

**2021RNDS**  
connect. care. cure.™

# Acute Disseminated Encephalomyelitis

Cynthia Wang, MD

October 8, 2021

2021 Rare Neuroimmune Disorders Symposium

# Disclosures

- I received the James T. Lubin Clinician-Scientist Fellowship Award from the Siegel Rare Neuroimmune Association
- I will be discussing off-label use of therapies

# Case Presentation

- 5-year-old previously healthy boy
- Developed a posterior headache, right eye blurry vision, and vomiting over 2-3 weeks
- Presented to local ER where physical examination and laboratory studies were unremarkable except for a positive SARS-CoV-2 RNA PCR nasopharyngeal swab
- His symptoms were attributed to this illness and the patient was discharged home



# Case Presentation

- Returned to ED for continued headache symptoms
- Tested positive again for SARS-CoV-2
- Neurological exam was reportedly unremarkable, irritability was attributed to headaches
- MRI brain and spinal cord imaging were obtained

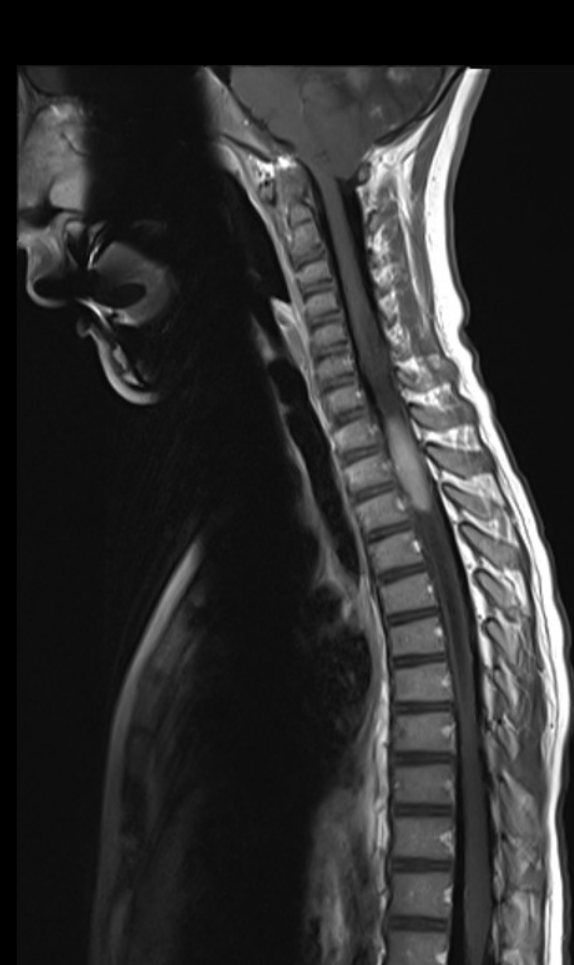
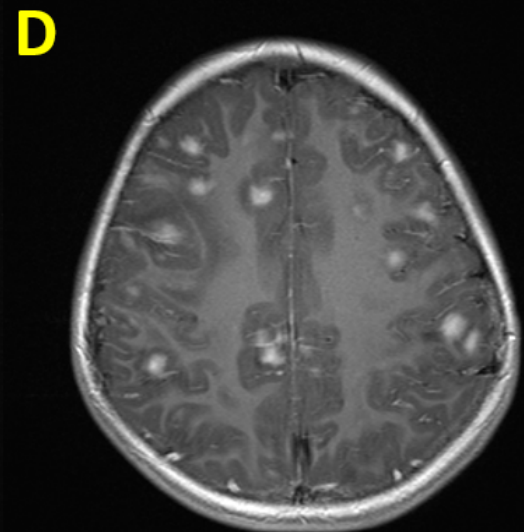
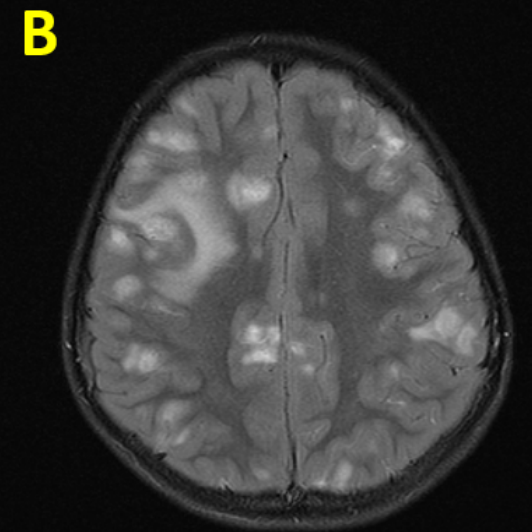
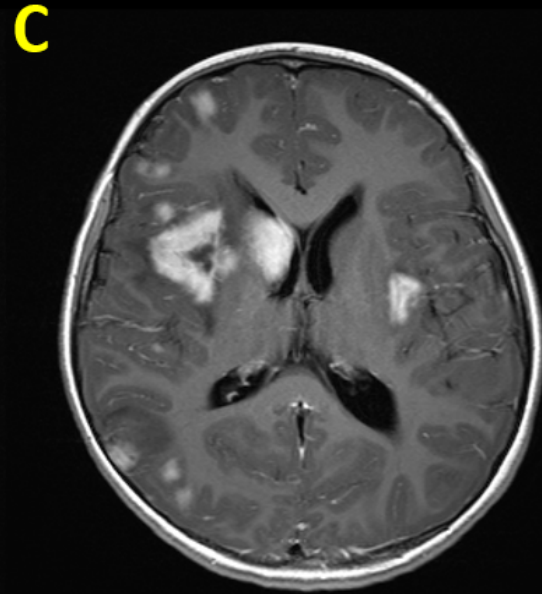
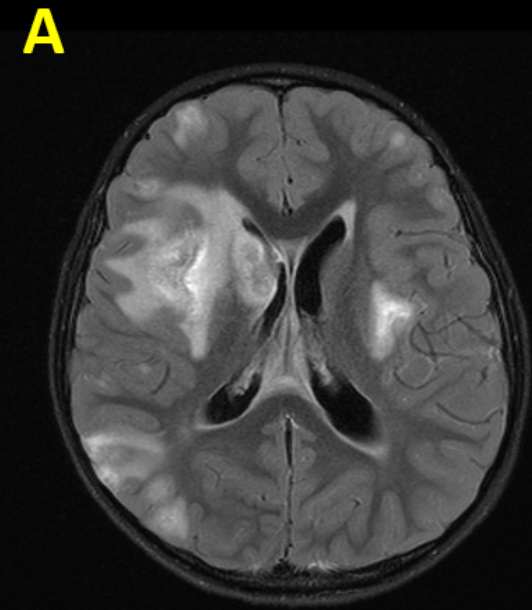


