



CNS immune mediated demyelinating diseases

Predicting MS

Coriene Catsman-Berrevoets, paediatric neurologist

Case 1

- 14 year old girl
- No medical history
- Progressive loss of vision of the left eye since 3 days
- Left eye hurts when moving
- Neurological examination:
 - Vision 1.0/ 0.2
 - No other abnormalities

Case 1

- Natasja 14 years old
- No medical history
- Progressive loss of vision of the left eye since 3 days
- Left eye hurts when moving
- Neurological examination:
 - Vision 1.0/ 0.2
 - Left papil is abnormal
 - No other abnormalities



Clinically isolated syndrome (CIS)

- first demyelinating episode with presumed inflammatory cause
- may be monofocal or polyfocal

Optic nerve: neuritis optica (usually unilateral)

Hemisphere: for example hemiparesis, hemi-sensory disorder

Brainstem: for example eye movement disorder

Cerebellum: for example (hemi) ataxia

Myelum: paralysis legs, bladder dysfunction

Question

which statement is correct

- A: The papillary edema is a contraindication for a spinal fluid tap
- B: In children with MS oligoclonal bands often occur in serum
- C: In children with MS neuritis optica is almost always bilateral
- D: The chance that Natasja develops MS is $> 80\%$
- E: The chance that Natasja develops MS is $< 50\%$

Multiple Sclerosis

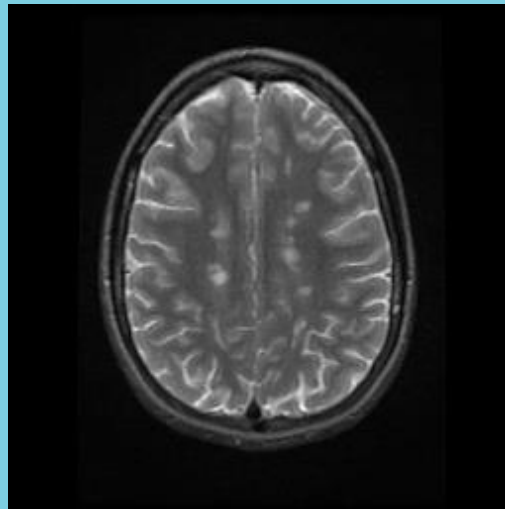
- MS
- Symptoms occur in episodes named Schubs or Relapses
- May last for hours to days
- Typical MRI abnormalities
- CSF: raised IgG index and oligoclonal bands present

Clinically isolated syndrome (CIS)

- first demyelinating episode with presumed inflammatory cause
- maybe monofocal or polyfocal

MRI lesions are:

- * well demarcated
- * discrete and situated mainly in the white matter
- * hypointense white matter lesions may be present

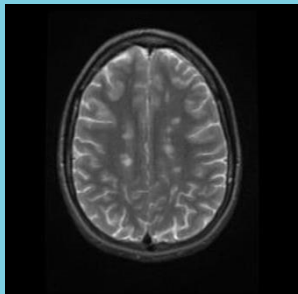


Multiple Sclerosis diagnostic criteria

- 1. Dissemination in place
- 2. Dissemination in time
 - Clinically
 - symptoms from lesions in 2 different neuroanatomical systems
 - MRI
 - A. neurological symptoms in 1 neuroanatomical system AND fulfilling specific MRI criteria
 - B. One neurological episode AND new lesions on 2^e MRI
- 3. No other diagnosis

MS in children is a difficult diagnosis

- Signs and symptoms are not always indicated by the child
- Symptoms often disappear spontaneously
- Parents do not always seek medical advice in case of subtle symptoms
- Rare disease with extensive differential diagnosis
- Symptoms and MRI abnormalities are often less defined than in adults



