Multiple Sclerosis Diagnosis and Care

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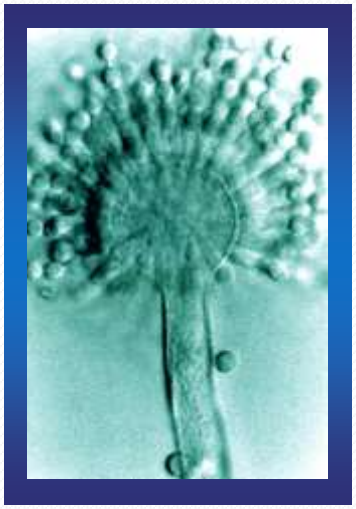
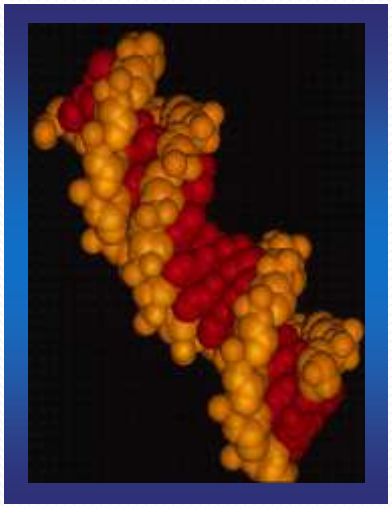
Underlying Factors of MS



Infectious agent



Genetic predisposition

Environmental factors

Abnormal immunologic response → MS

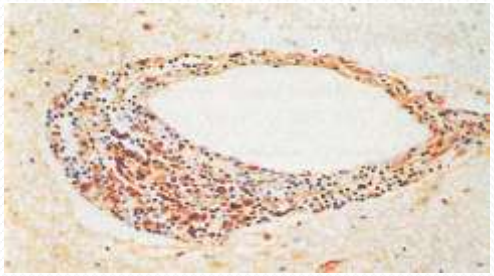
Multiple Sclerosis

- Disorder of CNS white matter
- Inflammation of myelin
- Loss of neurons, oligodendrocytes and osteocytes
- Atrophy of the brain
- Etiology unclear
  - viral infection
  - autoimmune disorder
  - heredity