T2 FLAIR

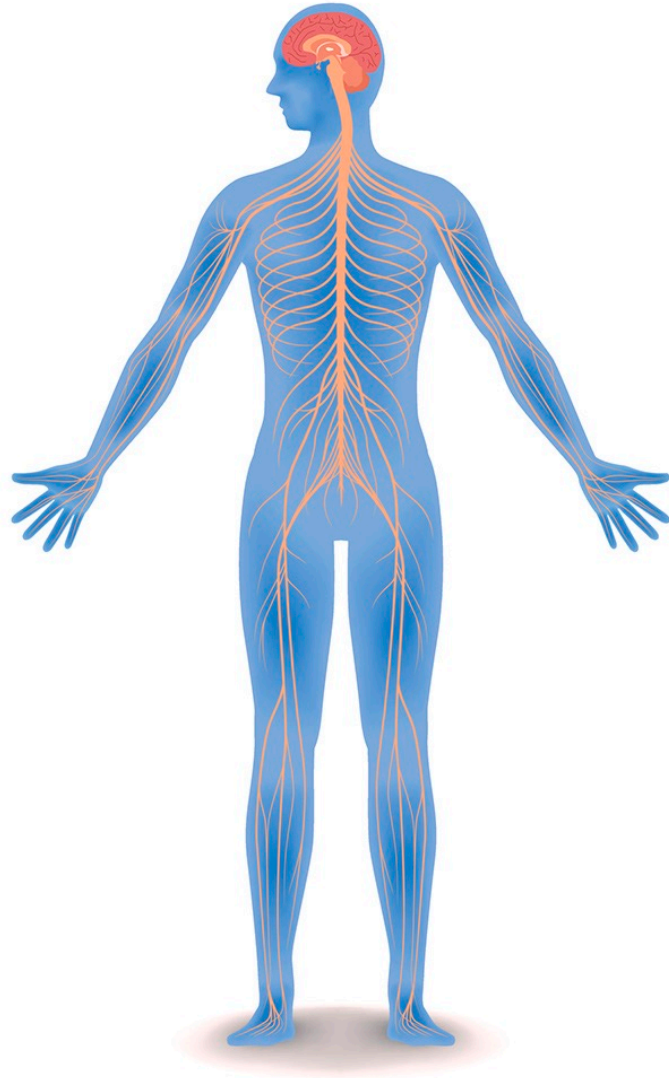
T1 post-gadolinium

STIR

T1 post-gadolinium



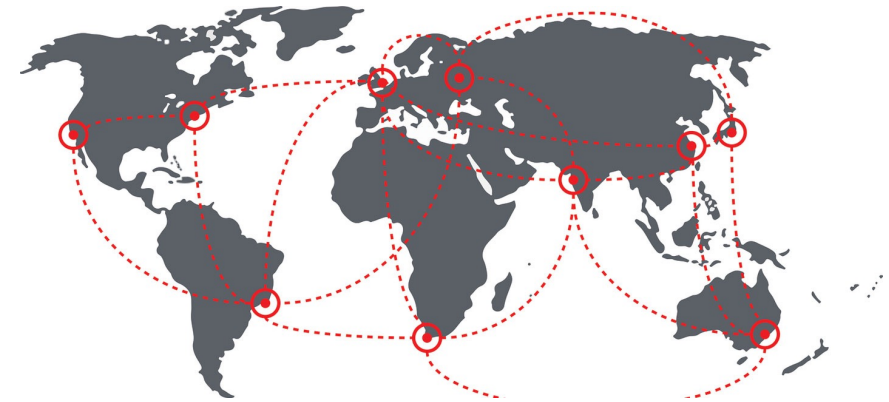
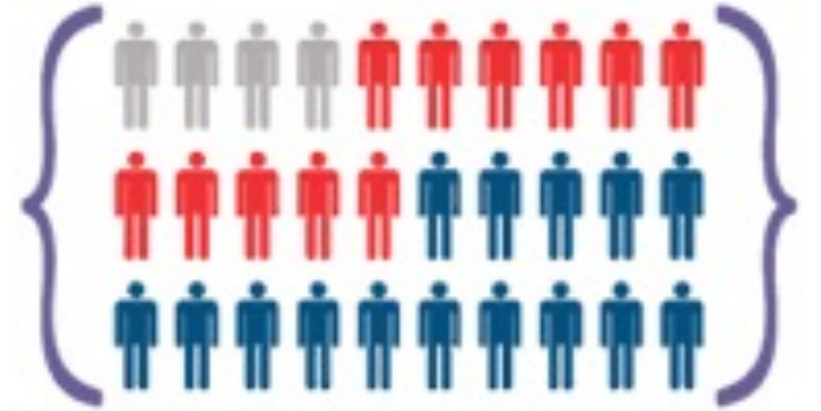
# What is ADEM?



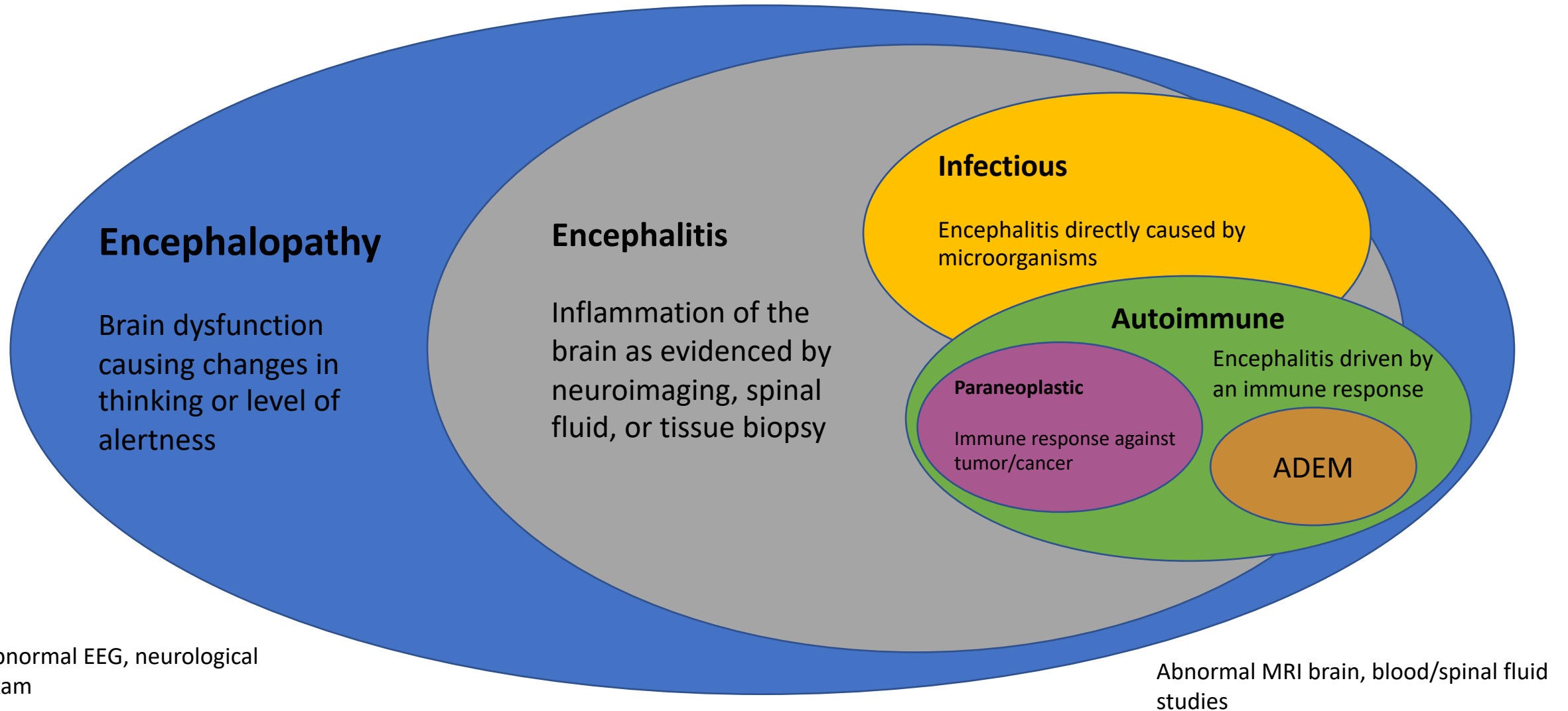
- Acute disseminated encephalomyelitis
- Sudden and widespread inflammation of the brain and spinal cord
- Leads to myelin injury within the central nervous system and abnormal functioning of brain (encephalopathy)