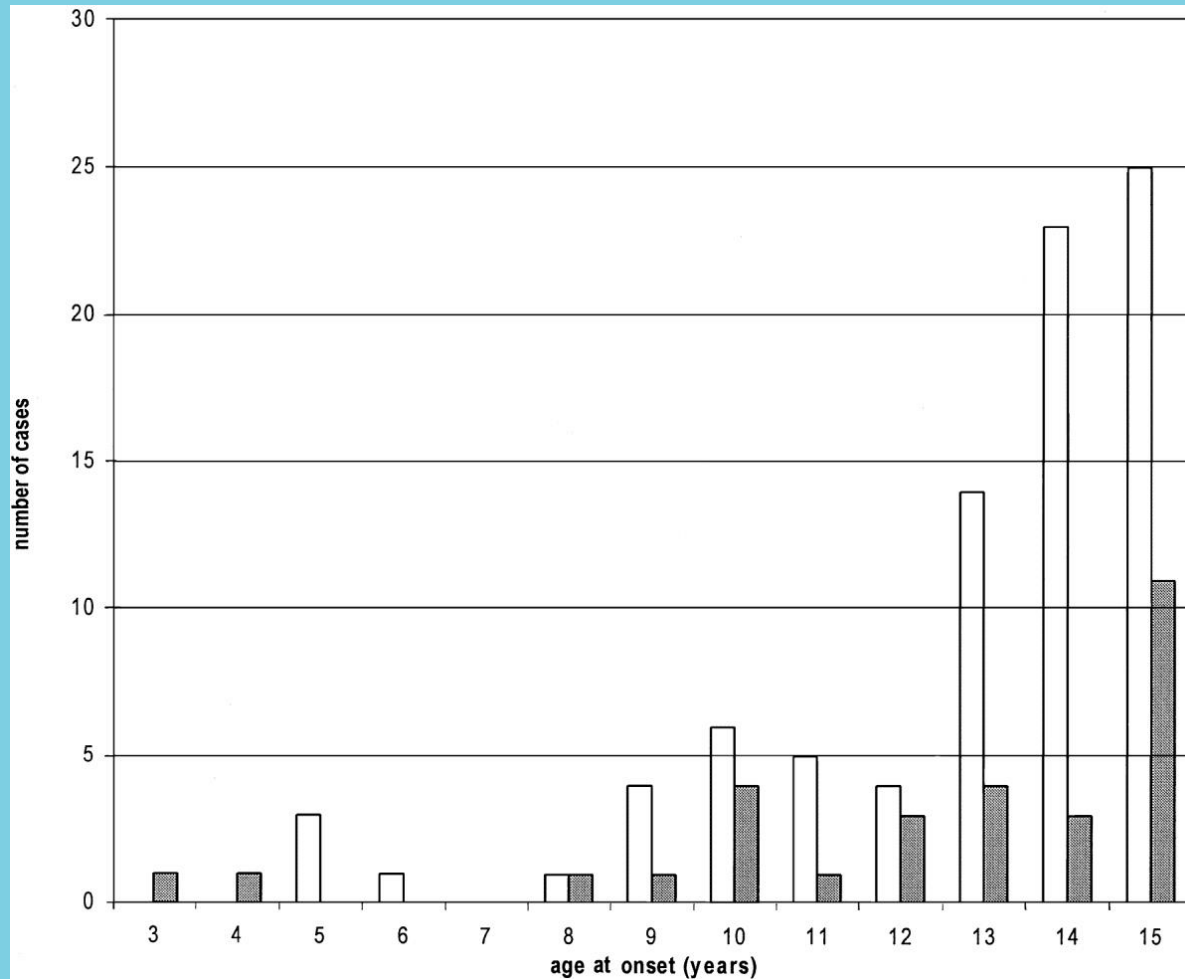
MS in children

- First episode before age 16: 2,7- 4,4 % of MS patients
- First episode before age 10: 0,2- 1,6% of MS patients

