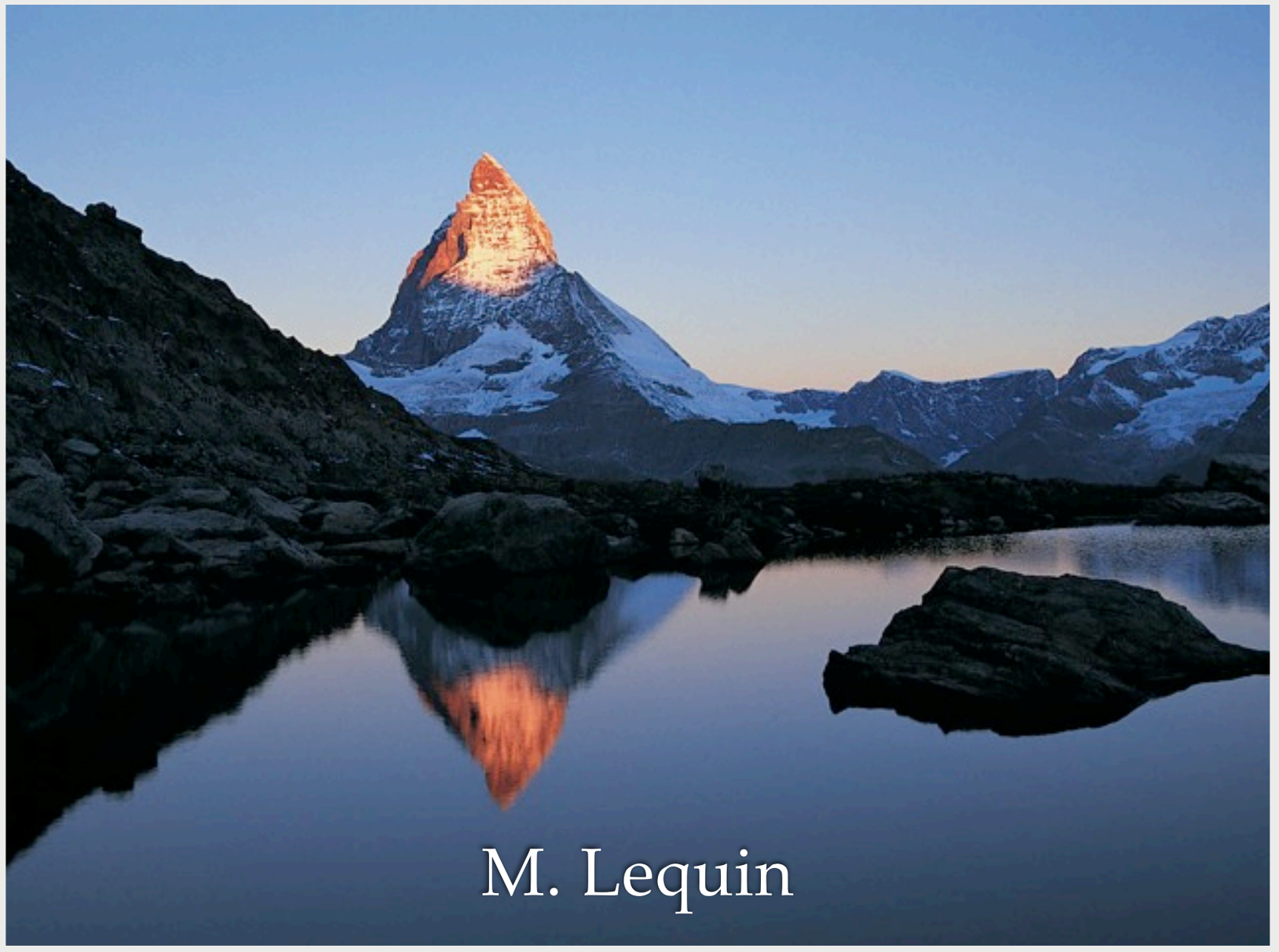
IMAGING IN DEMYELINATING DISORDERS AND ADEM



M. Lequin

LEARNING OBJECTIVES

- To learn about the most common demyelinating disorders in children and the diagnostic approach
- To recognize (a)typical imaging patterns and possible DD.
- To increase the knowledge on the relationship between the imaging pattern and its underlying pathology

THE DISORDERS

- Multiple sclerosis (MS)
- Acute disseminated encephalomyelitis (ADEM)
- Clinical isolated syndrome (CIS)
- Neuromyelitis optica (Devic)

IMAGING

- In acute phase often CT of the brain
- MR imaging modality of choice for the brain and especially for the spine/myelum

MR IMAGING PROTOCOL

BRAIN

• Head-coil, 256-512 matrix, 3mm slices
• Sagittal FLAIR
• Preferrable 3D with axial and coronal reconstructions
• Axial T2 (turbo/fast) spin-echo
• Axial T1spin-echo or 3D T1 gradient echo
• T1 spin-echo or 3D T1 gradient echo after Gadolinium
• Diffusion weighted imaging (DWI)
• Additional T2* or susceptibility weighted imaging (SWI)

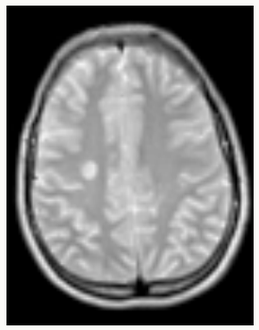
Optional:
• Magnetization transfer contrast (MTC)
• New techniques like 3D DIR (double inversion pulse suppressing CSF and WM)

MYELUM

• Presaturation heart/vessels; consider cardiac gating
• Phased-array coil, FOV 40-80 cm, 512matrix, 3mm slices
• Sagittal T2(turbo/fast)spin-echo and PD
• alternative STIR
• Sagittal T1spin-echo or T1 FLAIR
• In case of an abnormality, axial T2 (turbo/fast) spin-echo or 3D T2 sequence
• FLAIR T2 unsuitable for myelum imaging

BRAIN MR SEQUENCES

- conventional sequences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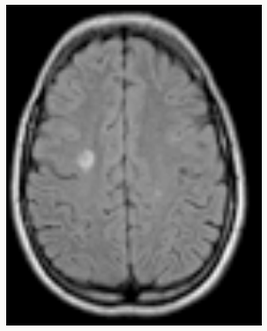
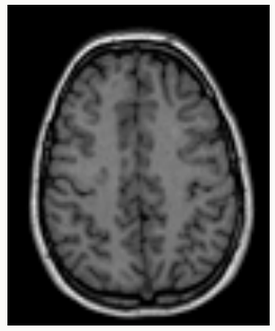
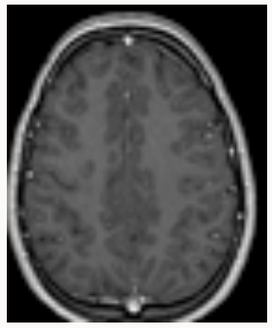
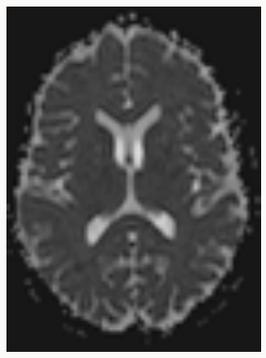

FLAIR


T1


T1Gd

- Additional sequences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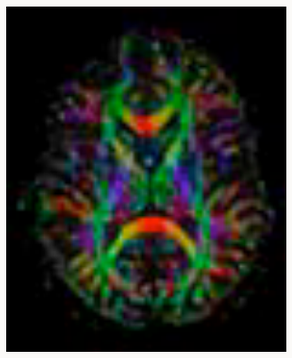
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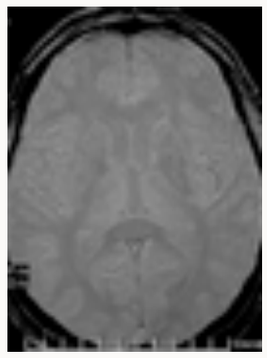
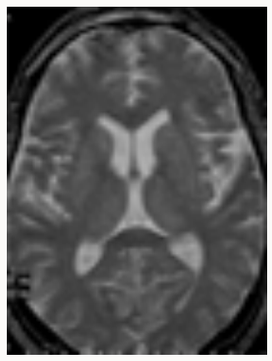

MTC



THE DISORDERS

- **Multiple sclerosis (MS)**
- Acute disseminated encephalomyelitis (ADEM)
- Clinical isolated syndrome (CIS)
- Neuromyelitis optica (Devic)

