ADEM and MOGAD RNDS Breakout Session

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Disclosures

- Dr. Gombolay
  - Part-time salary support as consultant to the CDC for acute flaccid myelitis case review for disease surveillance
- Dr. Levy
- Dr. Schreiner
  - Participates in research funded by Roche
  - Part-time salary support as consultant to the CDC for acute flaccid myelitis case review for disease surveillance
  - Off-label use of treatments will be discussed as majority of medications are not FDA approved

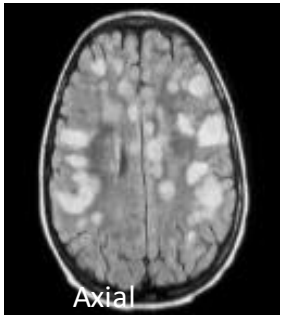
Outline

- ADEM
  - Definition
  - Clinical Presentation
  - Treatment
- MOGAD
  - Definition
  - Clinical Presentation
  - Relapses
  - Treatment
- Discussion and questions may be interspersed throughout

ADEM (Acute Disseminated Encephalomyelitis)

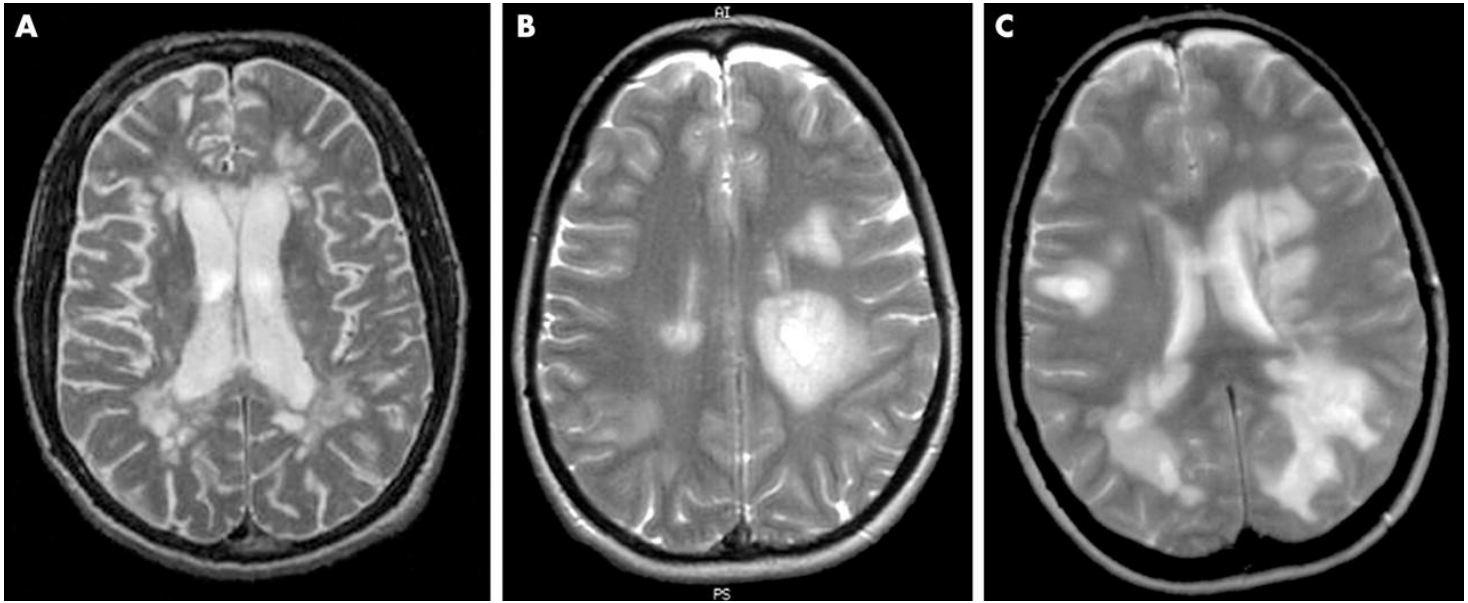
- A first multifocal, clinical CNS event of presumed inflammatory demyelinating cause
- Encephalopathy that cannot be explained by fever
- Abnormal brain MRI:
  - Diffuse, poorly demarcated, large (>1–2 cm) lesions predominantly involving the cerebral white matter
  - T1-hypointense lesions in the white matter in rare cases
  - Deep grey matter abnormalities (eg, thalamus or basal ganglia) can be present
- No new clinical or MRI findings after 3 months of symptom onset

