NMOSD: A New Era in Management & Treatment

SRNA Conference
Justin R. Abbatemarco, MD
Staff Physician
Mellen Center at Cleveland Clinic
October 8, 2021

Objectives

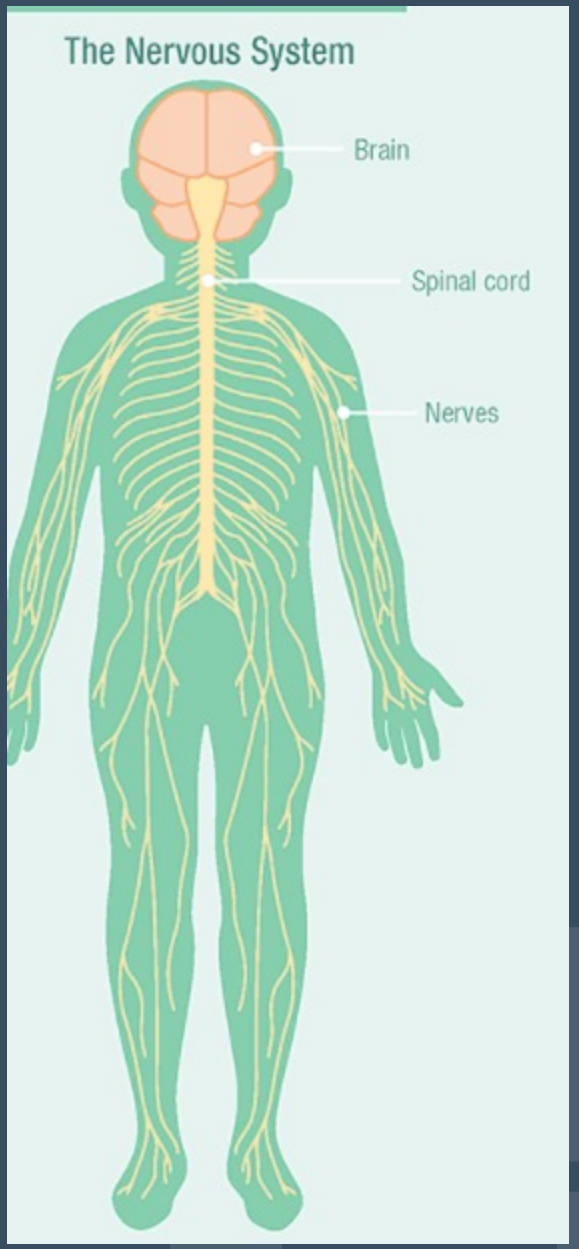
- Discuss common presenting symptoms in NMOSD
  - Diagnostic criteria
- Short and long term treatment options in NMOSD
  - Include the 3 new FDA approved options
- Symptom management NMOSD
- Defer discussion on anti-myelin oligodendrocyte glycoprotein (MOG) associated disorder (MOGAD)

Disclosures

- None
- No relation with any the pharmaceutical companies that we will be discussing
  - “borrowed” some of the nice graphics for today’s talk….

