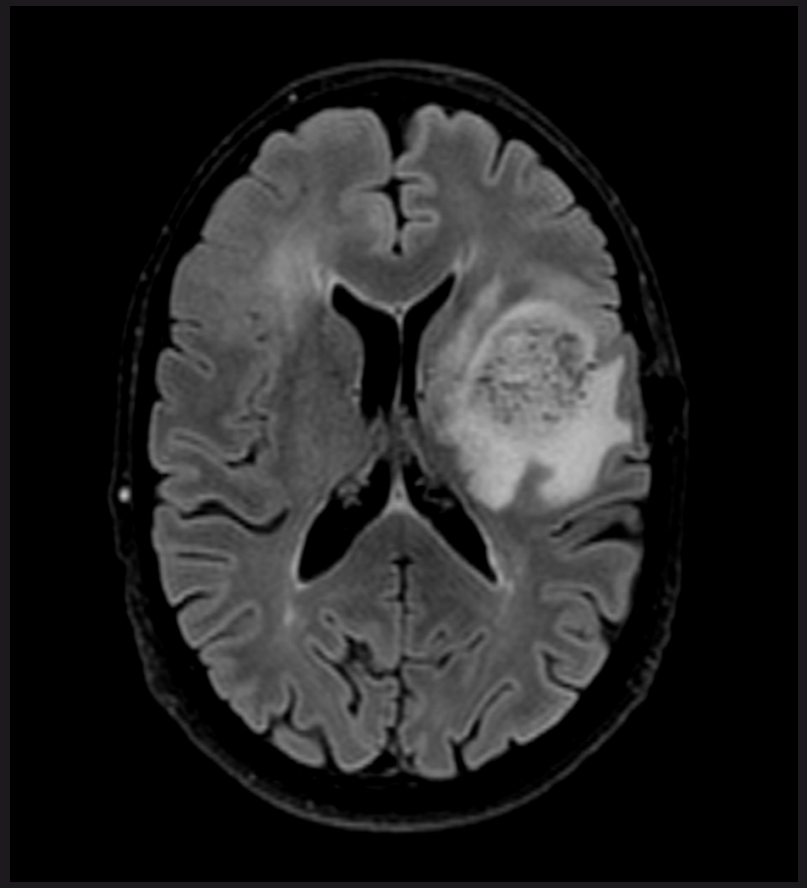

# *Myelin Oligodendrocyte Glycoprotein Antibody Disease (MOG-AD*

# *ICD-10-CM Proposal*

*ICD-10 Coordination and Maintenance Committee Meeting*

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# *What is MOG-AD?*

A large body of immunologic and clinical evidence has made clear that MOG-AD is a distinct entity.

- Myelin oligodendrocyte glycoprotein (MOG) antibody disease (MOG-AD) is an **inflammatory demyelinating condition** of the brain and spine characterized by a monophasic or relapsing course which does not meet the typical criteria for multiple sclerosis (MS) or other known neuroinflammatory conditions.
- It is associated with the presence of **MOG antibodies** which are **implicated in neuronal and axonal destruction**
- Patients may develop **optic neuritis** (54–61% of patients), **myelitis**, **acute disseminated encephalomyelitis (ADEM)** or a **polyphasic attack of multiple brain structures** such as neuromyelitis optica spectrum disorder (NMOSD)**.**
- A **relapsing course** has been reported in 44–83%

Ciotti JR, Eby NS, Wu GF, Naismith RT, Chahin S, Cross AH. Clinical and laboratory features distinguishing MOG antibody disease from multiple sclerosis and AQP4 antibody-positive neuromyelitis optica. Mult Scler Relat Disord. 2020;45:102399.
Weber MS, Derfuss T, Metz I, Brück W. Defining distinct features of anti-MOG antibody associated central nervous system demyelination. Ther Adv Neurol Disord. 2018;11:1756286418762083; Chen JJ, Bhatti MT. Clinical phenotype, radiological features, and treatment of myelin oligodendrocyte glycoprotein-immunoglobulin G (MOG-IgG) optic neuritis. Curr Opin Neurol. 2020;33(1):47-54.
Lennon VA, Kryzer TJ, Pittock SJ, Verkman AS, Hinson SR. IgG marker of optic-spinal multiple sclerosis binds to the aquaporin-4 water channel. J Exp Med. 2005;202(4):473-477.

# *MOG-AD v. MS & NMOSD*

Differences in pathology of MOG-AD, MS, and AQP-4-positive NMOSD result in distinct clinical symptoms and prognoses.

- MOG antibodies have a unique target, and the disease has **unique immunologic mechanisms** that distinguish it from other conditions, such as NMOSD and MS.