ADEM



- Clinically
  - Most children present before age 10
  - Acute or subacute onset
    - Viral infection or vaccination within one month
  - Multifocal neurologic deficits with encephalopathy
  - Additional clinical features: headache, fever, meningismus, seizures
  - Monophasic, with duration up to 3 months
- Multiphasic: 2 episodes consistent with ADEM separated by 3 months

MRI - ADEM



https://adc.bmj.com/content/90/6/6

Differential diagnosis for ADEM

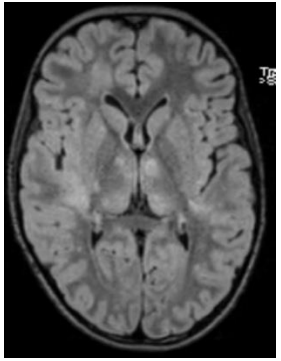
- ADEM
- MS
- NMOSD

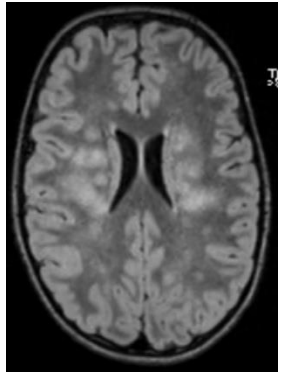
} Can include MOG

- CNS vasculitis (small vessel, angiography-negative)
- CNS Hemophagocytic lymphohistiocytosis (HLH) – primary/secondary
- Neuro-Behcet's
- CNS Lupus
- Sarcoid
- Chronic enteroviral meningoencephalitis
- Mitochondrial disorders (i.e. POLG, MELAS)
- CTLA-4 haploinsufficiency
- Aicardi-Goutieres syndrome

Management of acute exacerbations

- IV solumedrol 30 mg/kg (max 1G) IV x 3-7 days
- Consider IVIG 2G/kg divided over 2-5 days
- Severe episode (brainstem involvement) and not responding then consider plasmapheresis/plasma exchange (PLEX)
  - 5-7 cycles, every other day

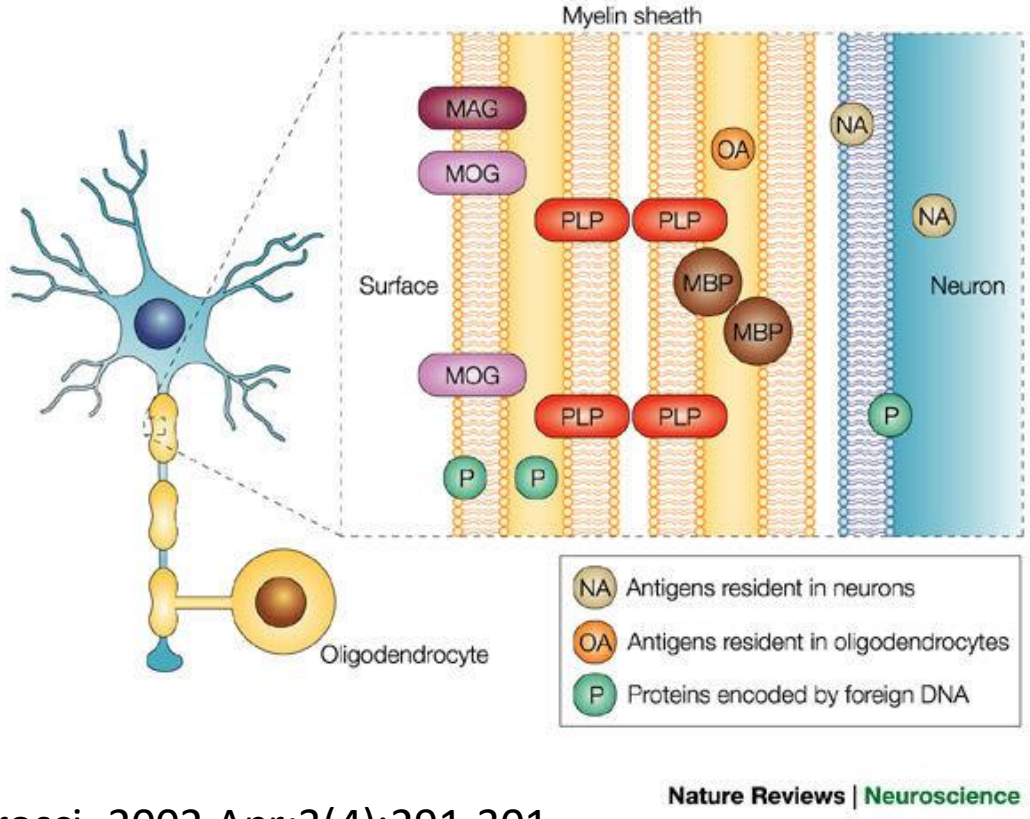




Myelin-Oligodendrocyte Glycoprotein Associated Disease (MOGAD)

Anti-MOG antibody associated disorder (MOGAD)

What is MOG?