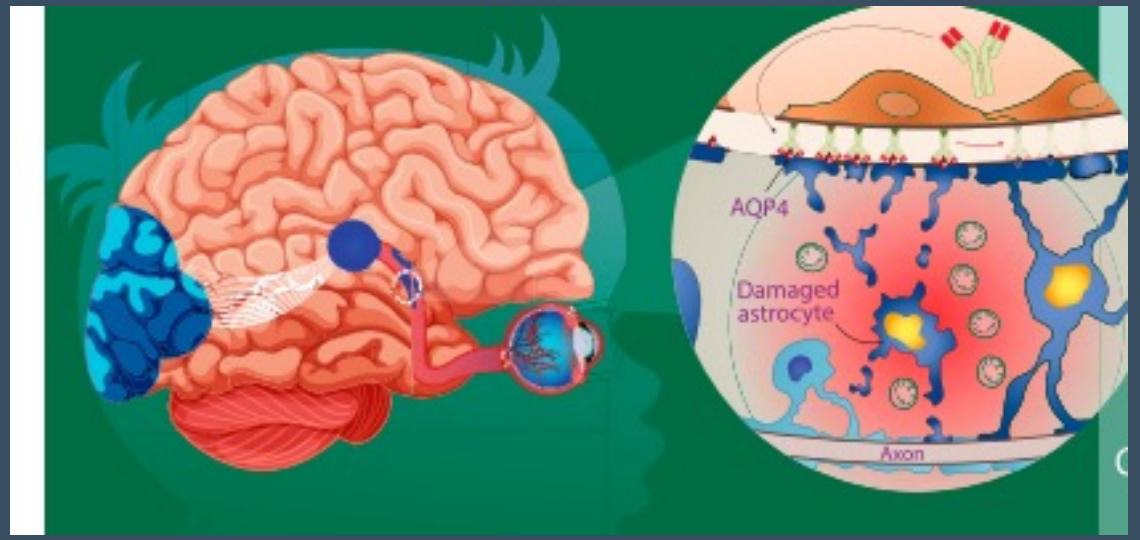
What is NMOSD?

- Neuromyelitis optica spectrum disorders (NMOSD)
  - Previously known as Devic disease or neuromyelitis optica (NMO)
- Inflammatory, antibody mediated disorder affecting distinct areas in the central nervous system (brain and spinal cord)



History

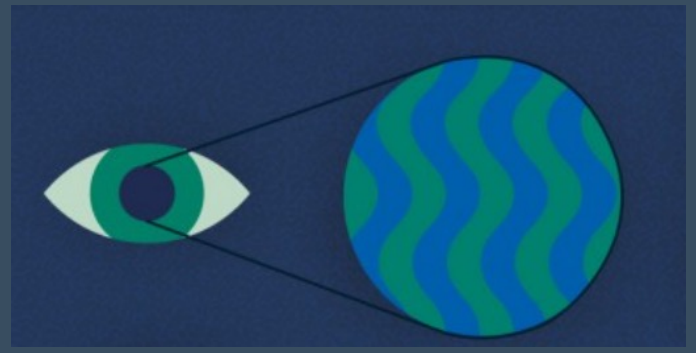
- Dr. Eugene Devic first described and published seminal case in 1894!
- In 2004, seminal discovery of the ***aquaporin-4 (AQP4) antibody***
- 2014-2015 several international treatment trials were initiated