OLD MS CRITERIA

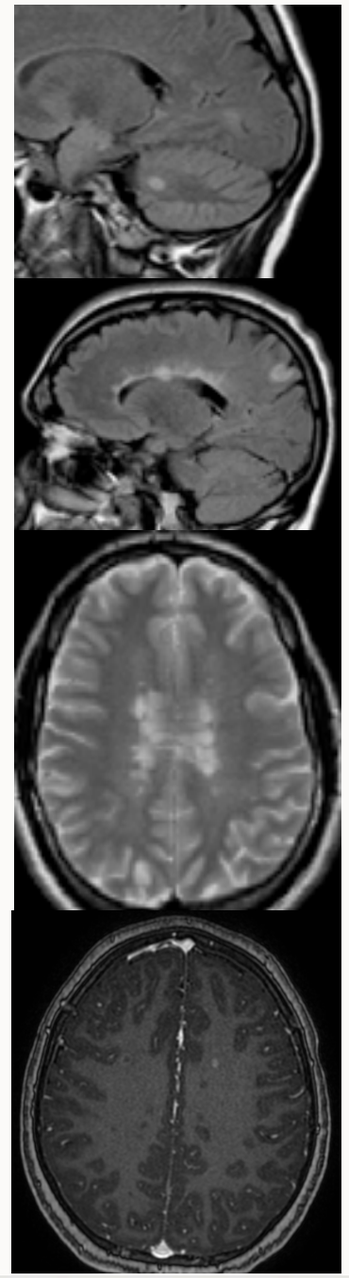
- Dissemination in space (DIS)

  •9 non enhancing lesions:

- At least 1 infratentorial lesion
- At least 1 juxtacortical lesion
- At least 3 periventricular lesions

- Dissemination in time (DIT)

  • a new T2 and/or enhancing lesion(s) on follow up MRI



Mc Donald J. et al, Ann. Neurol.2001;50:121-127

PRESENT MS CRITERIA IN SPACE AND TIME

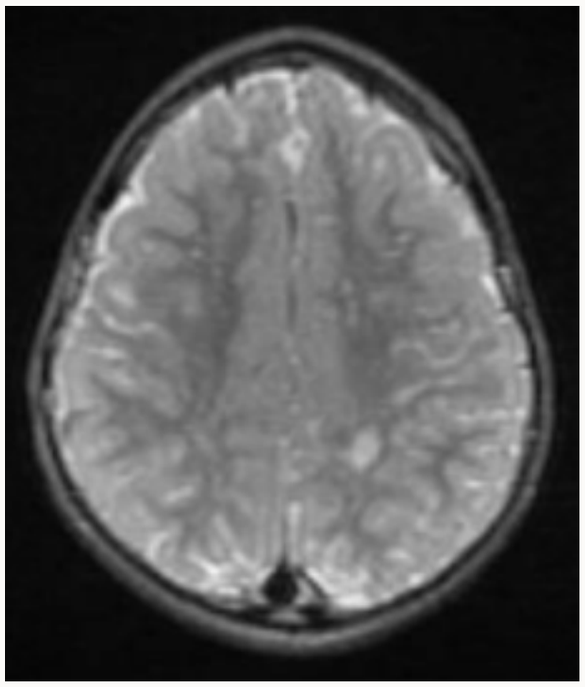
Revised McDonald 2010 criteria for MS

DISSEMINATION IN SPACE
At least 1 or more lesions in 2-4
different CNS areas:
≥1 juxtacortical lesion
≥1 periventricular lesion
≥1 infratentorial lesion
≥1 spinal lesion

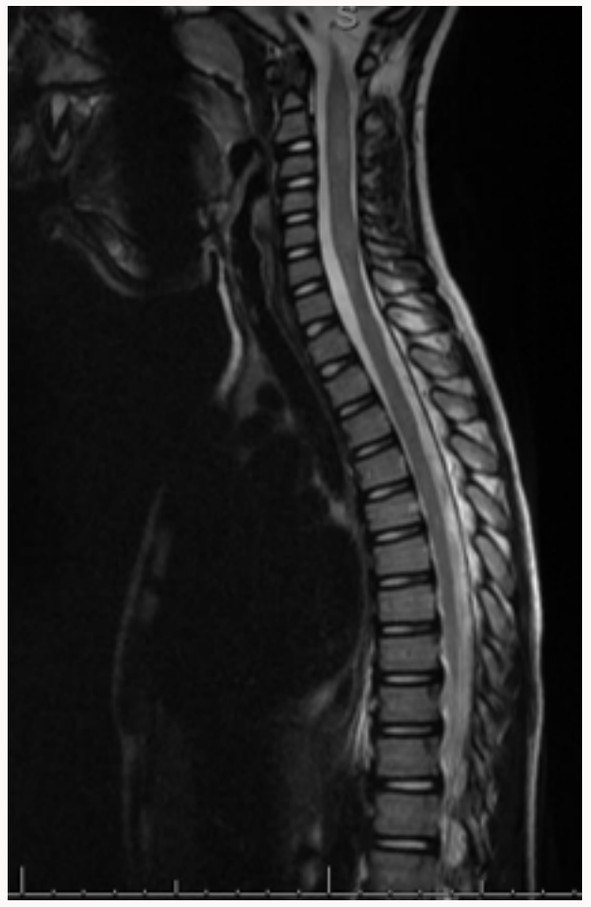
DISSEMINATION IN TIME
Fulfill 1 of the criteria mentioned below
≥1 enhancing lesion – even on the
baseline scan
≥1 new T2 lesion on a follow-up scan

age > 12 years
sensitivity 100%
specificity 86%

TYPICAL MR FINDINGS MS

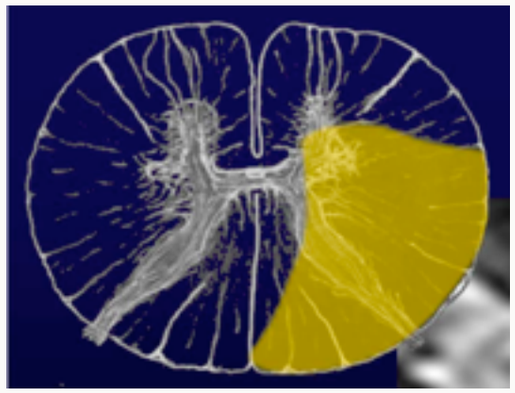


brain and spinal cord abnormalties

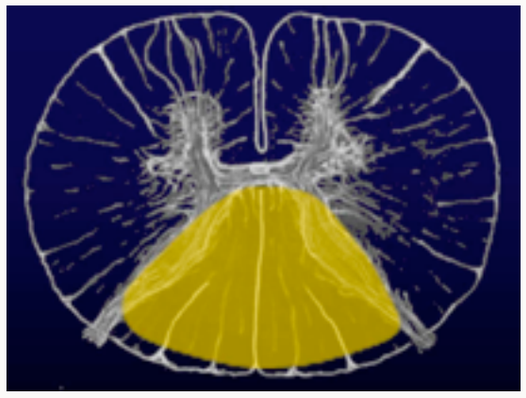


6y old boy with muscle weakness at the level of the legs and right arm and incontinentia

