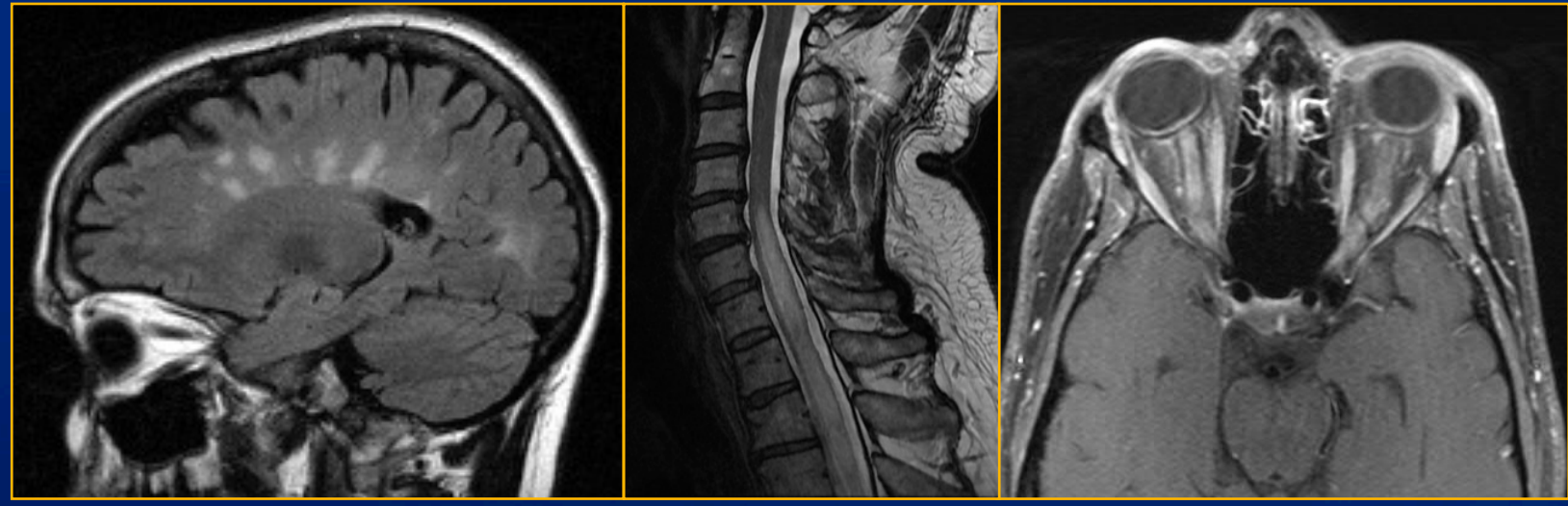
MAYO CLINIC



Management of vision after optic neuritis

John Chen, MD, PhD
Professor of Ophthalmology and Neurology
Mayo Clinic, Rochester, MN

Rare Neuroimmune Disorders Symposium
October 9, 2021

DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INDUSTRY

- Consultant to Roche and UCB

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

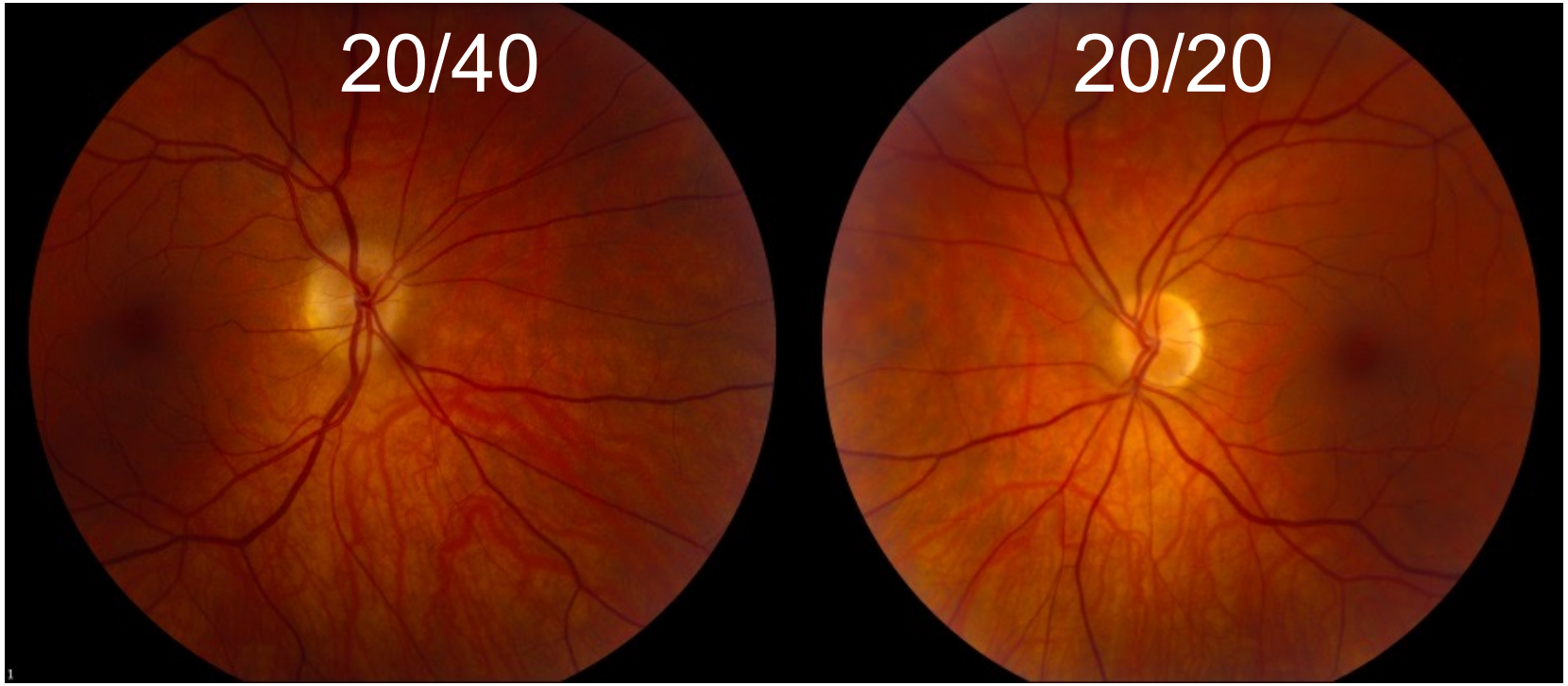
- None

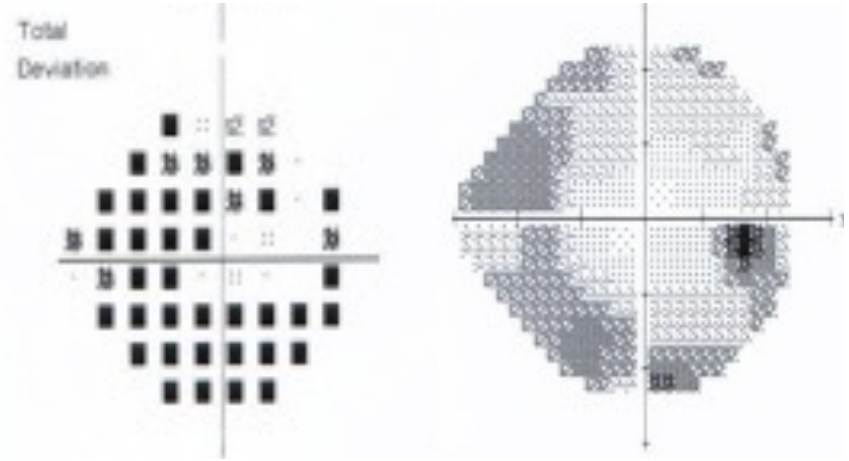
LEARNING OBJECTIVES

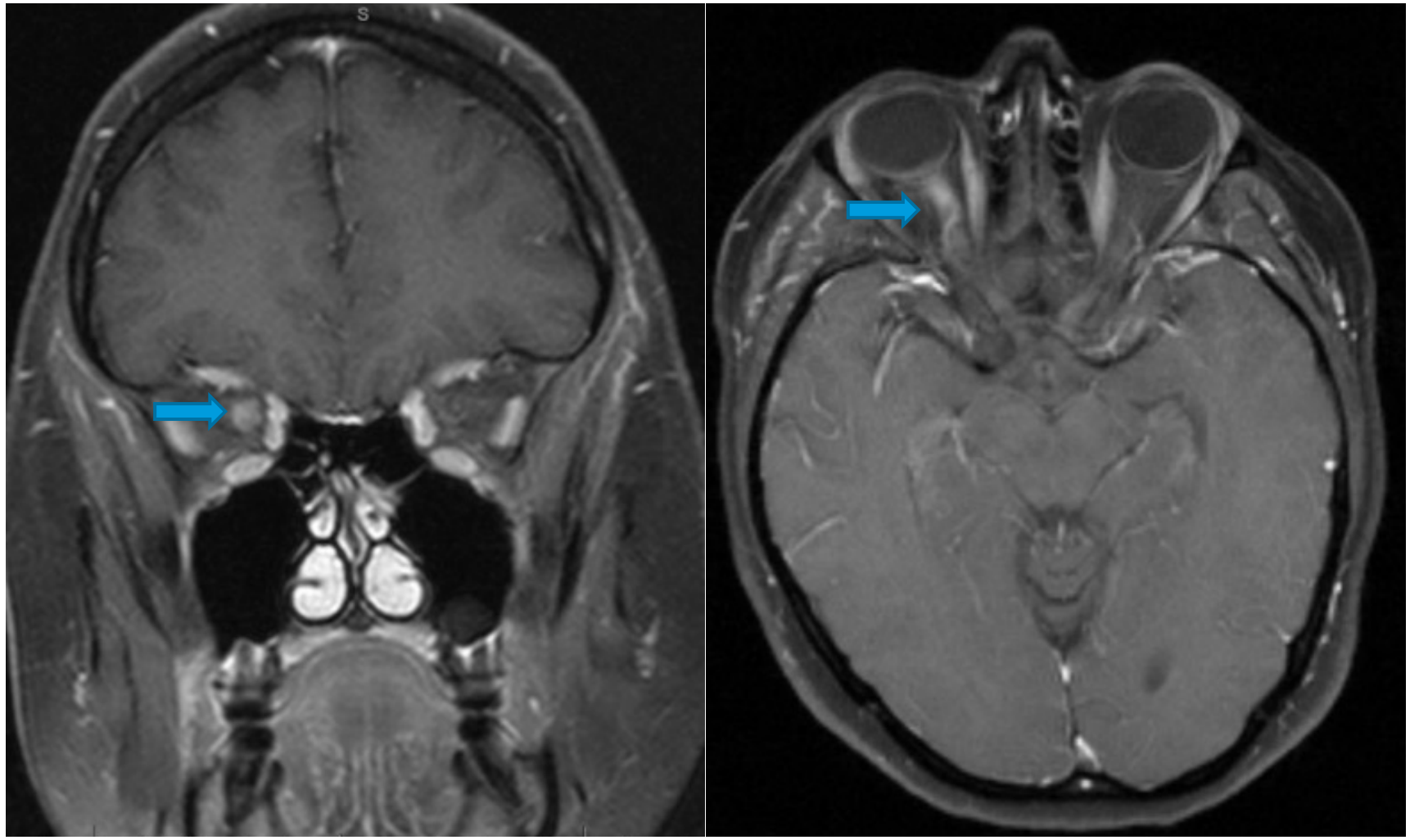
- Review how optic neuritis presents
- Discuss acute and chronic treatments for optic neuritis

A TYPICAL CASE OF OPTIC NEURITIS

- 34 year-old female developed blurred vision and pain in the right eye
  - Pain was worse with eye movements