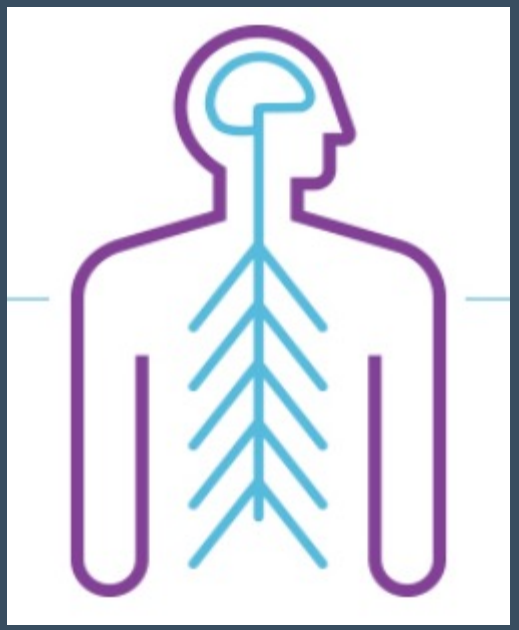


Barbosa et al. 2020. Neurol Neuroimmunol Neuroinflamm 2020;7:e837

Attribute	Multiple Sclerosis	AQP4-IgG
Antecedent infection/ immunization	Rare	Rare
Ages affected	Any (median age at onset in third decade)	Any (median age at onset in fourth decade)
Sex (female: male)	2:1	9:1
Epidemiology	Prevalence: common	Prevalence: rare
	Ethnicity: whites more predisposed	Ethnicity: African-Americans, Afro-Caribbeans more predisposed
	Geographic: regions farthest from equator	Geographic: higher proportion of total demyelinating disease is AQP4-IgG–positive neuromyelitis optica spectrum disorder (NMOSD) in regions where multiple sclerosis prevalence is low
Most common manifestations	Myelitis, optic neuritis, brainstem, cerebral episodes; myelopathy for progressive multiple sclerosis	NMOSD (any combination of single/recurrent myelitis, optic neuritis, area postrema syndrome)
Course	Relapsing-remitting from onset in 85% (most later develop secondary progression); 10–15% progressive from onset	Typically relapsing; usually no secondary progression
Attack severity	Usually mild to moderate	Usually moderate to severe
Recovery from attacks	Good	Often incomplete

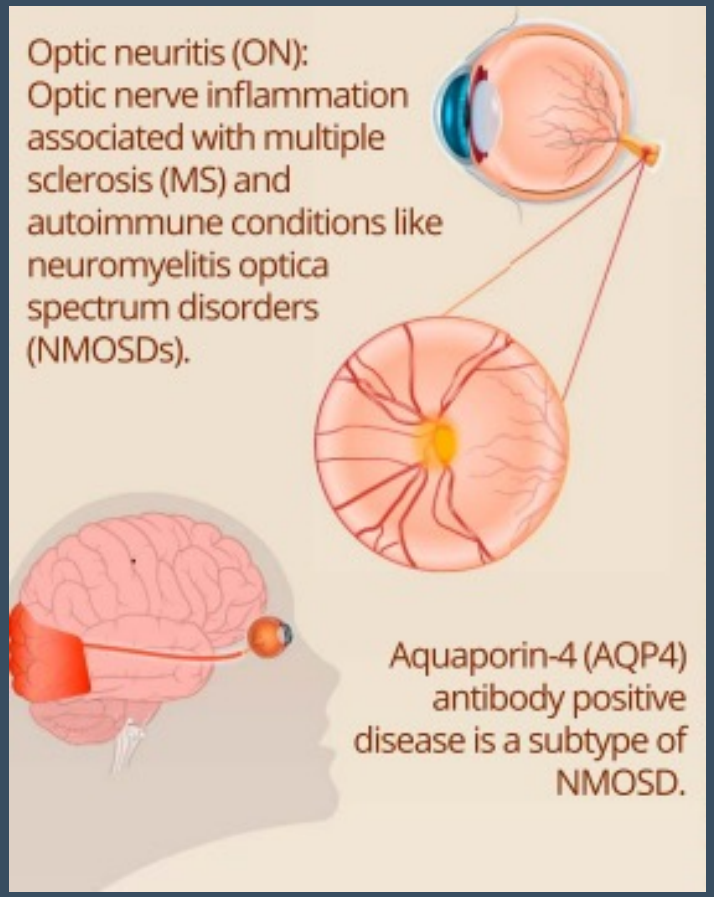
Flanagan. CONTINUUM. (3):815-844, June 2019.