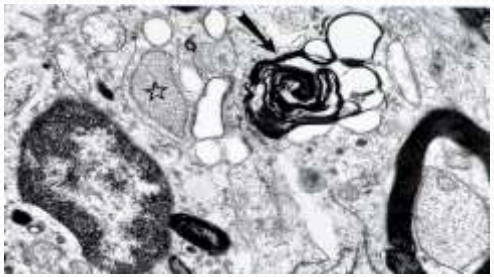
How MS Affects Nerve Cells

Underlying Factors of MS: Inflammatory Cascade

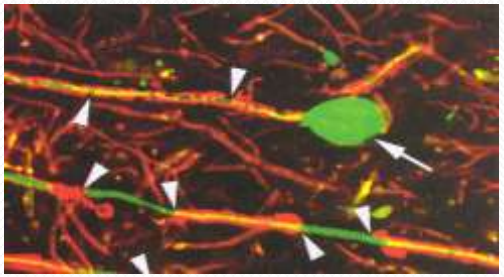
Inflammation



Demyelination



Axonal loss



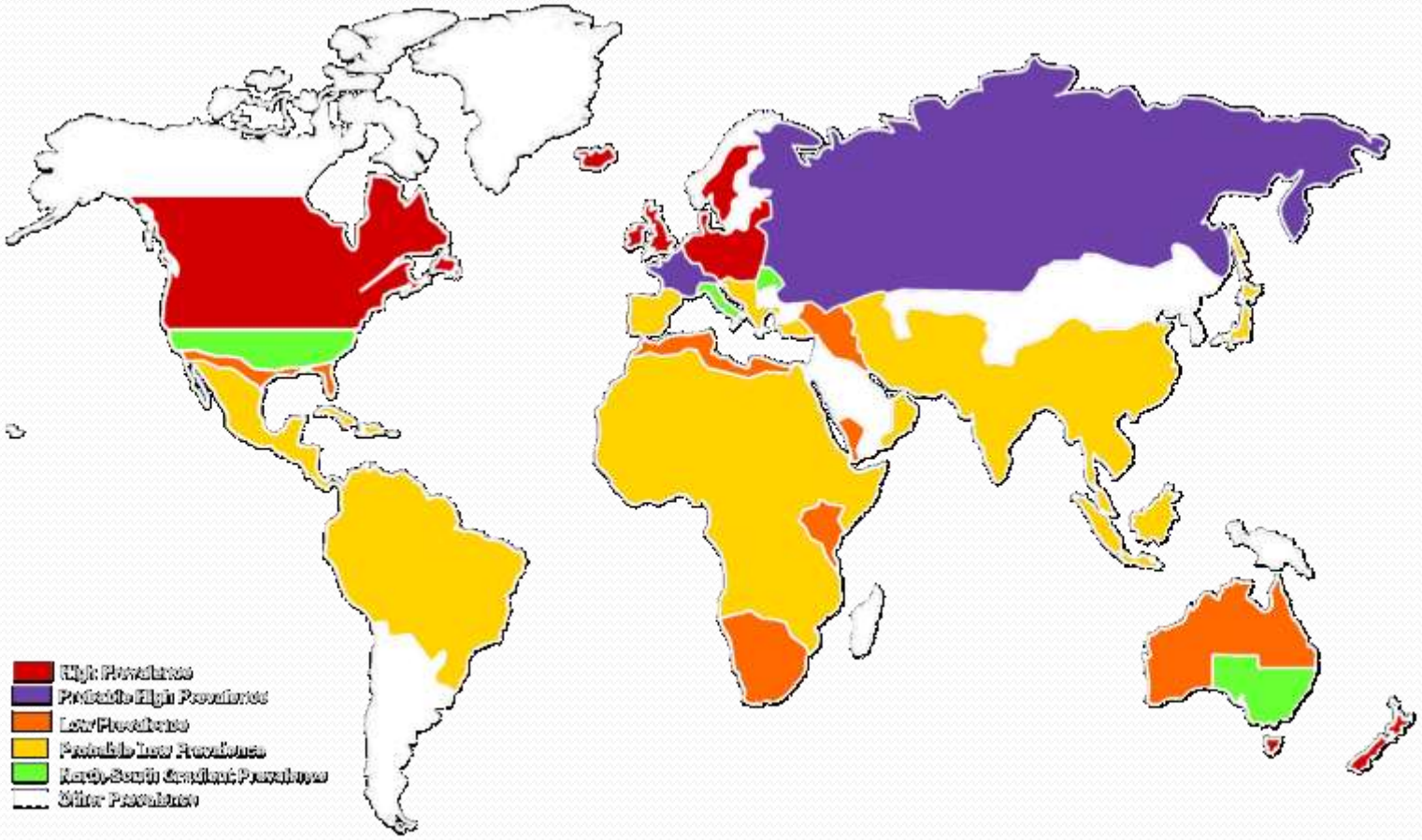
What causes MS ?

- ***MS is believed to be caused by an autoimmune destruction of myelin. MS patients have a decreased number of certain T-cells known as supressors / inducers which tell the immune system when to reduce its activity. The cells in the immune system actually fight each other and this causes destruction of myelin.***