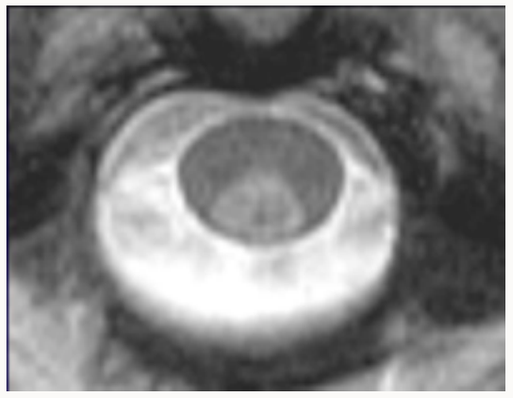
TYPICAL MR FINDINGS MS



dorsolateral location

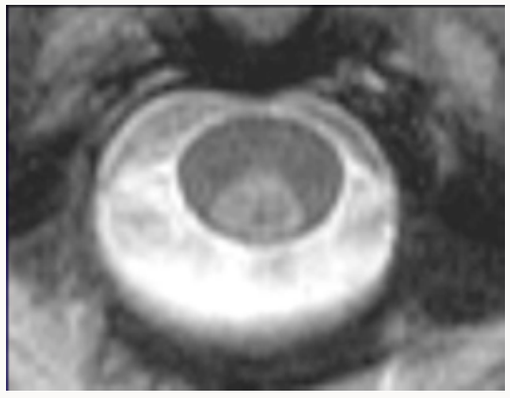


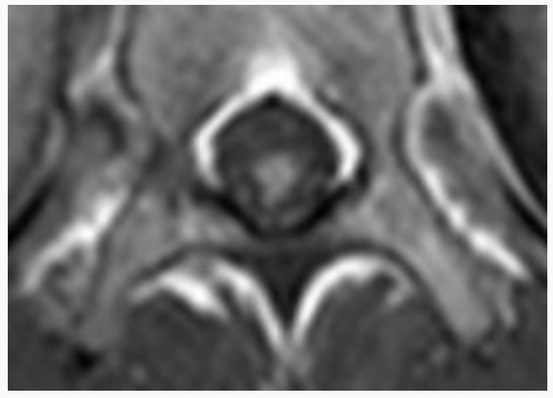
dorsocentral

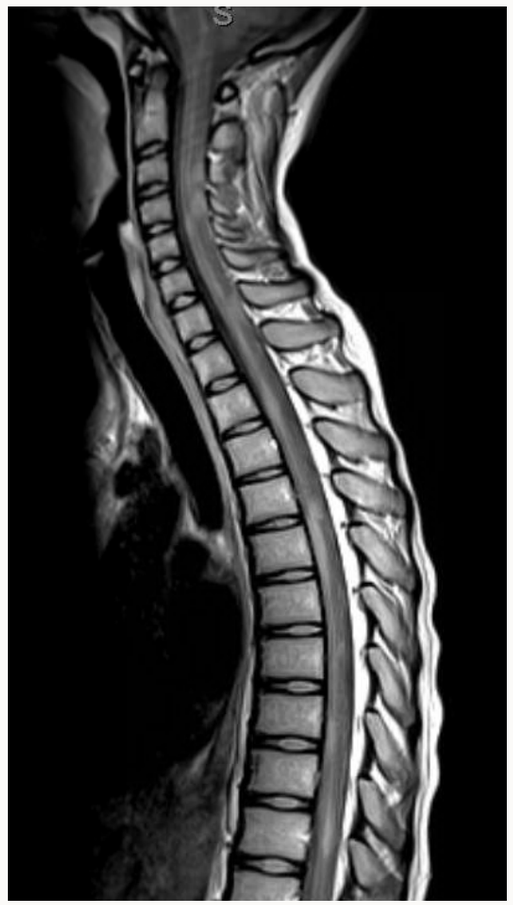


Could be multiple lesion and often lesion <2 vertrabral segments

TYPICAL MR FINDINGS MS



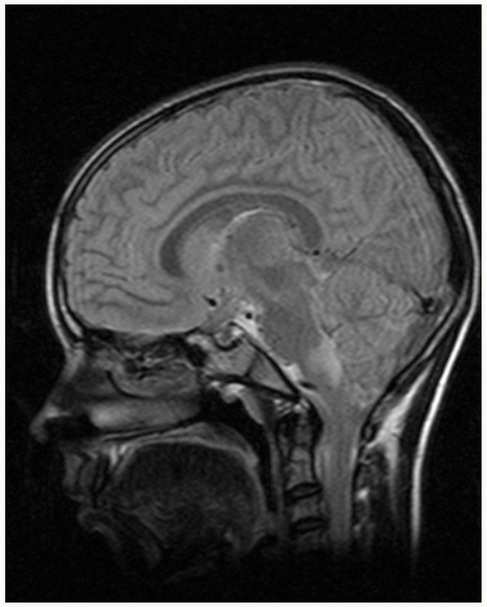


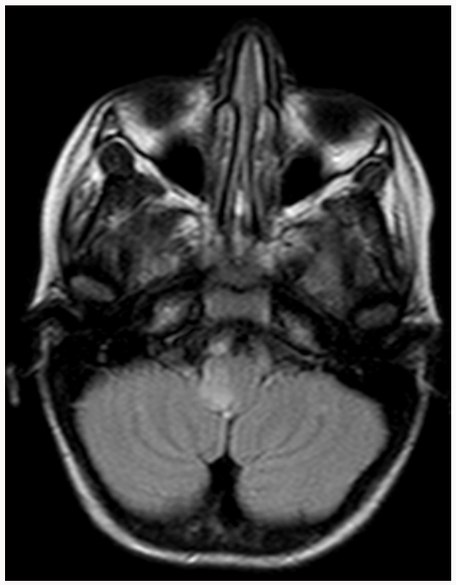


Gd enhancement insensitive marker for BBB disturbance, inflammation in progressive MS is trapped behind a closed or repaired BBB

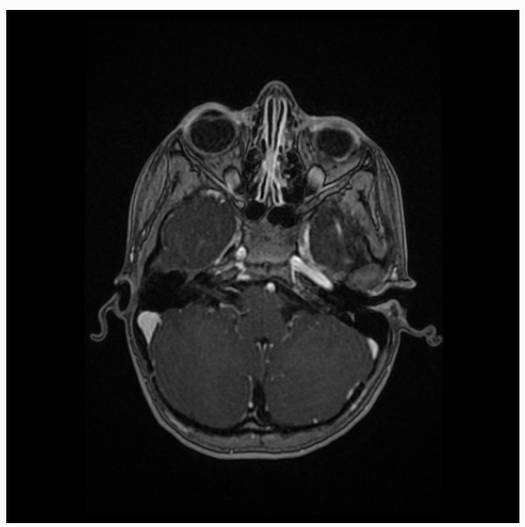
Lassmann H et al. The immunopathology of multiple sclerosis: an overview. Brain Pathol 2007