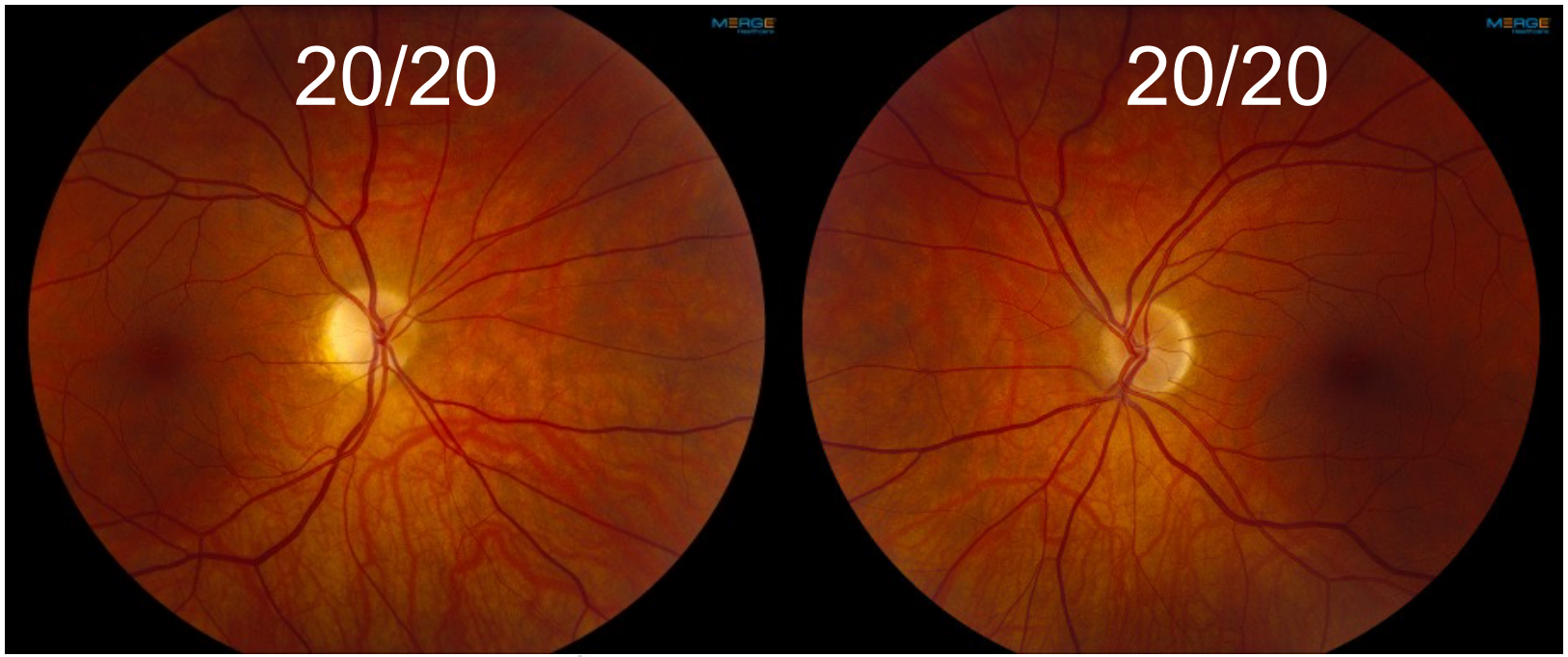


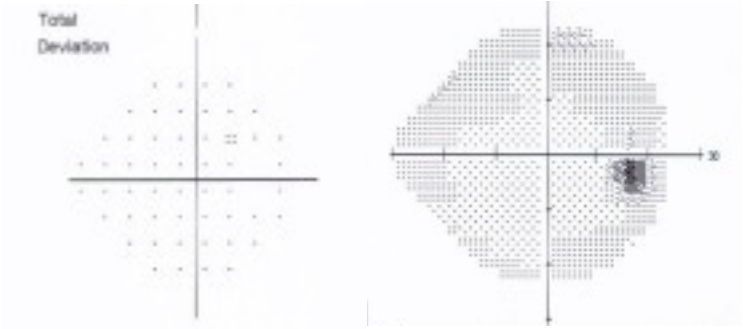


Enhancement of the right optic nerve confirming optic neuritis

The patient was treated with 5 days of IV steroids:
pain resolved and vision slowly improved over a month

3 MONTH FOLLOW-UP



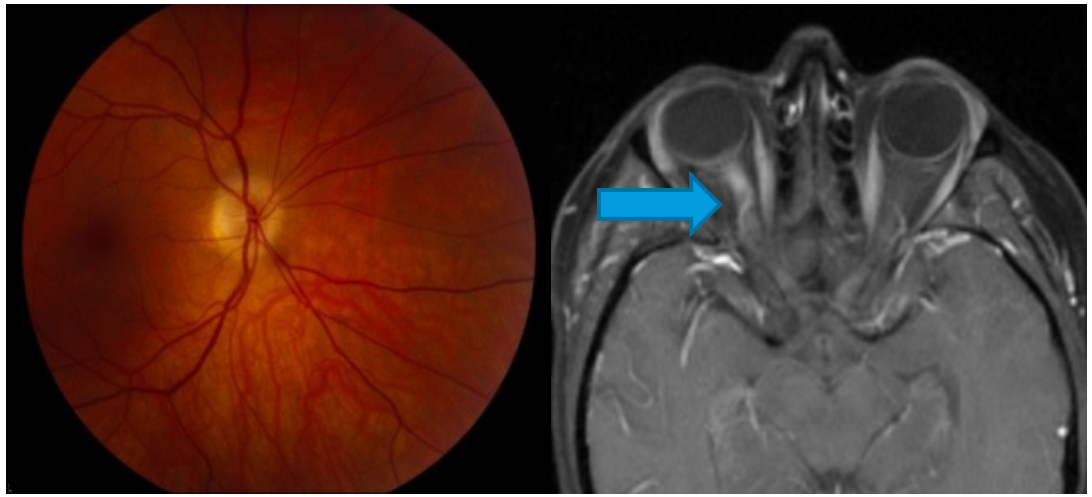


Recovery back to 20/20 with full visual fields, but residual paleness of the nerve

Per patient: “Vision is not the same and colors are more dull”

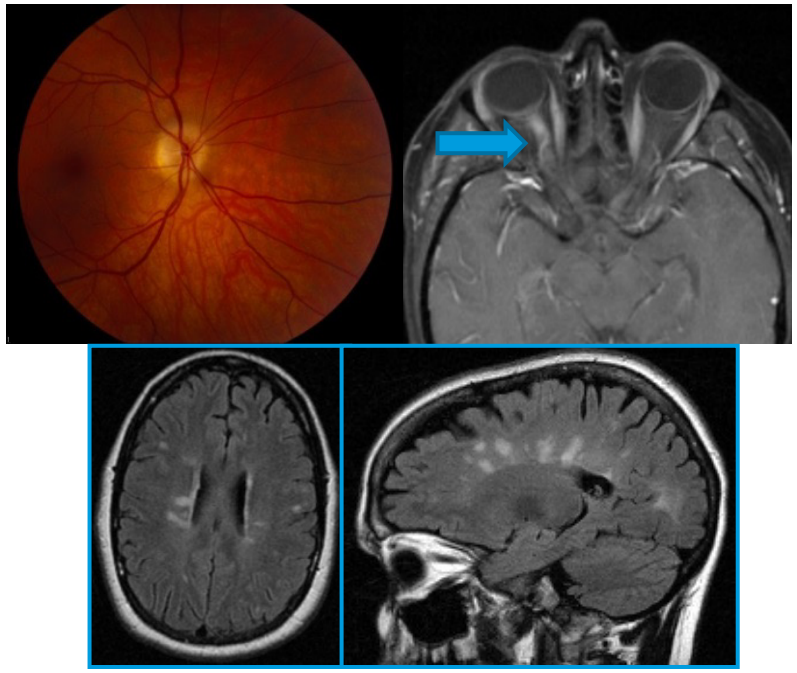
OPTIC NEURITIS

- Optic neuritis = inflammation of the optic nerve
- Most common cause of optic neuropathy in young patients (<50yo)
- Subacute monocular vision loss
  - 90% pain with eye movements
  - Dyschromatopsia
- 2/3 the disc is normal (retrobulbar optic neuritis)

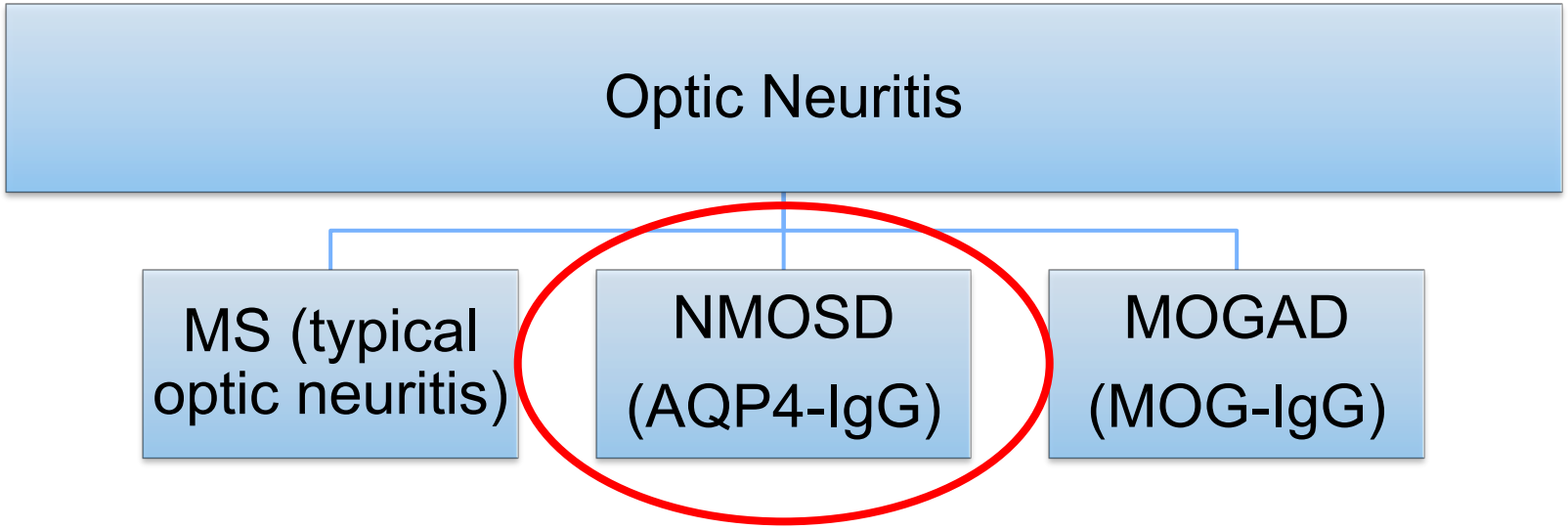


Multiple sclerosis = typical optic neuritis

- Young adult female
- Caucasians > black/asian
- Mild/moderate vision loss
- Good recovery
- 1/3 disc edema (mild)
- Periventricular lesions