# Epidemiology

- Primarily affects children
- Average age of onset around 4-8 years
- 3-6 cases per million children a year
- Slight male predominance
- More common in winter and in locations further from the equator
- Preceded by an acute illness 50-80% of the time



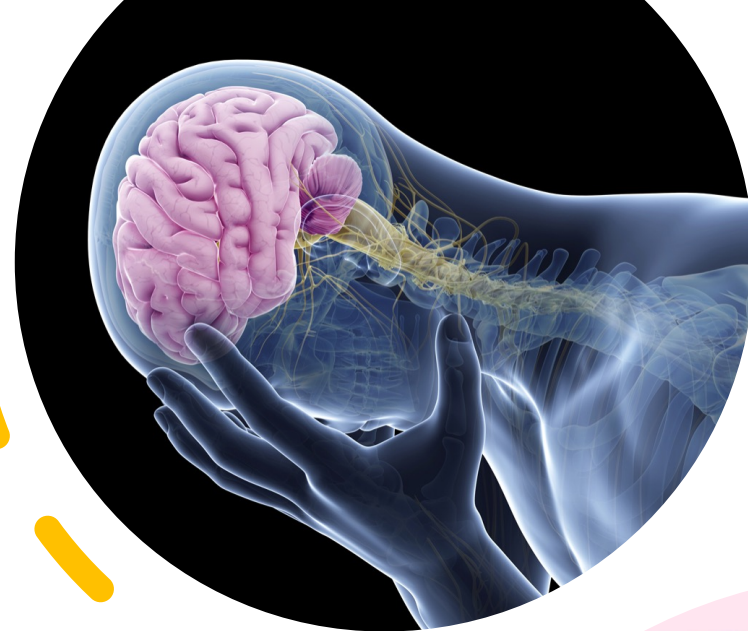
# Terminology





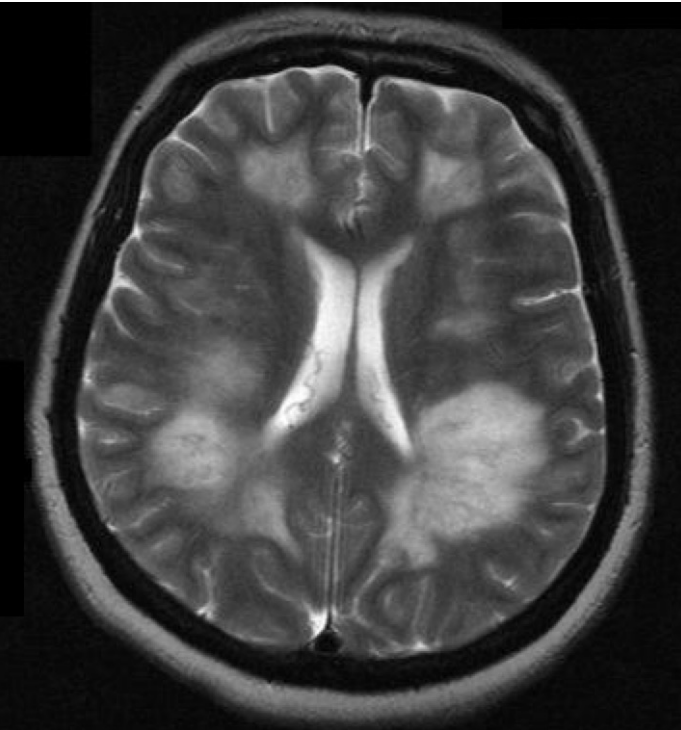
# Clinical Presentation

- Acute illness 1-2 weeks before
- Can have fever, headache, nausea 3-4 days before neurological symptoms
- Presenting symptoms depend where inflammation occurs
  - Brain → Irritability, confusion, sleepiness, coma, incoordination, gait problems
  - Spine → Weakness, numbness, paralysis of limbs
  - Optic nerve and cranial nerves → eye pain, blurry vision, double vision, facial weakness

