# APERTURE:
## New insights on ADEM

**Cynthia Wang, MD**

Assistant Professor

UT Southwestern/Children's Health Dallas

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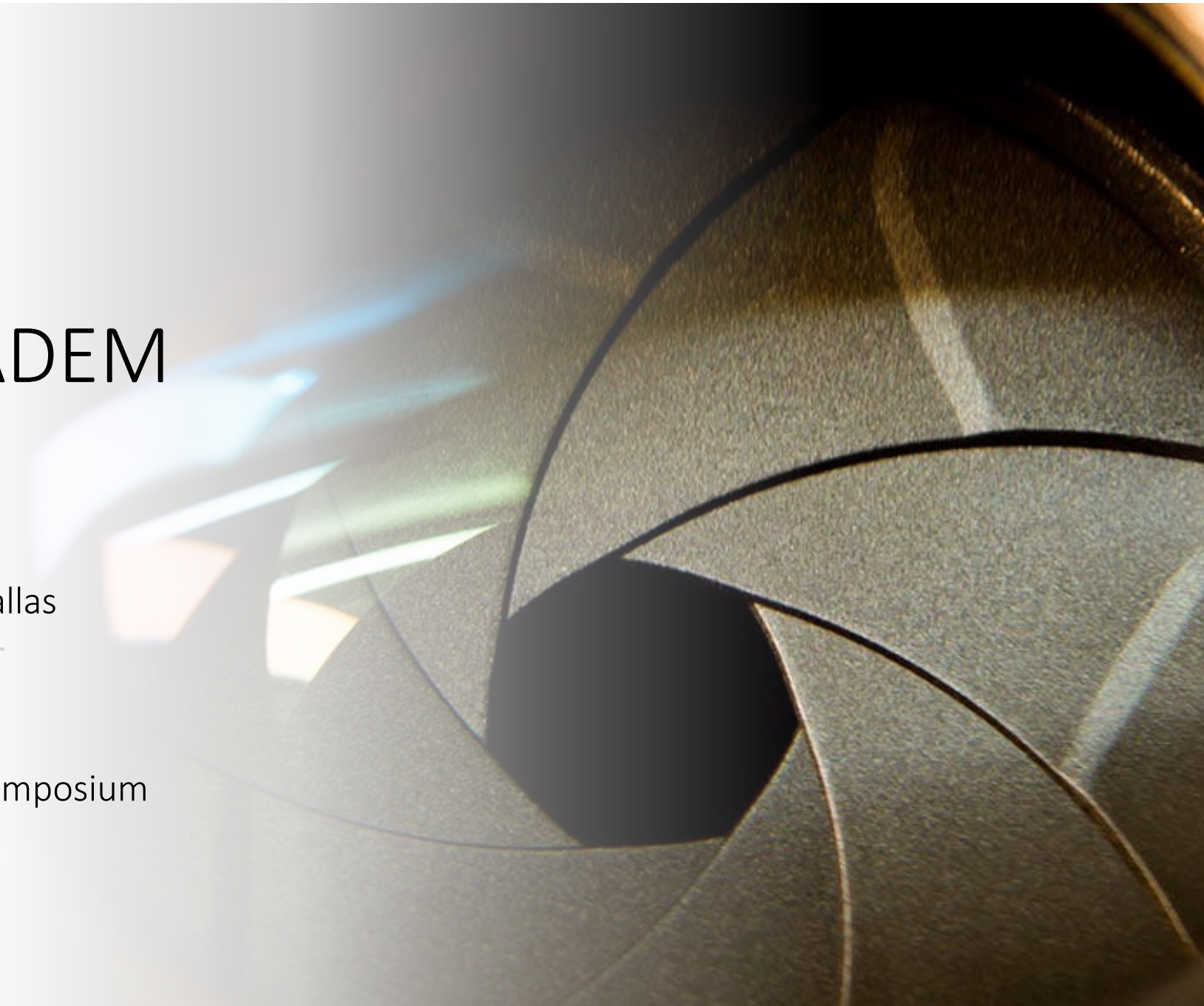
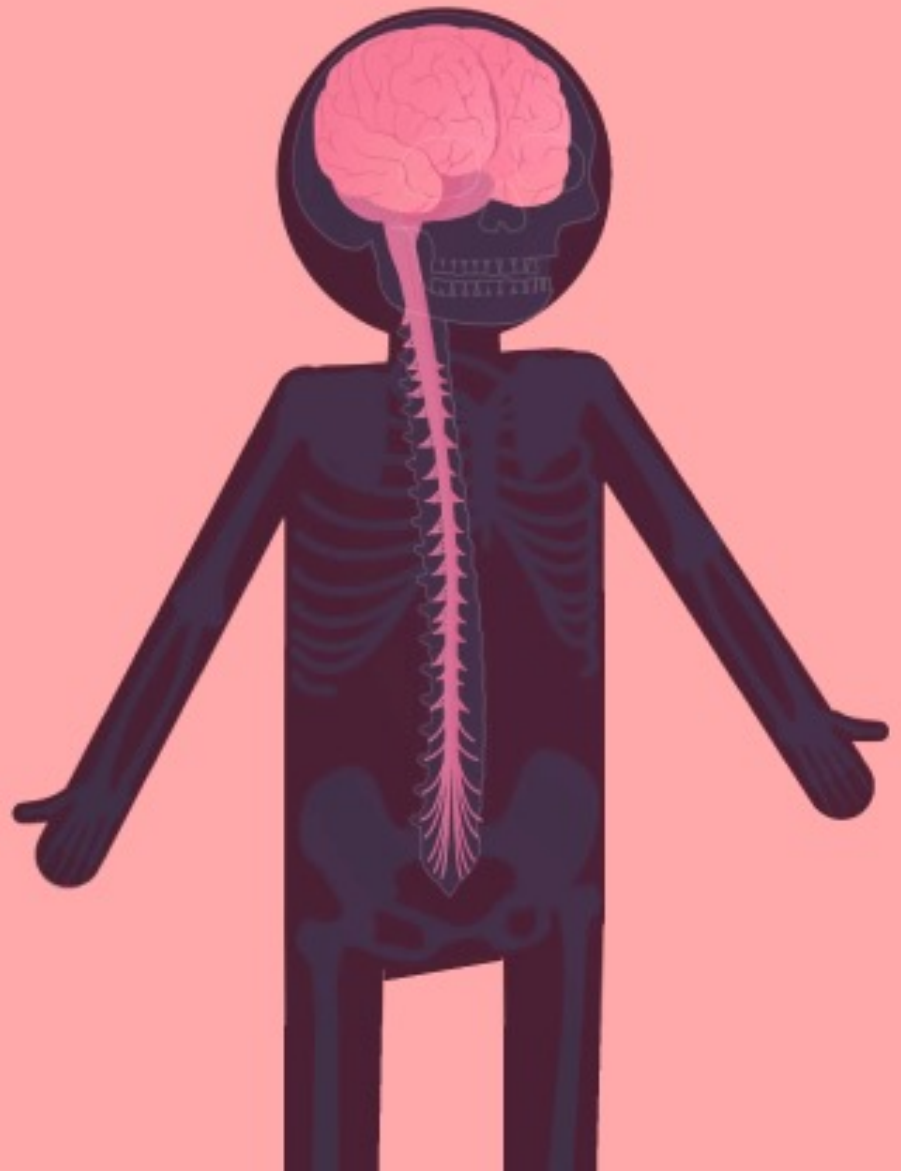
2022 Rare Neuroimmune Disorders Symposium