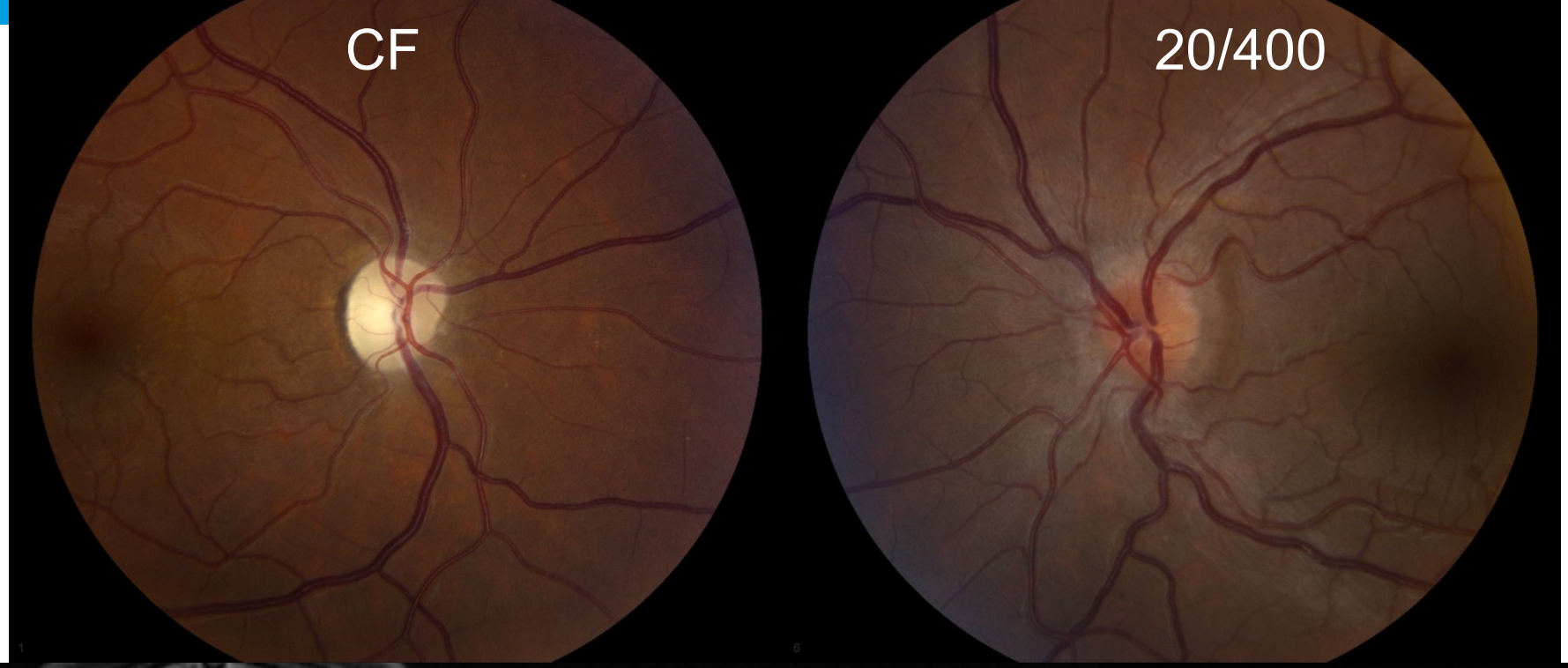


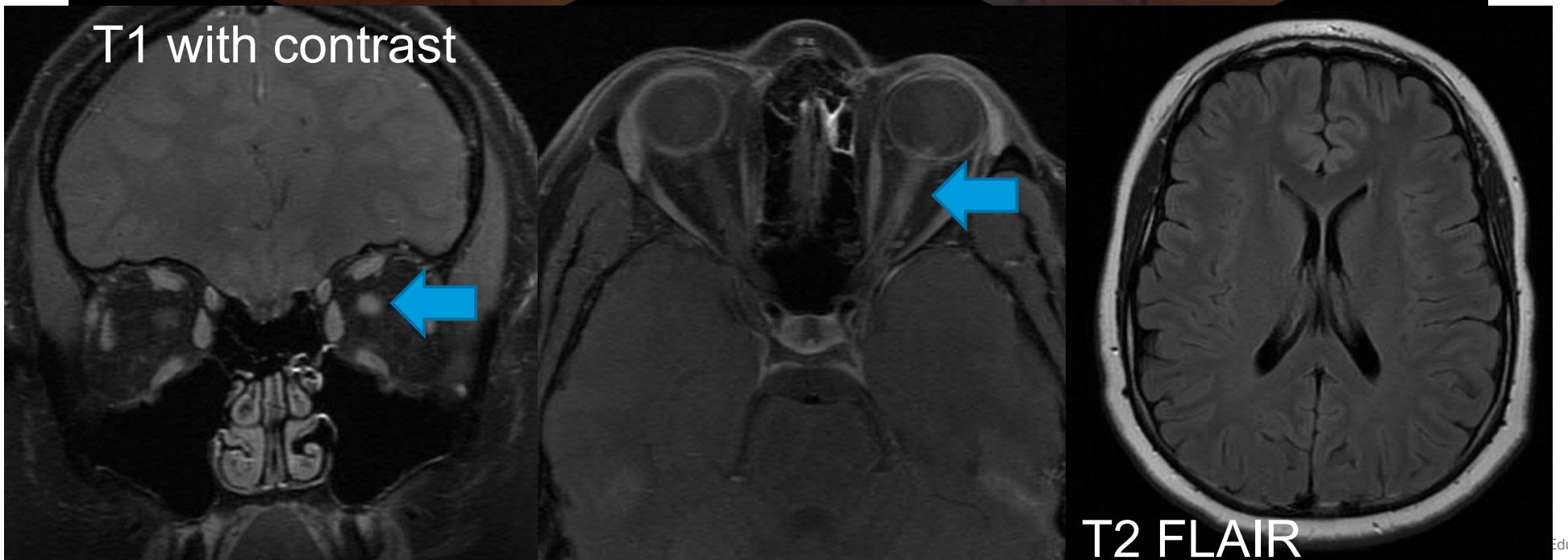
- 50% of patients with optic neuritis will develop MS
- Optic neuritis is the presenting symptom of MS in 25%
- In patients with MS, 50% will develop optic neuritis at some time point
- Only 3% 20/200 or worse



CLASSIC CASE OF NEUROMYELITIS OPTICA (NMO)

- 36yo African American female
  - Hx of optic neuritis in the right eye with poor recovery
  - Presents with vision loss in the left eye with eye pain
  - Also lower leg weakness and urinary incontinence

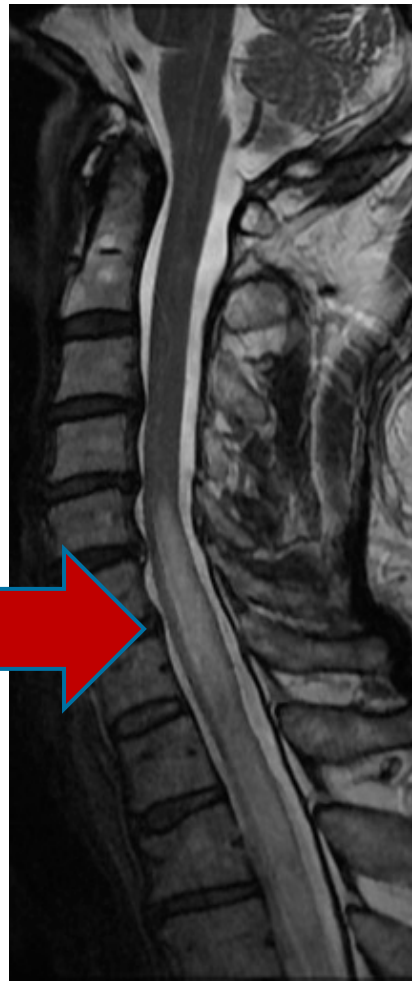

CF
20/400


T1 with contrast
T2 FLAIR

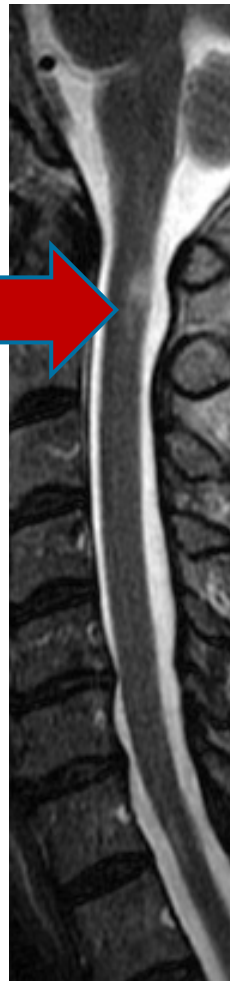
CLASSIC CASE OF NEUROMYELITIS OPTICA (NMO)

- Lower leg weakness and urinary incontinence
- AQP4-IgG (NMO ab) was positive
- Treated with IV steroids + PLEX
- Mild recovery to 20/200

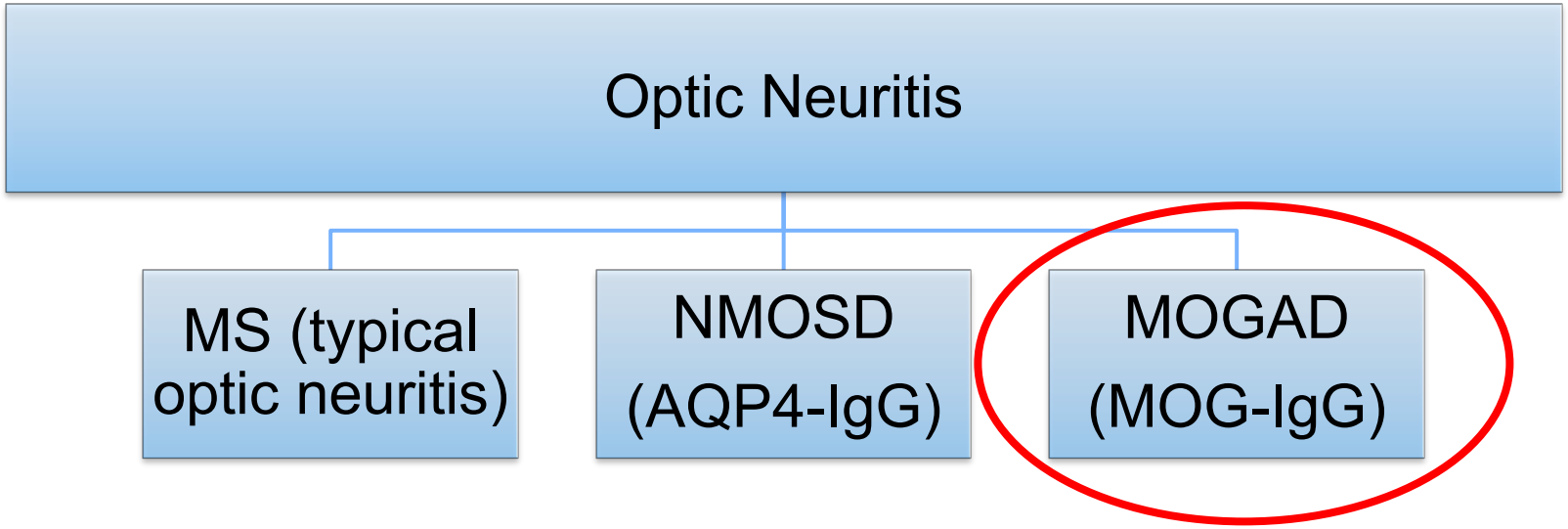
Longitudinally extensive transverse myelitis (>3 segments) *classic for NMO*