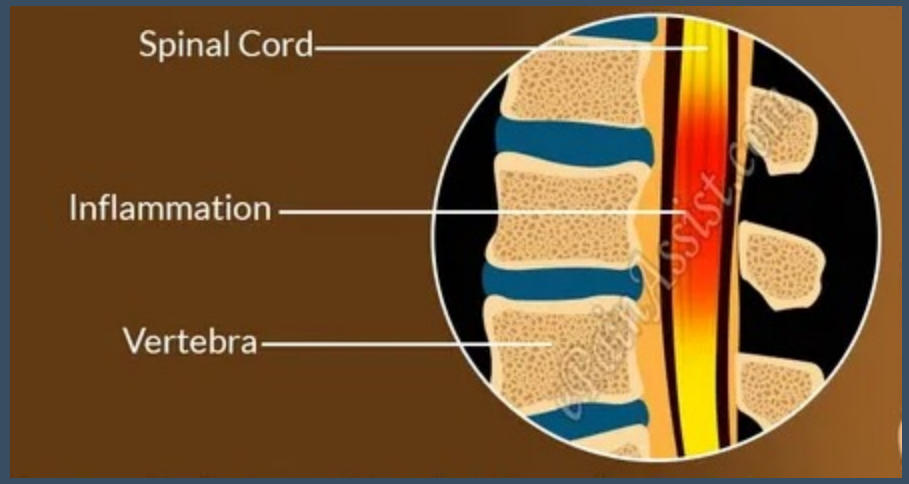


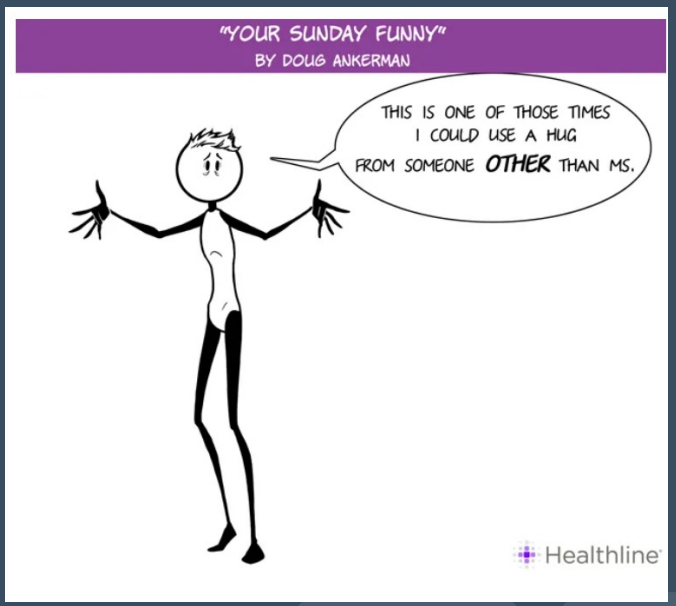
https://www.gene.com/stories/risk-of-relapse
https://www.uplizna.com/learn-about-nmosd/

Optic Neuritis



Myelitis, transverse myelitis vs longitudinally extensive TM (LETM)





Stiebel-Kalish et al. Neurol Neuroimmunol Neuroinflamm 2019;6:e572

Diagnostic criteria for NMOSD with AQP4-IgG

1. At least 1 core clinical characteristic
2. Positive test for AQP4-IgG using best available detection method (cell-based assay strongly recommended)
3. Exclusion of alternative diagnoses[a]

Diagnostic criteria for NMOSD without AQP4-IgG or NMOSD with unknown AQP4-IgG status

1. At least 2 core clinical characteristics occurring as a result of one or more clinical attacks and meeting all of the following requirements:
   a. At least 1 core clinical characteristic must be optic neuritis, acute myelitis with LETM, or area postrema syndrome
   b. Dissemination in space (2 or more different core clinical characteristics)
   c. Fulfillment of additional MRI requirements, as applicable
2. Negative tests for AQP4-IgG using best available detection method, or testing unavailable
3. Exclusion of alternative diagnoses[a]

Core clinical characteristics

1. Optic neuritis
2. Acute myelitis
3. Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting
4. Acute brainstem syndrome
5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions (figure 3)
6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions (figure 3)