# What is ADEM?

- Acute disseminated encephalomyelitis
- Sudden and widespread inflammation of the brain and spinal cord

Encephalopathy

Multiple neurological symptoms and corresponding MRI lesions

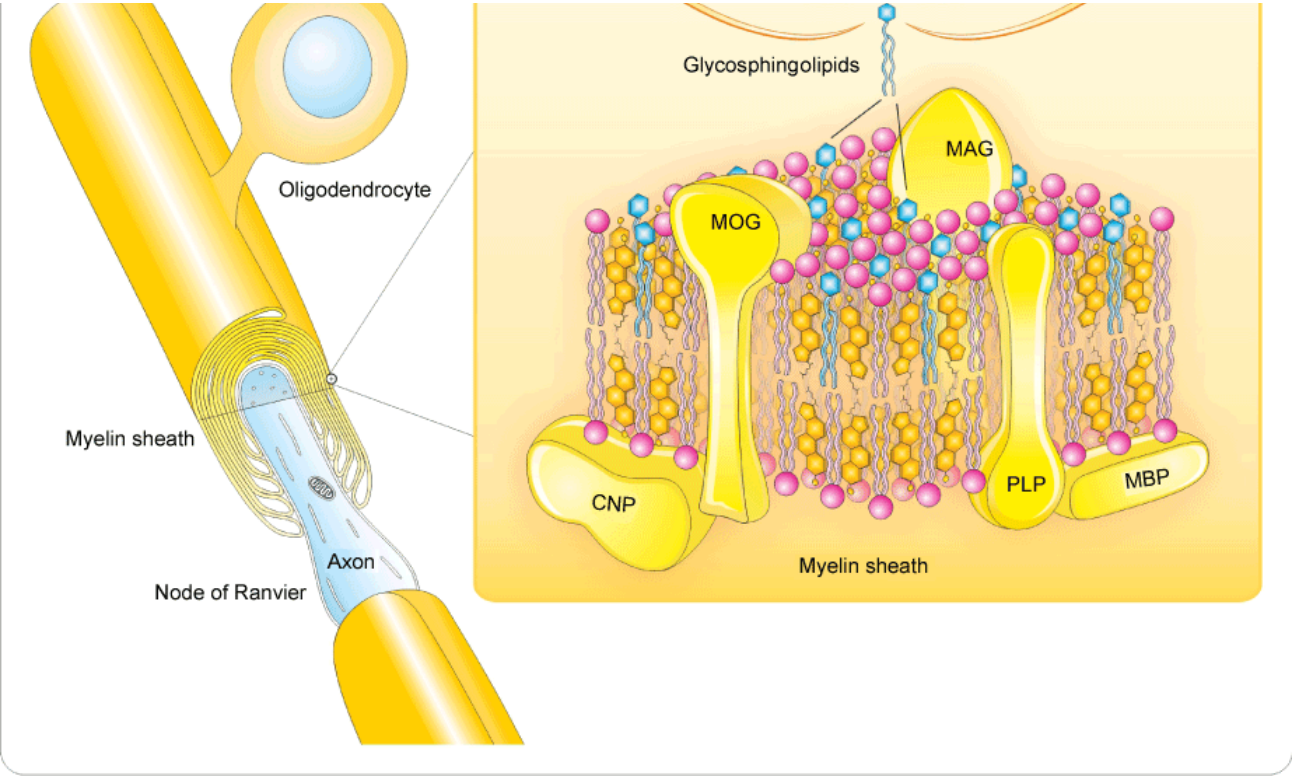
Affects children more than adults

Usually occurs following an infection

# Management of ADEM

- No large scale, prospective, randomized controlled clinical trials
  - High dose intravenous steroids
  - Therapeutic plasma exchange (PLEX)
  - Intravenous immunoglobulin (IVIG)
  - Oral corticosteroid taper
- Supportive care
  - 25% require ICU level care
- Prognosis
  - Most improve significantly within a 1-3 weeks
  - PT, OT, ST can help with recovery
  - May have lasting cognitive, mood, sensory and motor symptoms


- “ADEM doesn’t relapse”
  - MOGAD can
- “ADEM is a benign illness”
  - Severe brain swelling can be fatal
- “ADEM is primarily a white matter disease”
  - Affects both white and gray matter structures in brain and spinal cord




# Myelin Oligodendrocyte Glycoprotein

- Myelin protein expressed on the outermost surface of myelin in the central nervous system
- Produced by oligodendrocytes in the later stages of myelination
- Testing for MOG antibodies has become more accurate and widely available

aperture

Assessment of pediatric and adult encephalomyelitis related outcomes: understand, reveal, educate

- Hypothesis that what we call ADEM is actually composed of different disorders
- Goal of evaluating neuroimaging and clinical features and their relationship to clinical outcomes

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Assessment of pediatric and adult encephalomyelitis related outcomes: understand, reveal, educate

- Inclusion criteria
  - Age 0-64 years at time of ADEM onset
  - Availability or ability to access hospital records
  - Individuals/parents with proficiency in English (for neuropsychological and patient reported outcome surveys)
- Exclusion criteria
  - Initial diagnosis of Multiple Sclerosis, Neuromyelitis Optica Spectrum Disorder