Hemmer B et al., Nat Rev Neurosci. 2002 Apr;3(4):291-301.

International MOGAD Consensus Criteria

Diagnosis of MOGAD (requires fulfilment of A, B, and C)			
(A) Core clinical demyelinating event	Optic neuritis* Myelitis† ADEM‡ Cerebral monofocal or polyfocal deficits§ Brainstem or cerebellar deficits¶ Cerebral cortical encephalitis often with seizures‖		
(B) Positive MOG-IgG test	Cell-based assay: serum‡‡	Clear positive**	No additional supporting features required
		Low positive††	• AQP4-IgG seronegative AND • ≥1 supporting clinical or MRI feature
		Positive without reported titre	
		Negative but CSF positive§§	
Supporting clinical or MRI features	Optic neuritis	• Bilateral simultaneous clinical involvement • Longitudinal optic nerve involvement (> 50% length of the optic nerve) • Perineural optic sheath enhancement • Optic disc oedema	
	Myelitis	• Longitudinally extensive myelitis • Central cord lesion or H-sign • Conus lesion	
	Brain, brainstem, or cerebral syndrome	• Multiple ill-defined T2 hyperintense lesions in supratentorial and often infratentorial white matter • Deep grey matter involvement • Ill-defined T2-hyperintensity involving pons, middle cerebellar peduncle, or medulla • Cortical lesion with or without lesional and overlying meningeal enhancement	
(C) Exclusion of better diagnoses including multiple sclerosis¶¶			

Mayo clinic assay:

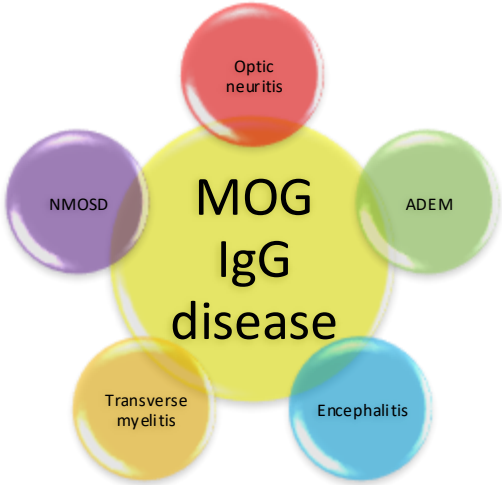
Clear positive:
≥1:100

Low positive:
1:20-1:40

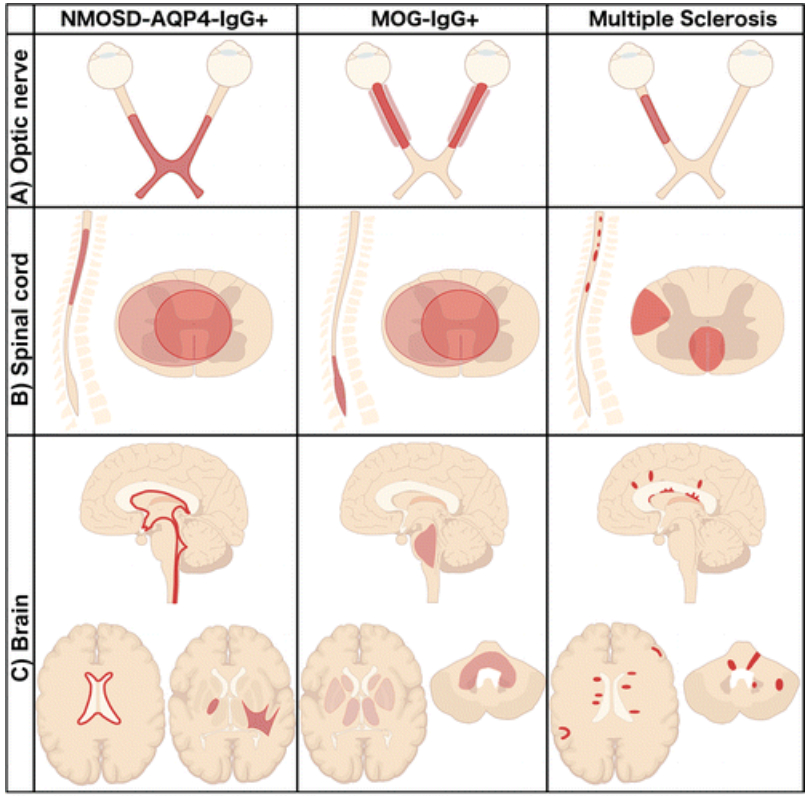
Banwell, Lancet Neurol. 2023:
PMID: 36706773