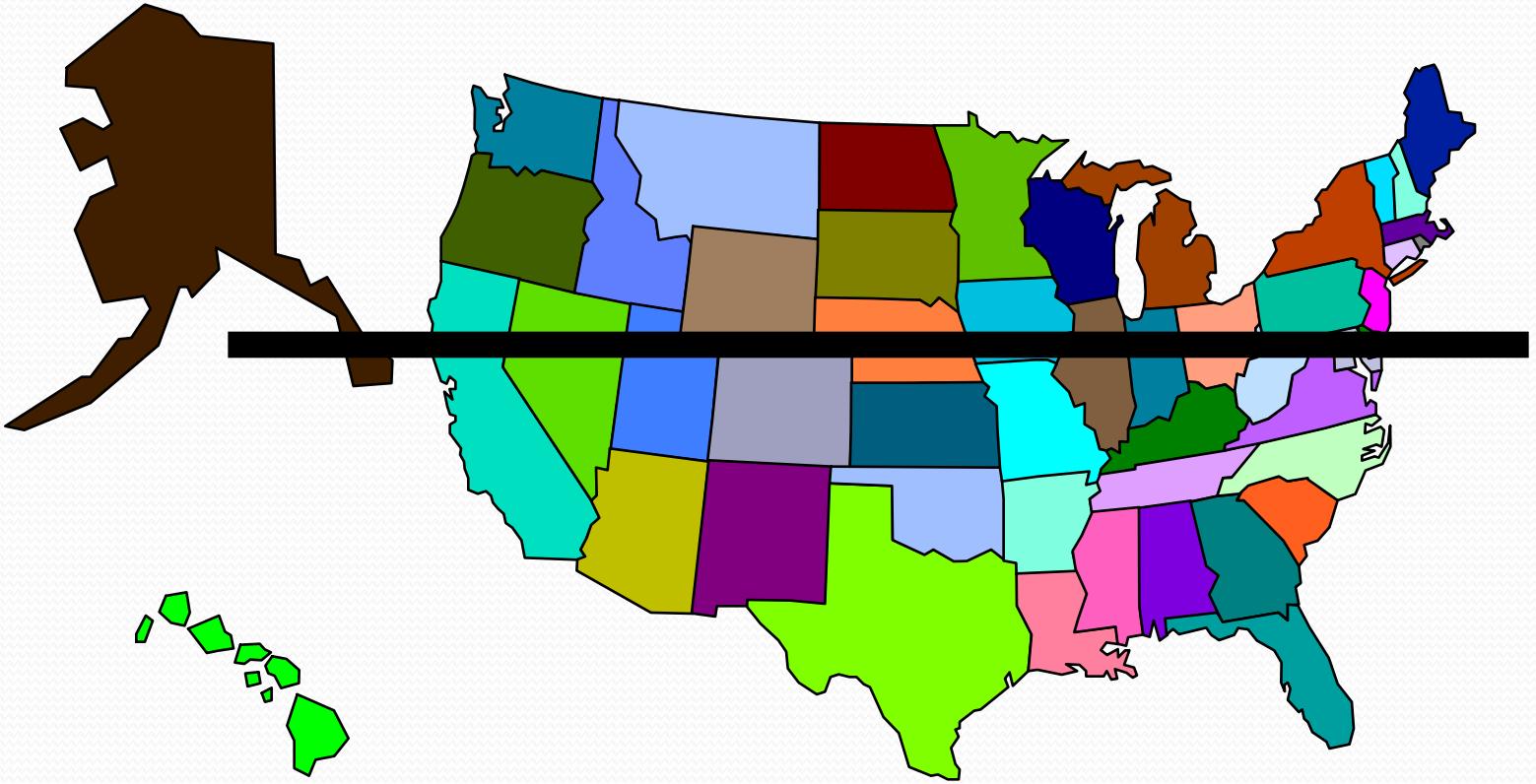
Epidemiology of MS

- .1-2% of the adult population in US affected
- Ages 15-50 years
- Women2: Men 1
- White especially people of northern European heritage
- Rare in tropics and polar regions
- Risk of MS changes with migration before age of 15 years

Worldwide Prevalence of MS



Incidence of Multiple Sclerosis



Neurological Signs & Symptoms of MS

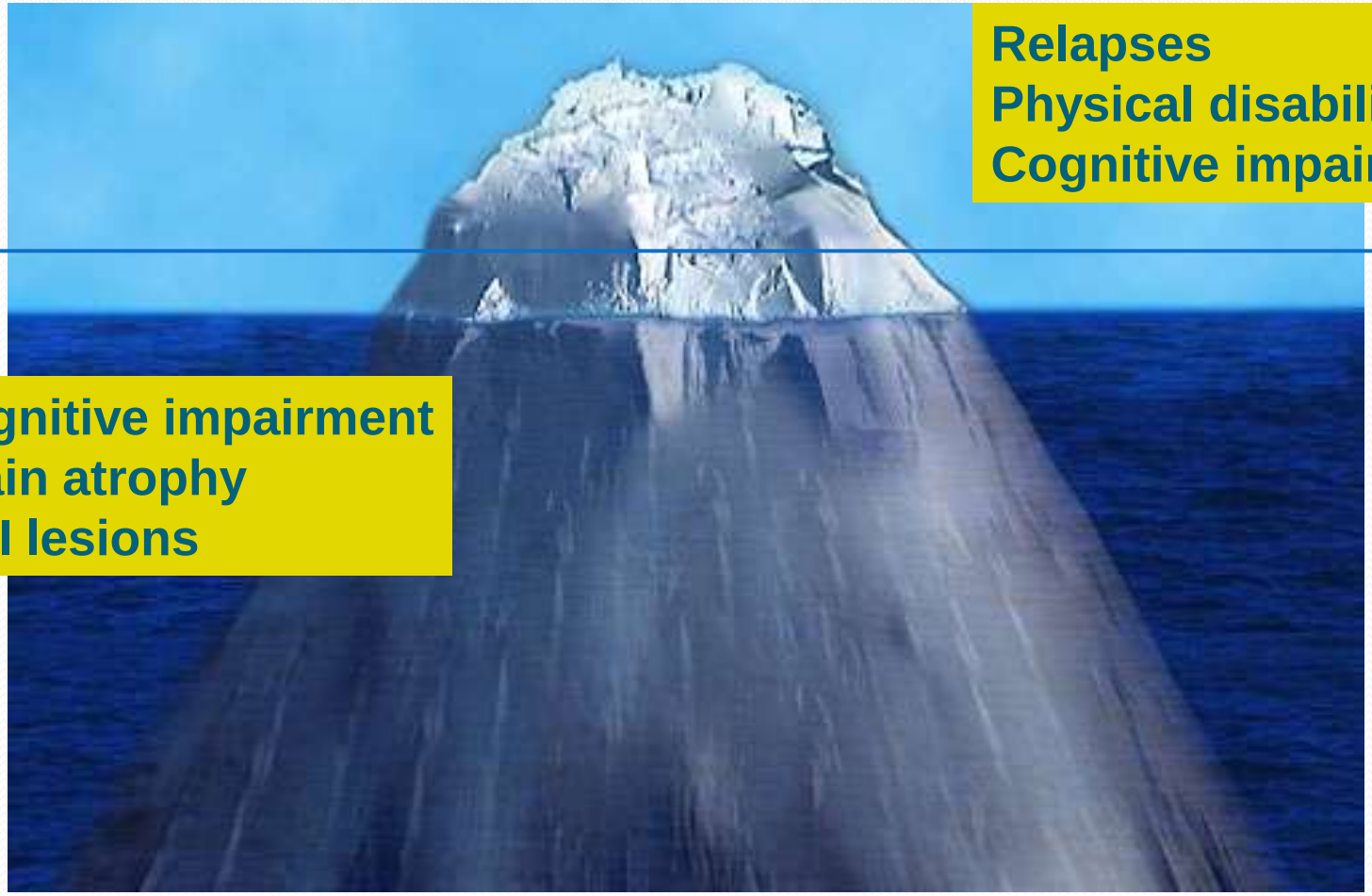
- As it can effect any portion of the white matter of the brain, it can promote any neurological deficit