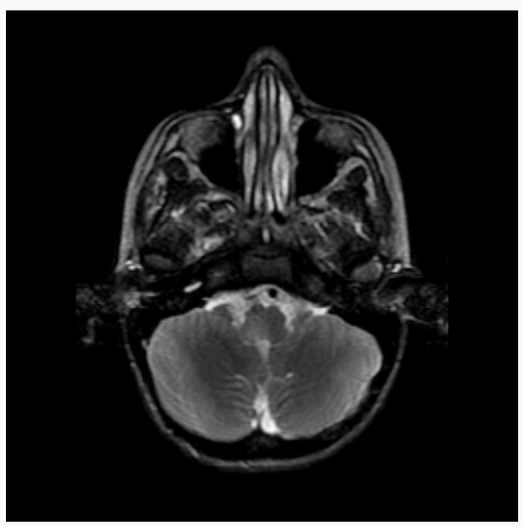
FOLLOW-UP IN MS





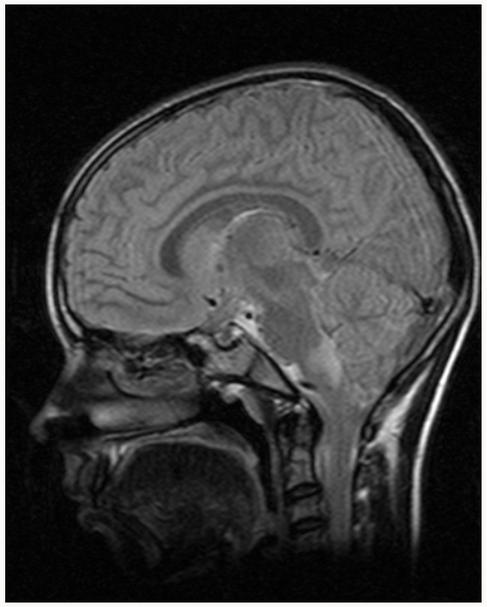
12y old girl with 12 days of vomiting

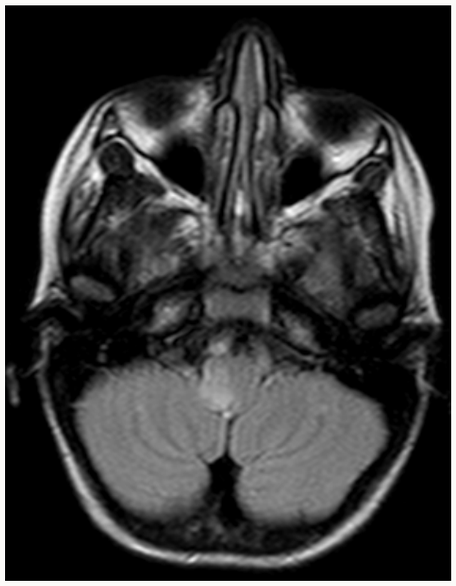




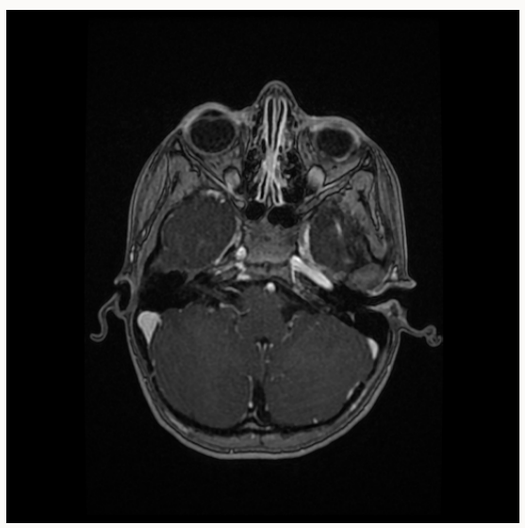
2 month follow-up

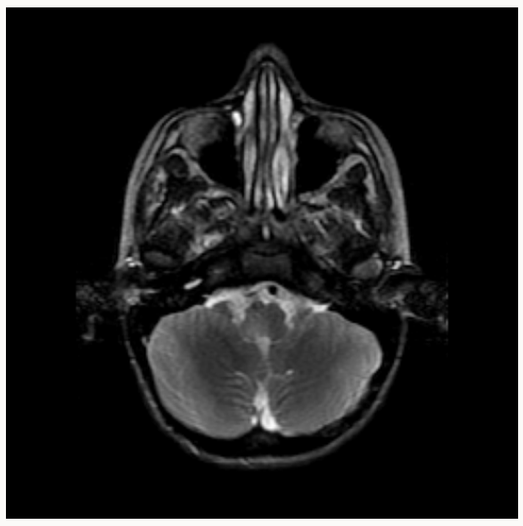
FOLLOW-UP IN MS



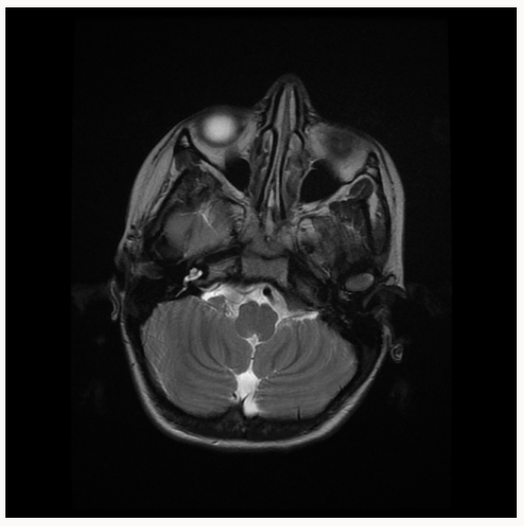


12y old girl with 12 days of vomiting





2 month follow-up



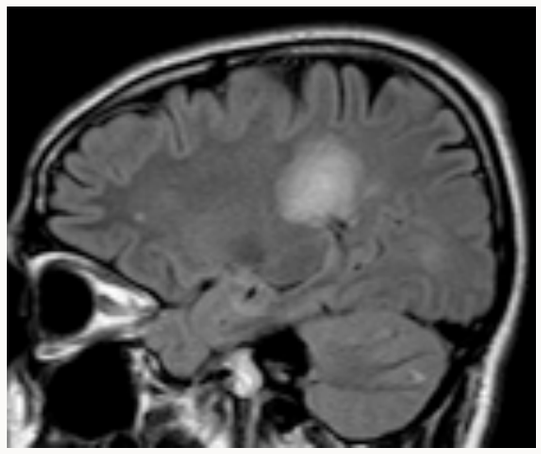
SUMMARY TYPICAL MR FINDINGS IN MS

- Periventricular lesions - touching the ventricles
- Involvement of the corpus callosum
- Juxtacortical lesions (U fibers) - touching the cortex
- Involvement of the temporal lobe
- Infratentorial lesions
- Lesions enhancement -“open ring”- “Dawson fingers”
- Black holes
- Spinal cord lesions

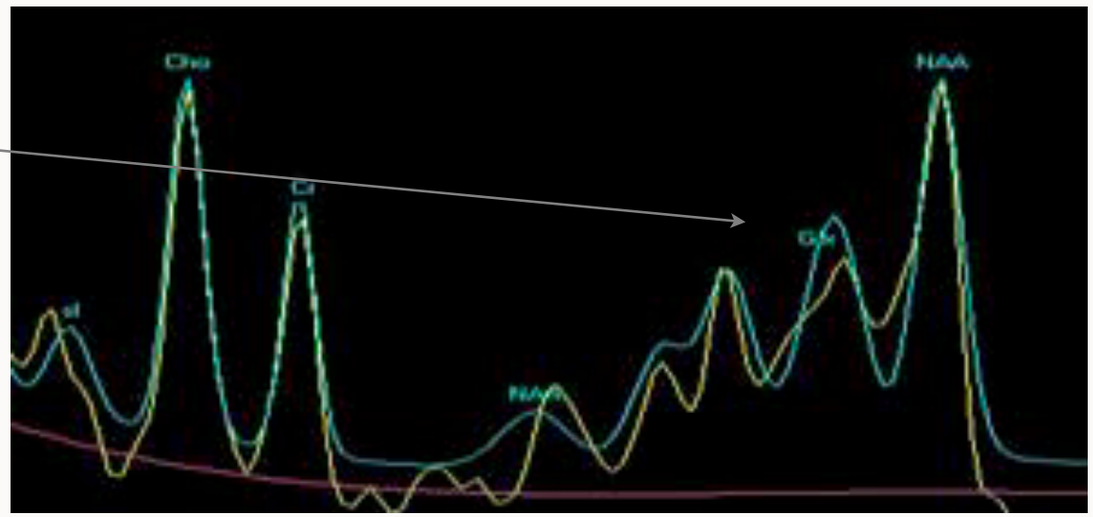
Children VS Adults at MS onset*
- Higher number of total T2 lesions in the posterior fossa
- Higher number of enhancing lesions
- Greater resolution of the initial T2 lesion burden on follow-up MRI
- Tumefactive T2-bright lesions > 0.3 / 100.000 /year

*E.Waubant, et al; Archives of Neurology(66):967–971, 2009

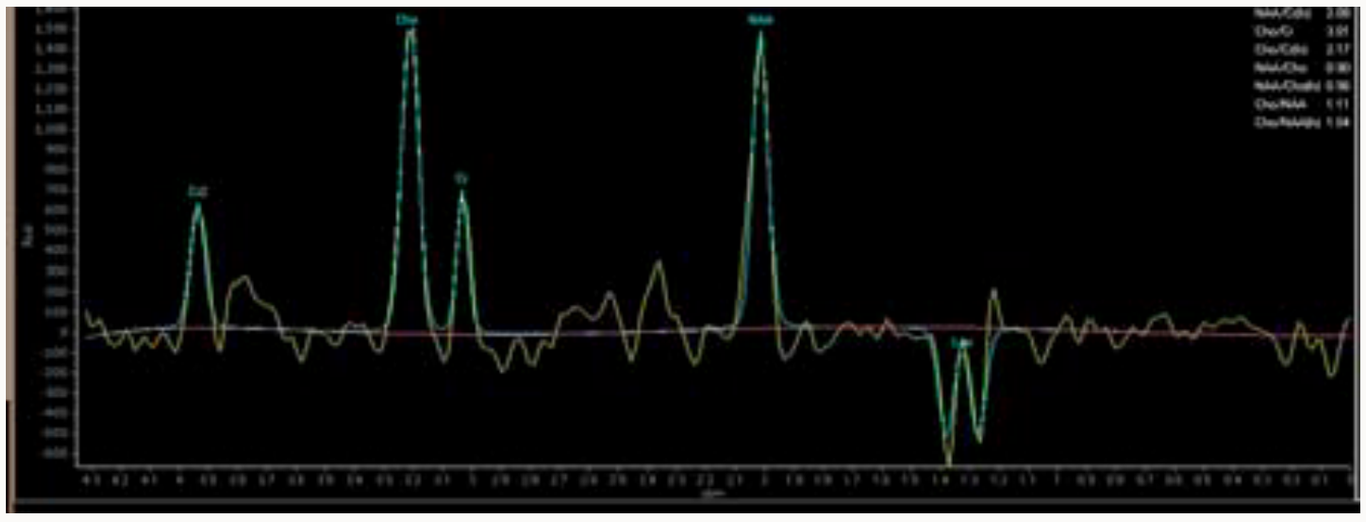
TUMEFACTIVE MS



ß-Glx



short TE: 25-35ms



Long TE: 144ms

TUMEFACTIVE MS

Summary Imaging Findings:

- Large lesion with Little Mass Effect and Edema
- Ringlike or Open-Ring Enhancement
- Central Dilated Veins Within the Lesion
- MR Spectroscopy (β-Glx peaks)
- Rapid Resolution After Steroid Therapy

THE DISORDERS

- Multiple sclerosis (MS)
- **Acute disseminated encephalomyelitis (ADEM)**
- Clinical isolated syndrome (CIS)
- Neuromyelitis optica (Devic)

