurology, Philipps University, 35033 Marburg, Germany; and ³Institute of Neuropathology, Georg August University, 37099 Göttingen, Germany

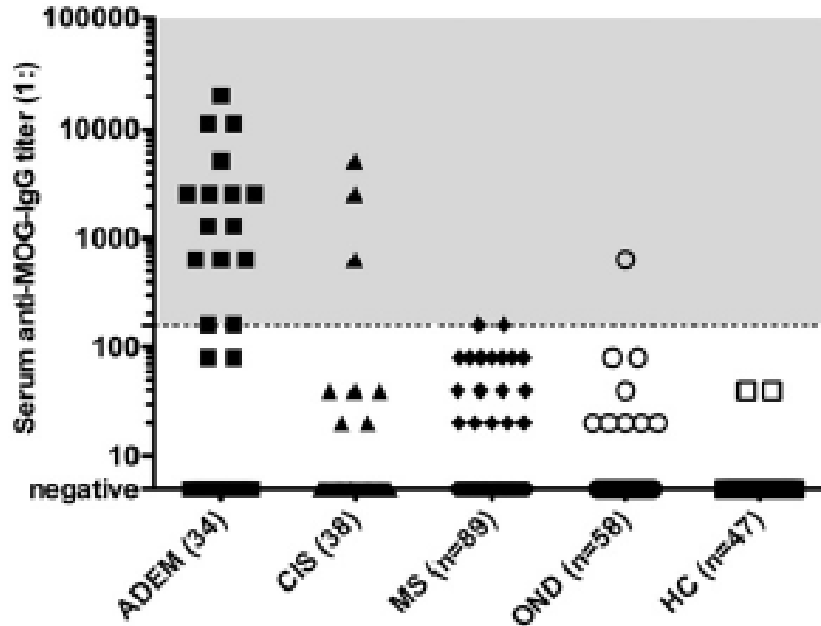
→ Cell based assay expressing natively folded MOG



Detection of Abs directed against conformational MOG epitopes increases specificity

Anti-MOG Abs are more frequent in children

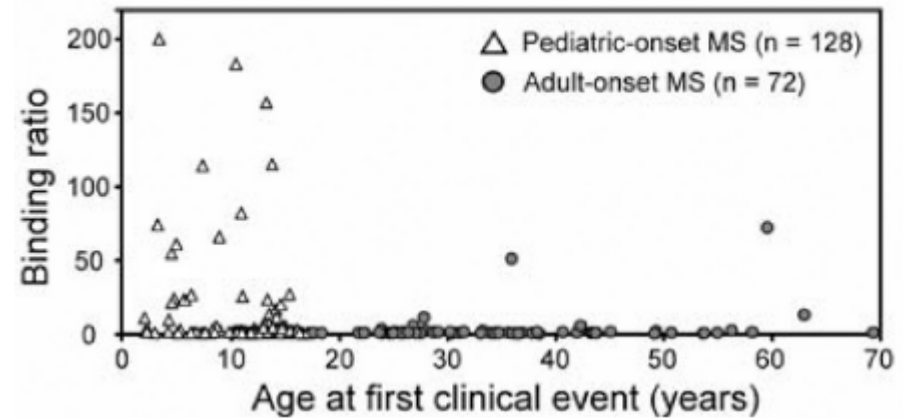
CNS demyelinating diseases



Anti-MOG Abs are more prevalent in ADEM than in MS

(Di Pauli et al. Clinical Immunology (2011) 138, 247–254)

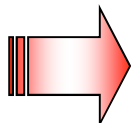
Pediatric vs adult MS



Anti-MOG Abs are more prevalent in pediatric than in adult-onset MS

(McLaughlin et al J Immunol 2009 Sep 15;183(6):4067-76)