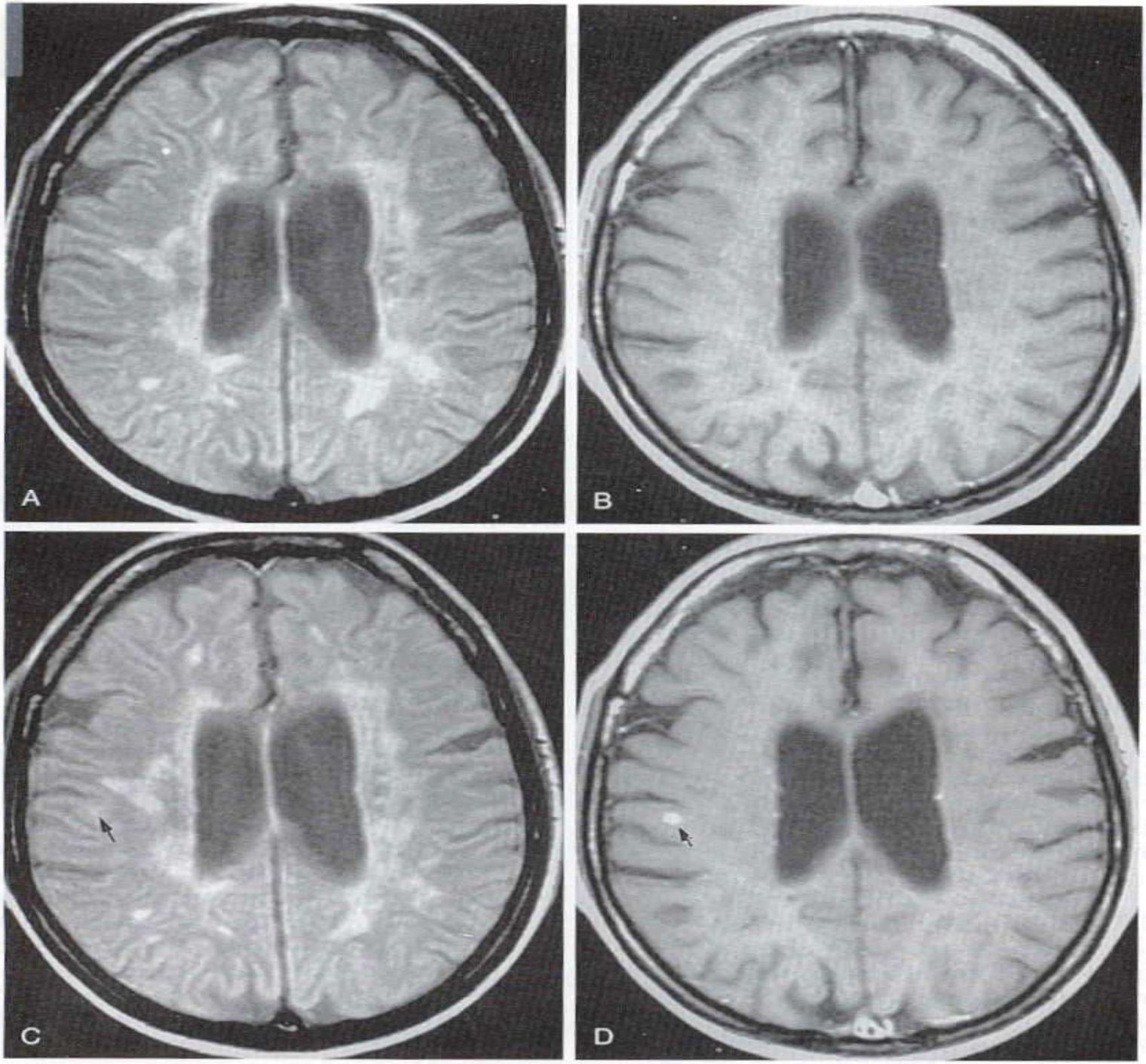
- Cognition/fatigue
- Speech
- Strength
- Sensation
- Balance & coordination
- Neurogenic bladder
- Vision
- Smell
- Walking
- Hearing/Dizziness

Work-up of MS

- Serum workup
- MRI brain with contrast and diffusion weighting/MS protocol
- Spinal fluid analysis
  - Cell count
  - Myelin basic protein
  - Oligoclonal bands
  - IgG index
  - Total protein/glucose
- Transesosphageal echo
- Evoked potentials
  - Visual (VEP)
  - Auditory (BAEP)
  - Somatic (SEP)