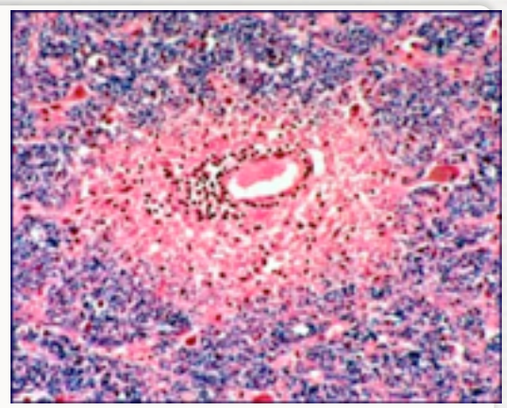
ACUTE DISSEMINATED ENCEPHALOMYELITIS (ADEM)

- Past: Any monophasic episode of disseminated demyelination
- Present: IPMS study group

1. A first polyfocal clinical neurological event with presumed inflammatory cause
2. Encephalopathy that cannot be explained by fever only
3. No new symptoms, signs, or MRI findings after three months of the ADEM incident

L.B. Krupp et al, Multiple Sclerosis Journal;19 (10) : 1261-1267, 2013

ADEM



- Monophasic, immune-mediated demyelinating disease
- T cell hypersensitivity reaction
- A history of infections, vaccination or drugs in the recent past
- Rapid recovery (first 3 months)
- A new event after 3 months is termed multiphasic ADEM (2-4%)
- ADEM : first manifestation of pediatric onset MS (2-10%)
- 25-30% of pts have spinal cord involvement
- There are no clear prognostic factors that determine if a child with a first event of ADEM will eventually develop MS.
(relapse: 80% in the first 2 yrs)

Neuteboom et al 2008, Dale et al 2007, Atzori et al 2009, Dale and et al 2007, Mikaeloff et al 2007

ADEM

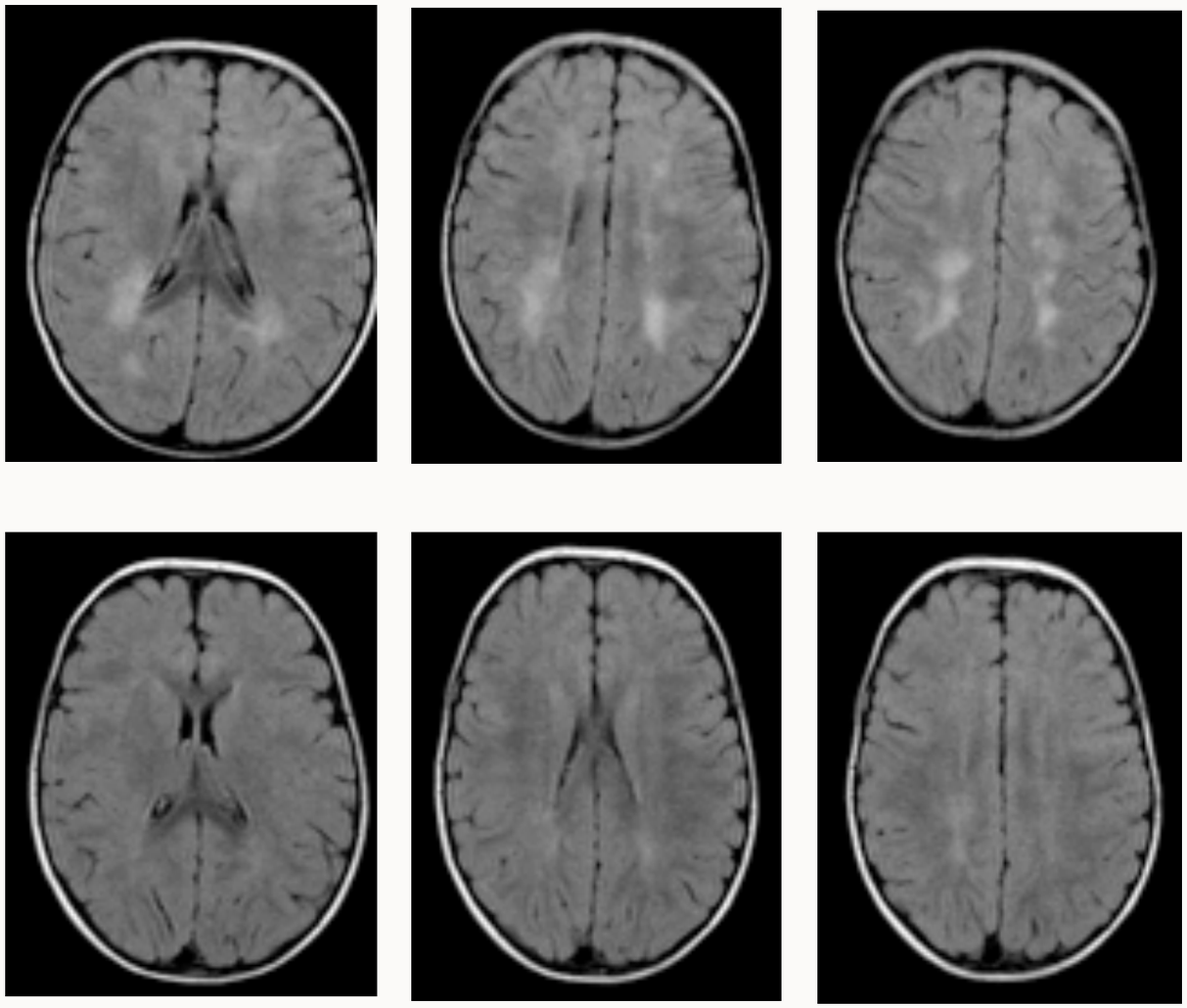
Brain imaging findings:

- large, hyperintense asymmetric lesions

- disseminated , confluent & blurred boundaries
- involving wm, cortex & deep grey nuclei
- On MR with gadolinium enhancement (+/-)

Rossi A. Imaging in acute disseminated encephalomyelitis. Neuroimag Clin N Am 2008

RAPID RECOVERY



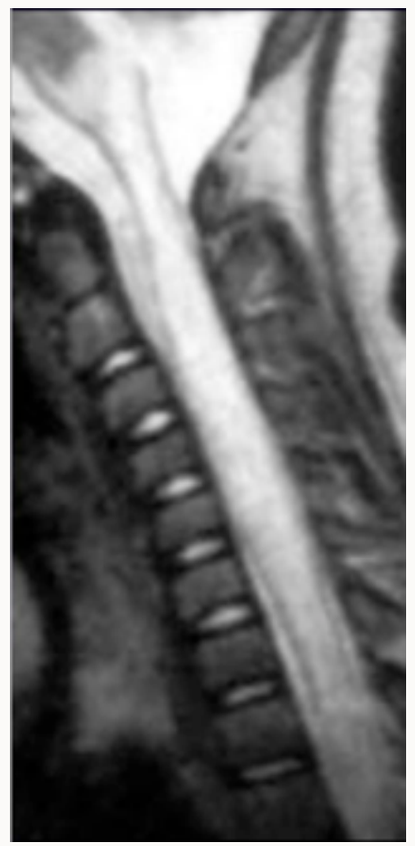
21m old girl

2m later recovery

ADEM

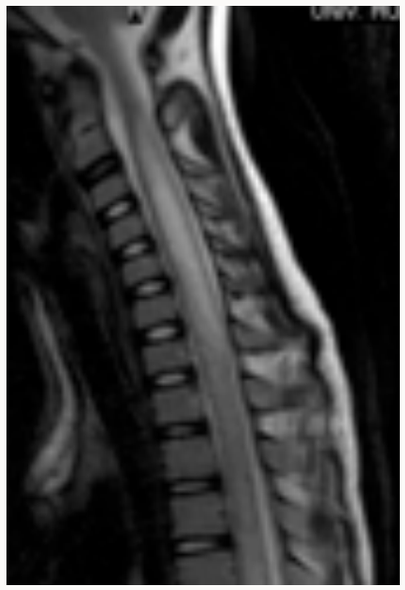
MR myelum imaging findings:

- multiple areas of high signal intensity
- no enhancement
- holocord involvement is possible
- gray matter, white matter or both