MOGAD phenotypes

- Demyelinating disease
  - Optic neuritis
  - Neuromyelitis optica spectrum disorder
  - Acute encephalomyelitis
  - “Multiple sclerosis”
  - Transverse myelitis
    - Gray matter predominant mimics AFM
- Meningoencephalitis



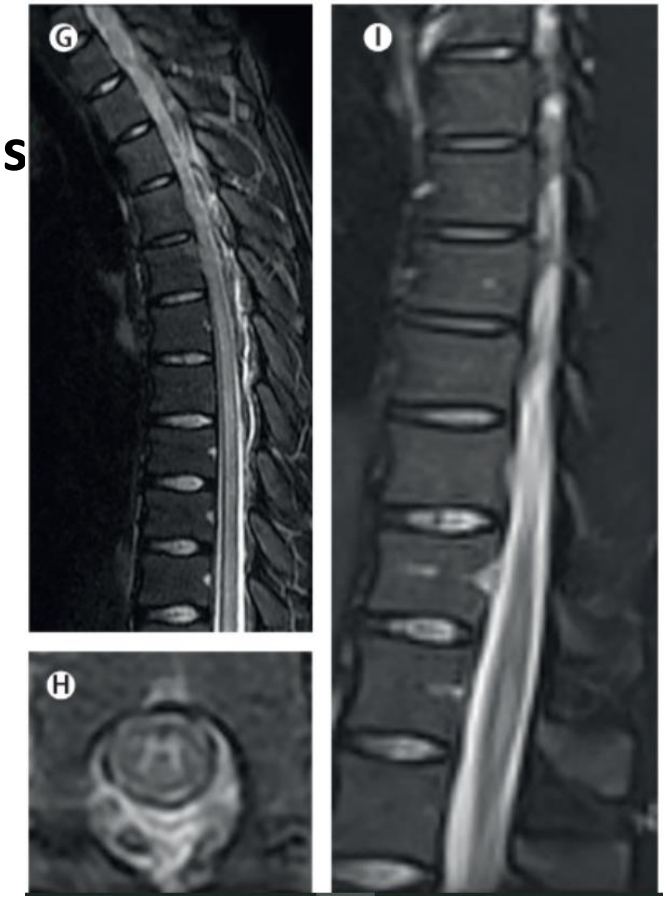
Differences in imaging in AQP4, MOG, and MS



Dutra, Radiographics, 2018, PMID: 29320331

MOGAD Demyelinating Presentations

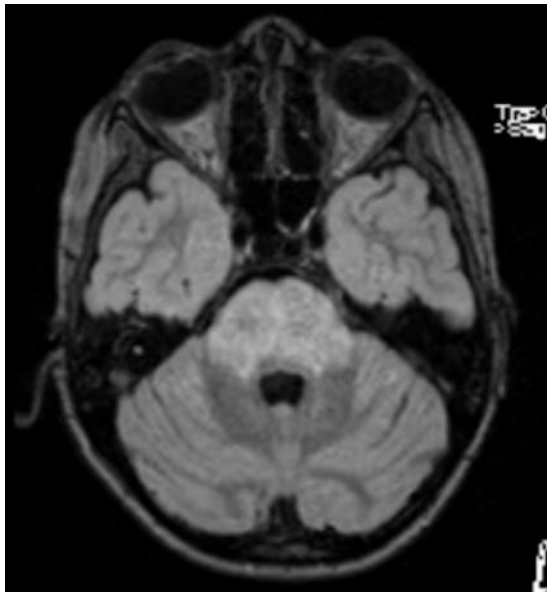
- Long segment transverse myelitis
  - Presentation
    - Weakness, numbness, may have urinary retention and constipation
  - MRI
    - >3 vertebral segments long
    - More thoracolumbar or conus



Banwell et al. 2022. Lancet Neurology.