Invisible vs Visible MS

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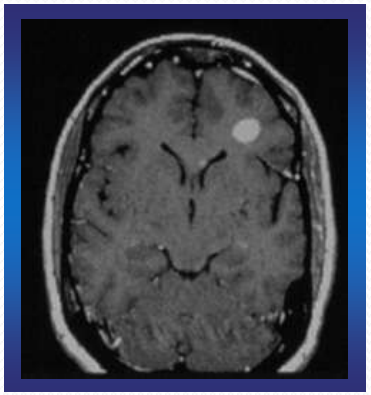
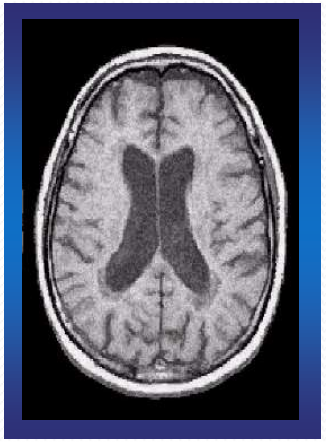
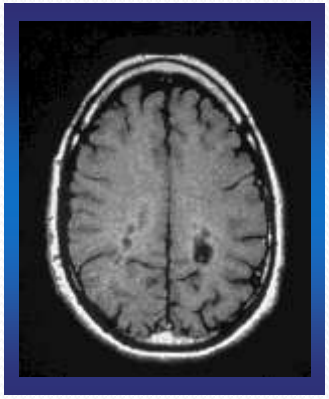
“Invisible” Neurologic Signs of MS



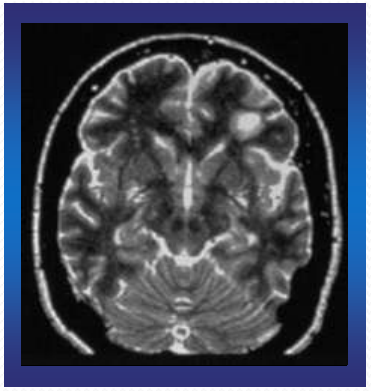
Gd enhancement



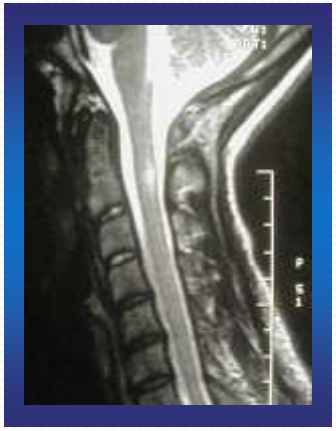
Brain atrophy (shrinkage)



T1 “black hole”