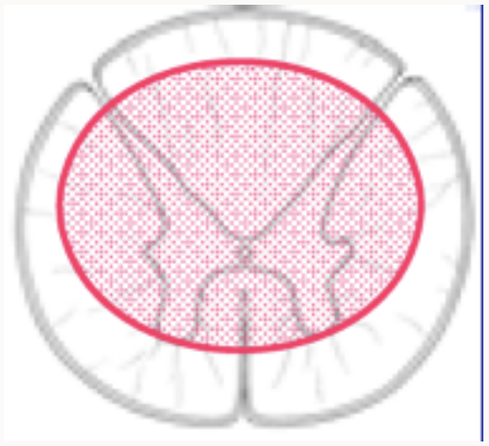


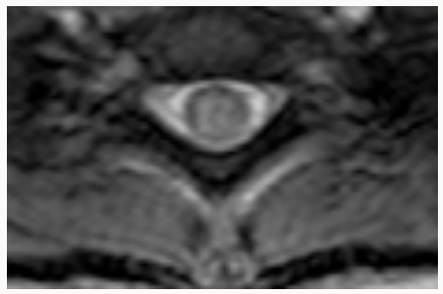
Rossi A. Imaging in acute disseminated encephalomyelitis. Neuroimag Clin N Am 2008

SPINAL CORD LESIONS



more than 2 segments





more than 2/3 cross sectional cord area

SUMMARY ADEM

Typical MRI characteristics of ADEM:

large, hyperintense asymmetric lesions
- disseminated , confluent & blurred boundaries
- involving wm, cortex & deep grey nuclei
- gadolinium enhancement (+/-)
- diffuse spinal cord lesions

* d.d. ADEM from MS:
a diffuse bilateral pattern, absence of black holes, few periventricular lesions (sensitivity 81%, specificity 95%)

***Callen et al. Neurology;72: 968–973, 2009.**

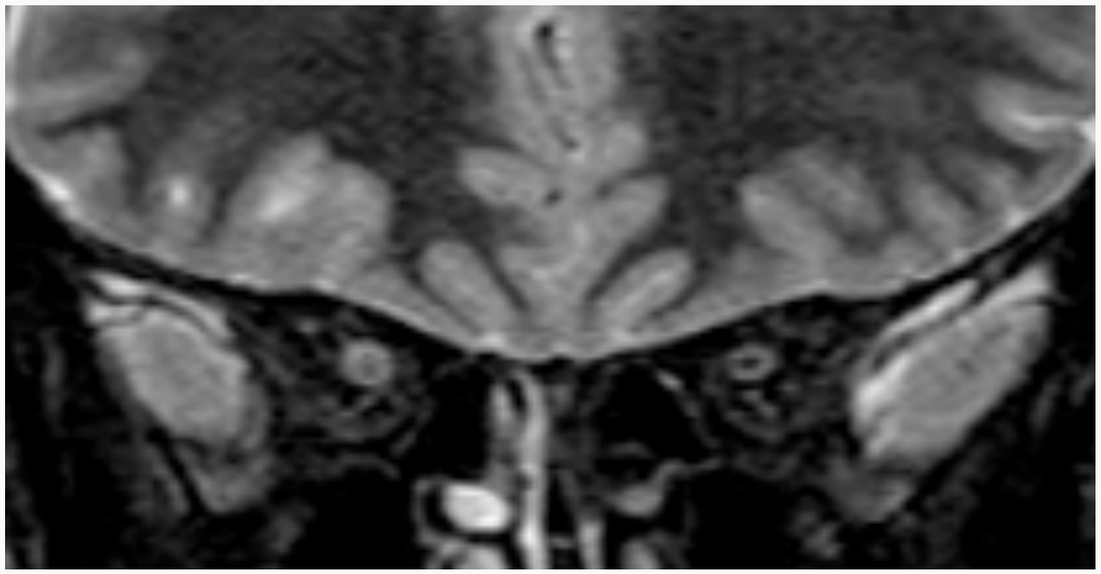
THE DISORDERS

- Multiple sclerosis (MS)
- Acute disseminated encephalomyelitis (ADEM)
- **Clinical isolated syndrome (CIS)**
- Neuromyelitis optica (Devic)

Clinically Isolated Syndrome (CIS)

- A monofocal first clinical demyelinating event (optic neuritis, acute transverse myelitis, brainstem, cerebellar or hemispheric dysfunction)
- or polyfocal first clinical demyelinating event
- no encephalopathy (unless explained by fever)
- diagnosis of MS on MRI is not met

Optic Neuritis (ON)

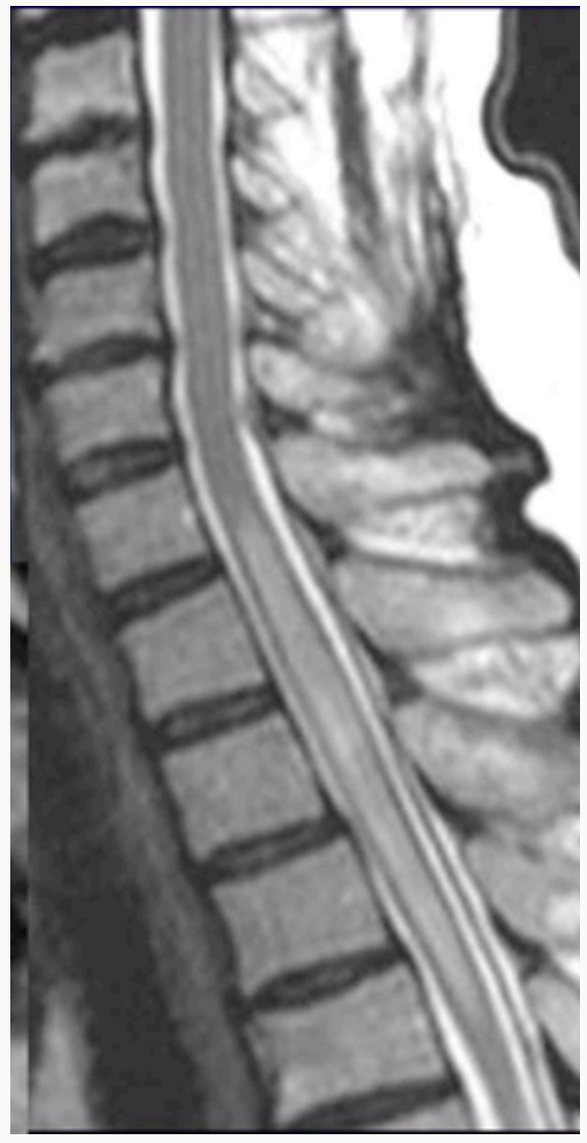


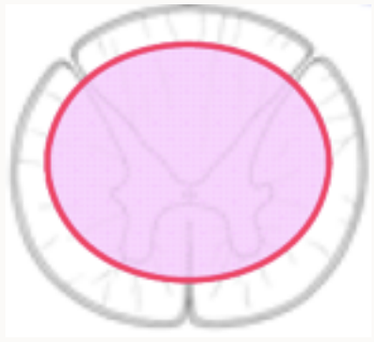
-Unilateral (58%) or bilateral (42%)
- high risk for MS (40-70%) in the next 2 years in children with ON and one or more wm lesions

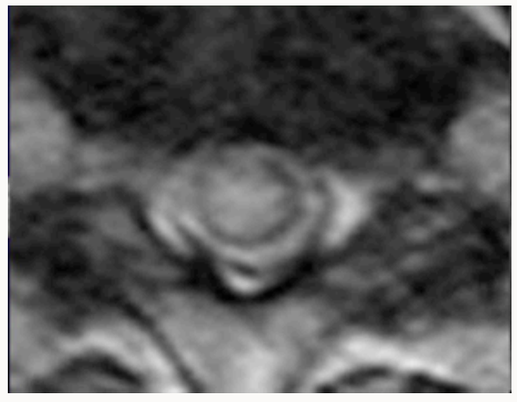
***M. Wilejto, et al. Neurology,(67):258–262,2006.**

Acute Transverse Myelitis

Long segment (> 3 vertebral segments)
Cord expansion
Central cord T2 hyperintensity
> 2/3 cross sectional area GM & surrounding WM







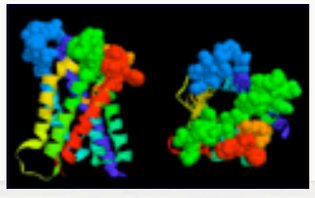
THE DISORDERS

- Multiple sclerosis (MS)
- Acute disseminated encephalomyelitis (ADEM)
- Clinical isolated syndrome (CIS)
- **Neuromyelitis optica (Devic)**