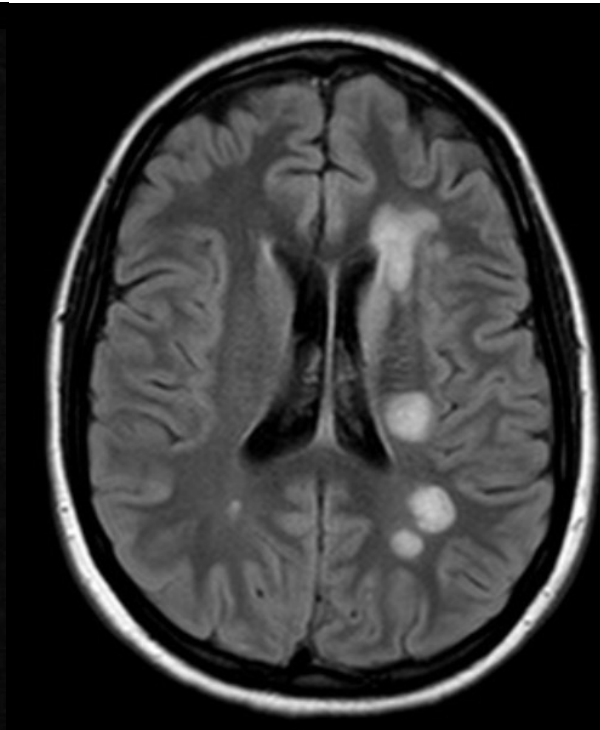


# Examples of ADEM on brain imaging

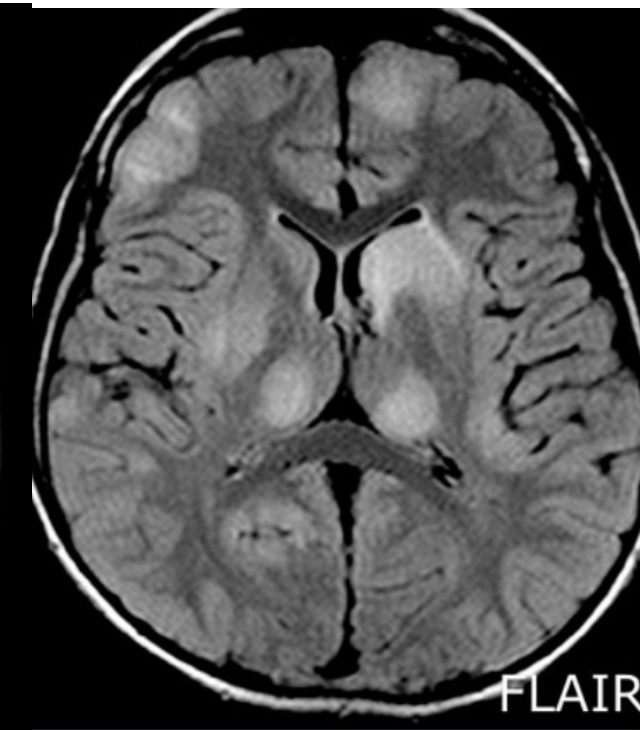
Large, diffuse white matter lesions



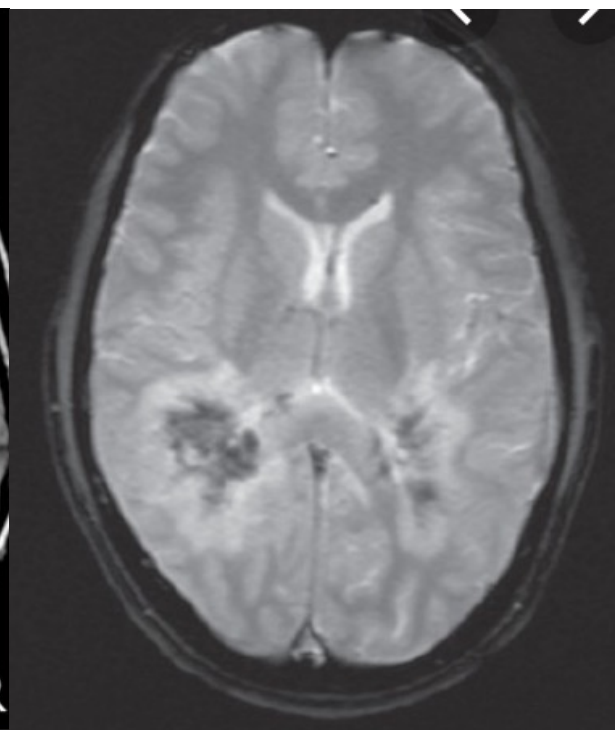
Smaller, more defined white matter lesions



Gray matter lesions (thalamus, basal ganglia)