MS lesion

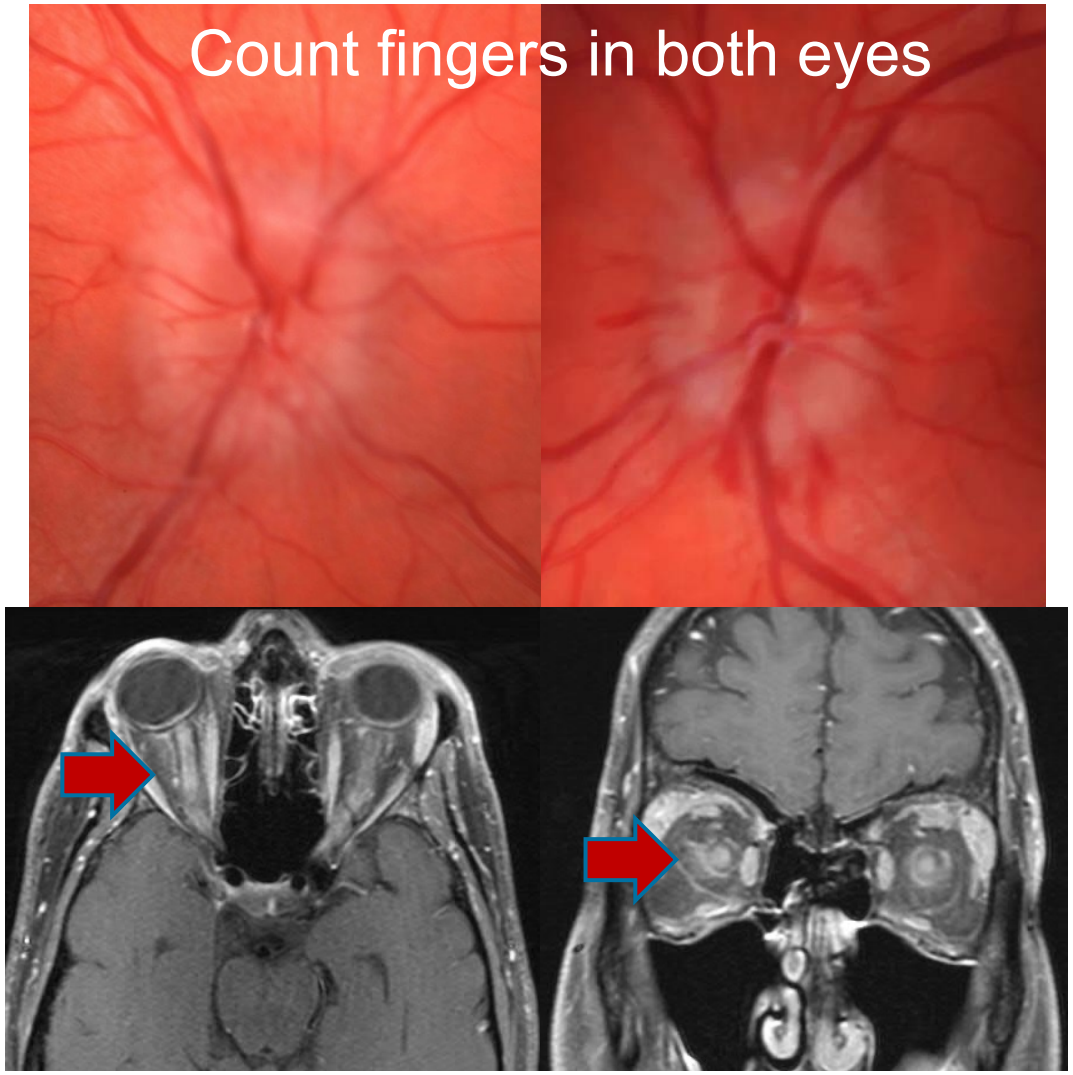


1/3 of optic neuritis attacks from NMO end up 20/200 or worse



CLASSIC CASE OF MOGAD OPTIC NEURITIS

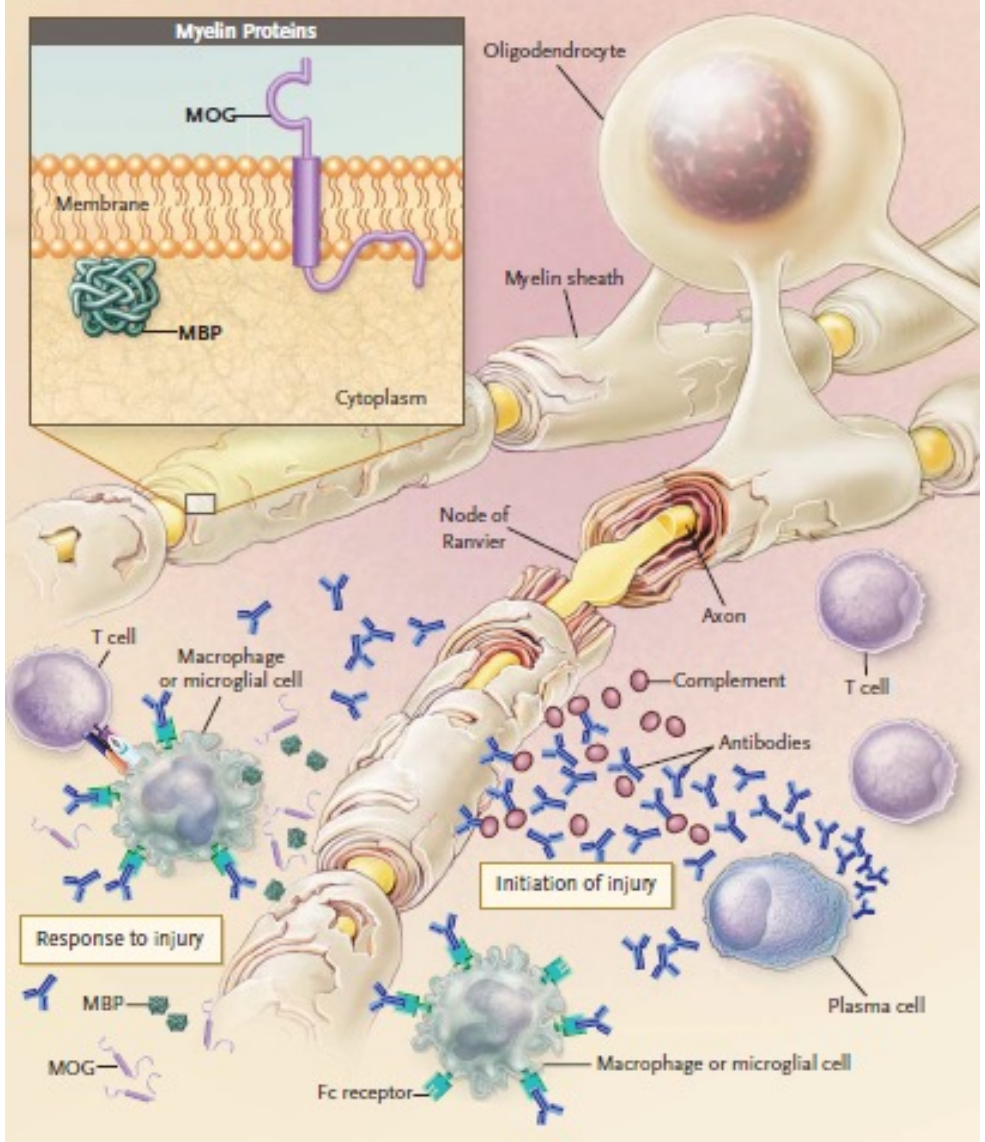
- 48yo male presented with blurred vision and pain in both eyes



CLASSIC CASE OF MOGAD OPTIC NEURITIS

- Treated 1 gm IV methylprednisolone x 5 days
  - Almost immediate recovery of vision
- Multiple relapses when tapered off prednisone
- Stabilized on azathioprine 100mg twice a day
- MOG-IgG was positive at 1:100

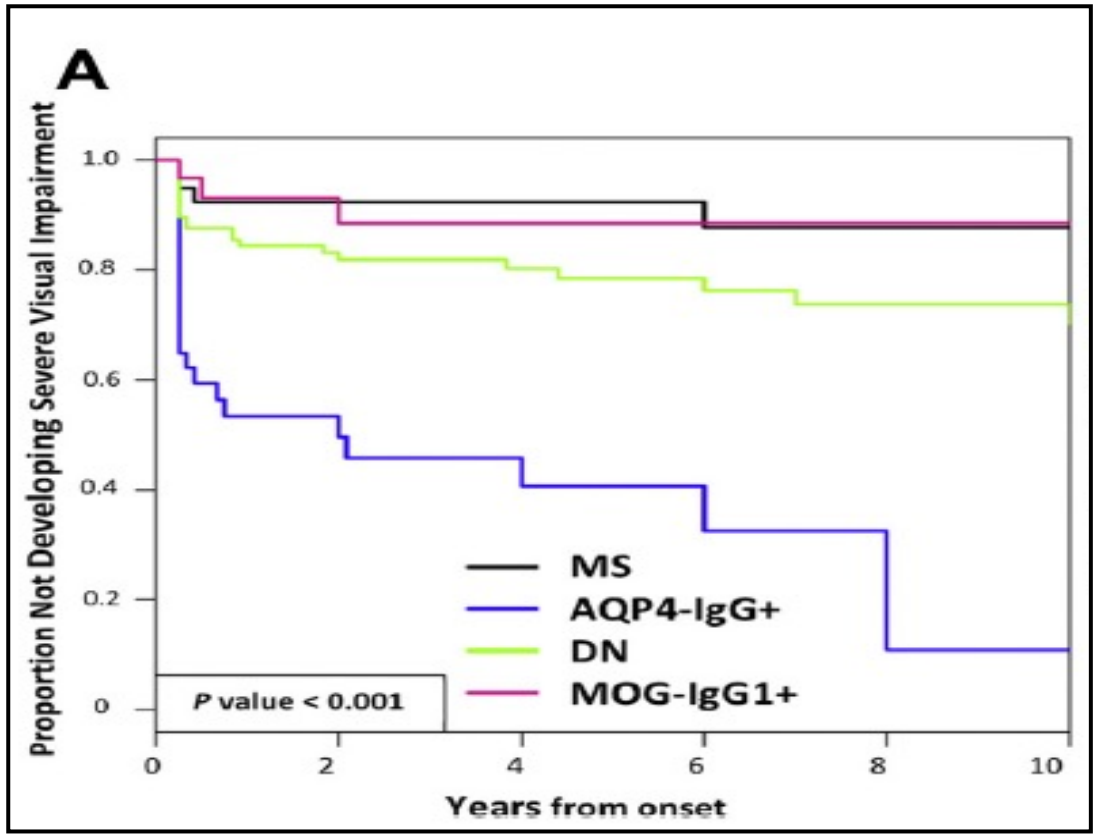
MYELIN OLIGODENDROCYTE GLYCOPROTEIN (MOG)



Antel et al. NEJM 2003

- MOG is a transmembrane protein found on the surface of oligodendrocytes and myelin
- Antibodies against MOG (MOG-IgG) are found in a distinct demyelinating disorder: MOG-IgG associated disease (MOGAD)
- MOG-IgG testing became commercially available in the US in October 2017 (Mayo FACS cell based assay)

MOGAD ON HAS SEVERE VISION LOSS AT ONSET, BUT RECOVERS MUCH BETTER THAN NMOSD

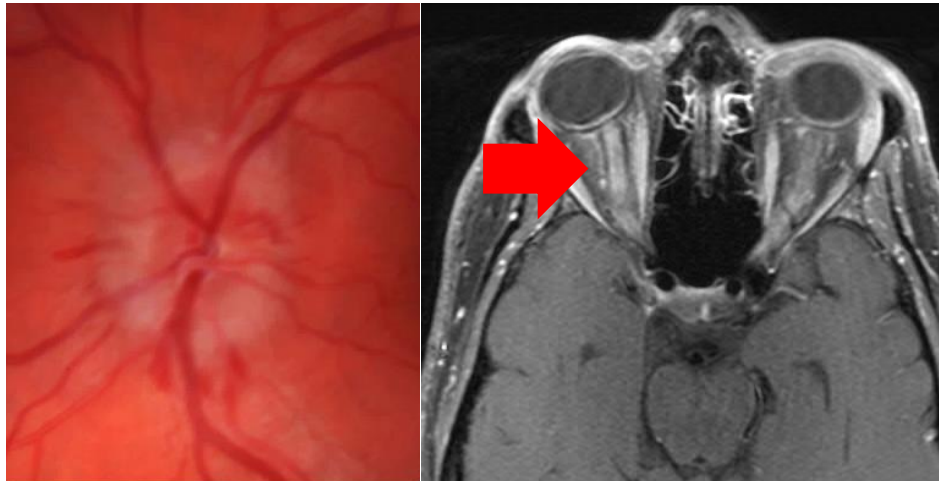


Jitprapaikulsan, Chen et al. Ophthalmology 2018

Only 6-10% ≤ 20/200 for MOGAD (vs 50% for AQP4-IgG NMO)

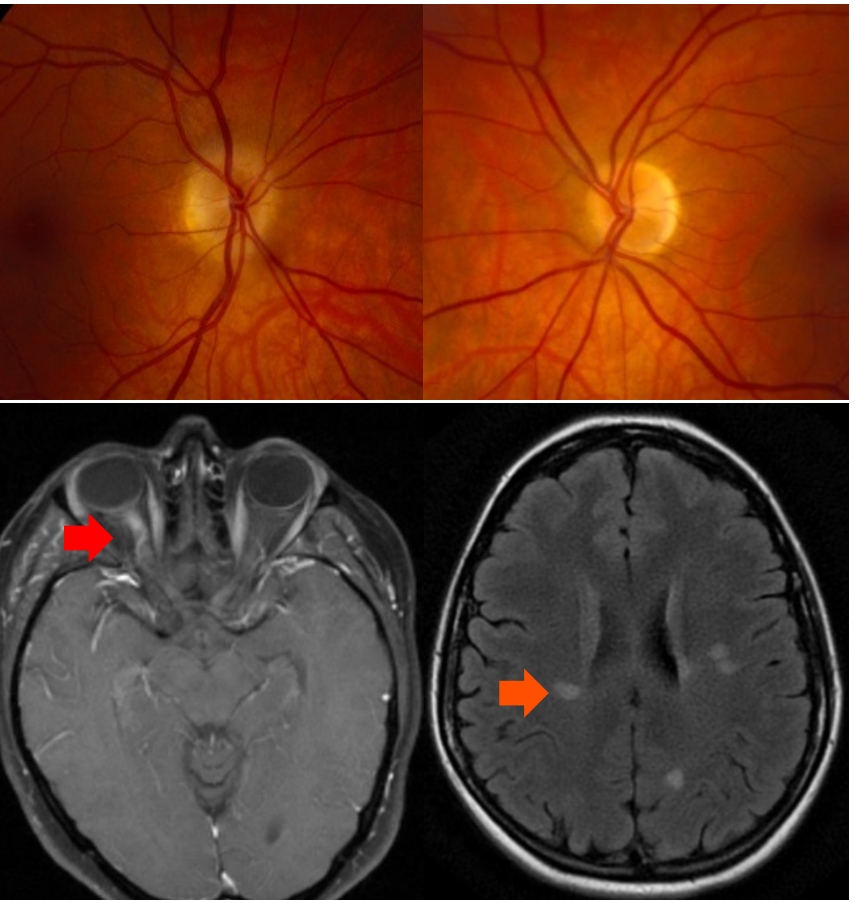
SUMMARY OF MOGAD OPTIC NEURITIS

- 50% bilateral
- 50% recurrent
- 89% painful
- 80% disc edema (swollen optic nerve)
- 50% perineural enhancement on MRI