Wingerchuk DM et al. Neurology 2015;85:1-13

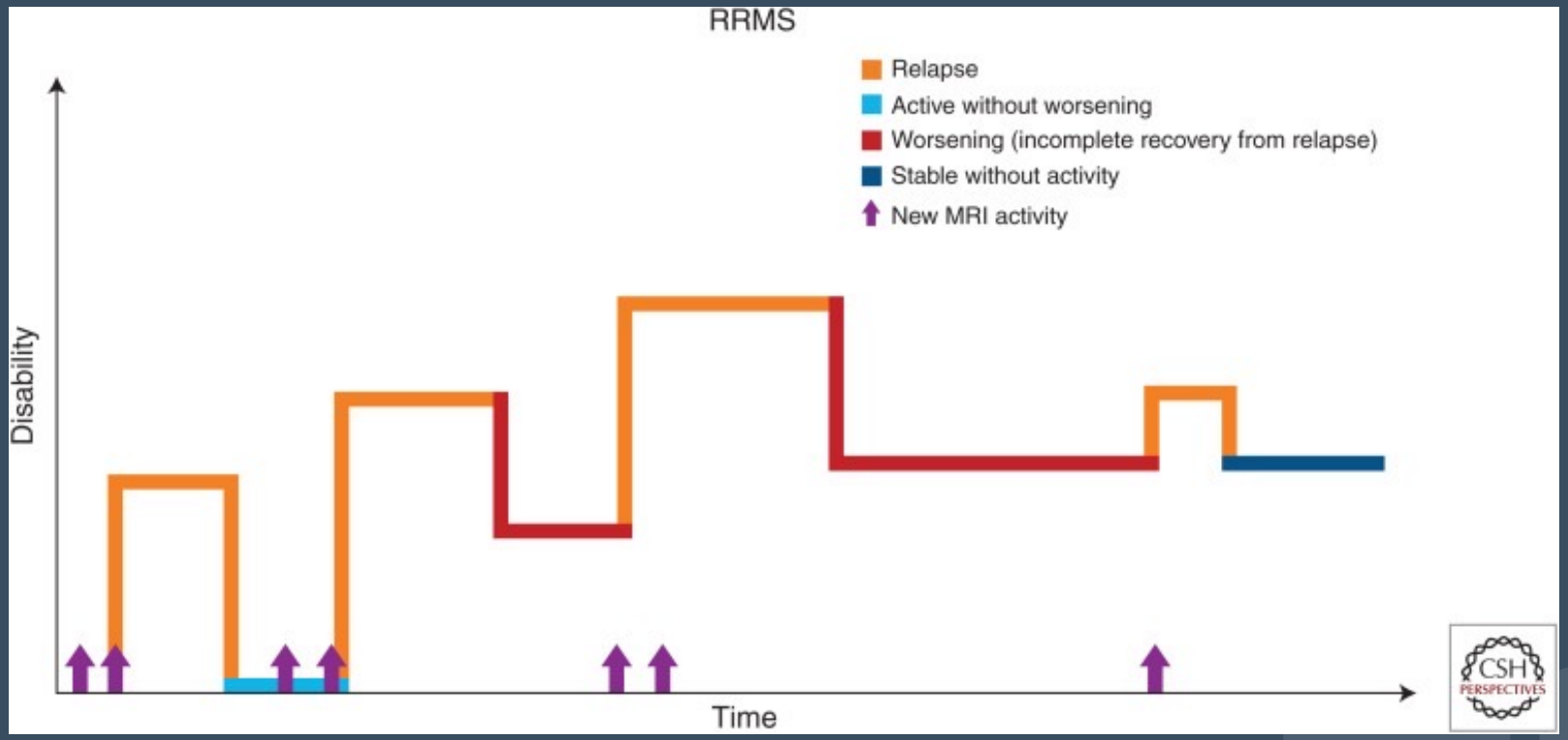
Acute Treatment

- High-dose intravenous methylprednisolone (IVMP) 1g daily 3-5 days
- +/- therapeutic plasma exchange (a.k.a: PLEX or apheresis)
  - IVIg is not usually utilized
- <u>Emphasize early treatment!</u>

Disability

Multiple Sclerosis disability is multifactorial
-- Relapses
-- Persistent inflammatory MRI activity
-- Neurodegeneration