T2 lesion

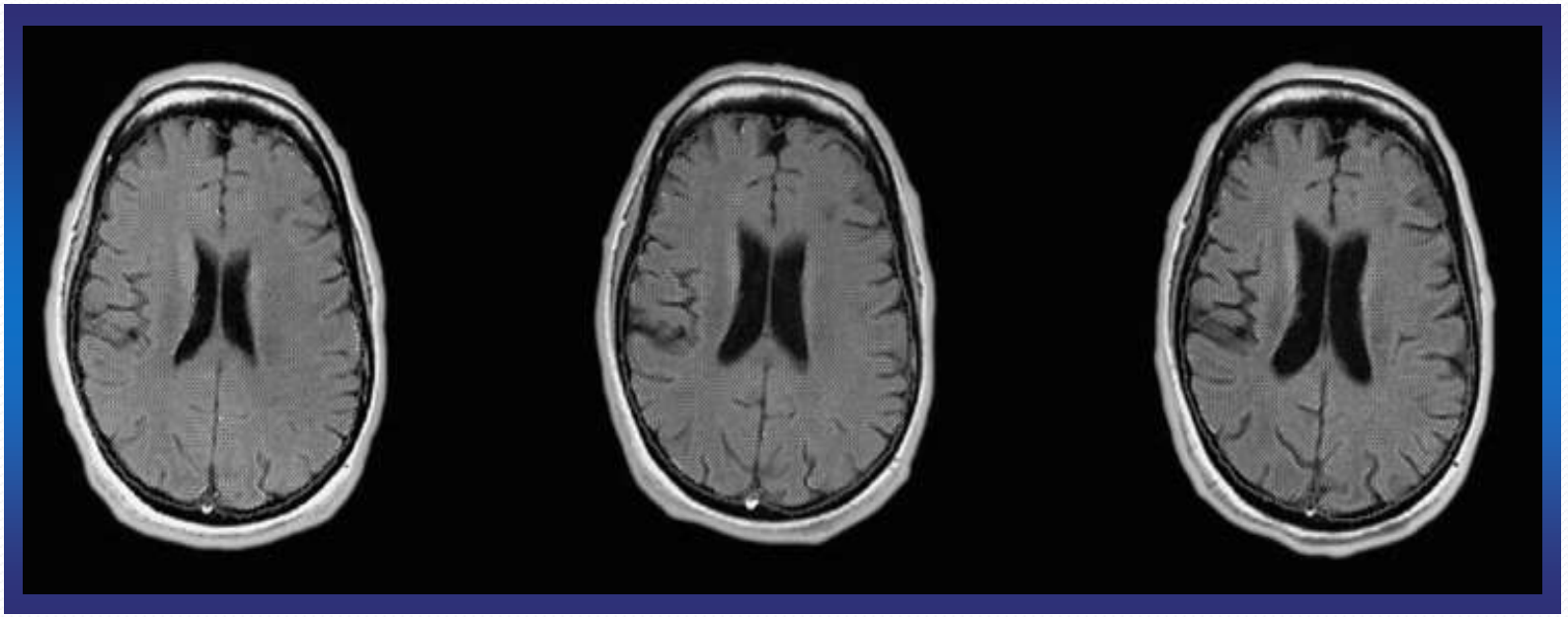


Spinal cord lesion

MS Treatment Goals

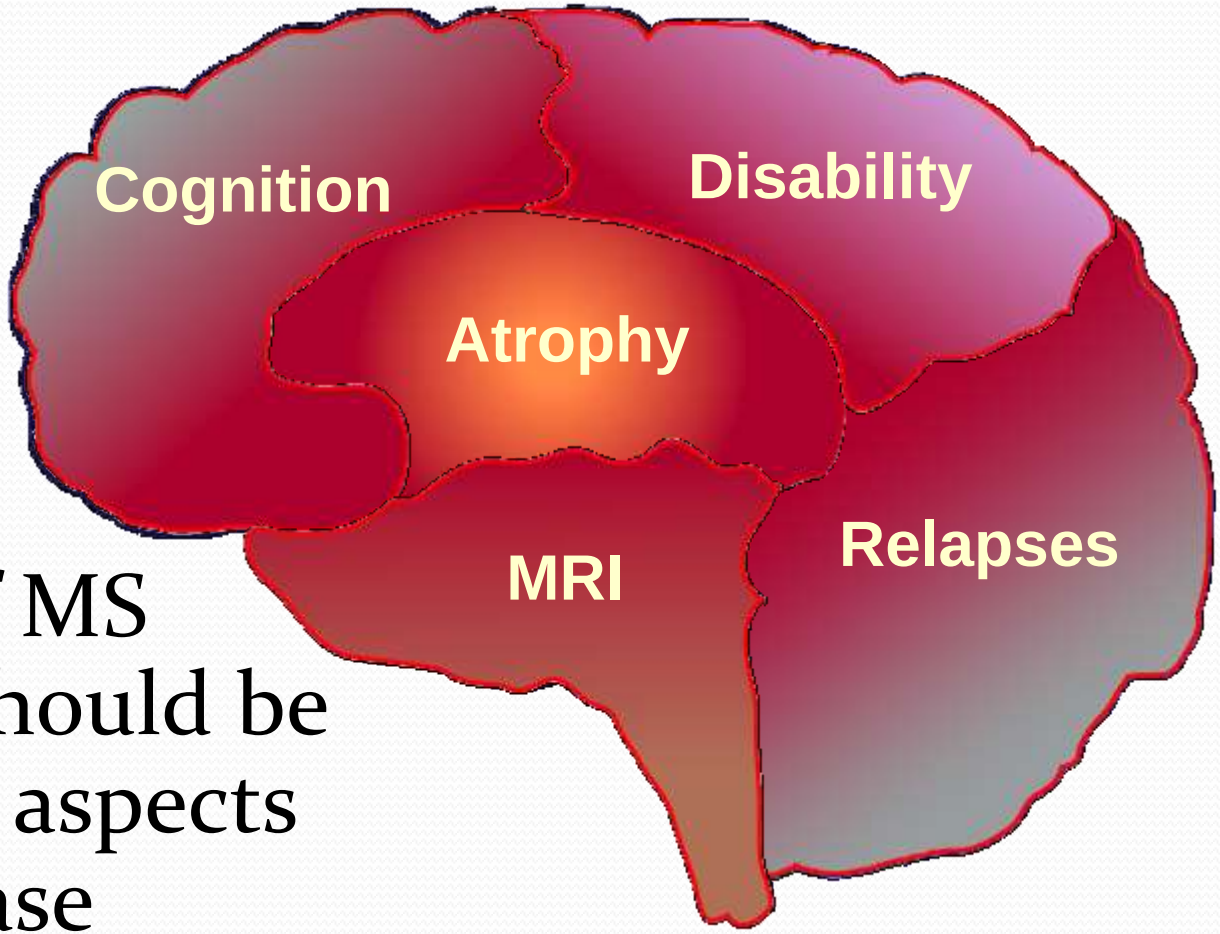
- Treat the whole disease
- Slow down the accumulation of sustained physical disability
- Reduce relapse rate
- Reduce CNS inflammation (lesions)
- Reduce progression of brain atrophy (shrinkage)
- Improve patients' quality of life
  - Cognitive function
  - Predictable, manageable side effects