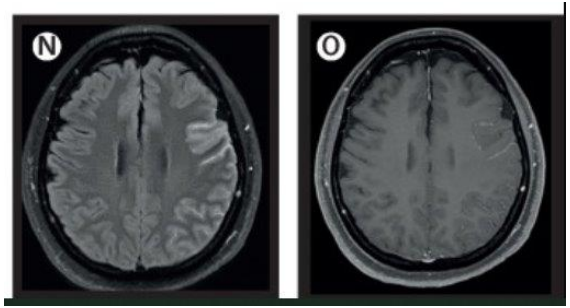
MOGAD Demyelinating Presentations

- Brainstem
    - Cranial nerve deficits, ataxia



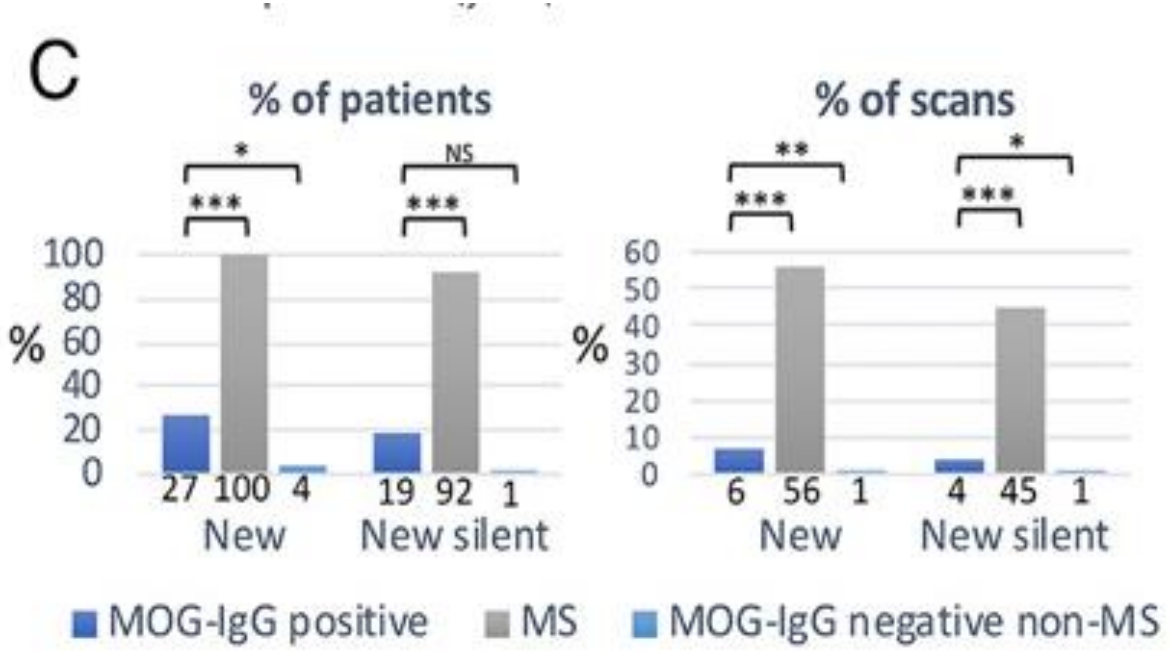
MOGAD Presentation - Encephalitis

- Cortical encephalitis
    - Presentation
        - Fever
        - Headache
        - Encephalopathy
        - Seizures
        - May become fulminant and progress to severe edema / herniation



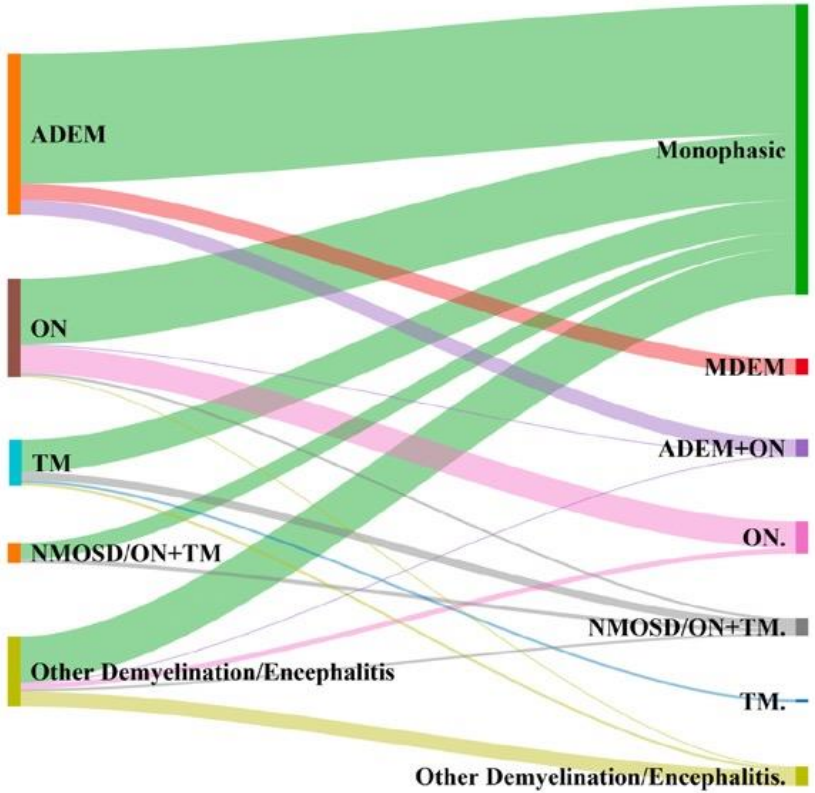
Silent new lesions in MOGAD

- Silent new lesions were detected in 14% of MOGAD, usually in the first months post-onset, with a 20% PPV for clinically relapse
- Detection of asymptomatic lesions alone need not prompt initiation of chronic immunotherapy



Fadda G et al; Canadian Pediatric Demyelinating Disease Network. Ann Neurol. 2021 Feb;89(2):408-413.