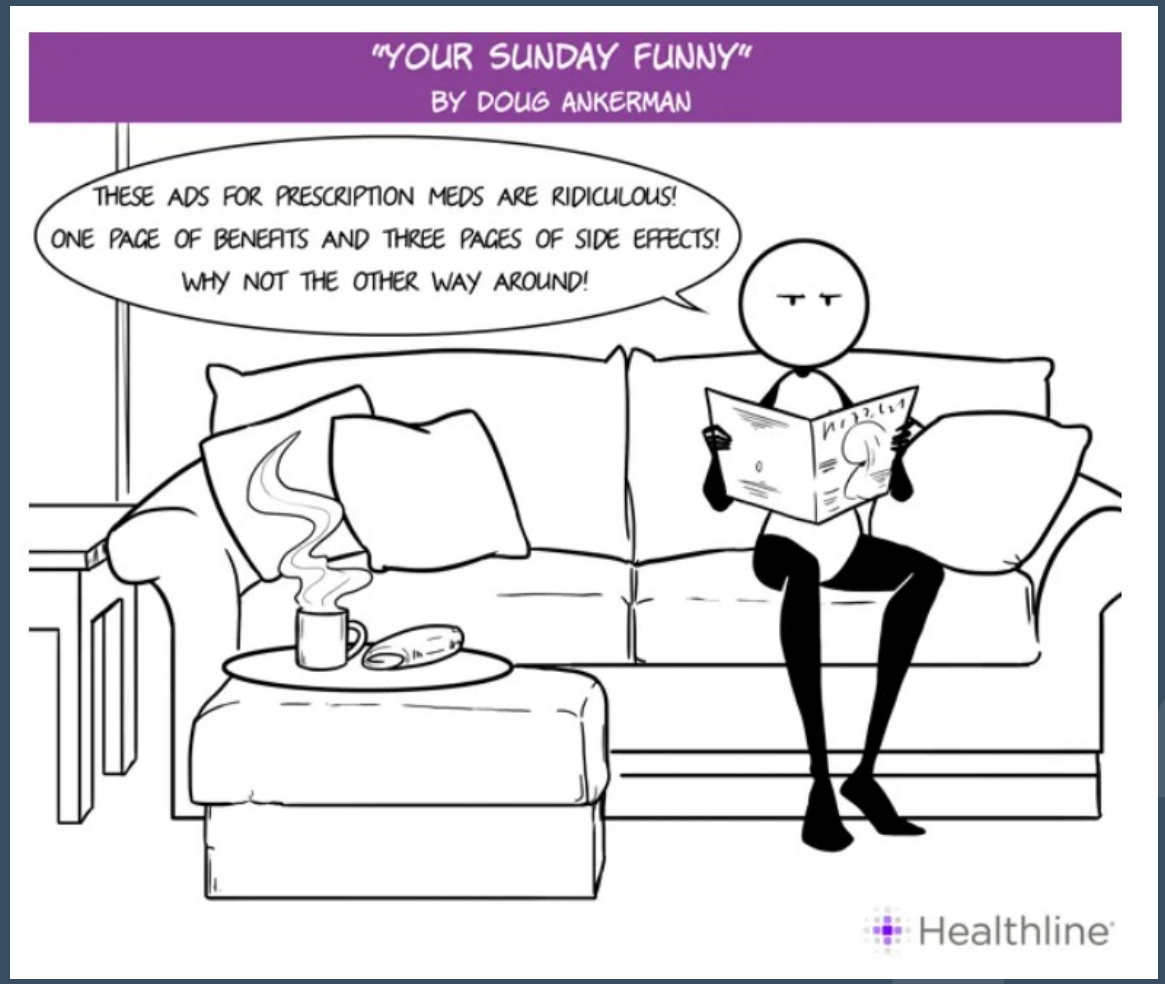
NMOSD Disability
-- INCOMPLETE RECOVERY FROM RELAPSE



National Multiple Sclerosis Society.

Long Term Treatment

- Prevention of relapses is essential in NMOSD
  - Long-term immunosuppression is vital