Brain Atrophy (Shrinkage) in Untreated MS



These images were acquired over the course of 7 years from a single person with untreated MS

MS Therapies: Treating the Whole Disease



- The goal of MS therapies should be to affect all aspects of the disease

Risk of Developing MS after First Attack

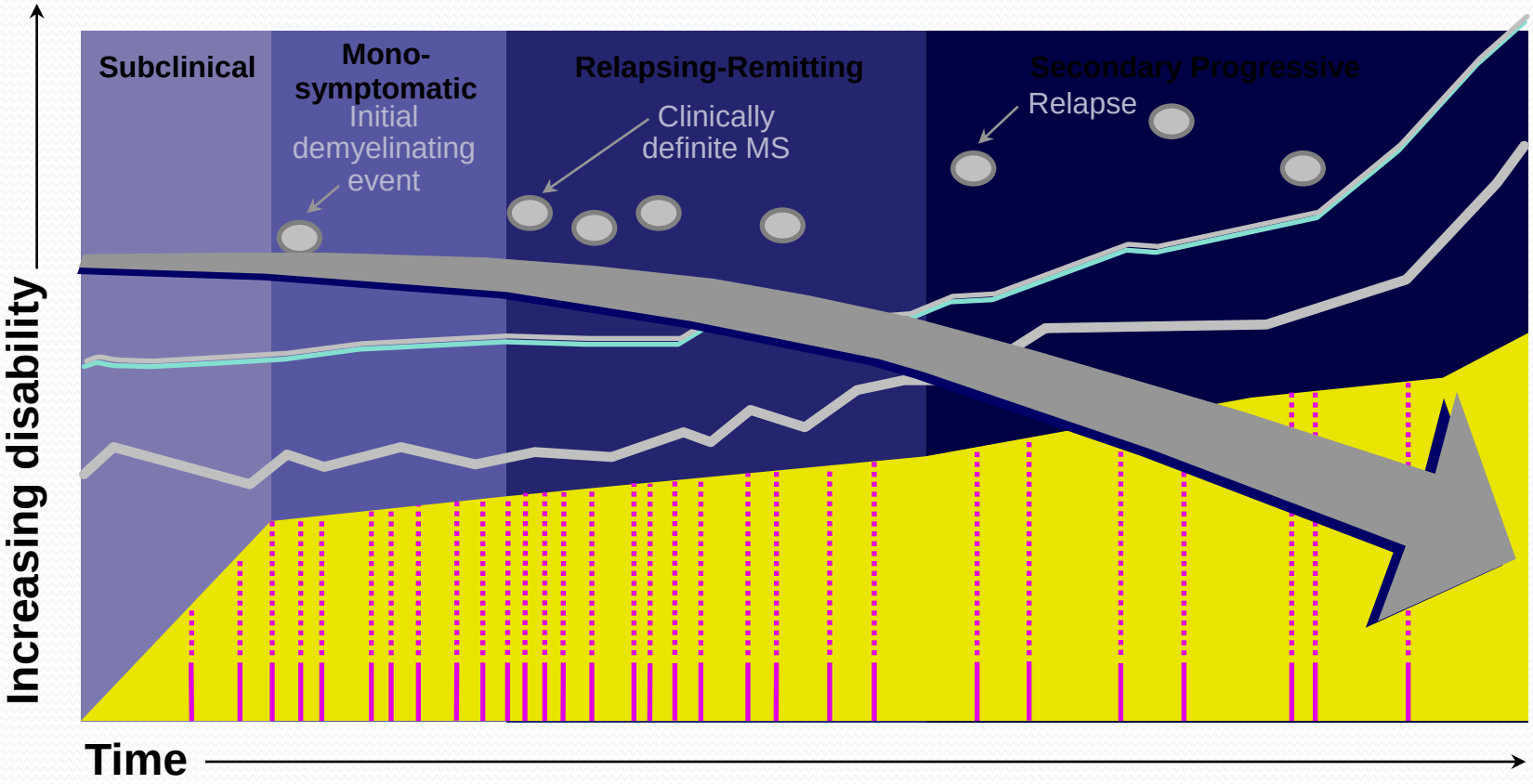
- Normal MRI - 40%
  - Normal CSF — < 20% at 5 years
  - Abnormal CSF — 20 - 50% at 5 years
- Abnormal MRI - 60%
  - 1 T2 lesion
    - Normal CSF — 20 - 50% at 5 years
    - Abnormal CSF — 50 - 90% at 5 years
  - 2 or more T2 lesions
    - No enhancement — 50 - 90% at 5 years
    - Enhancement — >90% at 5 years

What is the Range of MS Severity?