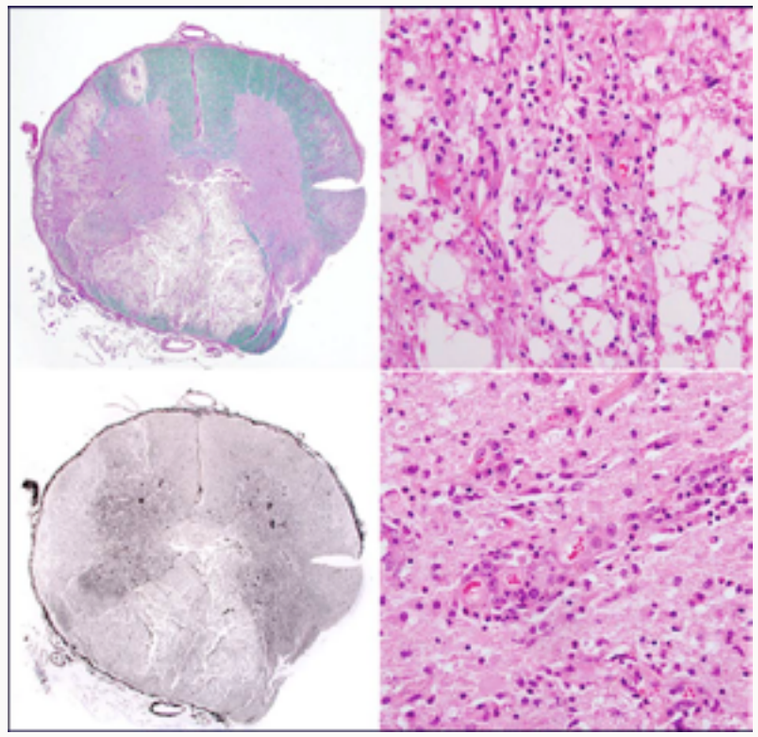
Neuromyelitis optica (Devic)

All required
1.optic neuritis
2.acute myelitis

At least 2 of these 3 criteria are considered:
(i) MRI evidence of a contiguous spinal cord lesion
(3 or more segments in length)
(ii) brain MRI non diagnostic for MS
(iii) anti-aquaporin-4 IgG seropositive status



Neuromyelitis optica (Devic)



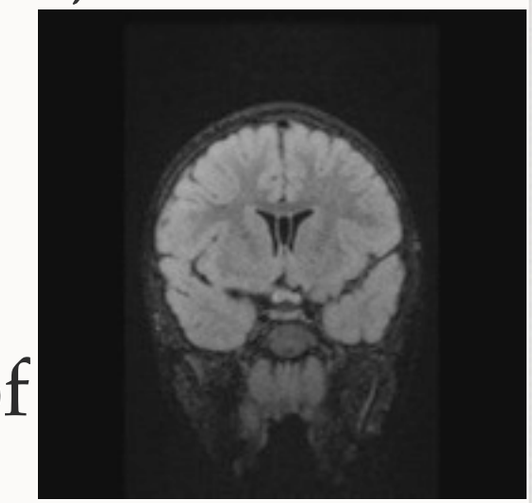
- extensive demyelination of the white and gray matter
- 80-90% relapsing course
- female : male 9:1

Wingerchuk DM et al. The spectrum of neuromyelitis optica. Lancet Neurol 2007

Neuromyelitis optica (Devic)

NMO – IgG against AQP-4 (AQP4 autoantibodies)

AQP-4 is the main water channel in the CNS
where it is expressed around cerebral microvessels,
pia mater and Virchow-Robin spaces

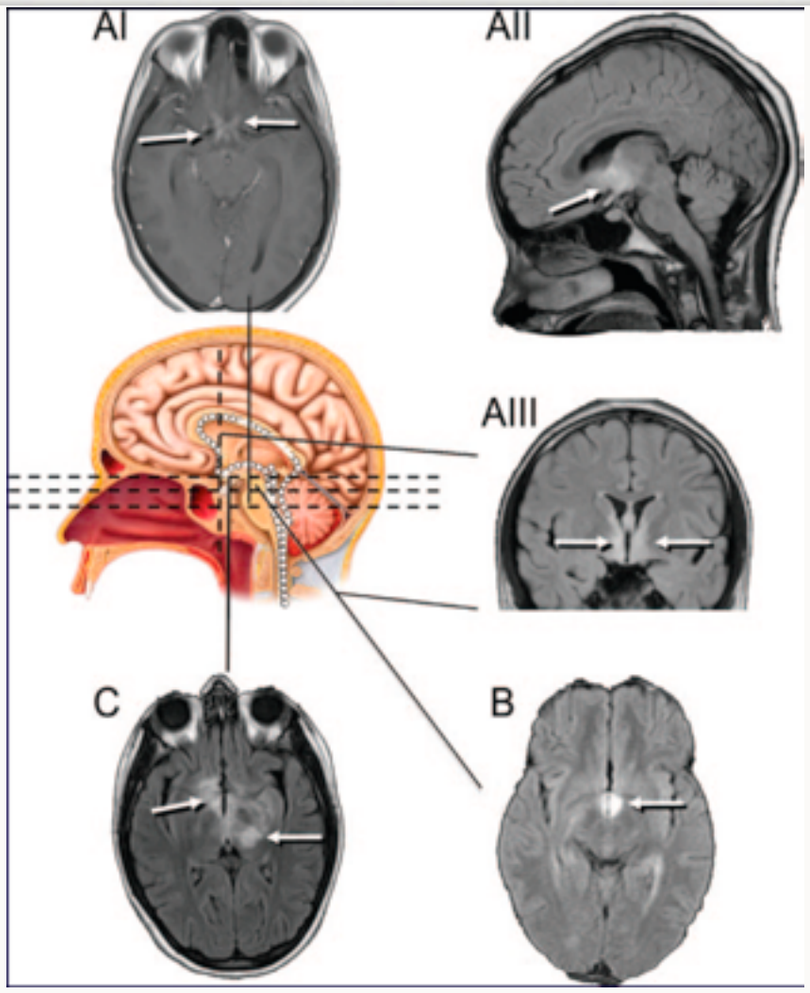


NMO IgG is a specific biomarker for NMO
spectrum disorders and is not simply a marker of
destructive CNS IDD !

Converting to the phenotype of relapsing-remitting
MS

Wingerchuk DM et al. The spectrum of neuromyelitis optica. Lancet Neurol 2007

Neuromyelitis optica (Devic)



10% had brain abnormalities

Wingerchuk DM et al. The spectrum of neuromyelitis optica. Lancet Neurol 2007

DIFFERENTIAL DIAGNOSES

Vascular/Inflammatory Disease

(i) CNS vasculitis/childhood primary CNS angiitis

(ii) Stroke

(iii) CADASIL/CARASIL

(iv) Autoimmune diseases

Metabolic/Nutritional

(i) Mitochondrial encephalopathy

(ii) Leukodystrophies

(iii) Vit B12 or folate deficiency

CNS Infection

(i) Neuroborreliosis

(ii) Herpes simplex encephalitis

(iii) Influenza ANE

(iv) Viral encephalitis

Malignancy

(i) Lymphoma

(ii) Astrocytoma

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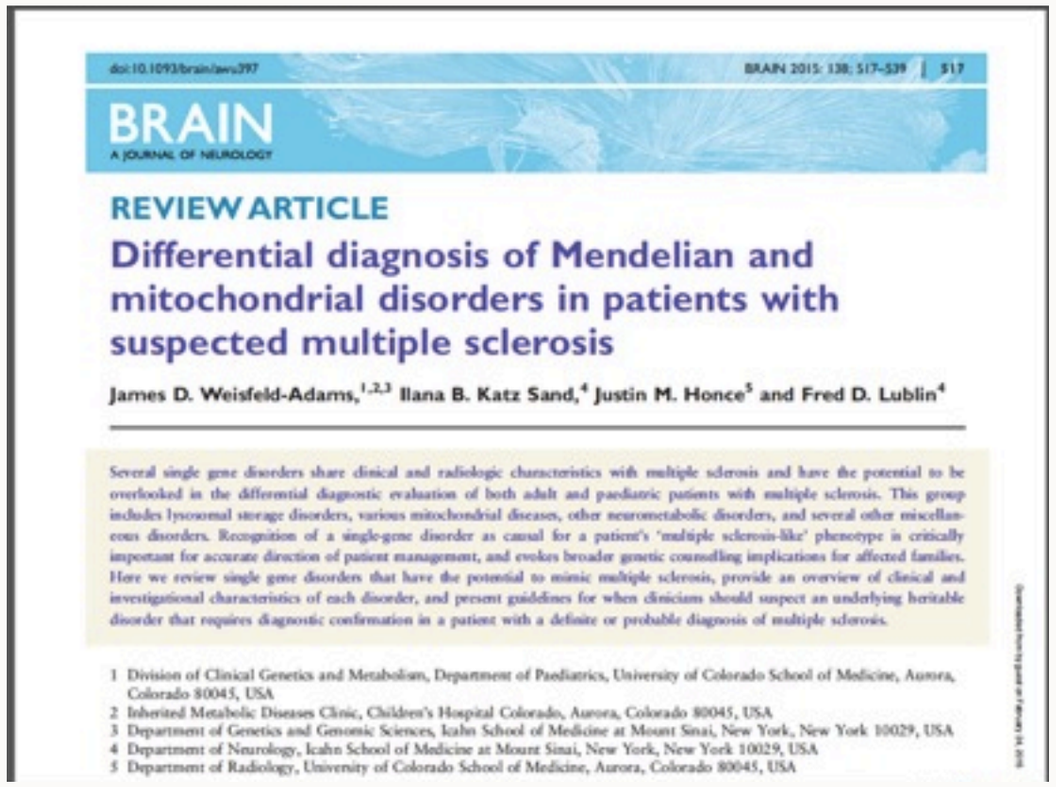