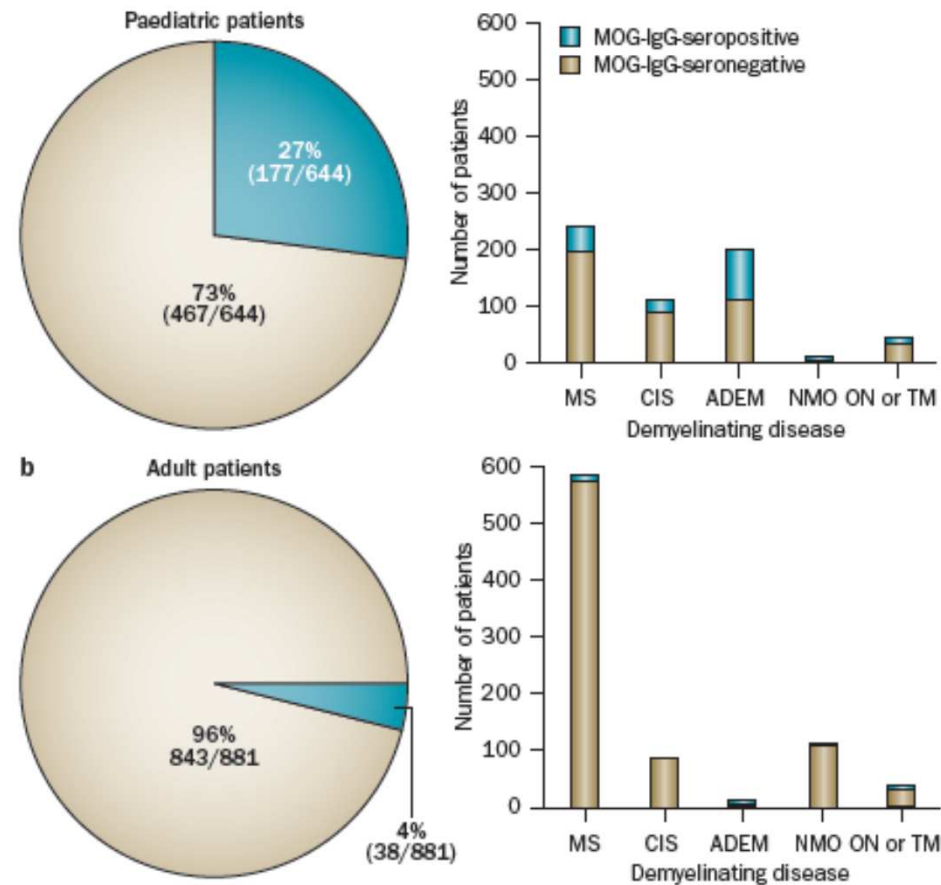
Transient in ADEM / Persistent in MS



Children + persistent anti-MOG → HR of MS (?)

The spectrum of MOG autoantibody-associated demyelinating diseases

Markus Reindl, Franziska Di Pauli, Kevin Rostásy and Thomas Berger



2- Anti-MOG auto-Abs in NMO

RESEARCH

Open Access

Complement activating antibodies to myelin oligodendrocyte glycoprotein in neuromyelitis optica and related disorders

Simone Mader¹, Viktoria Gredler¹, Kathrin Schanda¹, Kevin Rostasy², Irena Dujmovic³, Kristian Pfaller⁴, Andreas Lutterotti¹, Sven Jarius⁵, Franziska Di Pauli¹, Bettina Kuenz¹, Rainer Ehling¹, Harald Hegen¹, Florian Deisenhammer¹, Fahmy Aboul-Enein⁶, Maria K Storch⁷, Peter Koson^{8,9}, Jelena Drulovic^{3,10}, Wolfgang Kristoferitsch¹¹, Thomas Berger¹ and Markus Reindl^{1*}

OPEN

Distinction between MOG antibody-positive and AQP4 antibody-positive NMO spectrum disorders

**Presence of anti-MOG IgG
(16/215 NMOSD= 7.4%)**

- Male > Female

- Younger age

- More restricted phenotype (ON > myelitis)