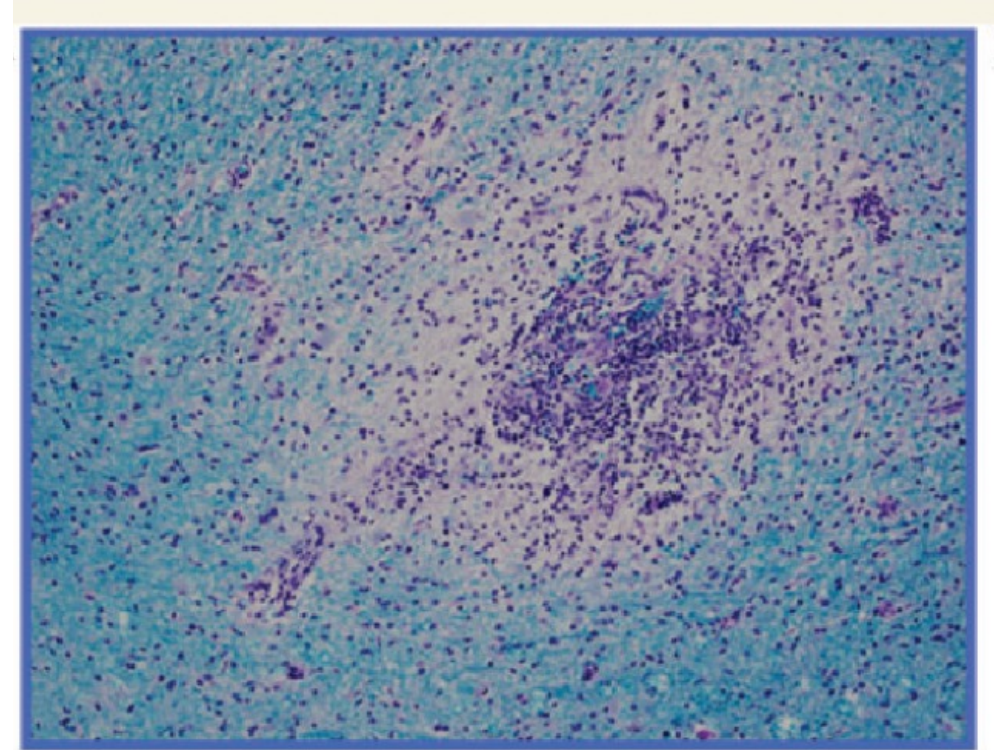
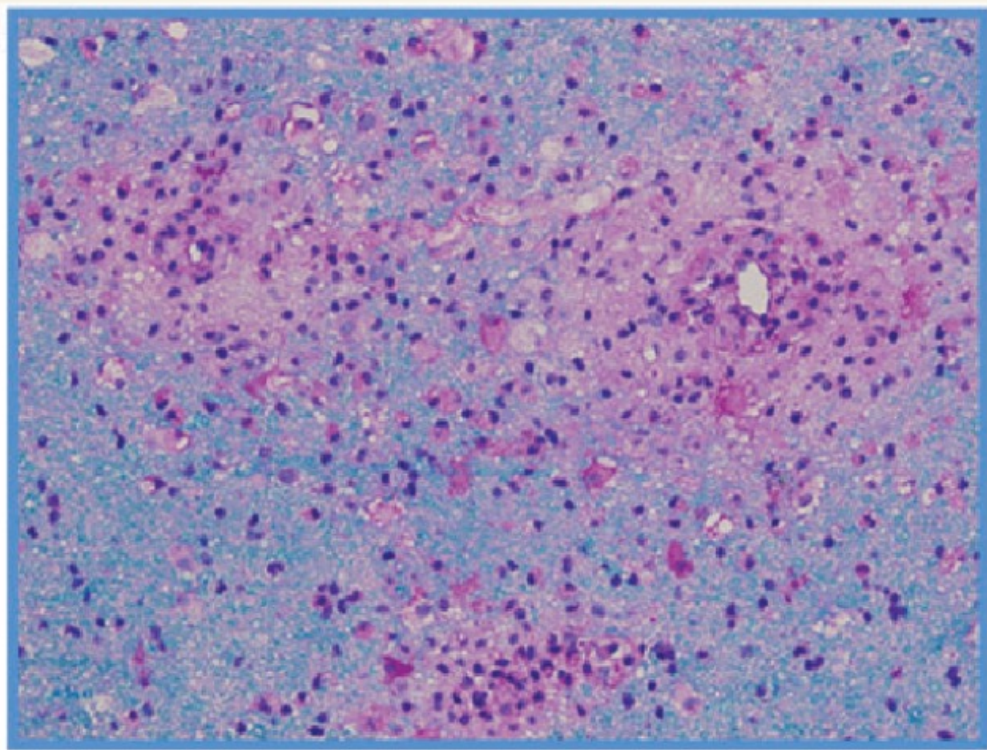


Hemorrhagic lesions



# Tissue biopsy

- Immune cells (macrophages and lymphocytes) gather around veins in the white matter
- Recognize and injure myelin and myelin-producing cells (oligodendrocytes)
- Severe presentations with hemorrhage and necrosis



# Diagnostic Criteria (IPMSSG, 2013)

A first polyfocal, clinical, CNS event with presumed inflammatory demyelinating cause

Encephalopathy NOT explained by fever, systemic illness, or postictal symptoms

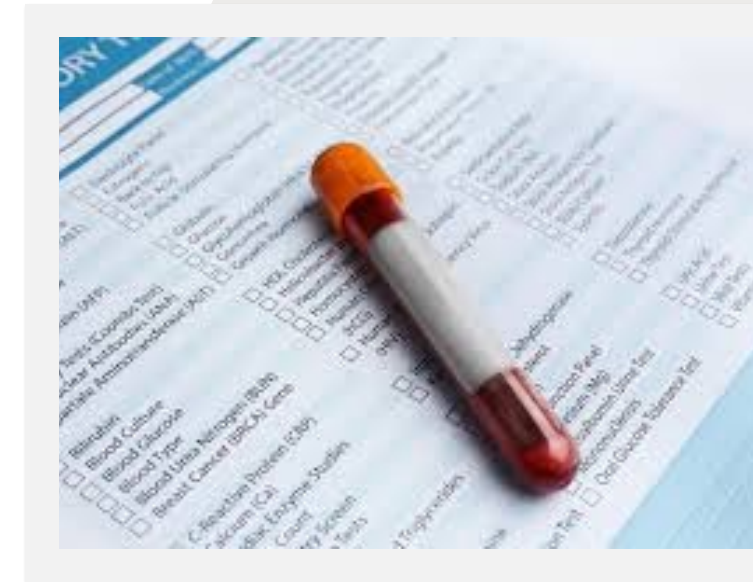
Brain MRI is abnormal during the acute (3 month) phase