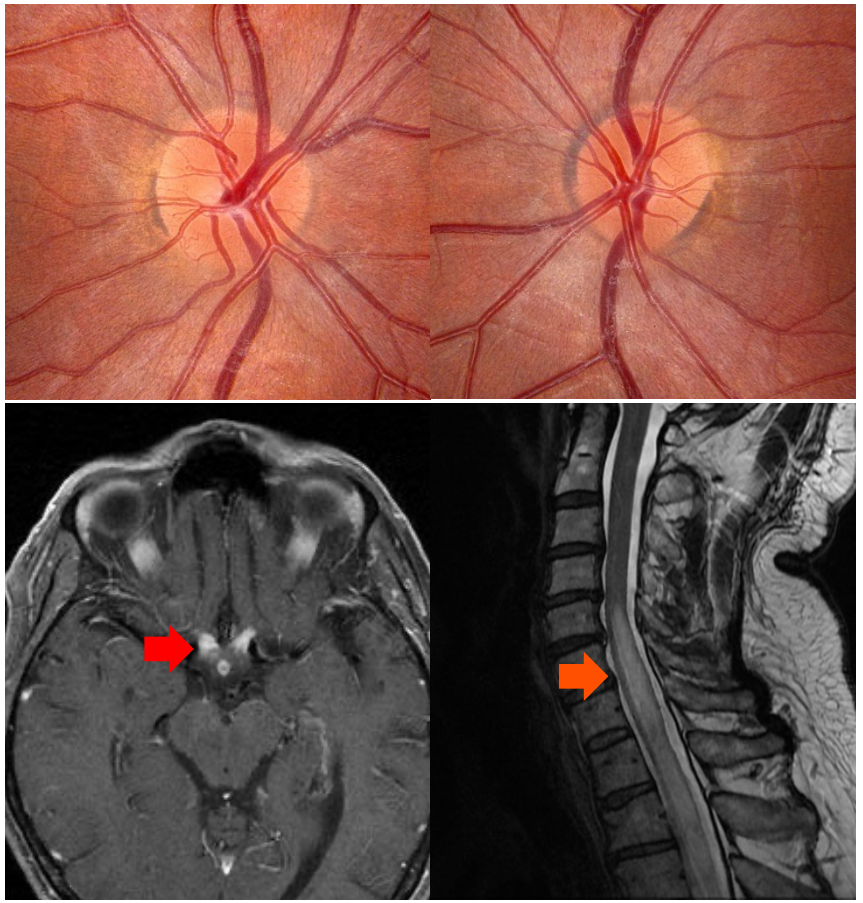


- Severe vision loss at onset
- Typically good recovery
  - ~6% 20/200 or worse

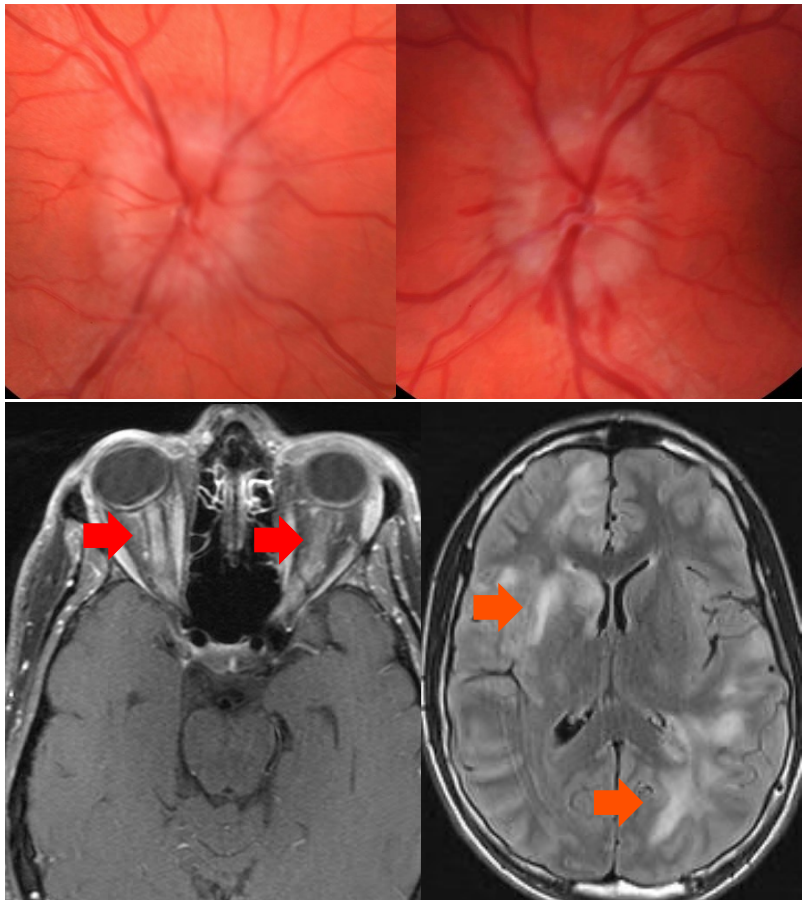
Multiple sclerosis



NMOSD



MOGAD



TREATMENT OF OPTIC NEURITIS

	Multiple sclerosis	NMOSD	MOGAD
Acute treatment	IV steroids quicken recovery	IV steroids + plasma exchange	IV steroids + oral prednisone for 1-3 months

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Outcome of legal blindness (20/200)	3%	Up to 50%	5-10%

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Acute treatment	IV steroids quicken recovery	IV steroids + plasma exchange	IV steroids + oral prednisone for 1-3 months
Outcome of legal blindness (20/200)	3%	Up to 50%	5-10%
Chronic treatment	MS disease modifying agent	All require chronic immunotherapy	Only patients with relapsing disease need chronic immunotherapy

VISUAL SEQUELAE FROM OPTIC NEURITIS

- Decrease visual acuity
- Decreased visual fields
- Decreased contrast
- Uhtoff’s phenomenon
- Pulfrich phenomenon

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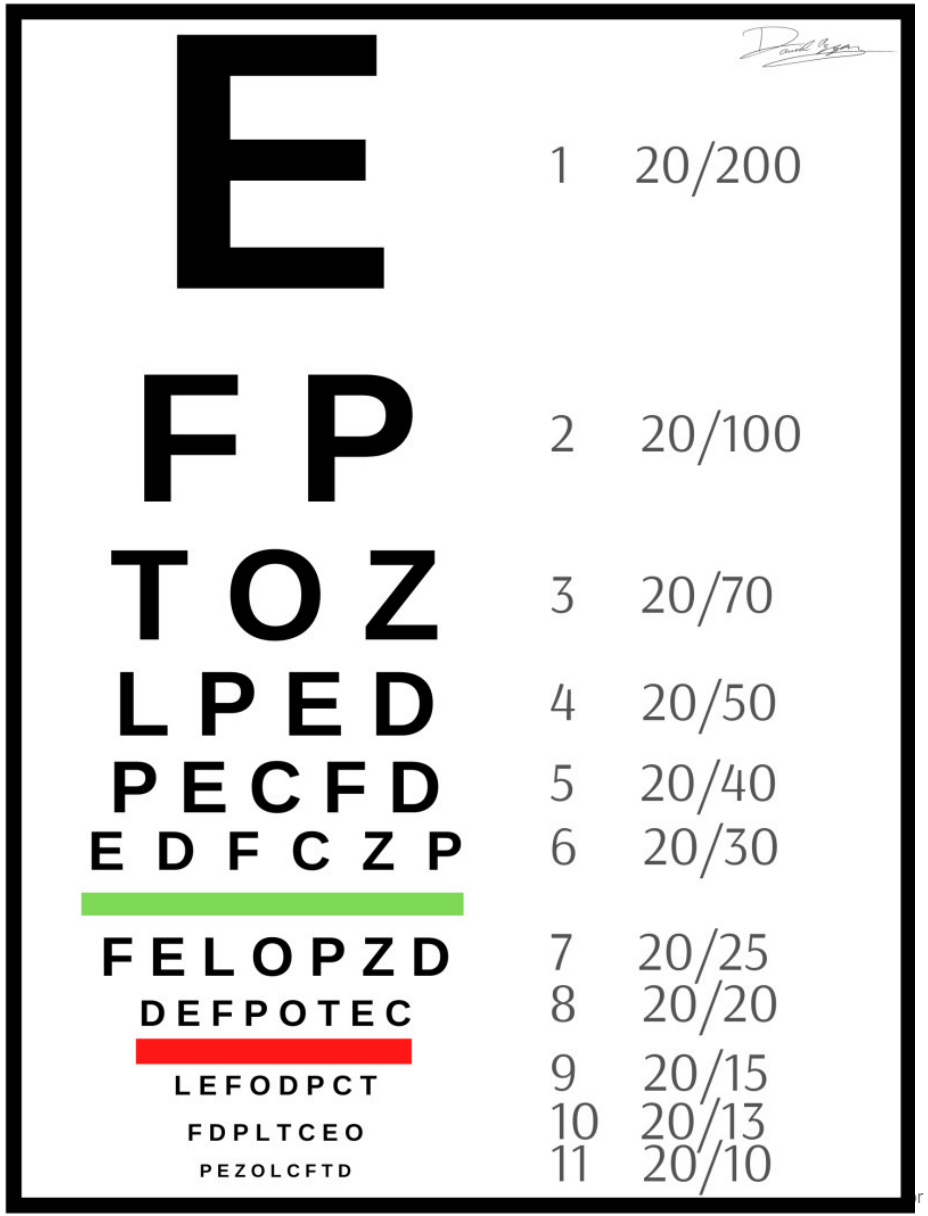

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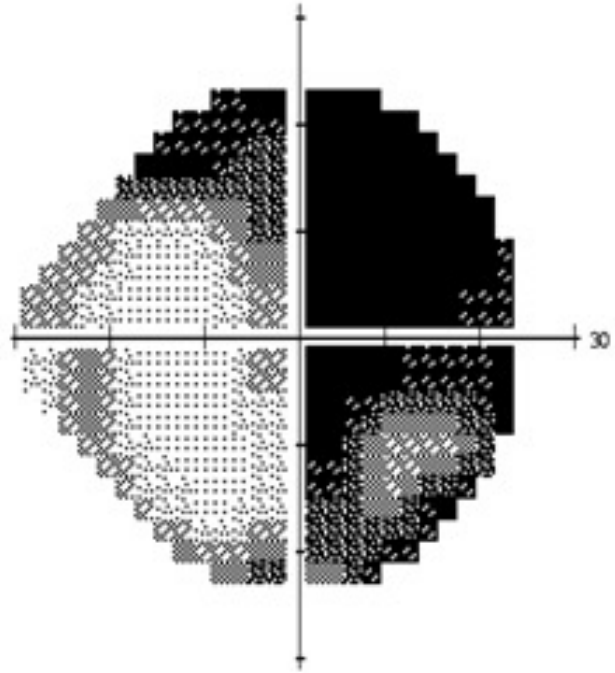

VISUAL SEQUELAE FROM OPTIC NEURITIS

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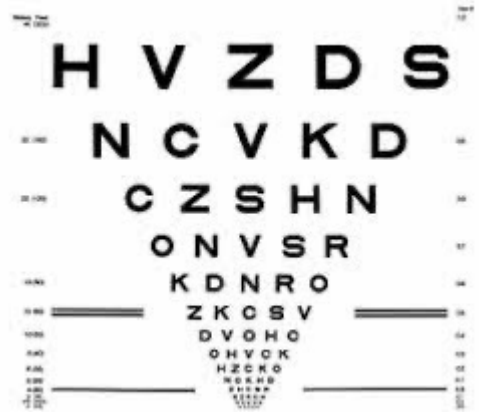

VISUAL SEQUELAE FROM OPTIC NEURITIS

- Decrease visual acuity
- Decreased visual fields
- Decreased contrast
- **Uhtoff's phenomenon:** Transient blurring of the vision with heat
- Pulfrich phenomenon

VISUAL SEQUELAE FROM OPTIC NEURITIS

- Decrease visual acuity
- Decreased visual fields
- Decreased contrast
- Uhtoff's phenomenon
- **Pulfrich phenomenon:** delay in conduction in one of the optic pathways causes a discrepancy in visual perception between the 2 eyes. Objects moving in a 2-D path are perceived to move in 3-D.