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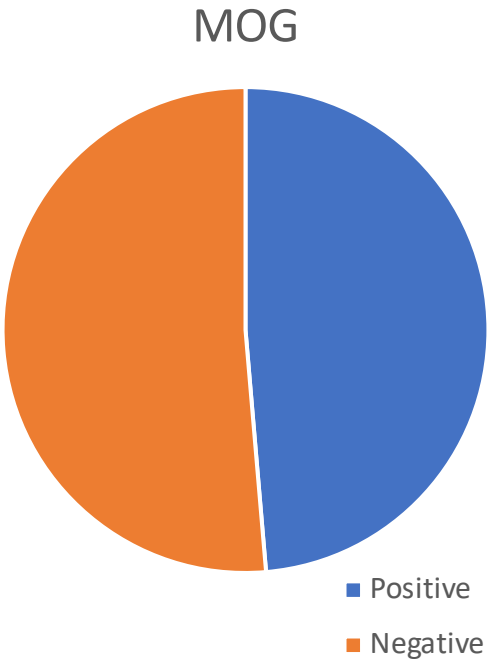
Assessment of pediatric and adult encephalomyelitis related outcomes: understand, reveal, educate

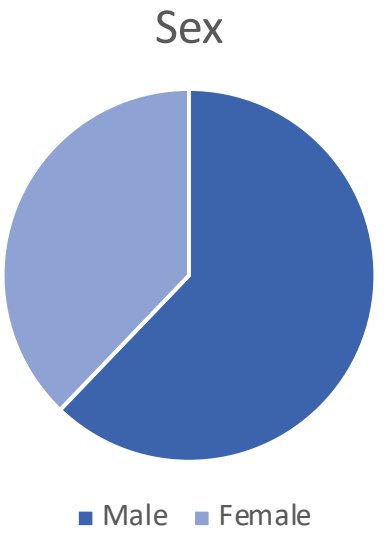
- Recruited from summer 2017 - 2020
- 41 Children
- 11 Adults

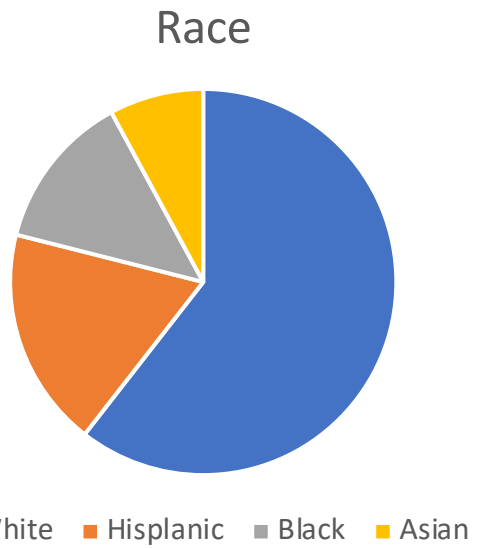
- I will present a subset of this data, children who were seen at Children's Dallas and tested for MOG antibody

# Demographic features

- 37 children
  - MOG positive: 18 (49%)
  - MOG negative: 19 (51%)
- Average age: 5.6 years, SD 2.9 years
- Sex: 23 males (63%), 14 females (37%)
- Race/ethnicity:
  - White: 23 (61%)
  - Hispanic: 7 (18%)
  - Black: 5 (13%)
  - Asian: 3 (8%)

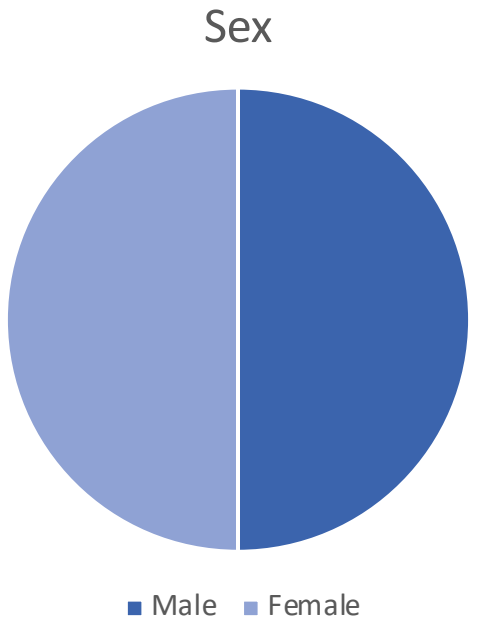


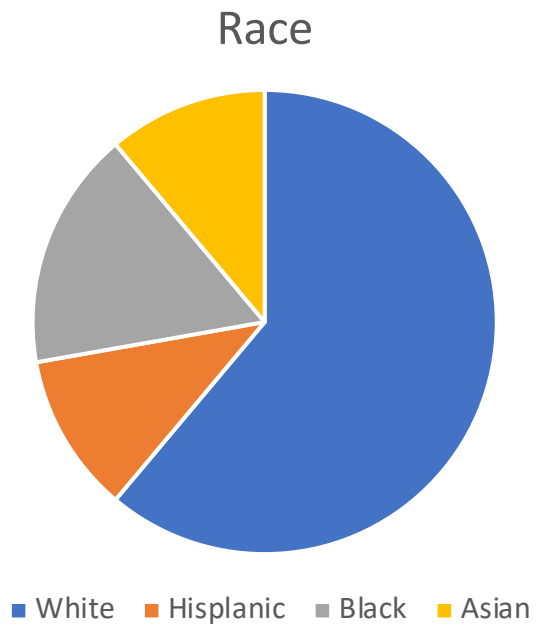



# Demographic features of MOG positive cohort

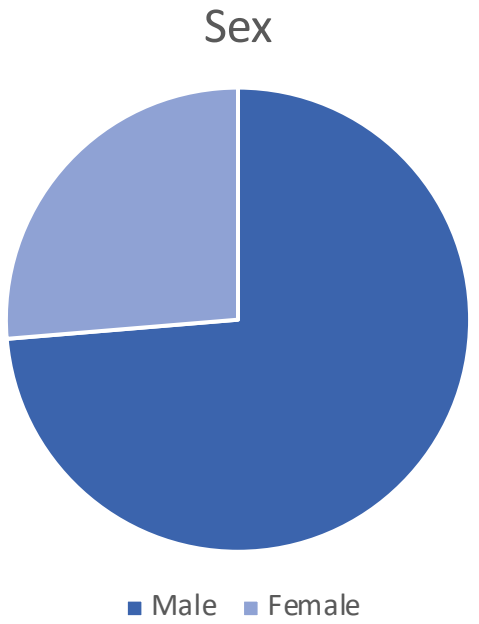
- 18 children (49%)
- Average age: 6.1 years, SD 3 years
- Sex: 9 males (50%) 9 females (50%)
- Race/ethnicity:
  - White: 11 (61%)
  - Black: 3 (17%)
  - Hispanic: 2 (11%)
  - Asian: 2 (11%)