- Diffuse, poorly demarcated, large (>1-2cm) lesions
- Predominantly involving cerebral white matter
- Deep gray matter lesions in thalamus or basal ganglia can be present

No NEW clinical or MRI findings emerge 3 months or more after onset

# Laboratory Studies

- Serum (blood)
  - Test for antibodies associated with CNS demyelination
    - Myelin oligodendrocyte glycoprotein (MOG), Aquaporin-4 (AQP4)
  - Test for infections, metabolic disturbances
  - Assess vitamin D level
- Cerebrospinal fluid
  - Increased WBCs in 29-85% of cases
  - Elevated protein in 17-48% of cases
  - Rare to see oligoclonal bands
  - May have elevated opening pressure



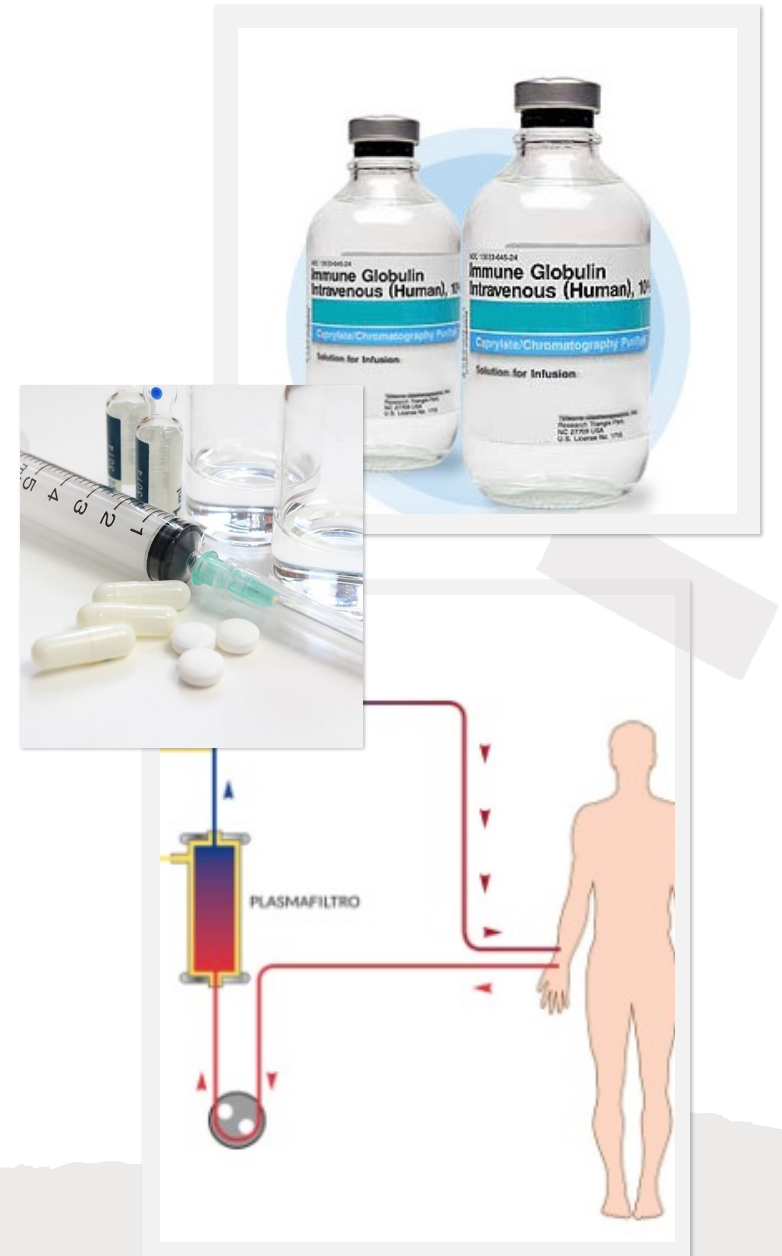
# Additional studies

- EEG
  - May show diffuse slowing (88%) or focal slowing and spikes (25%)
- Rule out mimics
  - Infectious meningoencephalitis, tumor, stroke, vasculitis, leukodystrophy, mitochondrial disorders, NMOSD, MS



# Acute Treatment

- No large scale, prospective, randomized controlled clinical trials
- 3-5 days of high dose intravenous corticosteroids
  - methylprednisolone 10-30 mg/kg/day
  - dexamethasone 1-2 mg/kg/day
- Therapeutic plasma exchange (PLEX) for 5-7 sessions
- Intravenous immunoglobulin (IVIG), 2 grams/kg divided over 2-5 days
- Followed by oral corticosteroid taper
  - prednisone 1 mg/kg/day, taper over 4-6 weeks



# Hospital course

- May spend 1-3 weeks in the hospital and rehabilitation
- 25% will require ICU level care (75% of whom are on ventilator)
- Supportive care for breathing, seizures, cerebral edema
- Once able to tolerate, can initiate therapy (PT, OT, ST) to help with neurological recovery