VISUAL SEQUELAE FROM OPTIC NEURITIS

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- Decreased visual fields
- Decreased contrast
- Uhtoff's phenomenon
- **Pulfrich phenomenon**

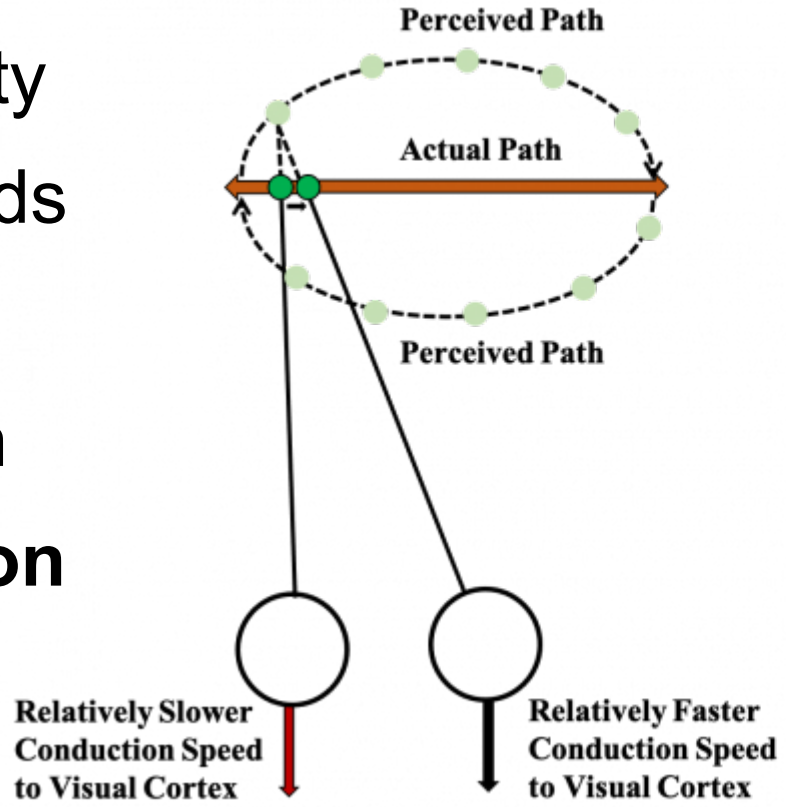

Figure courtesy of Peter Mortensen, Eyewiki

VISUAL SEQUELAE FROM OPTIC NEURITIS

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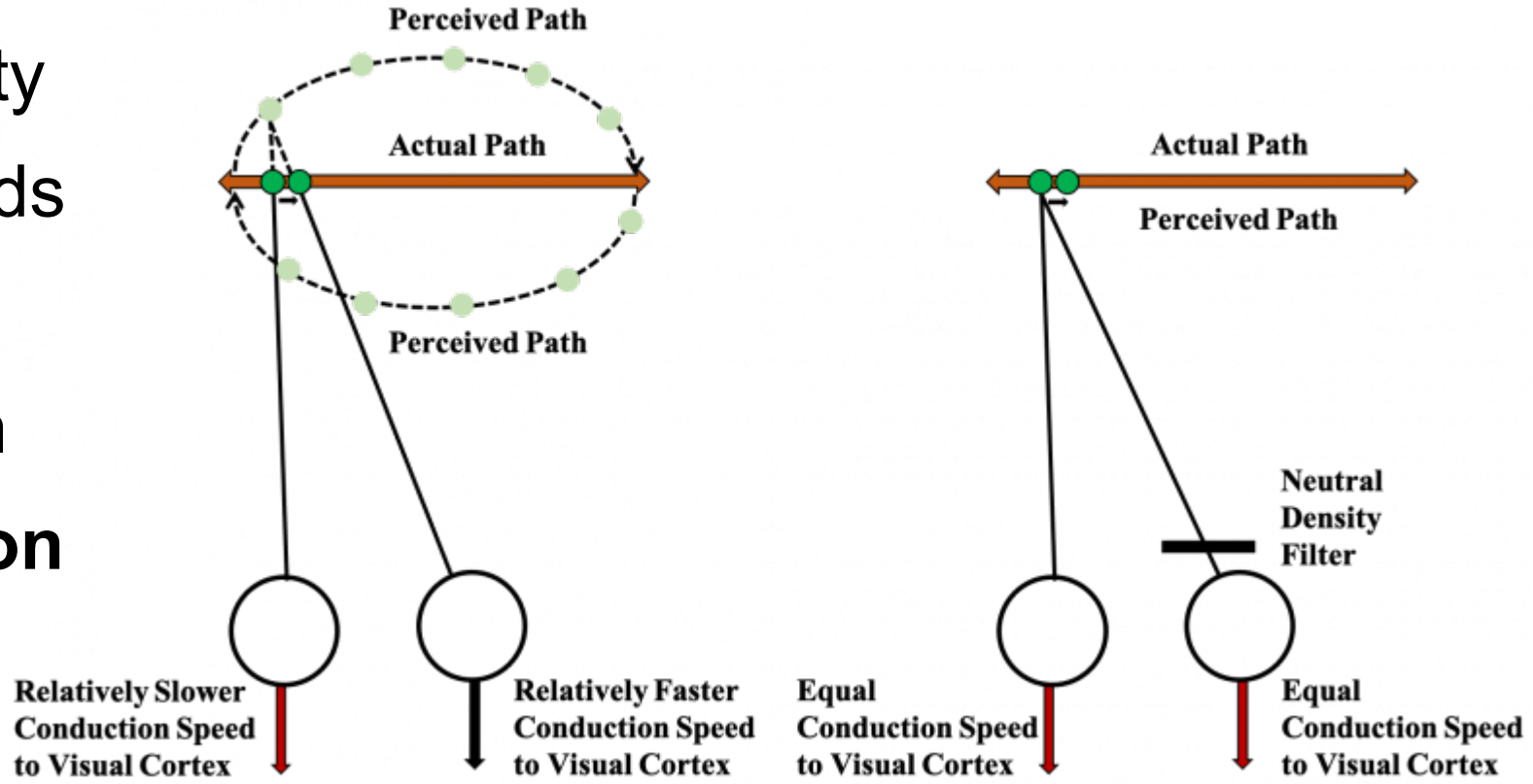


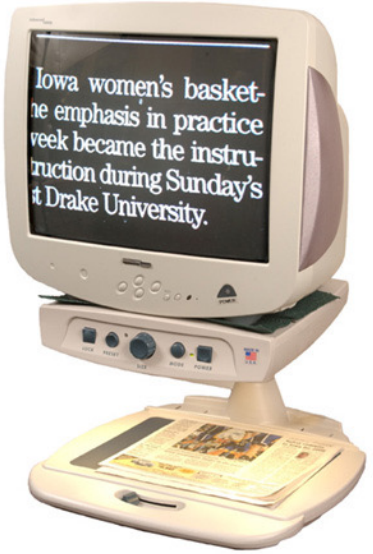
Figure courtesy of Peter Mortensen, Eyewiki

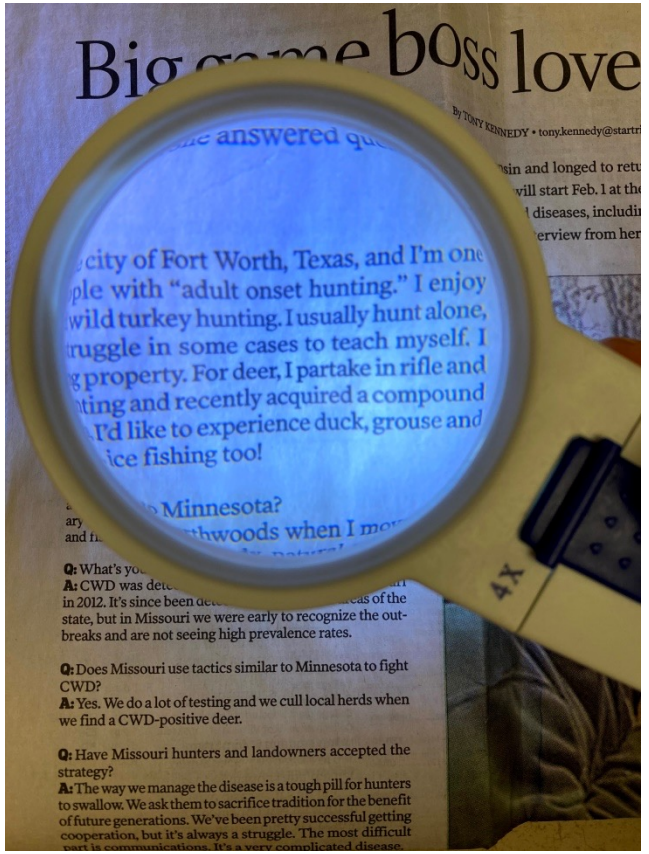
LOW VISION

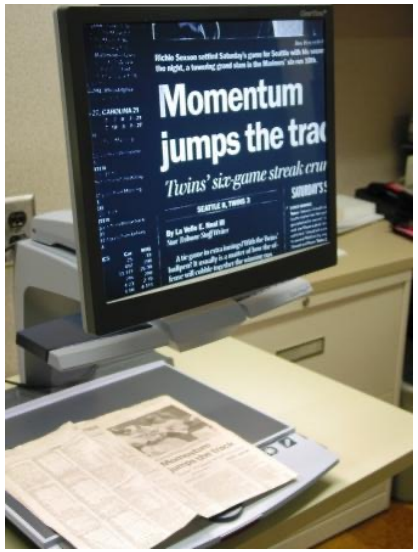
- State Services for the Blind
- Talking books, watch, IPAD

LOW VISION

- State Services for the Blind
- Talking books, watch, IPAD
- Low vision optometry



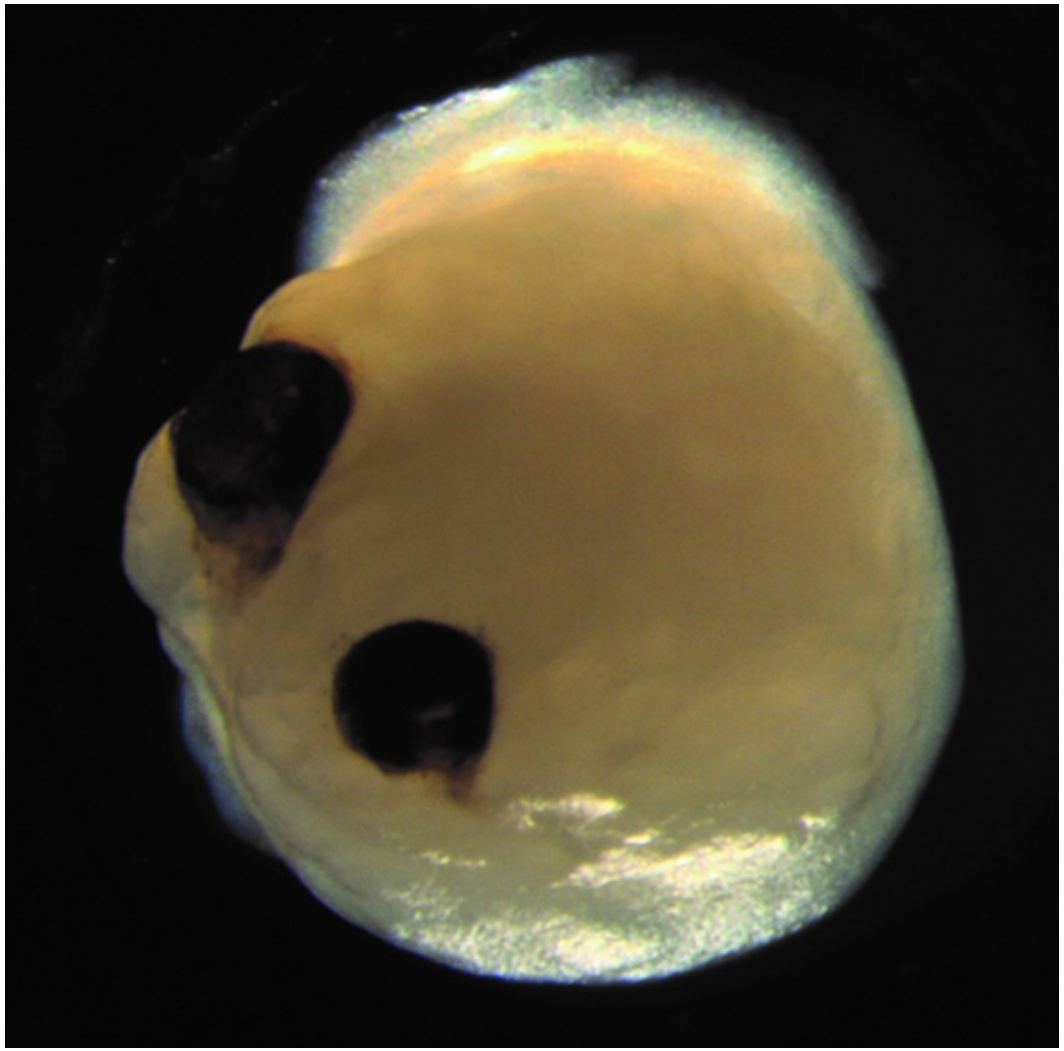




FUTURE OF VISION LOSS THERAPY

- **Stem cells**

Human induced pluripotent stem cells (iPSCs) can be used to generate brain organoids containing an eye structure called the optic cup