- Mean onset 12-13 years

- M : F ratio = 1 : 1.2-1.5
- In adults M : F ratio = 1 : 3

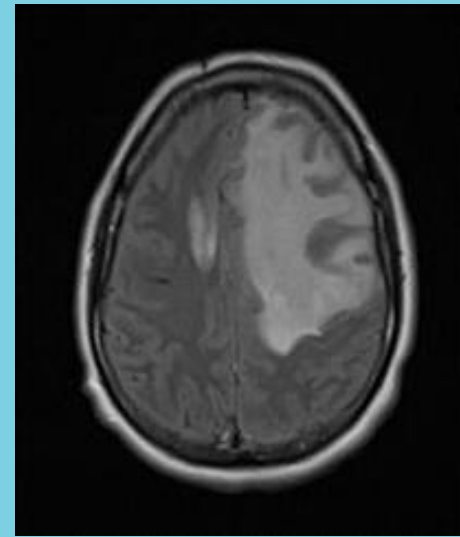
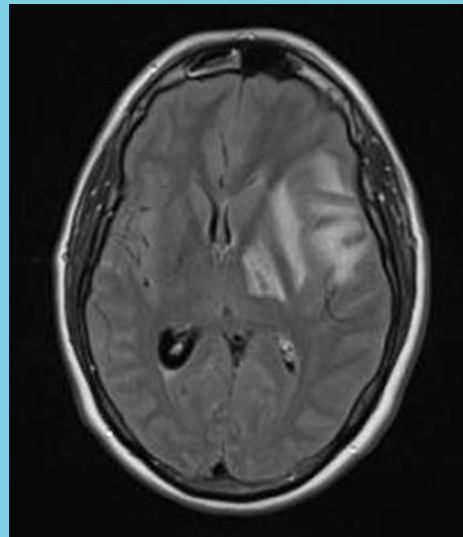
Influence of puberty on paediatric MS more severe in girls



Boiko, A. et al. Neurology 2002;59:1006-1010

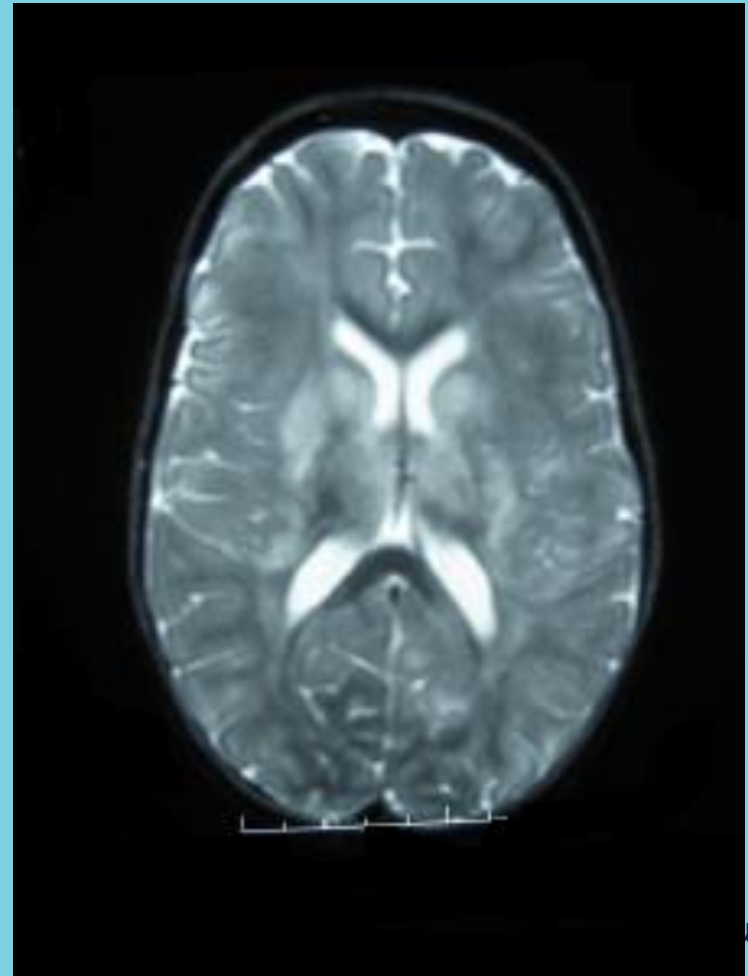
Symptoms of 1st episode of MS may differ from adults