- While MOG-AD was initially believed to represent a subset of patients with NMOSD it is now clear that this is not the case.

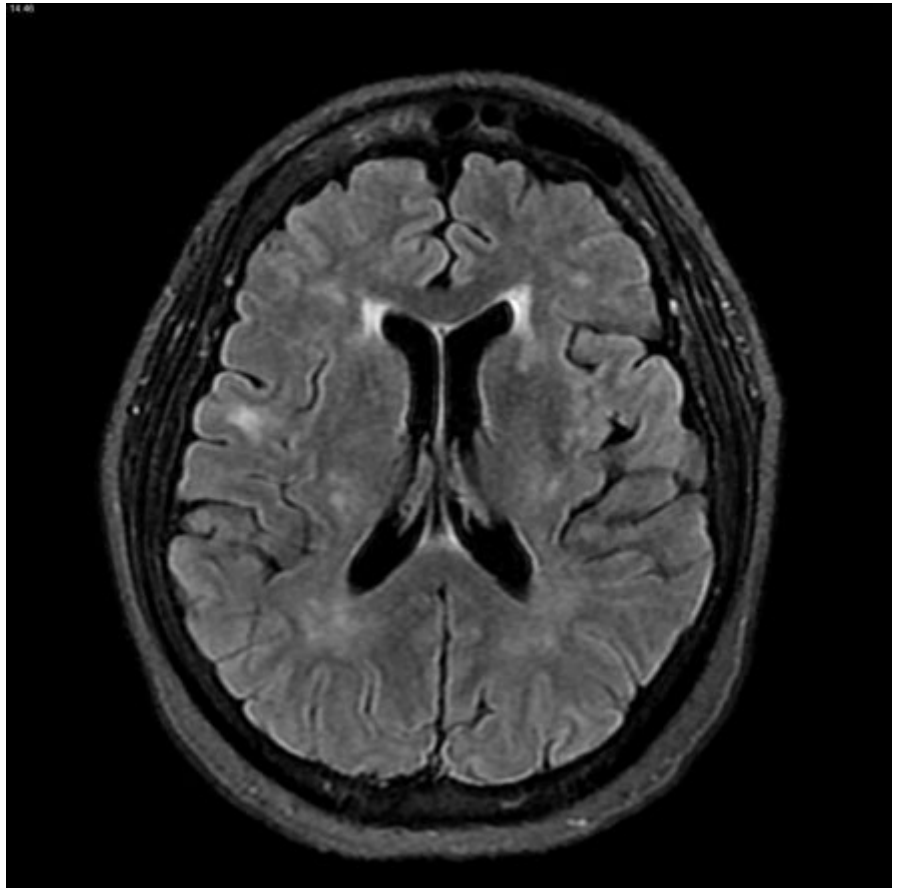
- MOG is located on the surface of myelin sheaths and oligodendrocyte processes, whereas AQP-4 water channels, the target of seropositive NMOSD, are located on astrocytic foot processes.

- It has also been shown that about **one-third of demyelinating lesions in patients with MOG-AD have MOG-dominant myelin loss, but relatively preserved oligodendrocytes**. This differs from AQP-4-positive NMOSD lesions, which exhibit myelin-associated glycoprotein-dominant oligodendrogliopathy.



·Nytrova P, Potlukova E, Kemlink D, et al. Complement activation in patients with neuromyelitis optica. J Neuroimmunol. 2014;274(1-2):185-191; Mader S, Kümpfel T, Meinl E. Novel insights into pathophysiology and therapeutic possibilities reveal further differences between AQP4-IgG- and MOG-IgG-associated diseases. Curr Opin Neurol. 2020;33(3):362-371.
Watanabe M, Schaedelin S, Maceski D, et al. Neutrophil granulocyte markers in cerebrospinal fluid differentiate NMOSD and anti-MOG antibody associated disease from MS in acute disease phase. Presented at ECTRIMS-ACTRIMS. 2020. LB01.03.