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BRAIN
A JOURNAL OF NEUROLOGY

REVIEW ARTICLE

Differential diagnosis of Mendelian and mitochondrial disorders in patients with suspected multiple sclerosis

James D. Weisfeld-Adams,[1,2,3] Ilana B. Katz Sand,[4] Justin M. Honce[5] and Fred D. Lublin[4]

Several single gene disorders share clinical and radiologic characteristics with multiple sclerosis and have the potential to be overlooked in the differential diagnostic evaluation of both adult and paediatric patients with multiple sclerosis. This group includes lysosomal storage disorders, various mitochondrial diseases, other neurometabolic disorders, and several other miscellaneous disorders. Recognition of a single-gene disorder as causal for a patient's 'multiple sclerosis-like' phenotype is critically important for accurate direction of patient management, and evokes broader genetic counselling implications for affected families. Here we review single gene disorders that have the potential to mimic multiple sclerosis, provide an overview of clinical and investigational characteristics of each disorder, and present guidelines for when clinicians should suspect an underlying heritable disorder that requires diagnostic confirmation in a patient with a definite or probable diagnosis of multiple sclerosis.

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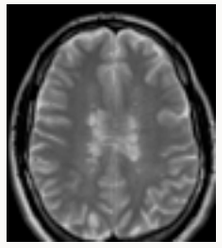
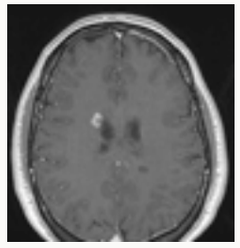
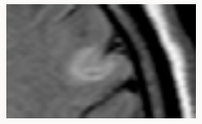
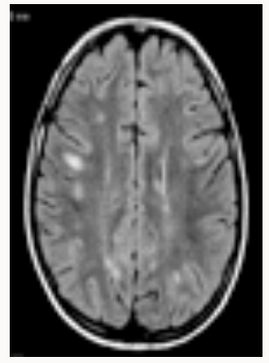
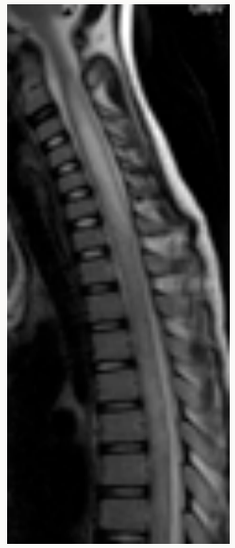
5 Department of Radiology, University of Colorado School of Medicine, Aurora, Colorado 80045, USA

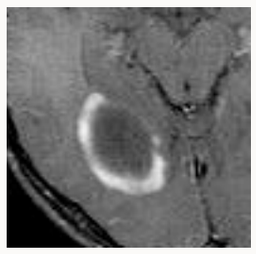
TAKE HOME MESSAGES


MS

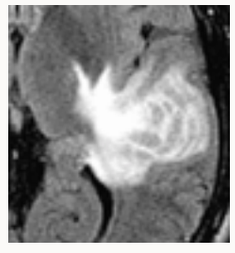



ADEM

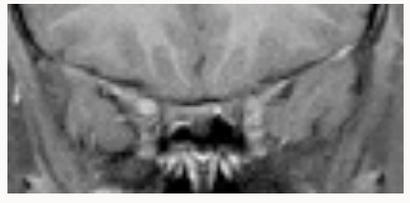
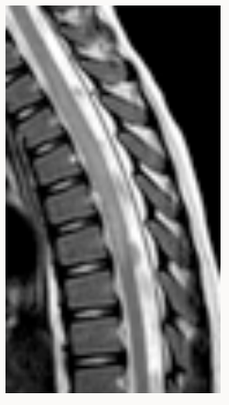


Tumefactive MS

CIS



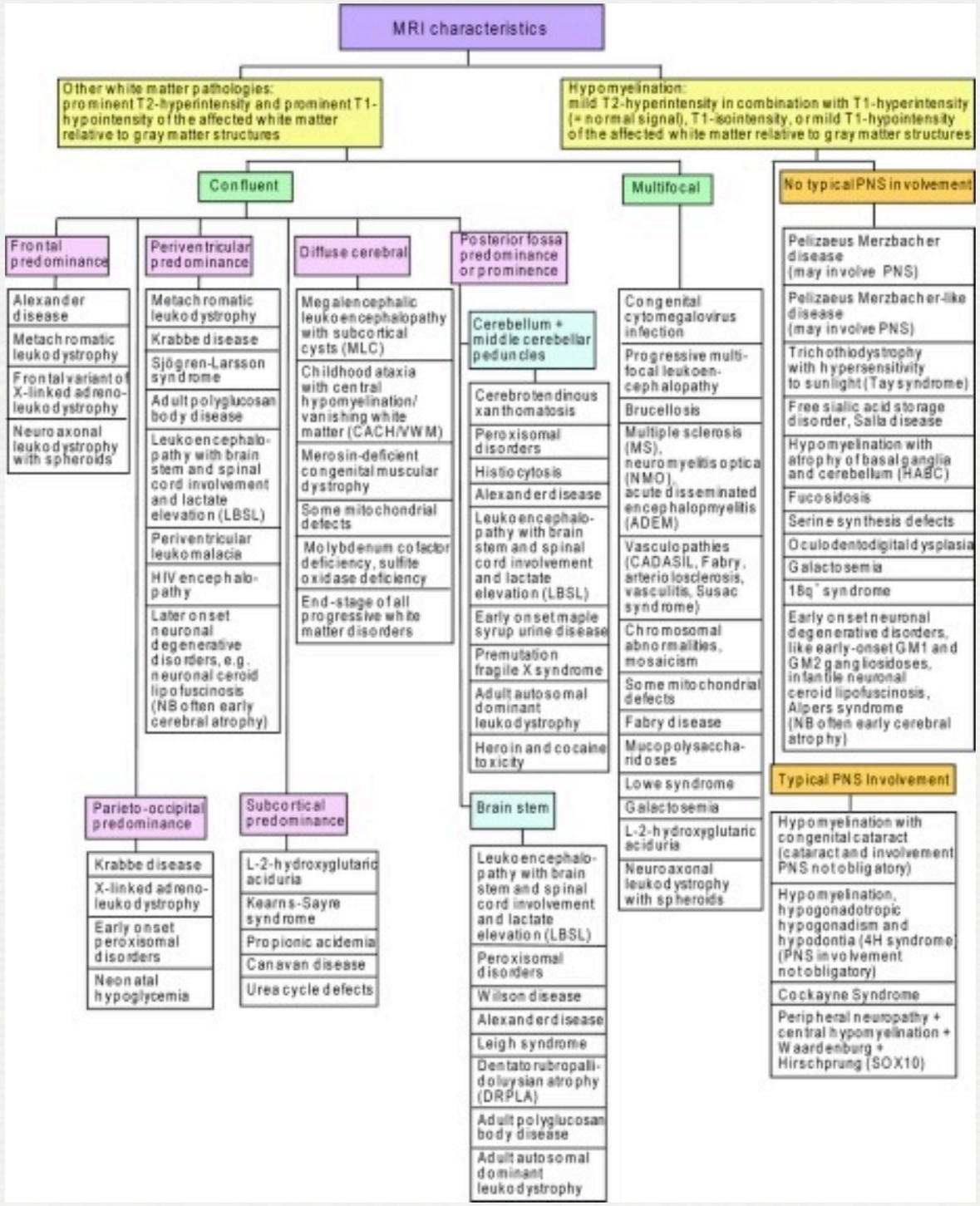
Ballo’s concentric sclerosis

NMO

TAKE HOME MESSAGES

- A lot of white matter abnormalities are non-specific (30-40%)
- Use pattern recognition tools
- Use discriminators like extent and location of the lesions
- Use standardised MR Protocols
- MS criteria of adults can be used in children suspected to have MS
- MS and ADEM can look alike on MR, think of MS mimicers (DD)
- Always combine a brain MR with a MR of the spine



Courtesy to Schiffmann and van der Knaap in 2009 (Neurology 2009; 72:750-9)