- Often more severe
- Encephalopathy may be present
- MRI at onset often ADEM-like abnormalities



Willem, 1 year and 5 months: will he develop MS??

- Diagnosis **ADEM**.
- Treatment: corticosteroids
- 5 years follow-up
 - No further events
 - Normal development
 - No residual deficits



Question

- Which statement on ADEM is correct
- A: The chance to develop MS after ADEM is $< 5\%$
- B: The chance to develop MS after ADEM is $> 5\%$
- C: ADEM is associated with cambylobacter infection
- D: ADEM more frequently occurs in girls

Initial diagnosis ADEM: 21-29% develops MS !

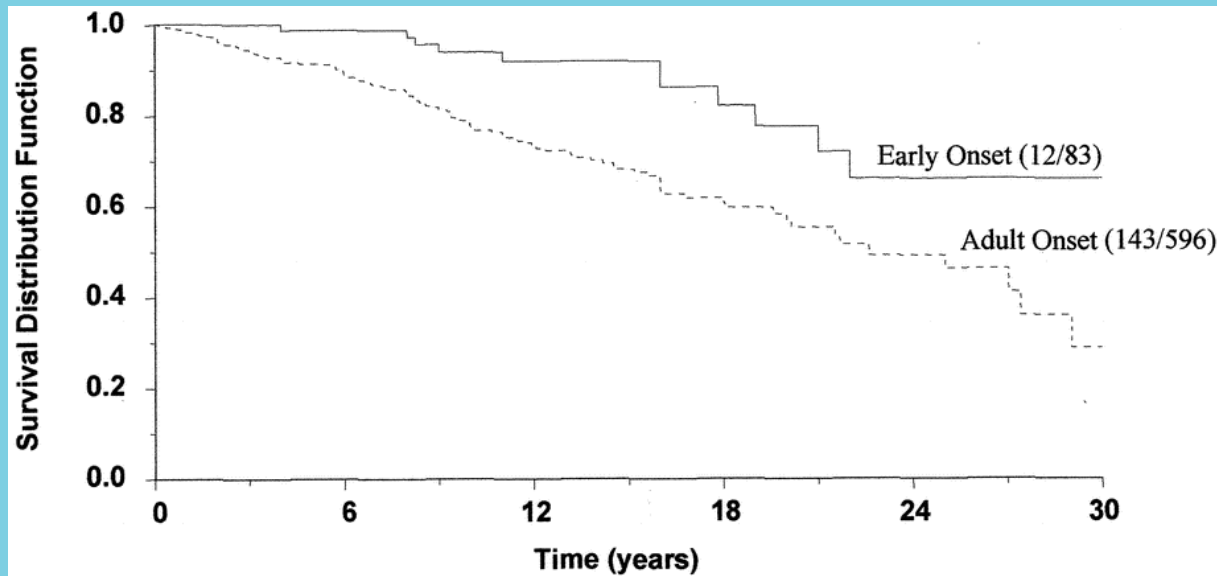


Mikaeloff et al. 2004, Neuteboom et al 2009

A second ADEM event after ADEM

- After ADEM a second event compatible with a diagnosis of ADEM may occur
- Dissemination in place: ✓
- Dissemination time: ✓
- ~~Diagnosis MS? = recurrent or multiphasic ADEM~~