# *Importance*



- Most **experts now consider MOG-AD a disease entity in its own right, immunopathogenetically distinct** from both classic multiple sclerosis (MS) and aquaporin-4 IgG-positive NMOSD

- Owing to a substantial overlap in clinical and radiological presentation, **MOG-AD was often unwittingly misdiagnosed as MS in the past.**

- In the past decade, clinical and radiographic phenotyping of this condition have allowed for the **development of distinct diagnostic criteria and therapeutic algorithms**

- **Children are disproportionally affected by MOG-AD and the impact of poor diagnosis or therapeutic intervention can mean a life of neurologic disability**

# *Historical Concerns & Importance*

- In 2014, a "polio-like" disease entity began occurring in children across the country. Although this was later coded as **acute flaccid myelitis**, delays in creating a code *severely* impacted diagnosis, monitoring and research in the field
  - Now coded as: **G04.82**, only became effective in October 2021, **nearly seven years AFTER the first cases were reported**

- Countless children suffered due to poor coding, highlighting the importance of having a clear and structured mechanism for the diagnosis of a similarly disabling condition in MOG-AD

HEALTH

**Acute flaccid myelitis, the polio-like disease that causes paralysis in kids, to peak this year, CDC says**

Adrianna Rodriguez
USA TODAY

Published 1:00 p.m. ET Aug. 4, 2020 | **Updated 7:35 p.m. ET Aug. 4, 2020**

The New York Times

*Acute Flaccid Myelitis Cases in Children Are Investigated in at Least 5 States*

CNN health Life, But Better Fitness Food Sleep Mindfulness Relationships • LIVE TV

**CDC escalates response to polio-like illness AFM**

By Elizabeth Cohen, CNN

Updated 1931 GMT (0331 HKT) November 20, 2018

# *Diagnosis*

A lack of definitive diagnostic criteria has also delayed coding although the current standards have been in place for over two years

*1*

Monophasic or relapsing acute ON, myelitis, brainstem encephalitis, or encephalitis, or any combination of these syndromes

*2*

MRI or electrophysiological (visual evoked potentials in patients with isolated ON) findings compatible with CNS demyelination

*3*

Seropositivity for MOG-IgG as detected by means of a cell-based assay employing full-length human MOG as target antigen