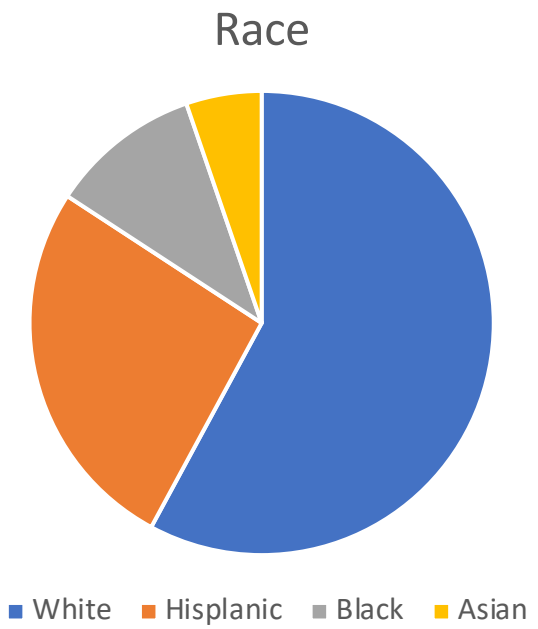


# Demographic features of MOG negative cohort

- 19 children (51%)
- Average age: 5.1 years, SD 2.7 years
- Sex: 14 males (74%), 5 females (26%)
- Race/ethnicity:
  - White: 11 (58%)
  - Hispanic: 5 (26%)
  - Black: 2 (11%)
  - Asian: 1 (5%)



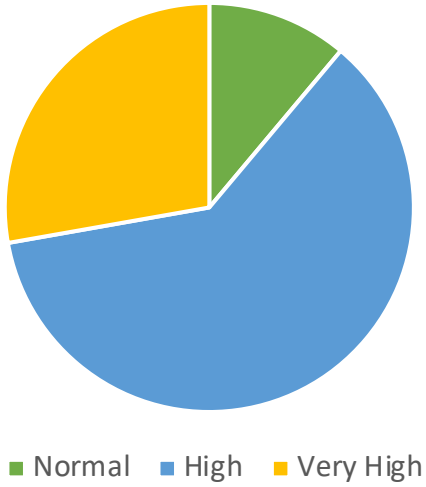



# Laboratory studies

CSF studies – # nucleated cells

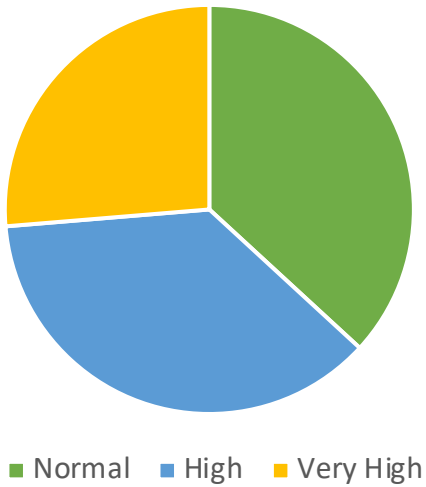
- Normal 0-5 cells/$mm^3$
- High 5-50 cells/$mm^3$
- Very high >50 cells/mm3

MOG positive




Normal: 2 (11%)
High: 11 (61%)
Very High: 5 (28%)