- More frequent bilateral simultaneous ON

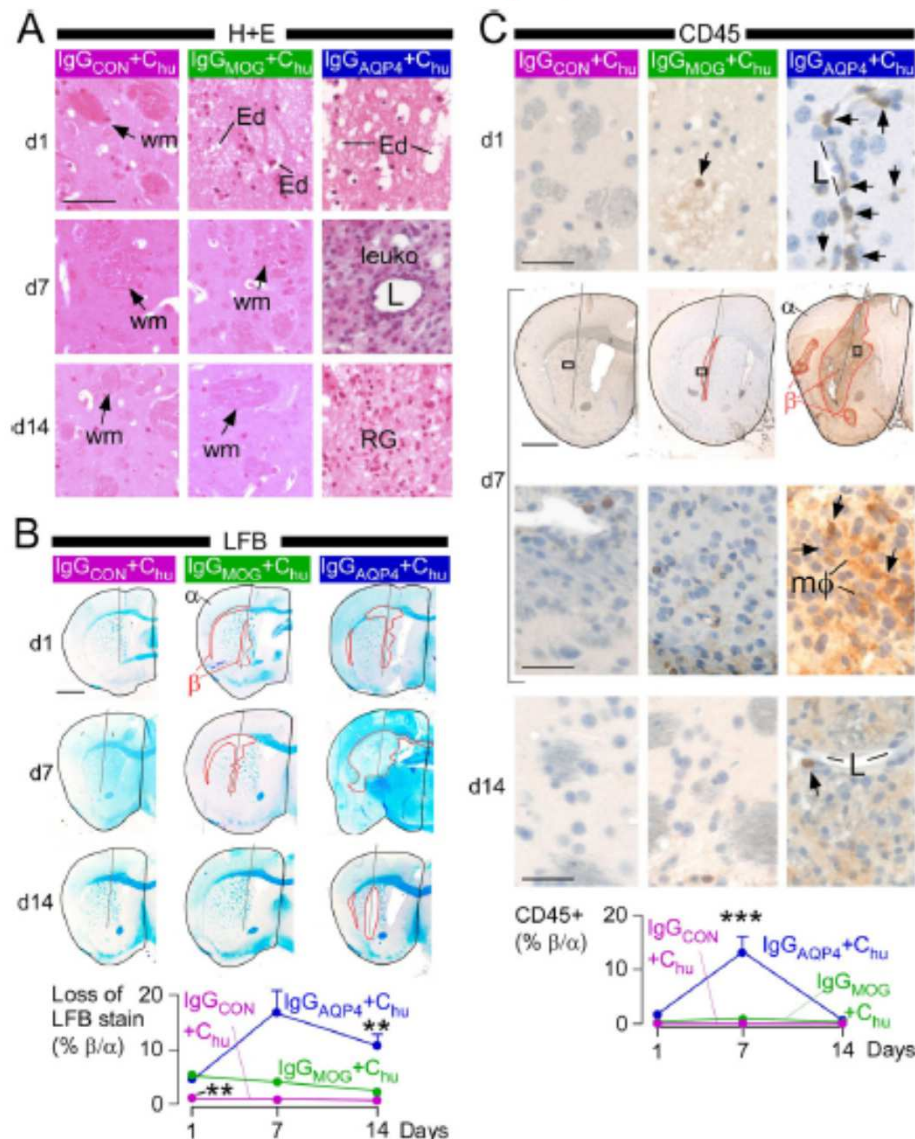
- Lower number of attacks

- Myelitis involving the lower portion of the SC

- Better functional recovery (but not all patients)

Neuromyelitis optica MOG-IgG causes reversible lesions in mouse brain

Samira Saadoun¹, Patrick Waters², Gregory P Owens³, Jeffrey L Bennett^{3,4}, Angela Vincent²
and Marios C Papadopoulos^{1*}



Anti-AQP4

- Myelin loss (C' mediated)
- inflammation
- neuronal and astrocyte death
- limited recovery at 2 weeks