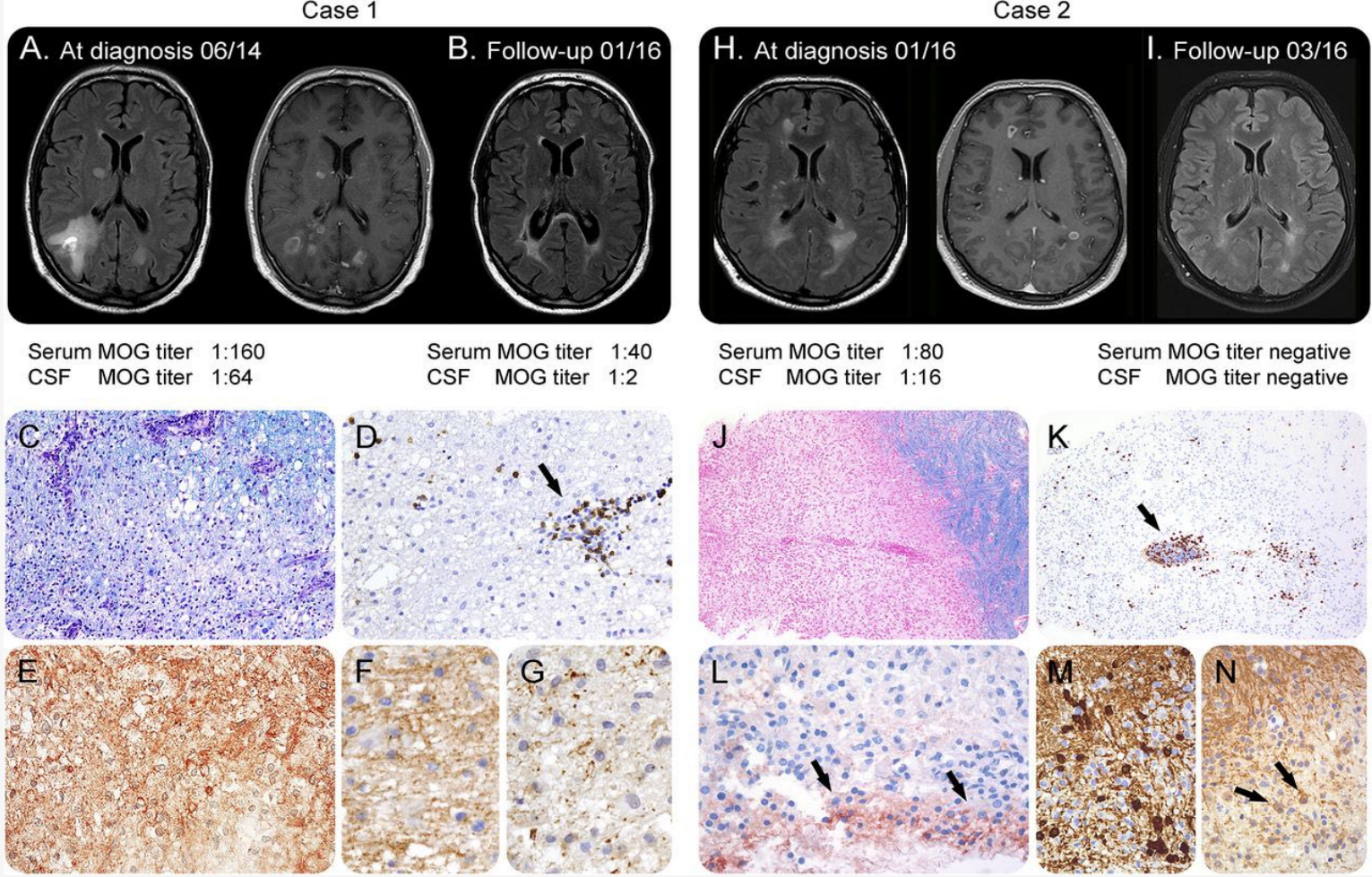
Expert Consensus from 2018

Jarius et al., *J Neuroinflammation,* 2018;15:134



Optic Neuritis (ON), Central Nervous System (CNS), myelin oligodendrocyte glycoprotein (MOG)

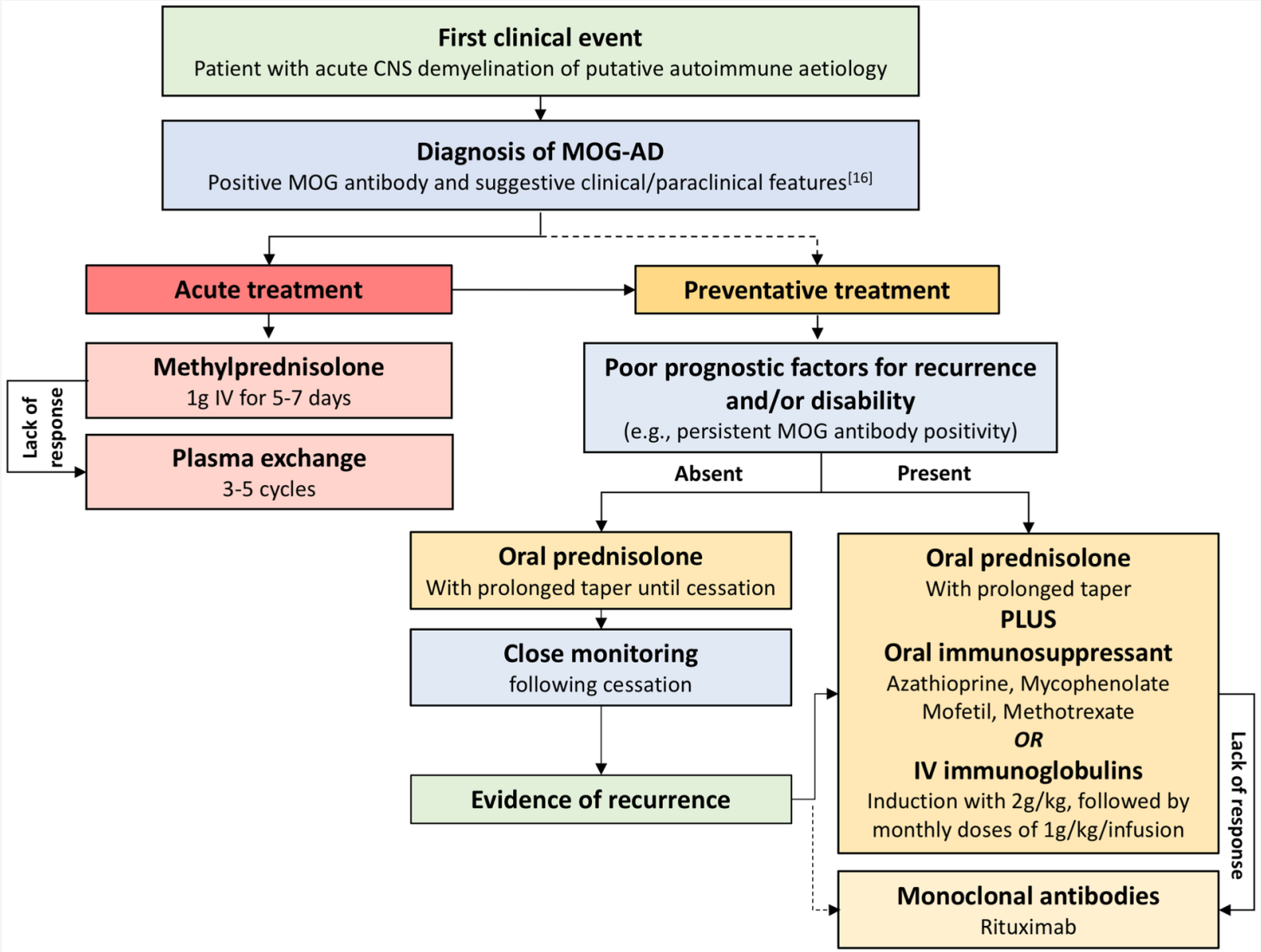
# *Differences Radiographically & Histologically*