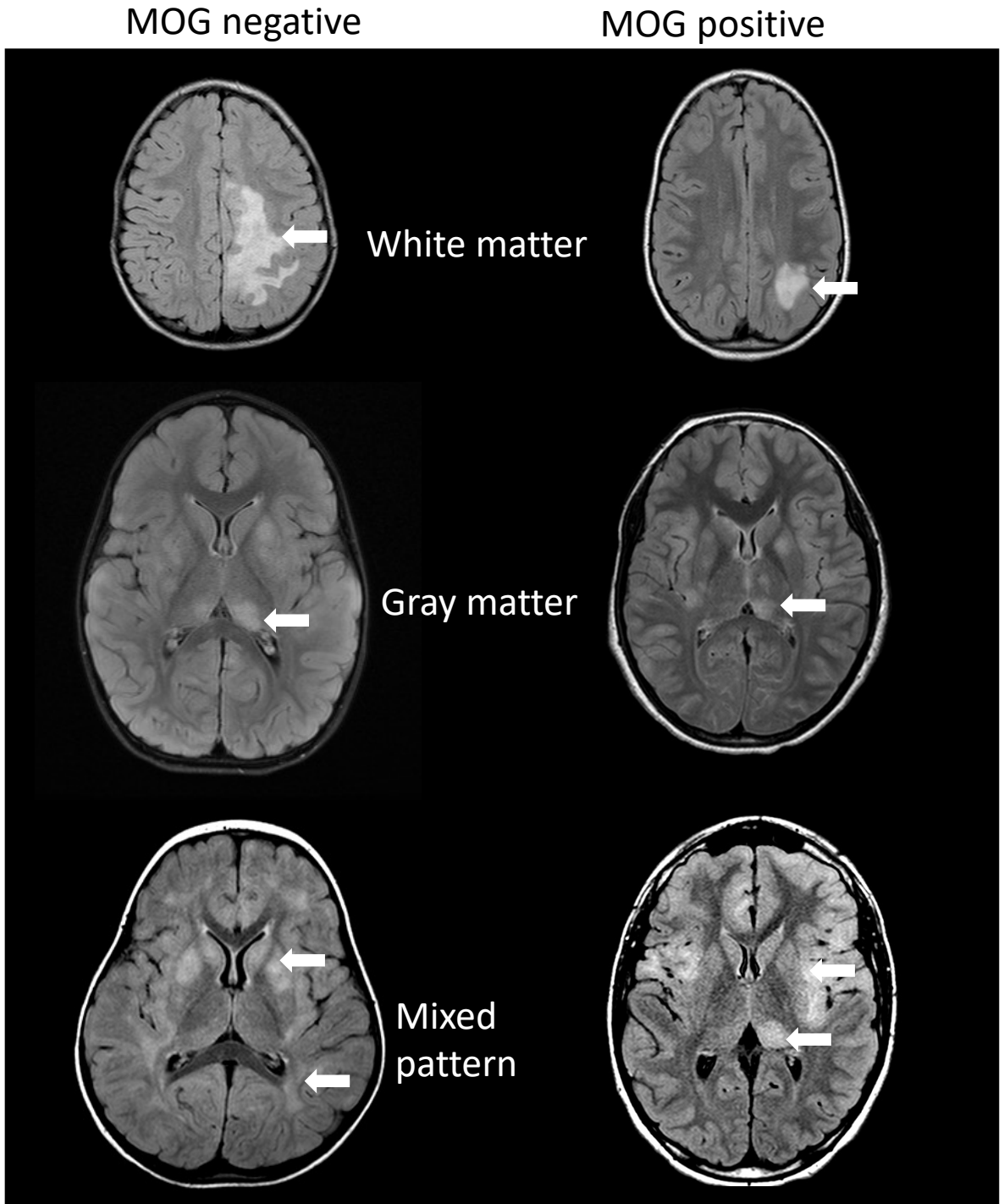
MOG negative




Normal: 7 (37%)
High: 7 (37%)
Very High: 5 (26%)

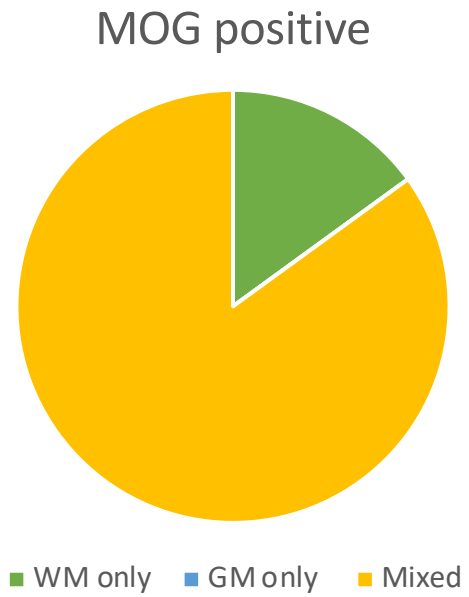
# Neuroimaging features

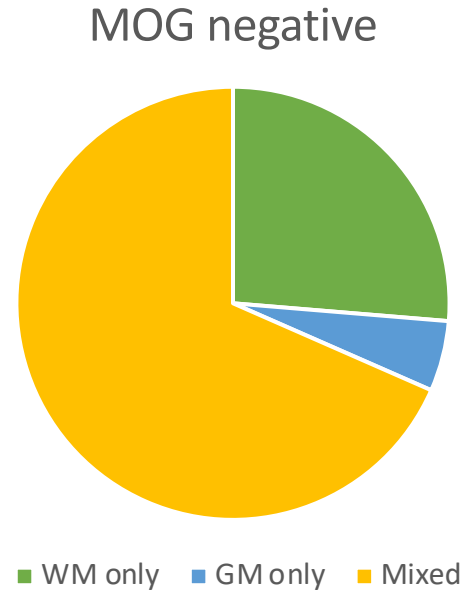
- Lesions in white matter, gray matter, or both?



# Neuroimaging features

- MOG positive
  - White matter only: 3 (17%)
  - Gray matter only: 0
  - Mixed: 15 (83%)
- MOG negative
  - White matter only: 5 (26%)
  - Gray matter only: 1 (5%)
  - Mixed: 13 (68%)



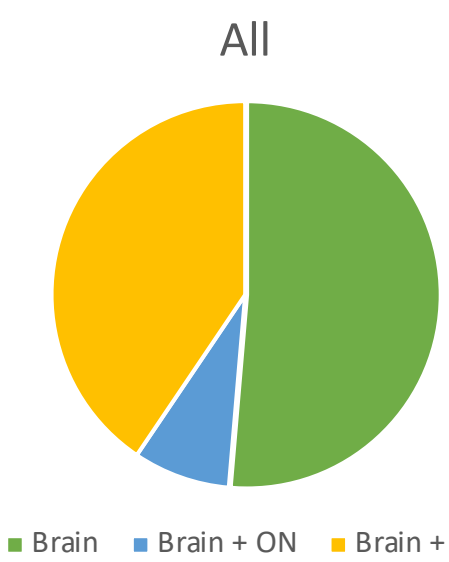



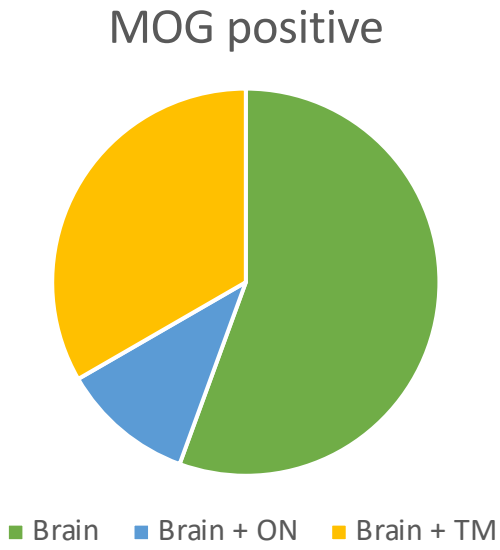
# Location of CNS Involvement

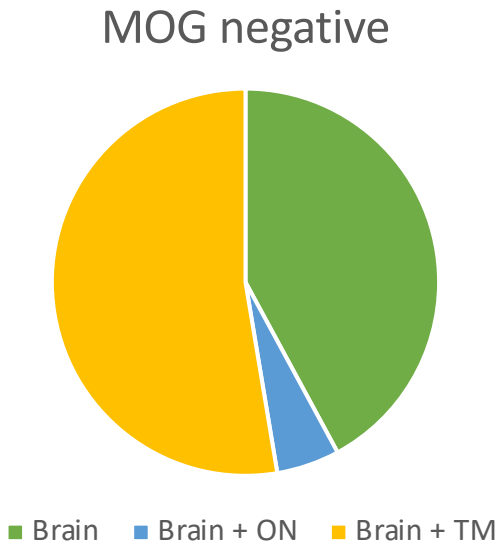
All (37)
- Brain only: 19 (51%)
- Brain and optic nerve: 3 (8%)
- Brain and spinal cord: 15 (41%)