First and second relapse phenotypes in pediatric MOGAD



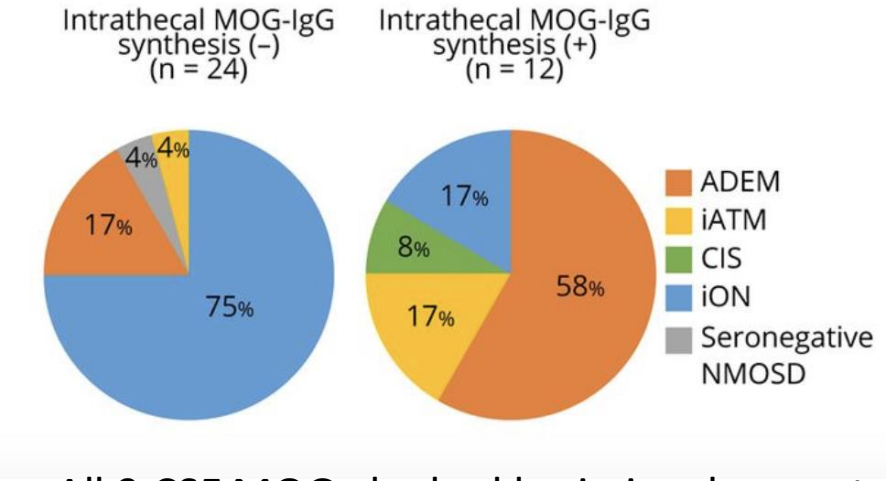
Santoro, ACTN, 2023, PMID 37000895

Serum vs CSF antibodies?

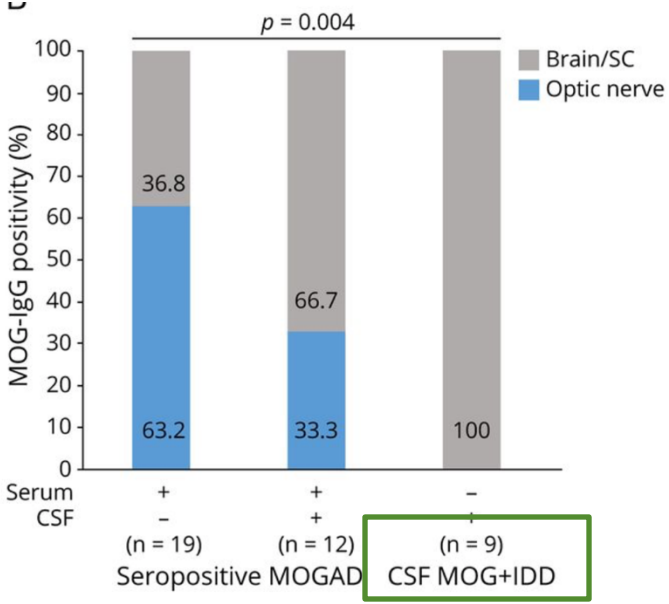
MOG and AQP4 antibodies are more sensitive in the serum than in CSF

In contrast to *most* antibody-positive autoimmune encephalitis (few exceptions) where CSF > serum

Do CSF MOG titers matter?



All 9 CSF MOG ab+ had brain involvement
CSF MOG Ab+ in one MS patient
CSF MOG Ab may predict disability and increased relapse, but small number (9)



Kwon et al. Neurol Neuroimmunol Neuroinflamm. 2021 Oct 28;9(1):e1095. PMID: 34711644; PMCID: PMC8554713.