Anti-MOG

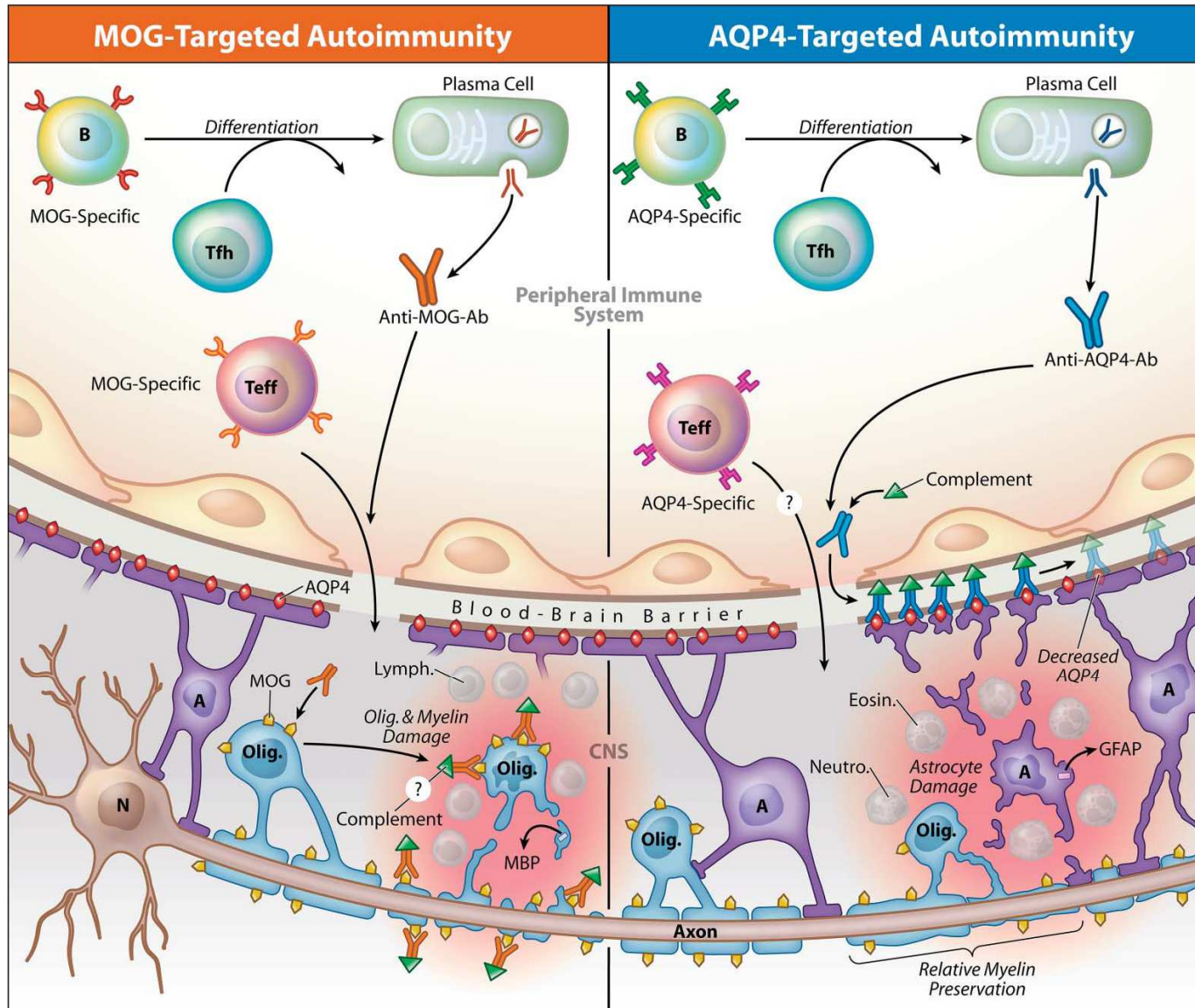
- Myelin loss (independent of C')
- no inflammation
- no neuronal or astrocyte death
- recovery within 2 weeks

Explanation for better outcome of anti-MOG patients ?

Does MOG Ig-positive AQP4-seronegative opticospinal inflammatory disease justify a diagnosis of NMO spectrum disorder?

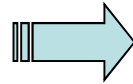
Scott S. Zamvil, MD,
PhD
Anthony J. Slavin, PhD

Neurol Neuroimmunol Neuroinflamm 2015;2:e62;



conclusion

Anti-(native) MOG



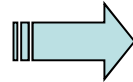
Pediatric ADEM and MS (# 30-40%)

Transient

→ ADEM

Persistent

→ HR of MS



Anti-AQP4 negative NMO (# 20%)

→ Better prognosis

But is it NMO, OSMS or OIND ??

→ which treatment ??