MOG positive (18)
- Brain only: 10 (56%)
- Brain and optic nerve: 2 (12%)
- Brain and spinal cord: 6 (33%)

MOG negative (19)
- Brain only: 8 (42%)
- Brain and optic nerve: 1 (5%)
- Brain and spinal cord: 10 (53%)



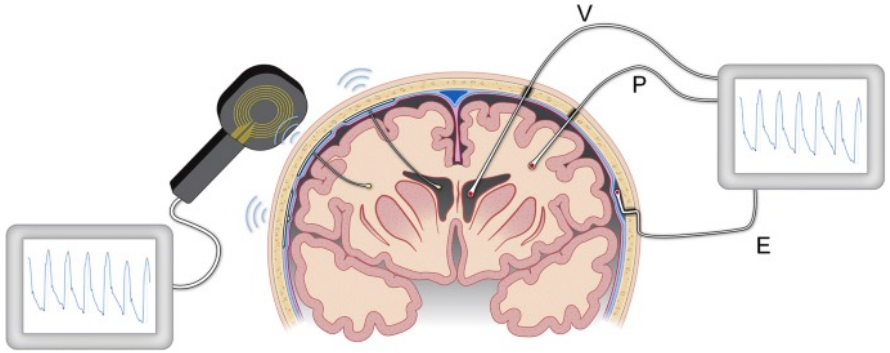



# Hospital course

All (37)
- ICU level care : 15 (41%)
- Neurosurgical or medical intervention for increased intracranial pressure: 5 (14%)
- Inpatient rehabilitation: 8 (22%)

MOG positive (18)
- ICU: 8 (44%)
- Neurosurgical or medical intervention for increased intracranial pressure: 4 (22%)
- Inpatient rehabilitation: 4 (22%)

MOG negative (19)
- ICU: 7 (37%)
- Neurosurgical or medical intervention for increased intracranial pressure: 1 (5%)
- Inpatient rehabilitation: 4 (21%)




# Treatments

All (37)

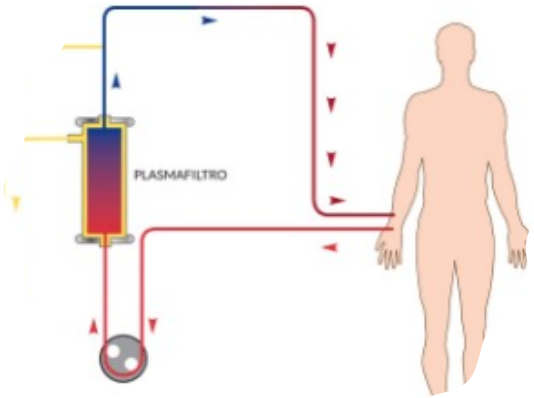
- Steroids only: 10 (27%)
- Steroids and IVIG: 10 (27%)
- Steroids and PLEX: 15 (41%)
- Steroids, IVIG, and PLEX: 2 (5%)

MOG positive (18)

- Steroids only: 5 (28%)
- Steroids and IVIG: 4 (22%)
- Steroids and PLEX: 8 (44%)
- Steroids, IVIG, and PLEX: 1 (6%)

MOG negative (19)

- Steroids only: 5 (26%)
- Steroids and IVIG: 6 (32%)
- Steroids and PLEX: 7 (37%)
- Steroids, IVIG, and PLEX: 1 (5%)

# Relapses and Outcomes

Total

- Relapse: 9 (24%)
  - Over average time of 6.6 years after ADEM diagnosis

MOG positive

- Relapse: 6 (33%)
- Immunotherapies:
  - Rituximab: 5
  - IVIG: 4
  - Mycophenolate mofetil: 3
  - Tocilizumab: 1

MOG negative

- Relapse: 3 (16%)
- Immunotherapies
  - Rituximab: 2
  - Mycophenolate mofetil: 3
  - Natalizumab: 1

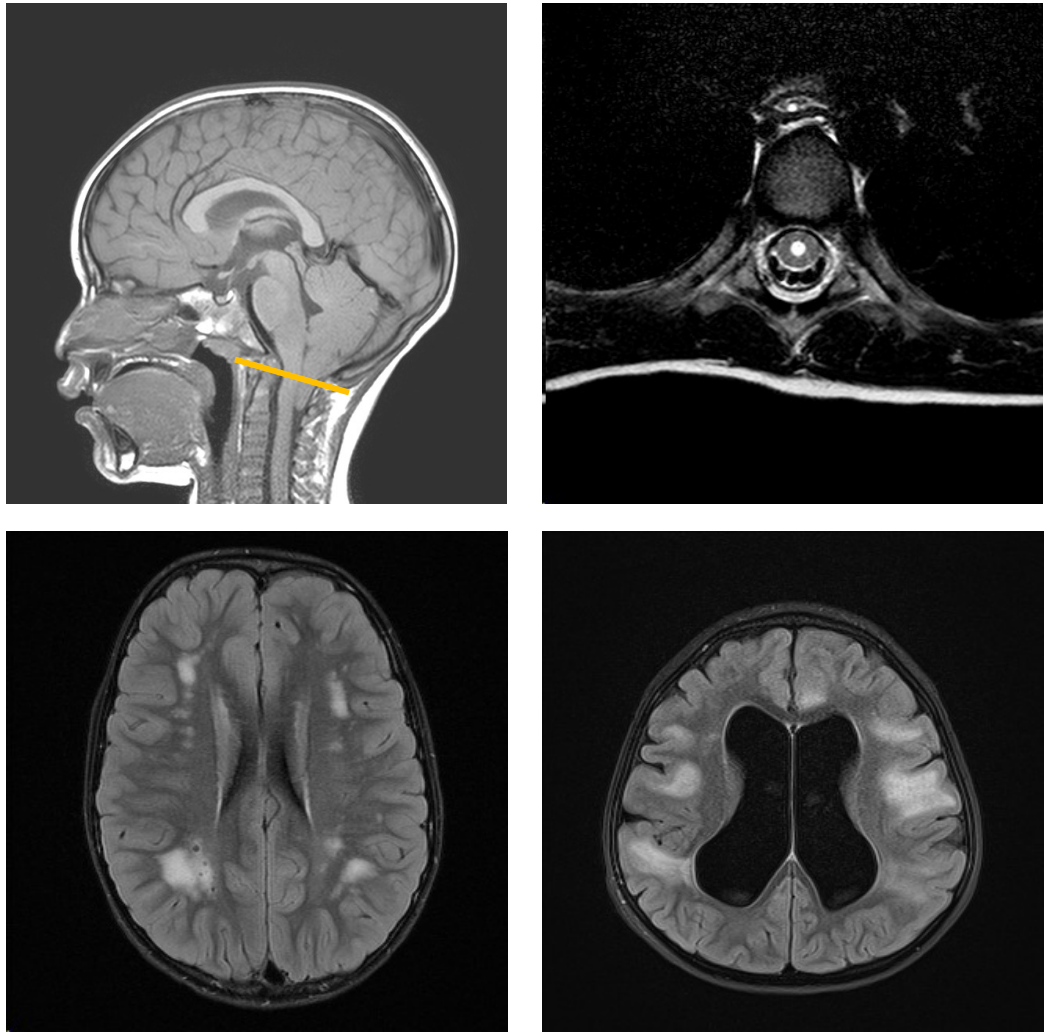
1 patient later died due to complications of ADEM (MOG positive)