Recovery from attacks in MOGAD

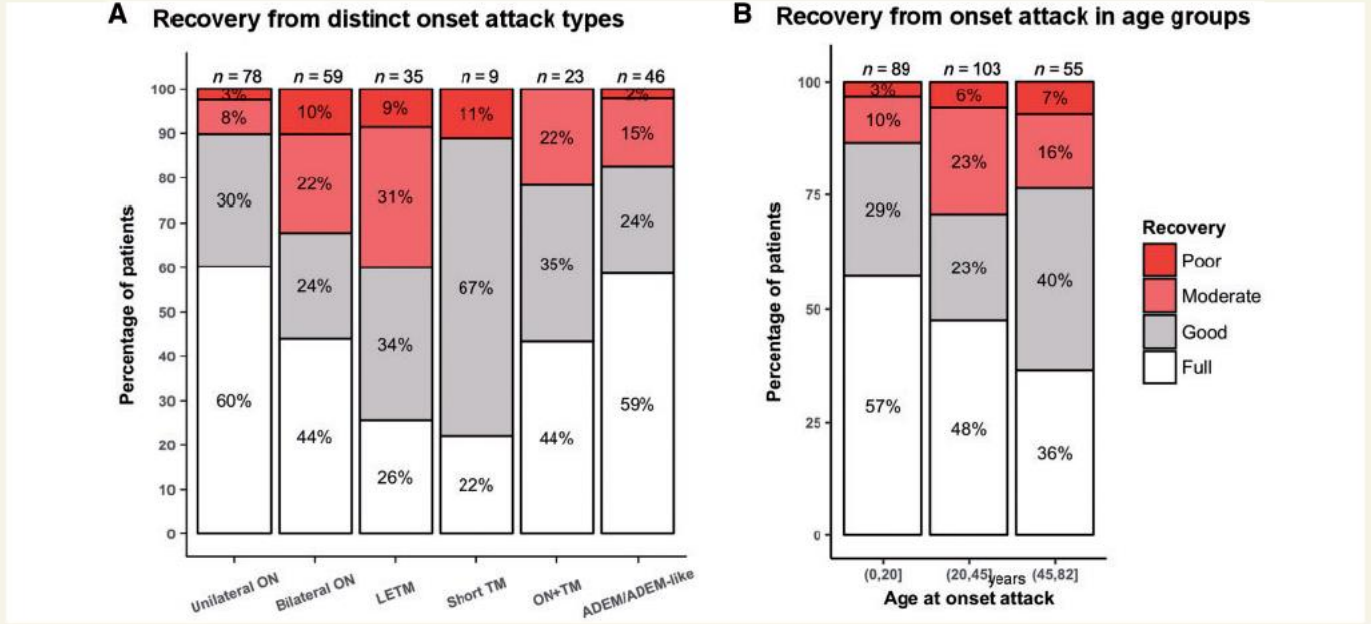


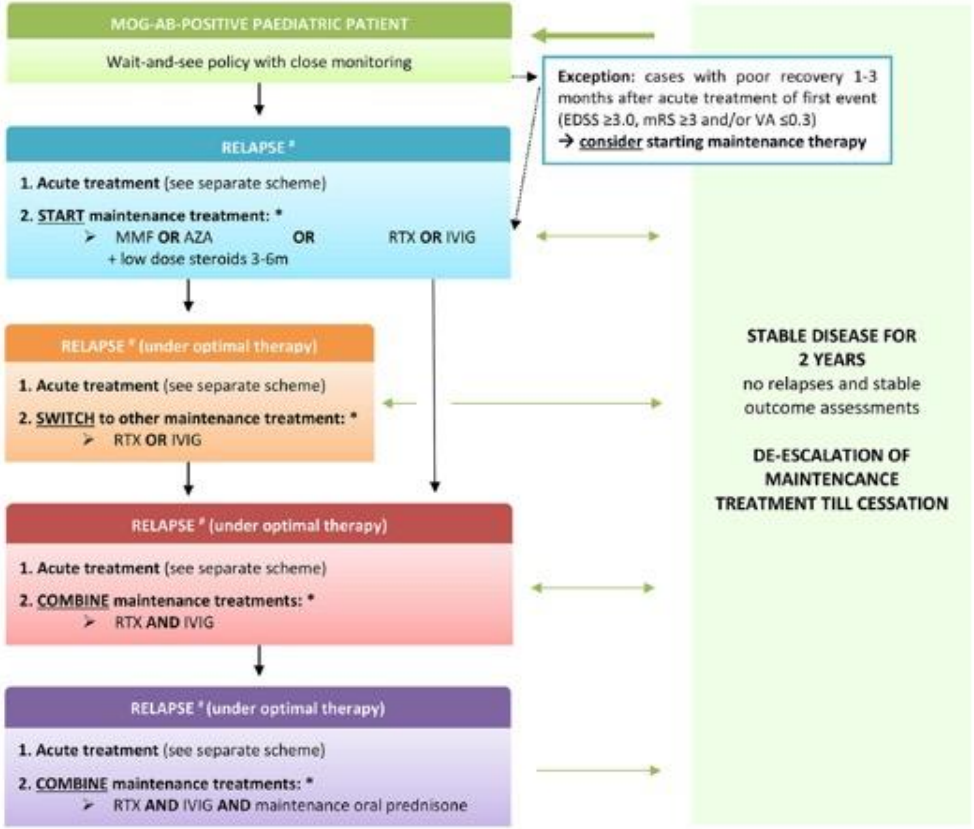
Figure 2 Recovery from the onset attack in the UK cohort. (**A**) Depending on the onset attack phenotype; (**B**) in different age groups. The total number of patients in each group is shown above the bar. ON = optic neuritis; TM = transverse myelitis.