*"These pathological features are clearly different from those of multiple sclerosis and AQP4 antibody-positive NMOSD, suggesting an independent autoimmune demyelinating disease entity."*
- *Takai et al.,* Brain, 2020; 143(5):1431-1446

# *Differences in Therapeutics*

With the collection of real-world data on MOG-AD, specific treatment algorithms have been developed which are distinct from the treatment of multiple sclerosis and/or neuromyelitis optica



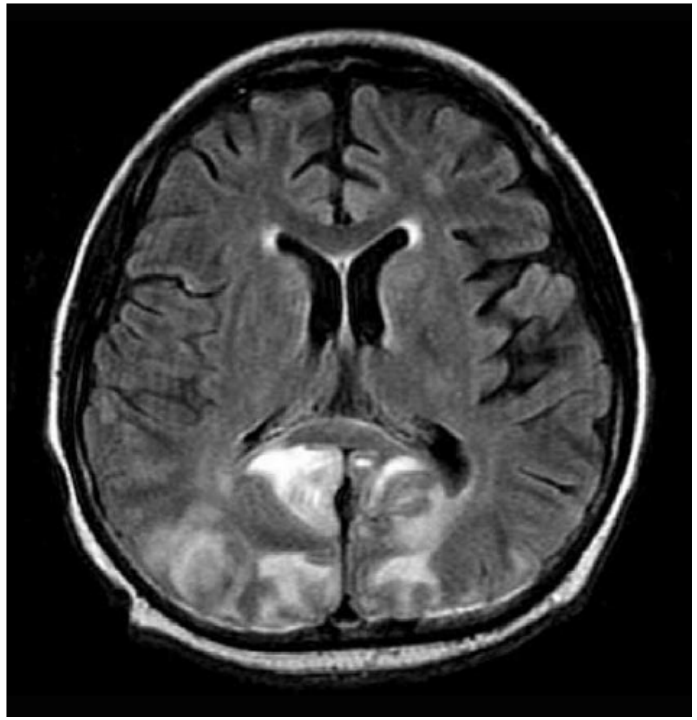


- Hacohen Y et al (2018) Disease course and treatment responses in children with relapsing myelin oligodendrocyte glycoprotein antibody–associated disease. JAMA Neurol 75(4):478–487
- Rynford-Thomas (2018) Neurological Update: MOG Antibody Disease. *J Neurol*; 266, 1280-1286
- Ramanathan S et al (2018) Clinical course, therapeutic responses and outcomes in relapsing MOG antibody-associated demyelination. J Neurol Neurosurg Psychiatry 89:127–137
- Jarius S et al (2016) MOG-IgG in NMO and related disorders: a multicenter study of 50 patients. Part 2: epidemiology, clinical presentation, radiological and laboratory features, treatment responses, and long-term outcome. J Neuroinflamm 13:280

# *Impact of an Independent ICD-10-CM Code*

Creating a coding structure for this condition will directly improve patient care by reducing misdiagnosis, improving ability to obtain standard of care therapeutics and improving research investigations into MOG-AD

- Improve Patient Care and Outcomes by Reducing Misdiagnosis
- Improve Ability to Obtain Appropriate Therapies
- Improve Disease Surveillance of MOG-AD
- Advance Therapeutic Investigations in MOG-AD
- Advance Research Efforts into MOG-AD
- Reduce Long-Term Neurologic Disability Over the Lifespan



# *Summary of Rationale*

- MOG-AD is now internationally recognized as a distinct disease entity, separate from multiple sclerosis, optic neurtitis, transverse myelitis, and neuromyelitis optica
- MOG-AD is treated differently and is responsive to non-traditional immuontherapeutics
- Inappropriate coding has reduced physician and researcher ability to track these patients longitudinally, stalling the development of therapeutics for this condition and preventing epidemiologic monitoring
- Development of a dedicated ICD-10-CM code will **improve diagnosis**, **improve access to appropriate therapeutics**, **improve epidemiologic disease monitoring, and spark research and drug development in this condition**
- Creation of this new category is supported by the American Academy of Neurology (AAN) and the MOG Project