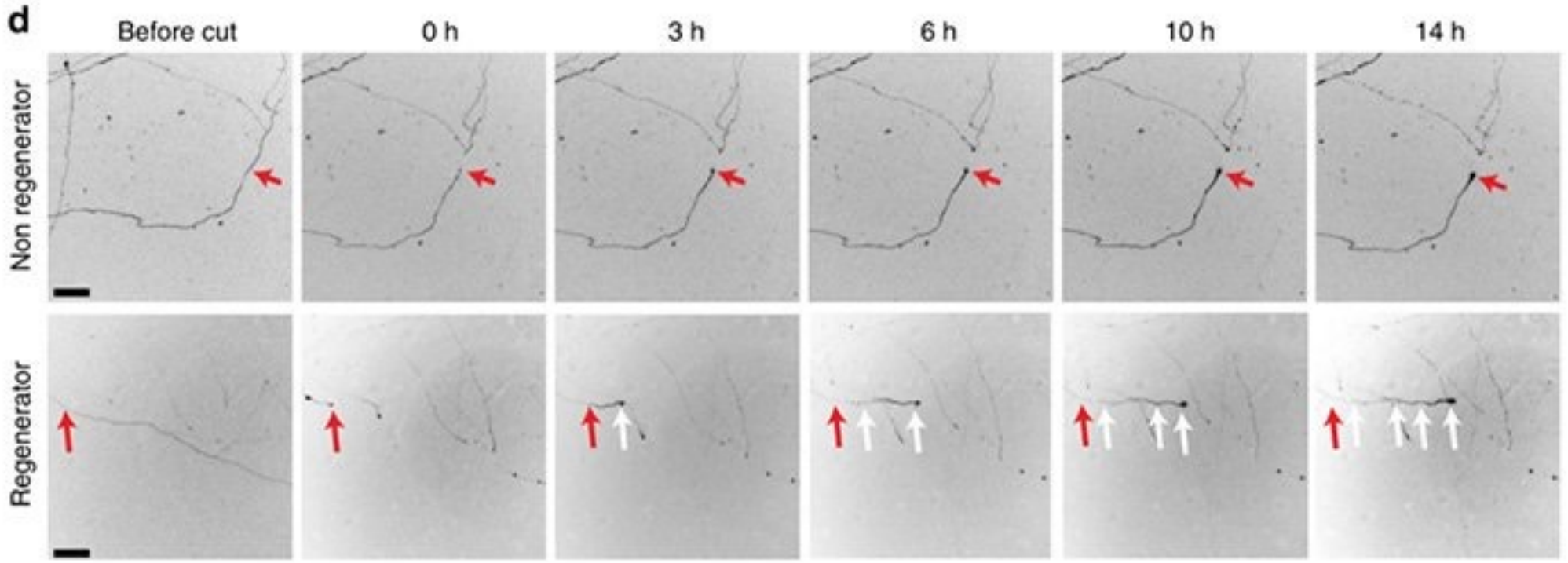


Gabriel, Elke, et al. "Human brain organoids assemble functionally integrated bilateral optic vesicles." *bioRxiv* (2021).

QUESTIONS & DISCUSSION

FUTURE OF VISION LOSS THERAPY

- Stem cells
- **Gene therapy**



Petrova et al, Nature Communications, 2020

Expressing protrudin led to more regeneration of a cut nerve

CHRONIC TREATMENT FOR MOGAD

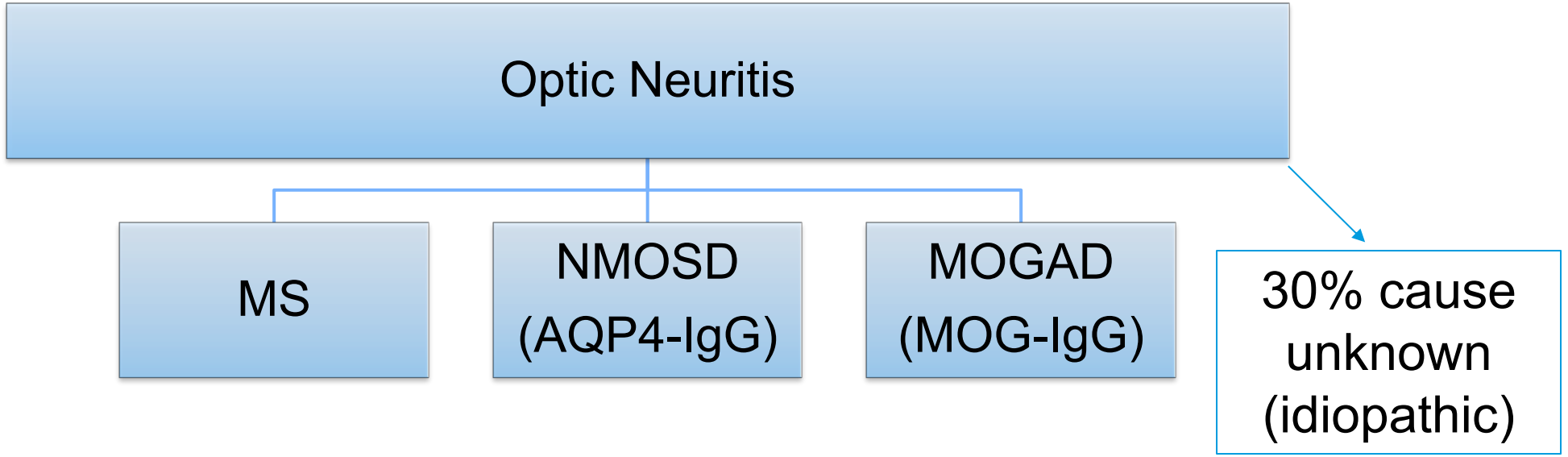
- For MOGAD relapsing disease
  - Our first line is typically rituximab or azathioprine +/- low dose maintenance PO prednisone
  - For severe relapsing disease that breaks through, we will use monthly IVIG

Steroid-sparing maintenance immunotherapy for MOG-IgG associated disorder

John J. Chen, MD, PhD, Eoin P. Flanagan, MB, BCh, M. Tariq Bhatti, MD, Jiraporn Jitprapaikulsan, MD, Divyanshu Dubey, MBBS, Alfonso (Sebastian) S. Lopez Chiriboga, MD, James P. Fryer, MS, Brian G. Weinshenker, MD, Andrew McKeon, MB, BCh, MD, Jan-Mendelt Tillema, MD, Vanda A. Lennon, MD, PhD, Claudia F. Lucchinetti, MD, Amy Kunchok, MBBS, MMED, Collin M. McClelland, MD, Michael S. Lee, MD, Jeffrey L. Bennett, MD, PhD, Victoria S. Pelak, MD, Gregory Van Stavern, MD, Ore-Ofe O. Adesina, MD, Eric R. Eggenberger, DO, Marie D. Acierno, MD, Dean M. Wingerchuk, MD, Byron L. Lam, MD, Heather Moss, MD, PhD, Shannon Beres, MD, Aubrey L. Gilbert, MD, Veeral Shah, MD, PhD, Grayson Armstrong, MD, MPH, Gena Heidary, MD, PhD, Dean M. Cestari, MD, Hadas Stiebel-Kalish, MD, and Sean J. Pittock, MD

Correspondence
Dr. Chen
Chen.john@mayo.edu

Neurology® 2020;95:1-10. doi:10.1212/WNL.0000000000009758



HOW COMMON IS MOGAD AND NMOSD IN OPTIC NEURITIS?

- Population-based incidence of optic neuritis in Olmsted County in 1985 was 5.1 per 100,000
  - 52% were from MS, 48% were idiopathic
  - This study was done before the knowledge of AQP4-IgG and MOG-IgG

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  - 52% were from MS, 48% were idiopathic
  - This study was done before the knowledge of AQP4-IgG and MOG-IgG
- Given these new biomarkers, we did an updated incidence study from 2000-2018

Population-Based Incidence of Optic Neuritis in the Era of Aquaporin-4 and Myelin Oligodendrocyte Glycoprotein Antibodies

  - 57% were from MS, 31% were idiopathic
  - 5% MOGAD, 3% AQP4-IgG NMOSD, 1% seronegative NMOSD

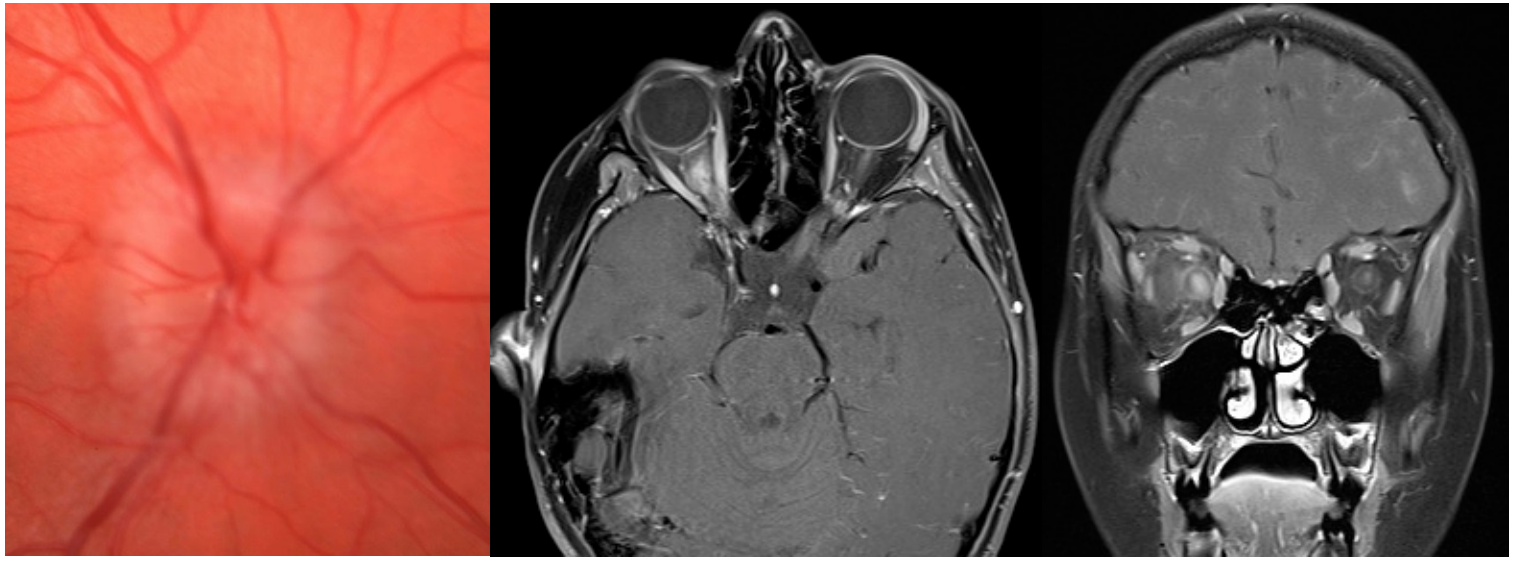
9% of optic neuritis is either NMOSD or MOGAD

WHEN TO TEST FOR AQP4-IGG AND MOG-IGG?

- Consider for any optic neuritis unless classic MS

WHEN TO TEST FOR AQP4-IGG AND MOG-IGG?

- Consider for any optic neuritis unless classic MS
- Required for any atypical optic neuritis
  - Severe vision loss, bilateral and/or recurrent optic neuritis, prominent disc edema, long segment of enhancement, enhancement of optic nerve sheath or chiasm