# Prognosis

- Up to 3% mortality
- Often marked improvement within 30 days
- Follow-up MRI in 3-4 months can show complete or partial resolution of lesions
- Cognitive recovery takes longer and can be incomplete; fatigue may persist
- May not have normal rates of white matter and gray matter growth
- Up to 1/3 with recurrent attacks (often MOG positive)
- Epilepsy uncommon (0-16%, often MOG positive)





RECOVERY

RELAPSE

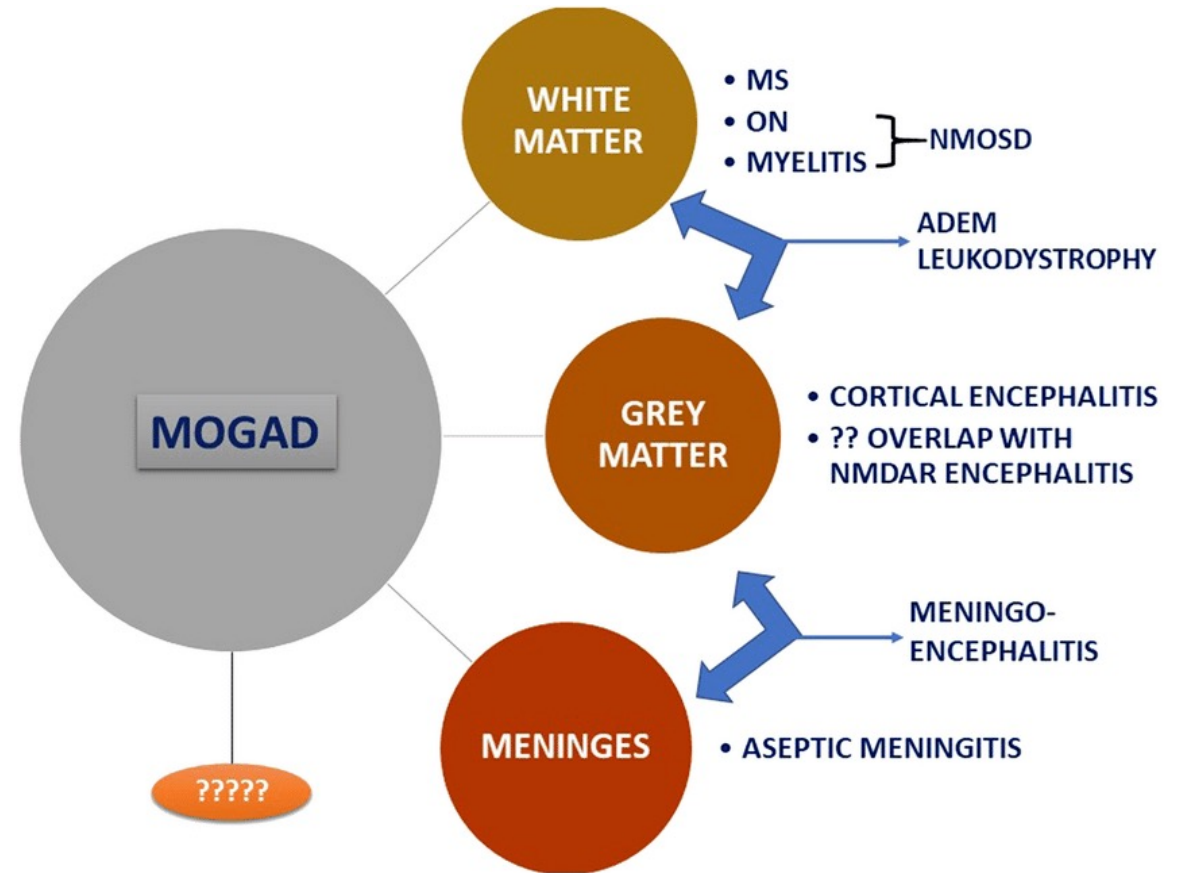
# Relapsing or Multiphasic ADEM

---

- Monophasic ADEM
  - A single ADEM episode with no further demyelinating events or new MRI lesions outside the acute three-month period after onset
- Multiphasic ADEM
  - Two episodes of ADEM separated by at least three months in time.
  - The second event can involve the same or new symptoms, signs or MRI lesions compared with the first event.
  - This diagnosis is limited to two episodes of ADEM.
  - Three or more suggest ultimate diagnosis of MS, NMO, or other disorder

# Myelin Oligodendrocyte Glycoprotein (MOG) Antibody Disease (MOGAD)

- MOG is a protein expressed on myelin and myelin producing cells
- Common cause of ADEM and acute demyelination in children
- Can also affect the optic nerves, spinal cord, and gray matter of the brain
- Relapse is possible, and risk may be related to persistent MOG antibody production



# Supporting Recovery from ADEM

- Comprehensive neuropsychological testing
- School Accommodations
- Cognitive and Behavioral therapies
- Follow-up of neuropsychiatric symptoms
- Monitor for relapses
- Provide immunosuppressive therapy when appropriate



Q&A

---