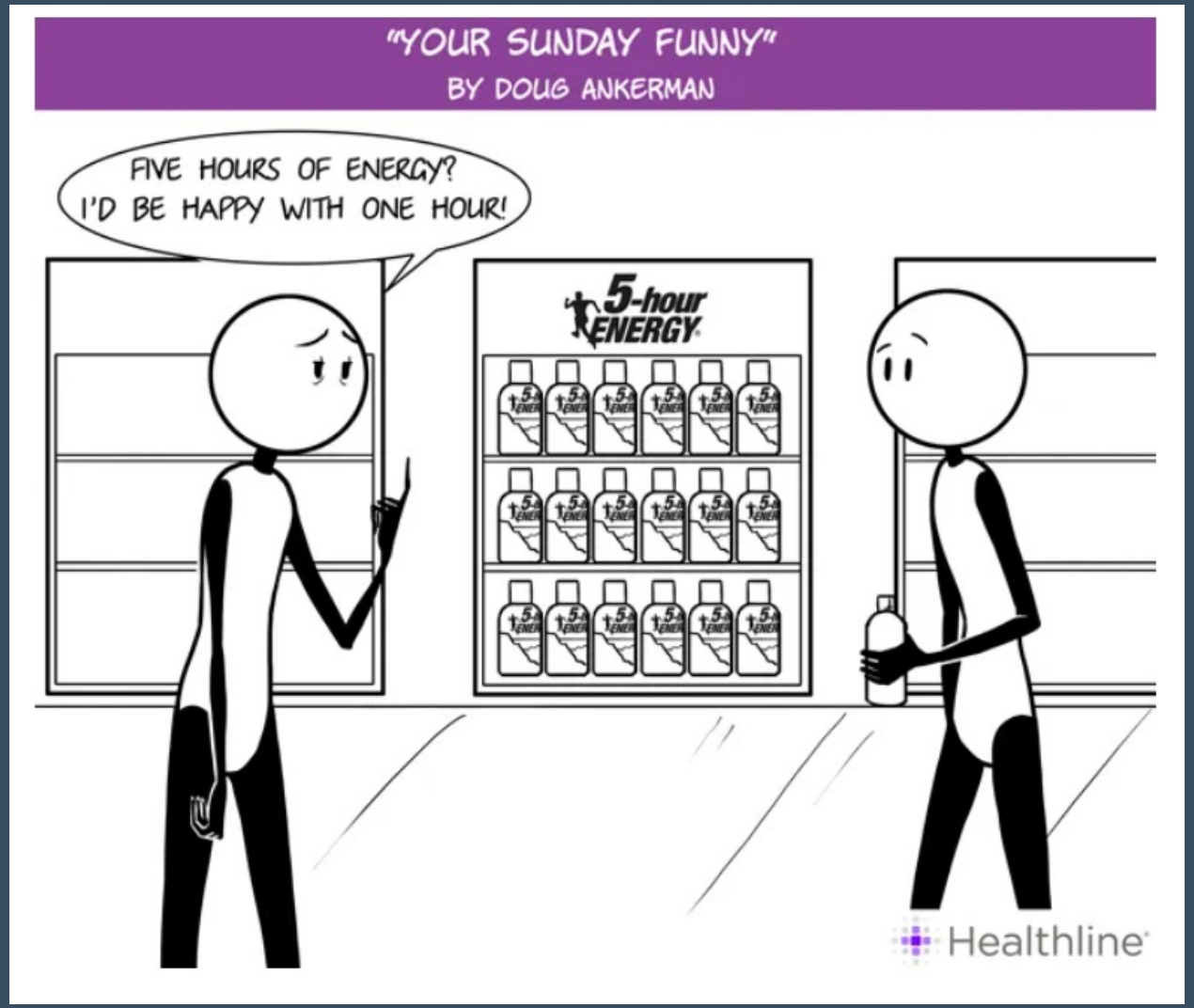


Intervention	Mechanism	Frequency of Dosing	Safety
Rituximab **Rituxan** (Off-label use)	Anti-CD20 (B cells)	Day 1 and day 15, then ever 6 months	- Infusion related reactions - Mild infections (URI, UTI) - Hypogammaglobulinemia
Inebilizumab Uplizna (FDA)	Anti-CD19 (B cells)	Day 1 and day 15, then ever 6 months	- Infusion related reactions - Mild infections (URI, UTI) - Hypogammaglobulinemia
Satralizumab Enspryng (FDA)	Anti-interleukin 6 (inflammatory marker)	Week 0, 2, 4, then Every 4 weeks	- URI - Nasopharyngitis - Headache
Eculizumab Soliris (FDA)	Anti-complement antibody (C5)	Weekly for 4 weeks, then every 2 weeks	- Meningococcal infections - URI - Nasopharyngitis