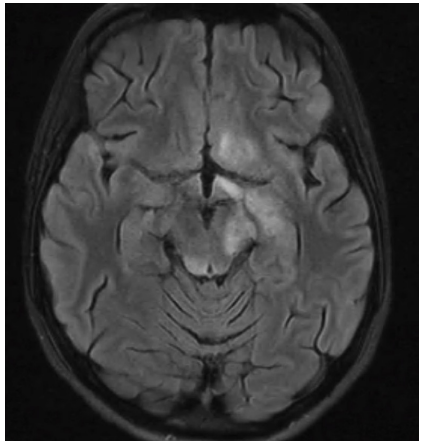
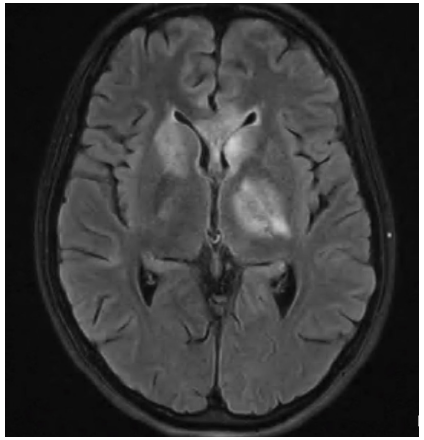
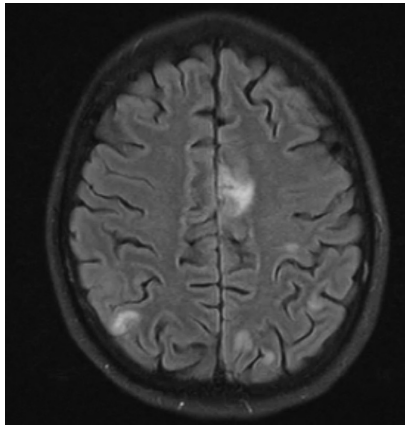

# Neuropsych testing

- Of the 29 subjects who had neuropsychological evaluation, 26 (90%) were functioning within average range
- Lower range scores included 1 MOG positive patient and 2 MOG negative patients (ADEM onset at 4 years; 1, 2 years respectively)
  - Deficits in attention, hyperactivity/impulsivity, processing speed, language/vocabulary, visual spatial abilities and visuomotor integration

# What is MOG negative ADEM?

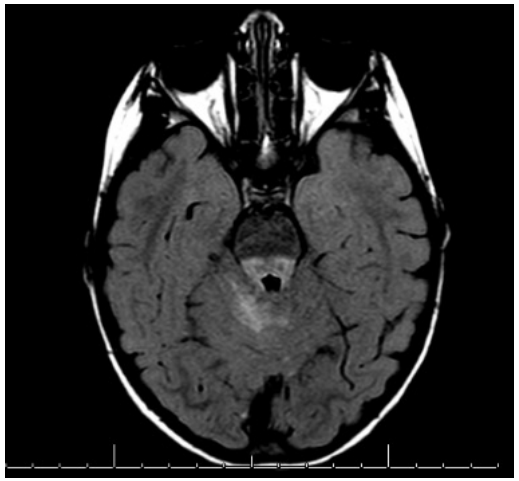
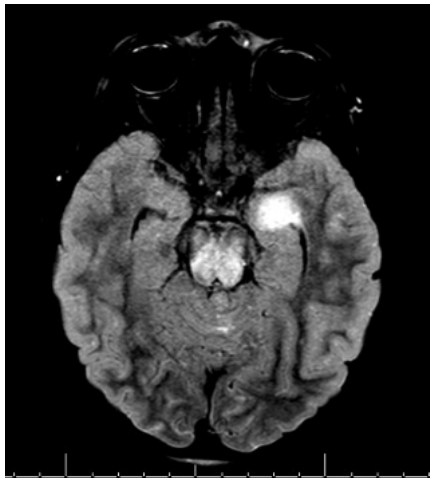
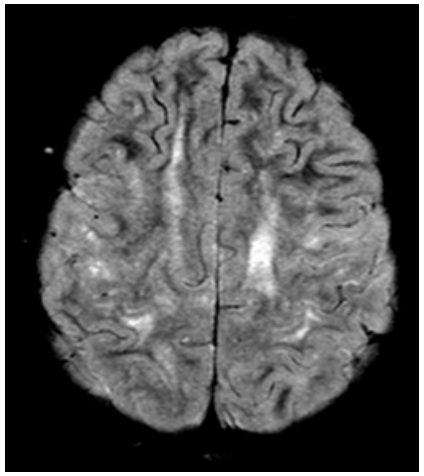
- Idiopathic?
- Alternate diagnoses?