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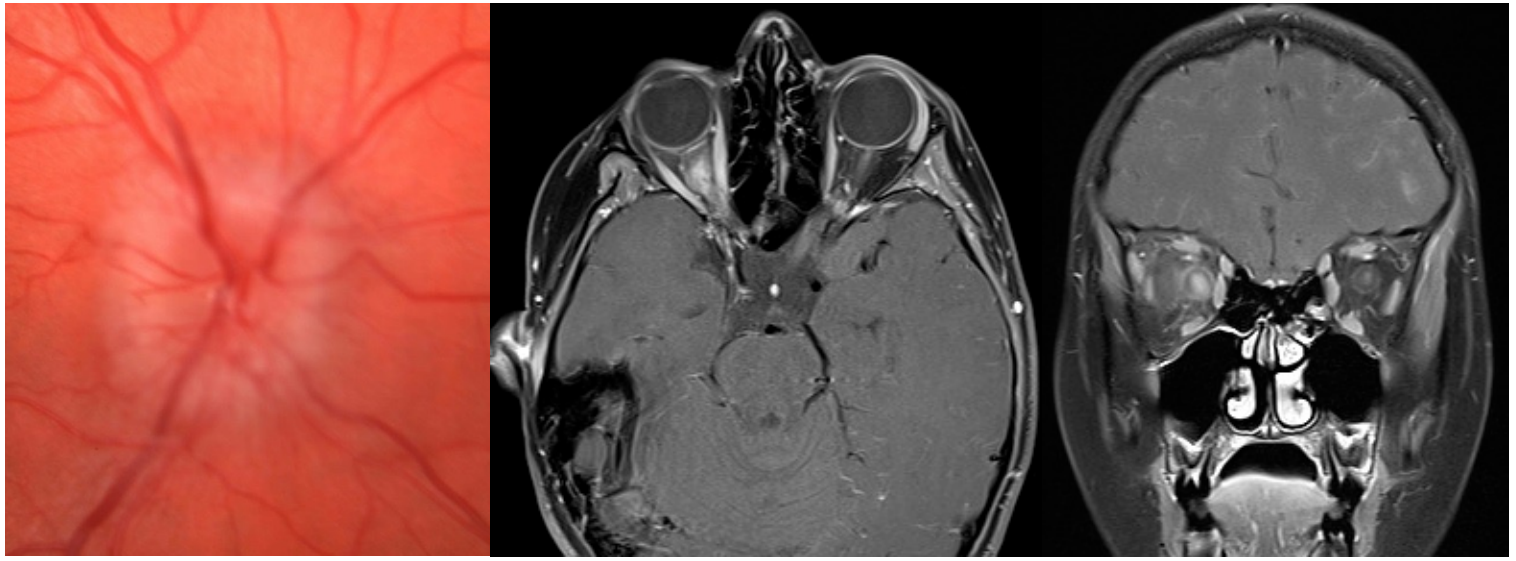
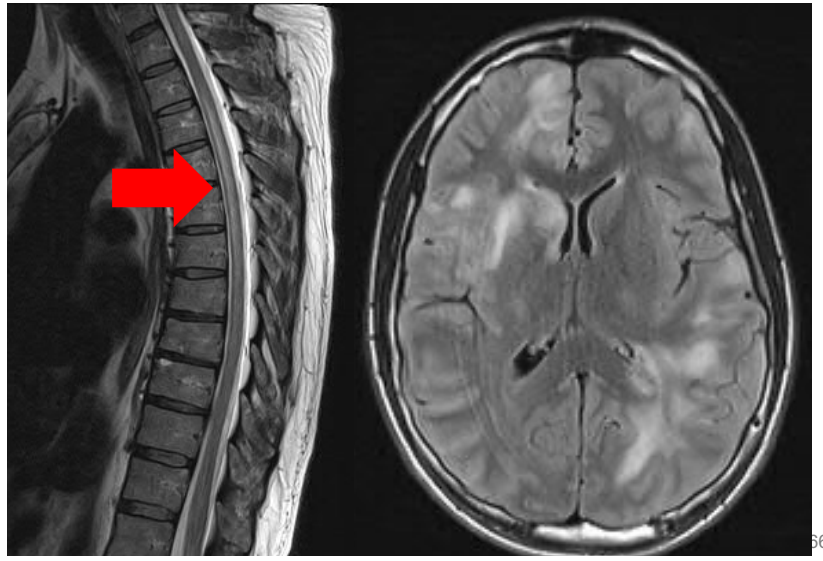
  - ADEM, long transverse myelitis, area postrema, atypical MS





Multiple sclerosis

- Young adult female
- Caucasians > black/asian
- Mild/moderate vision loss
- Good recovery
- 1/3 disc edema (mild)
- Short enhancement
- Short transverse myelitis
- Periventricular lesions

AQP4-IgG NMOSD

- Middle-aged adult female
- Black/asian > Caucasian
- Severe vision loss at onset
- Poor recovery
- <1/3 disc edema
- Optic chiasm
- Long transverse myelitis
- Area postrema

MOGAD

- Any age/sex + children
- Any race
- Severe vision loss at onset
- Good recovery
- 80% disc edema, 50% OU
- Perineural enhancement
- Long transverse myelitis
- ADEM

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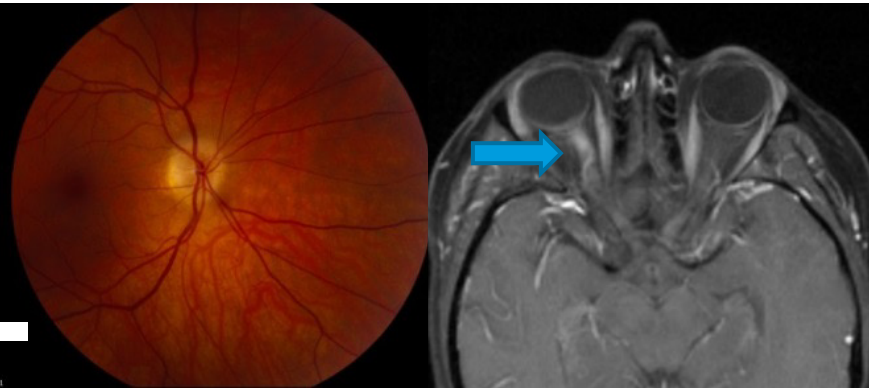

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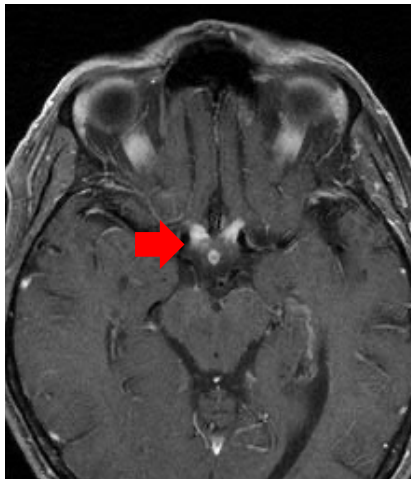
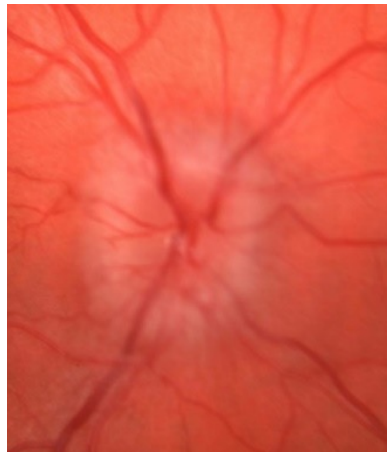
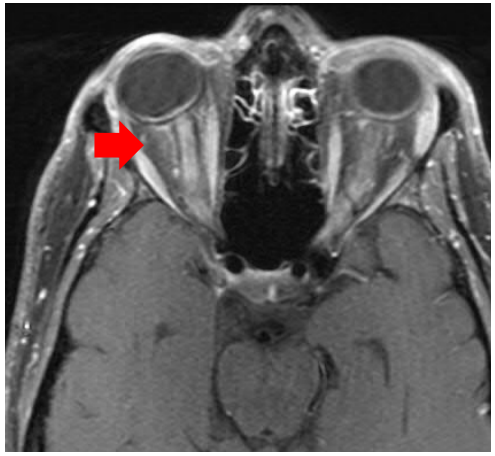
- Middle-aged adult female
- Black/asian > Caucasian
- Severe vision loss at onset
- Poor recovery
- <1/3 disc edema
- Isolated optic chiasm
- Long transverse myelitis
- Area postrema



MOGAD

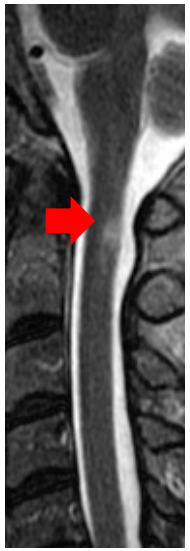
- Any age/sex + children
- Any race
- Severe vision loss at onset
- Good recovery
- 80% disc edema, 50% OU
- Perineural enhancement
- Long transverse myelitis
- ADEM





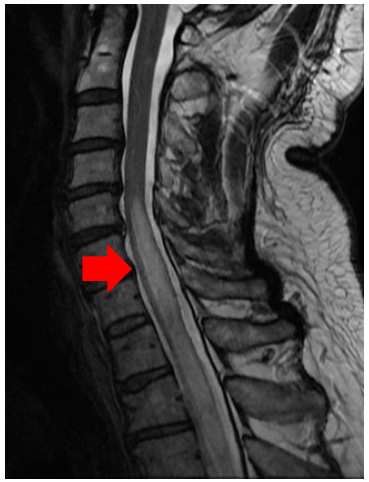
Multiple sclerosis

- Young adult female
- Caucasians > black/asian
- Mild/moderate vision loss
- Good recovery
- 1/3 disc edema (mild)
- Short enhancement
- Short transverse myelitis
- Periventricular lesions



AQP4-IgG NMOSD

- Middle-aged adult female
- Black/asian > Caucasian
- Severe vision loss at onset
- Poor recovery
- <1/3 disc edema
- Optic chiasm
- Long transverse myelitis
- Area postrema



MOGAD

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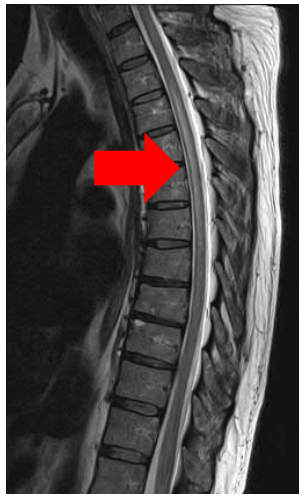
- Good recovery
- 80% disc edema, 50% OU
- Perineural enhancement
- Long transverse myelitis
- ADEM



MOGAD explains 1/3 of AQP4-IgG negative NMOSD

Multiple sclerosis

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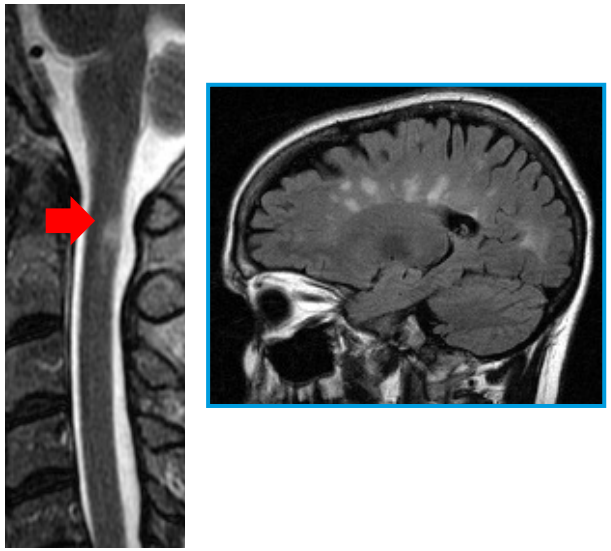

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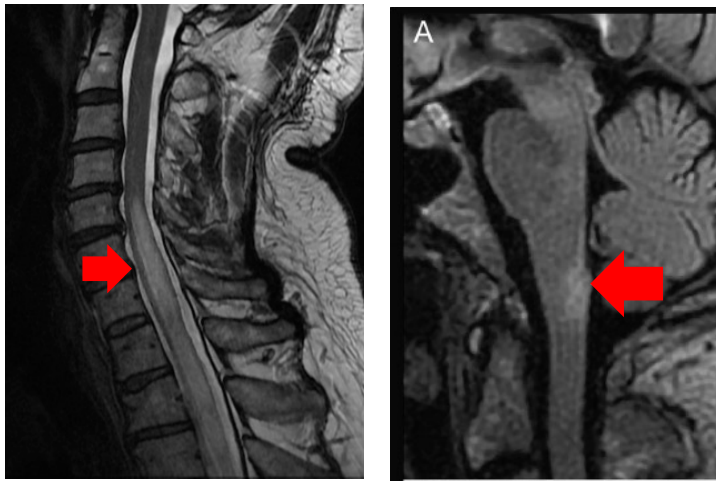

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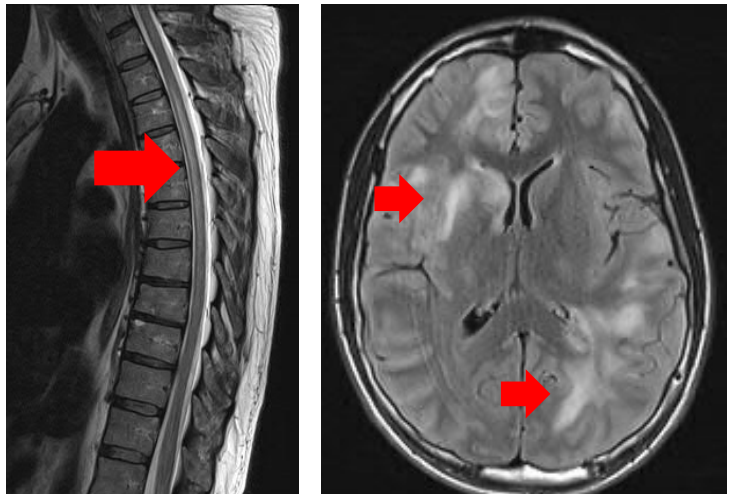

SUMMARY

- Optic neuritis has multiple causes, including MS, AQP4-IgG NMOSD, and MOGAD
  - Treatments and prognosis are different for these diseases
- AQP4-IgG and MOG-IgG should be tested for any atypical optic neuritis
- Treatments are different for MS, AQP4-IgG NMOSD, and MOGAD

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