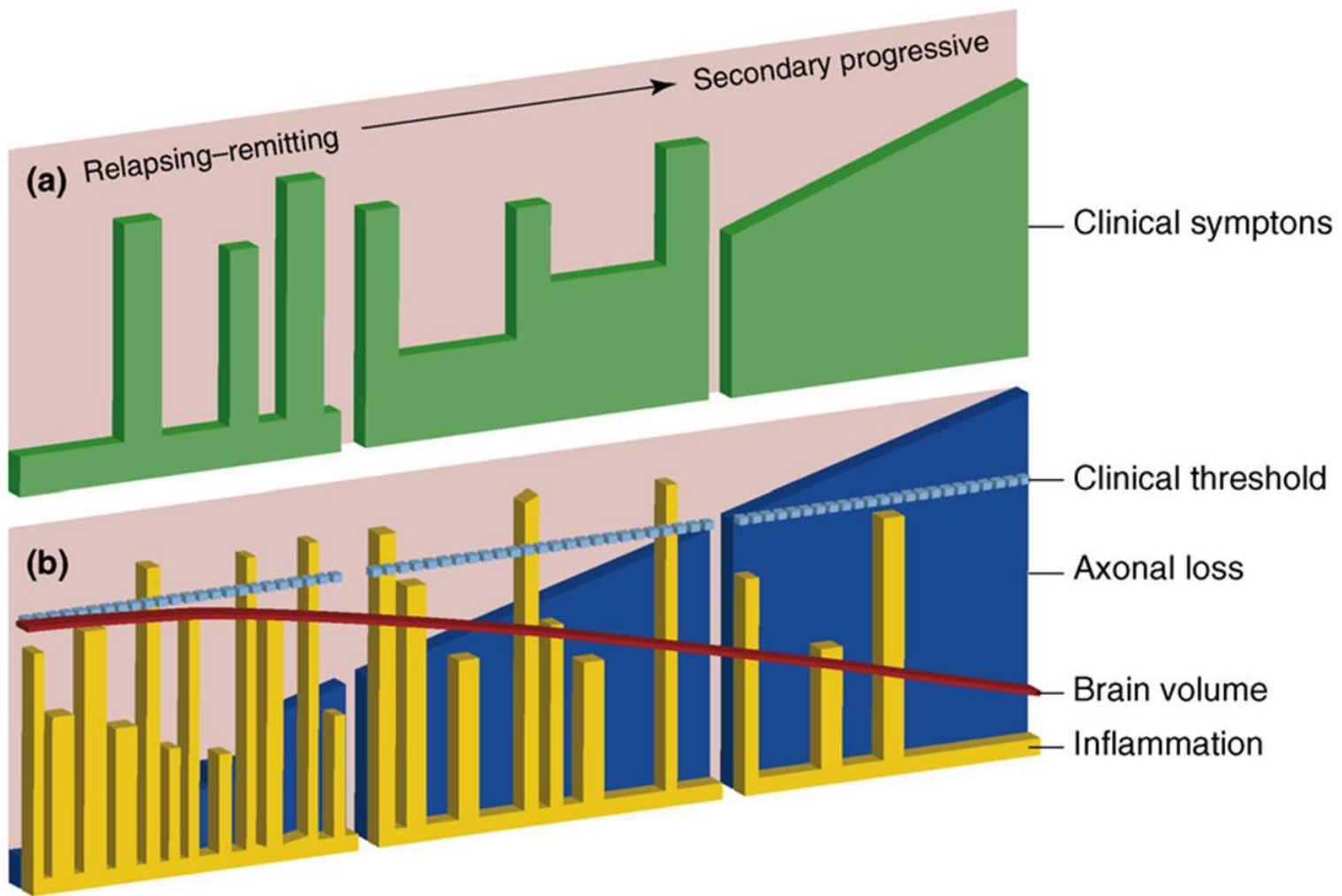
Course of MS in children is slower than in adults