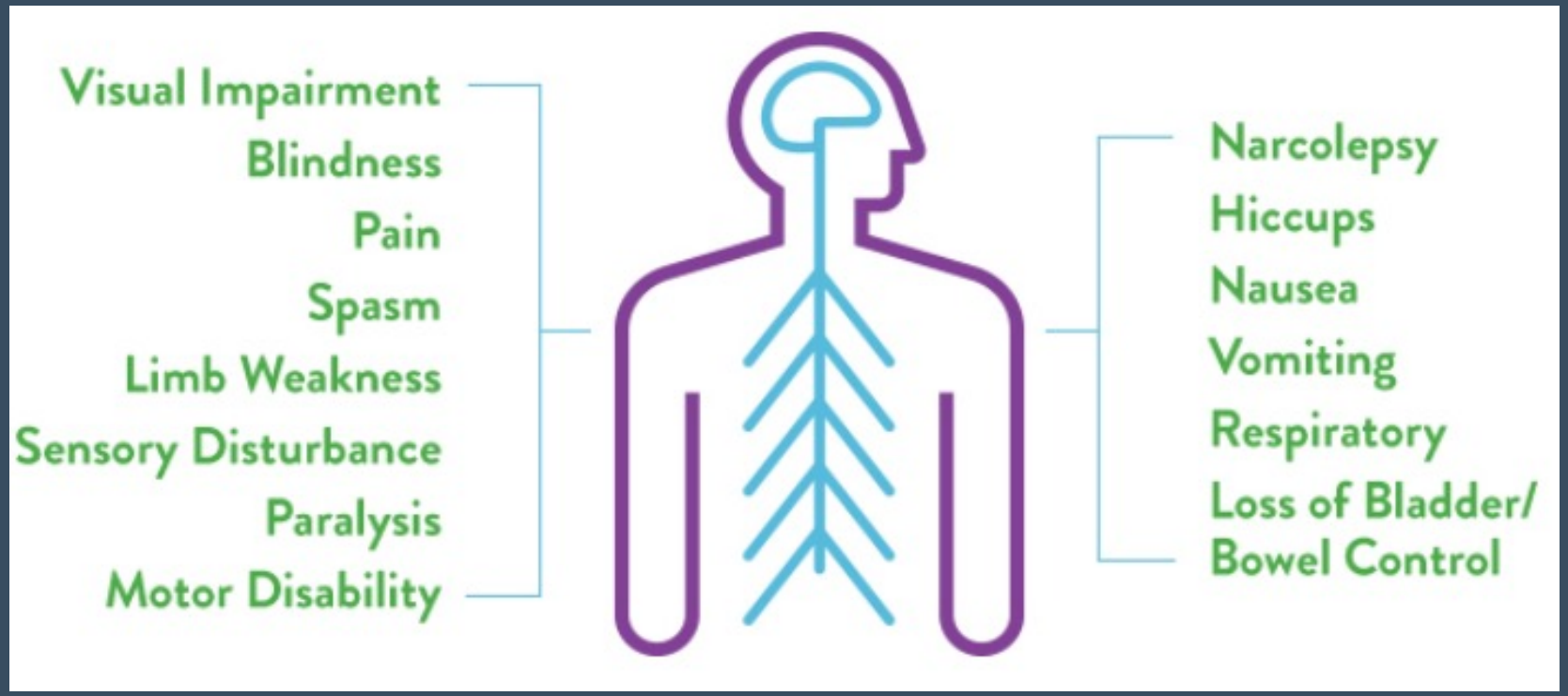
Other potential treatments..

Azathioprine (Imuran)	Guanosine nucleotide biosynthesis inhibition	Malignancy Infections Hepatotoxicity Myelosuppression, Gastrointestinal upset Hair thinning
Mycophenolate (Cellcept)	Inosine monophosphate dehydrogenase inhibition	Infections Myelosuppression Malignancy Gastrointestinal upset Peripheral edema Elevated blood pressure

Symptom Management



Symptom Management



https://www.uplizna.com/learn-about-nmosd/

A complex disease requires a comprehensive approach

- Involves the expertise of many different healthcare professionals including mental health professionals

Questions?