Jurynczyk, Brain 2017, PMID: 29136091

Treatment of MOGAD

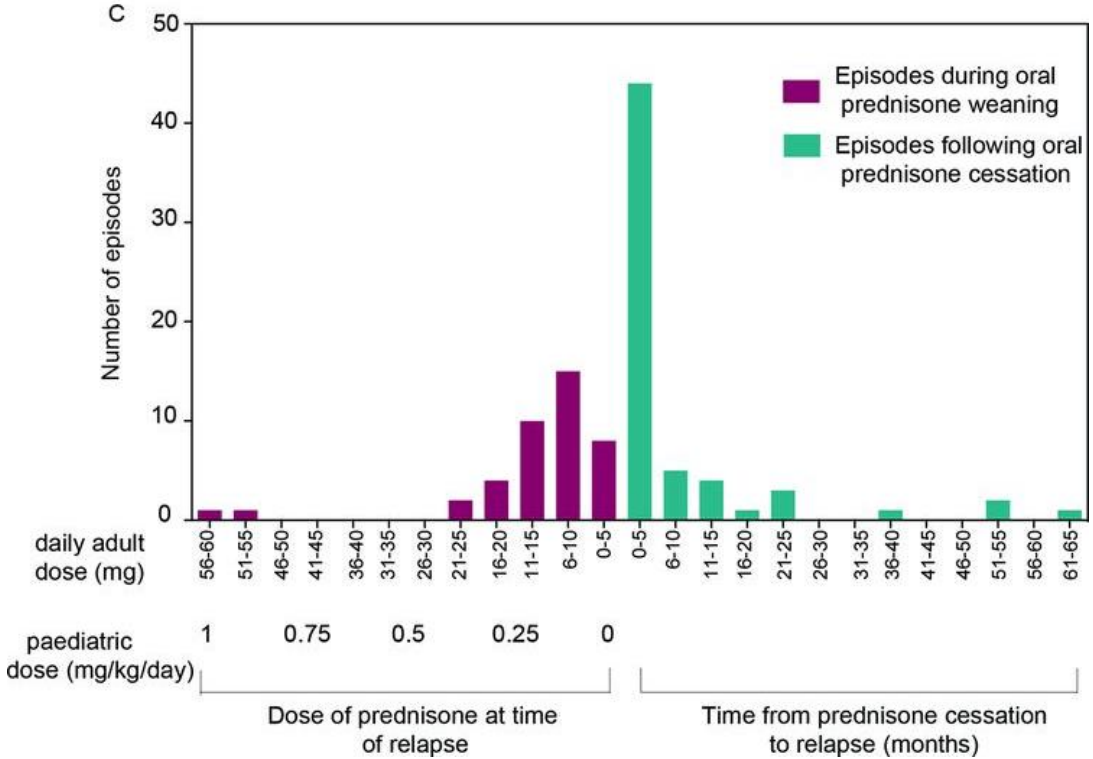
- Important to check MOG antibody on everyone with demyelinating disease or persistent leptomeningeal enhancement
- Traditional MS therapies can cause relapses
- One time episode: IV steroids, IVIG, steroid taper (length is debated)
  - Relapse risk is highest during taper or 6 months after stopping steroids
- Recurrent episodes in 30-50%:
  - IVIG
  - Mycophenolate mofetil
  - Rituximab (may be less efficacious in MOGAD vs AQP4 ab NMOSD)
  - Azathioprine
  - Cytoxan

European treatment consensus



Bruijstens, Eur J Ped Neurol, 2020, PMID: 33176999

Relapses related to steroid wean



Ramanathan et al., J Neurol Neurosurg Psychiatry. 2017 Nov 15.

Conclusion

- We are still learning the full spectrum of MOGAD disease
- MOGAD can mimic most neuroimmune and neuroinfectious disease
- Treatment is based upon the clinical scenario and symptoms not just the positive test

Questions to spark discussion

- How to interpret symptom fluctuation vs. New relapse?
- How to connect with others with ADEM/MOGAD?
  - SRNA, MOG project, Sumaira Foundation
- When is the right time to stop treatment for relapsing MOGAD?
- Does the amount (titer) of MOG antibody matter?
- Symptoms that affect quality of life: cognitive changes and fatigue.