Simone et al. Neurology 2002;59: 1922- 1928

Early onset MS = a severe disease

- Relapse frequency 1-1.9 relapses /year in the first few disease years
- Physical disability at relatively young age
- 30% of children and adolescents perform below age-expected levels



Decursus early onset MS

Early onset MS

Protracted course

Disability at relatively young age

Time to EDSS 6.0



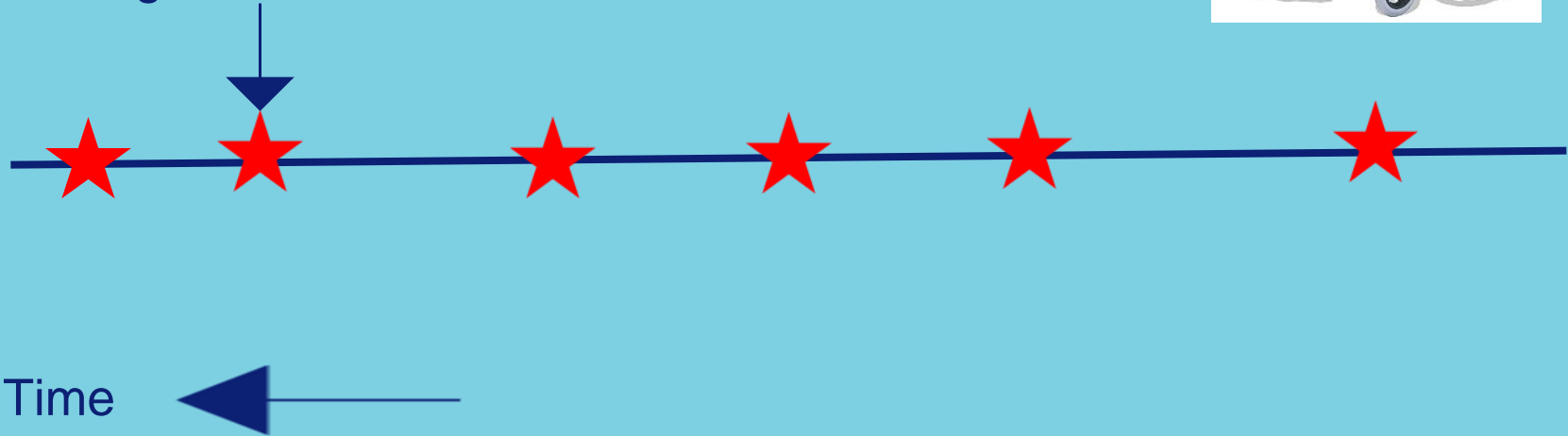
Adult onset MS

Time to EDSS 6.0

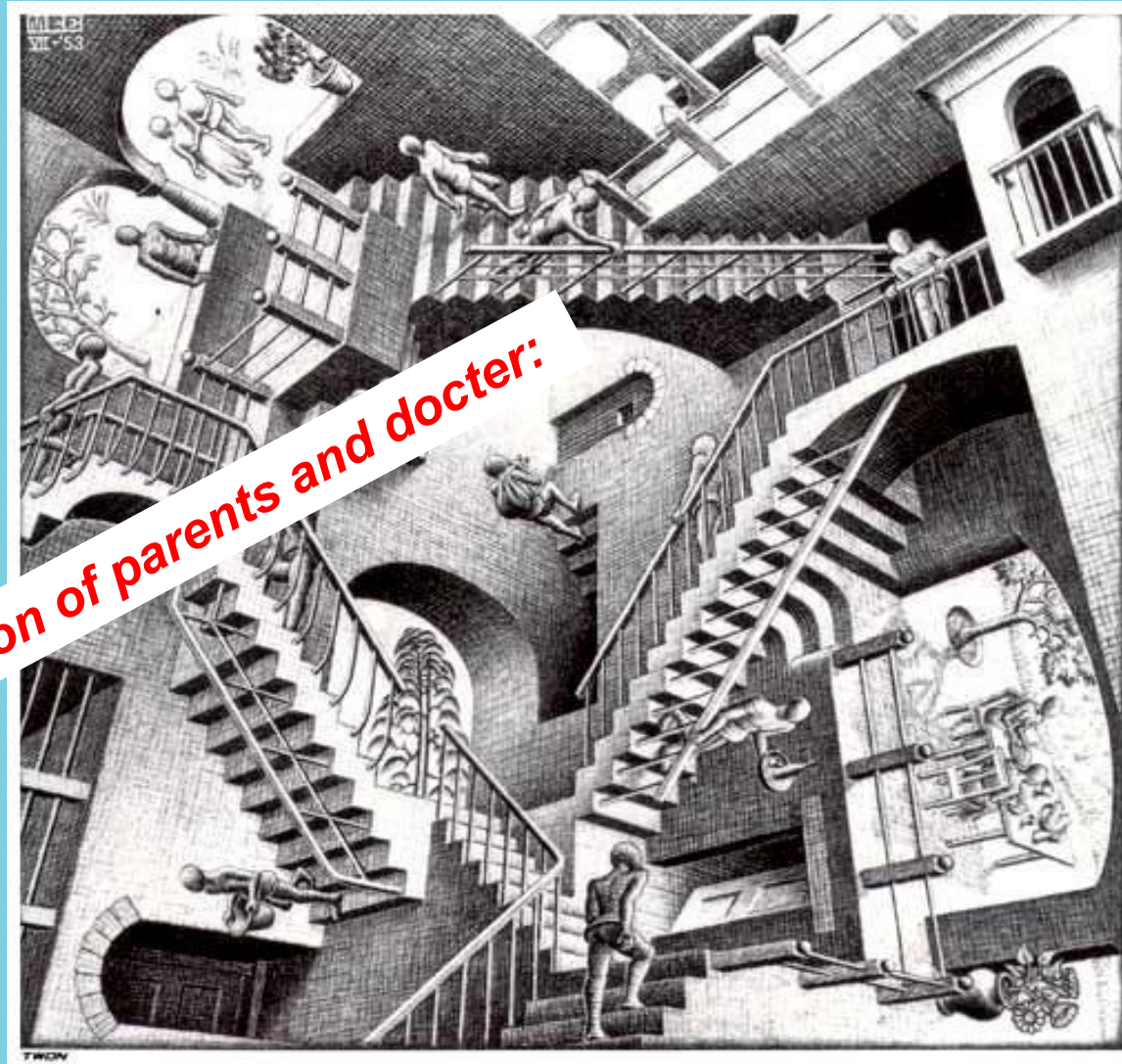


Early diagnosis is important to start immune modulating treatment as young as possible!

- Diagnosis MS



Is this Clinically Isolated Syndrome the first episode of MS?



Question of parents and doctor:

2012: MRI criteria for childhood MS

1. Dissemination in space (DIS)

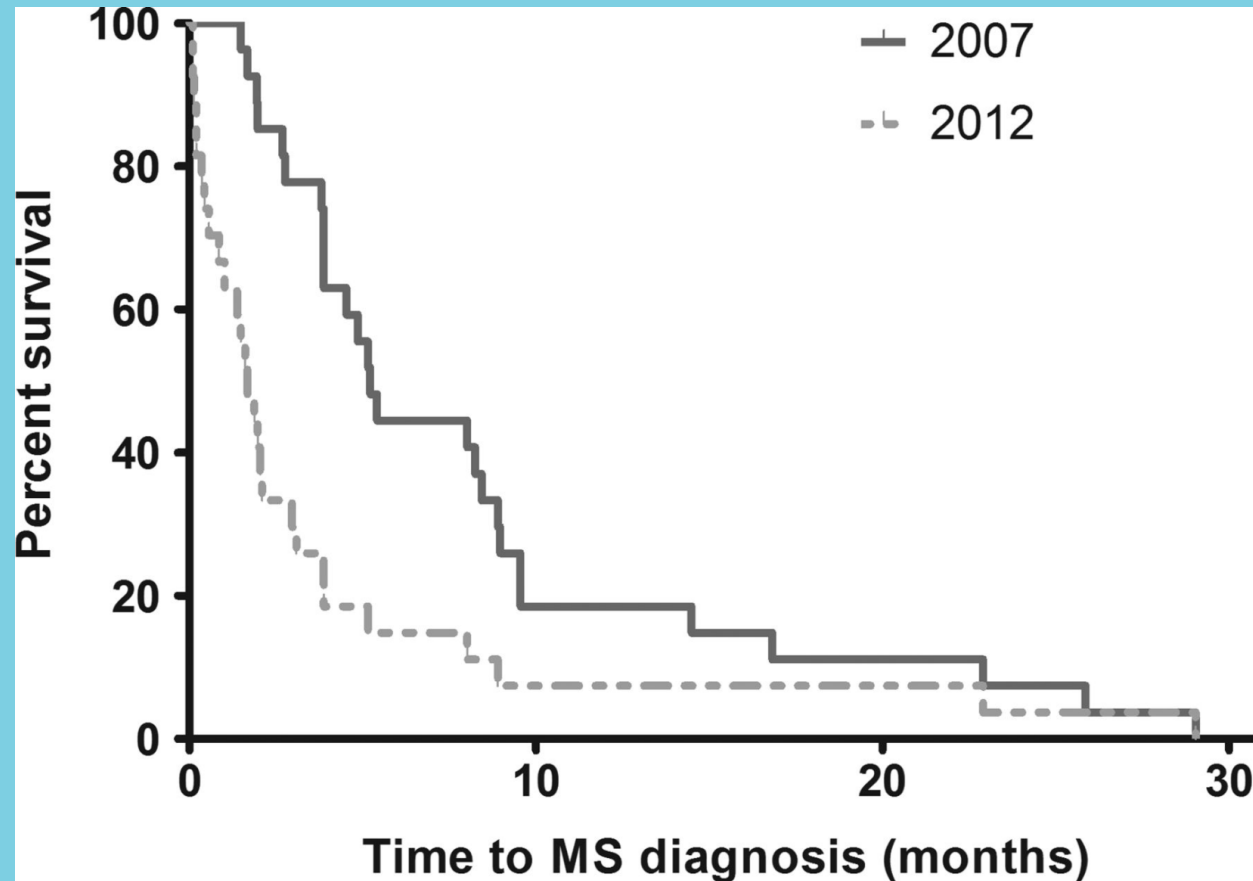
- 1 or more juxtacortical lesion
- 1 or more periventricular lesion
- 1 or more infratentorial lesion
- 1 or more spinal lesion

2. Dissemination in time (DIT) (only if >11 years)

- on 1st MRI non symptomatic GADO enhancing lesion
- new lesion T2 or GAD+ lesion on 2e MRI

3. ADEM does not count as first event

2012 MRI criteria voor children



Time to diagnosis MS: CDMS 10m, 2007: 8.5m, 2012: 5m.

2011: Verhey criteria for prediction that a 1st Acute Demyelinating Syndrome develops into MS

	Dutch cohort	Canadian cohort
□ Sensitivity:	91%	84%
□ Specificity:	78%	93%

Positive Predictive Value: 61%
Negative Predictive Value: 96%

- **Minimal 1 T2 or flair periventricular lesion**

AND

- **Minimal 1 T1 hypo-intense lesion**



Verhey et al. Lancet Neurology 2011; 10: 1065-1073.

ERASMUS

Paediatric MS team

Rinze Neuteboom

Coriene Catsman

Femke Aarsen

Danielle van Pelt

Immy Ketelslegers

Sarita van den Berg

Rogier Hintzen



ErasMS