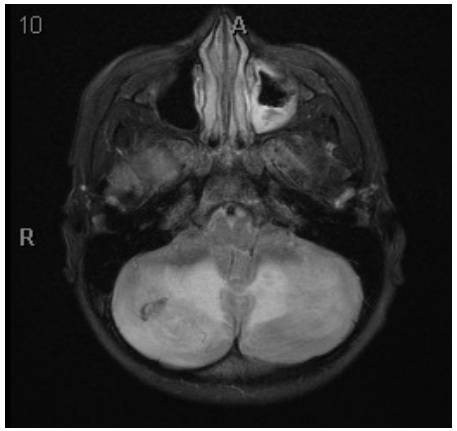
## Lymphomatoid granulomatosis

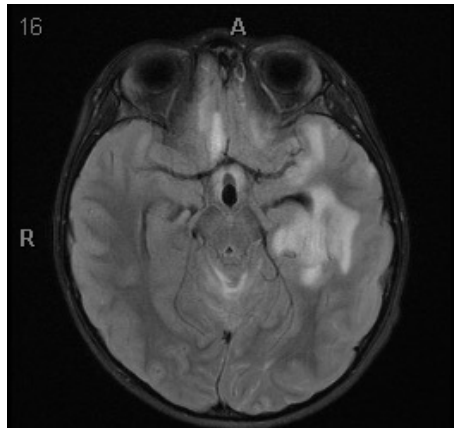
A rare Epstein-Barr virus (EBV)–driven B-cell lymphoproliferative disease

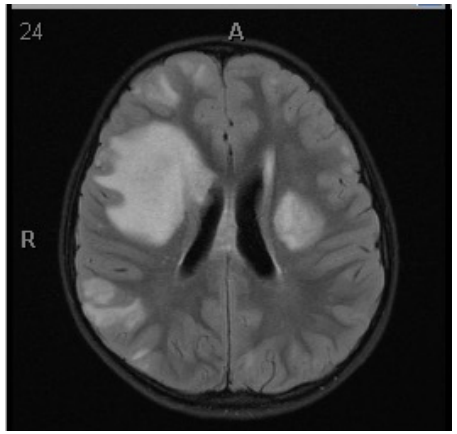




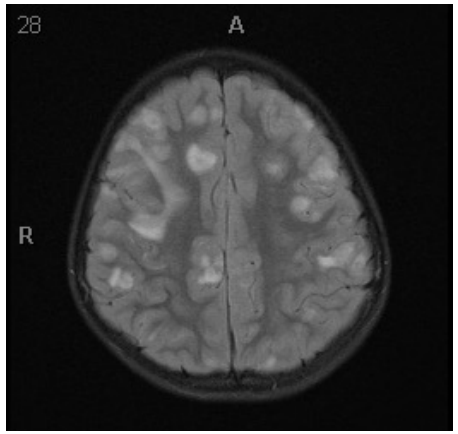
## Melioidosis

A bacterial infection caused by Burkholderia pseudomallei



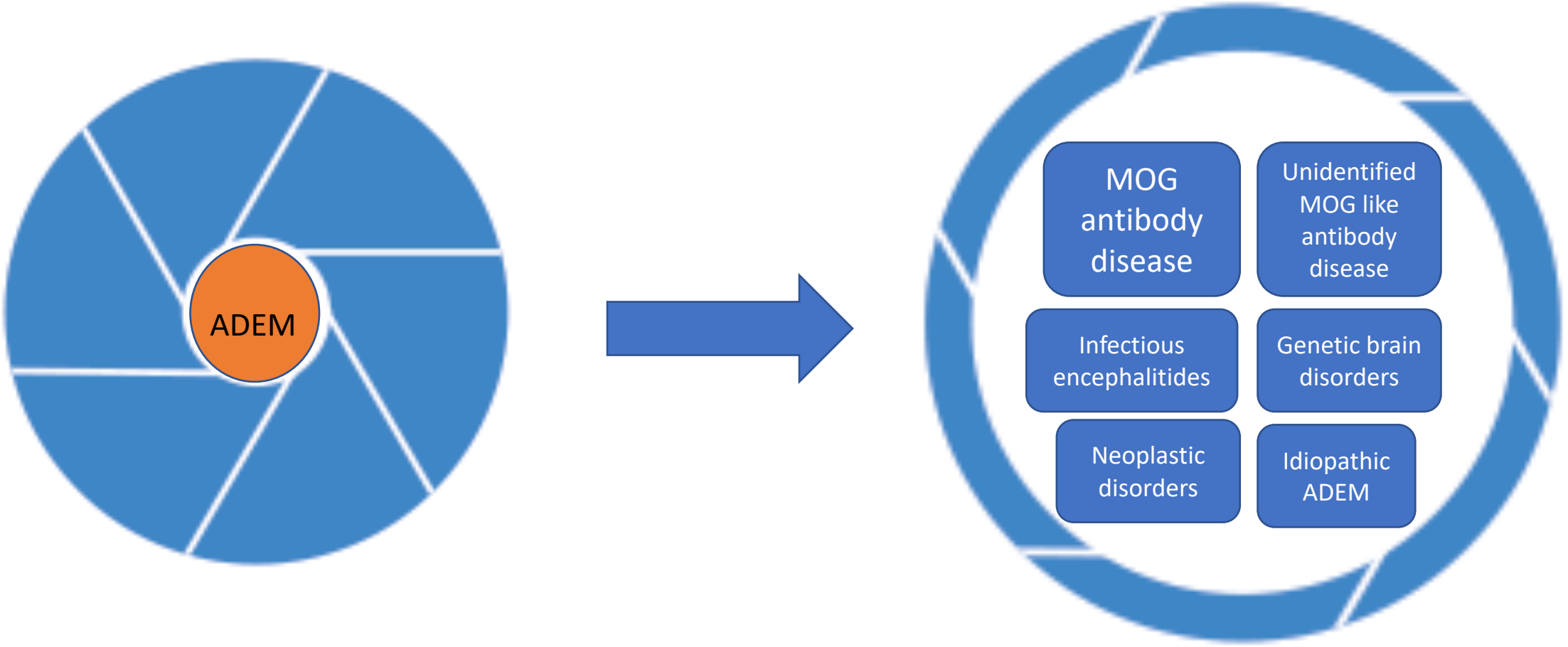







## CNS isolated familial hemophagocytic lymphohistiocytosis

Due to PRF1 mutation


ADEM
MOG antibody disease
Unidentified MOG like antibody disease
Infectious encephalitides
Genetic brain disorders
Neoplastic disorders
Idiopathic ADEM

# Summary

MOG antibody disease makes up a significant proportion of ADEM

- Generally good outcomes, but has potential for life-threatening complications, and relapses can occur

ADEM without MOG antibodies likely consist of a heterogenous group of conditions that requires further study and characterization

Understanding the individual disorders that are classified as ADEM will help devise more effective and targeted acute treatments, surveillance strategies, and long-term therapies

# Thank you

SRNA
connect. care. cure.

Siegel
Rare Neuroimmune
Association