- People with MS usually fit into one of two general categories according to the predominant course of the disease:
  - Relapsing
  - Progressive

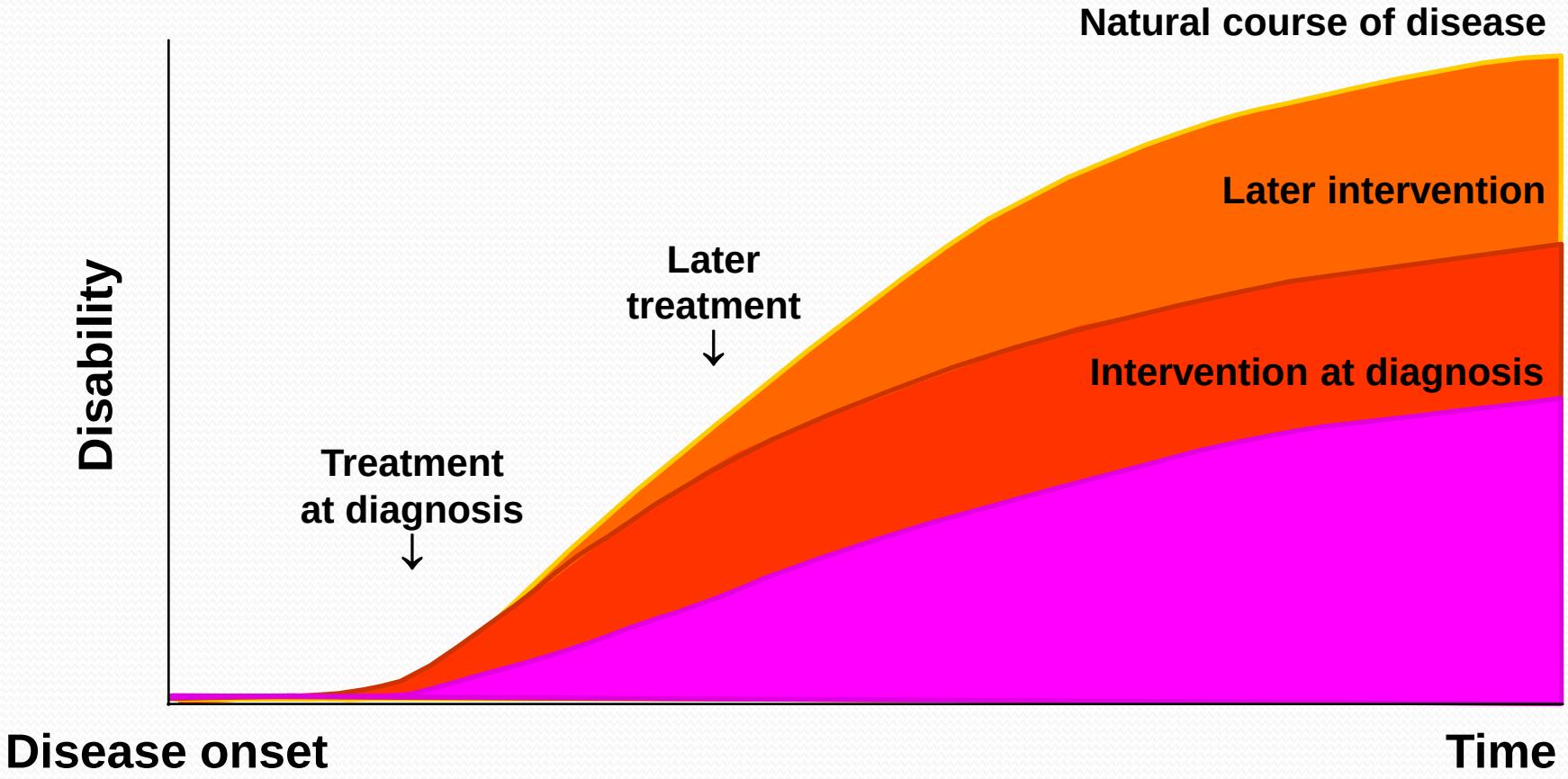
"Invisible" MS

Relapsing forms



Gd = gadolinium.

Current Opinion of the Hypothetical Effect of Treatment



Rationale for Treatment

- Relapsing-remitting multiple sclerosis (RRMS) leads to progressive MS within about 10 years in 50% of cases.[1]
- 30%-50% of patients worsen by 1.0 Expanded Disability Status Scale (EDSS) unit within 2 to 3 years.[2]
- 15%-44% of patients need an assistive device for walking within 5 years.[2]
- Once inflammatory demyelination has resulted in either gliosis preventing remyelination or frank axonal disruption, the ability to recover function is severely limited.

1. Weinshenker BG, et al. The natural history of multiple sclerosis: a geographically based study. Clinical course and disability. *Brain*. 1989; 112: 113-146.
2. Munschauer FE, Stuart WH. Rationale for early treatment with Interferon beta-1a in relapsing and remitting multiple sclerosis. *Clin Ther*. 1997; 19: 868-88g2.

Disease Modifying Therapies for MS

- Interferons
  - Avonex
  - Beta Seron/Extavia
  - Rebif
- Copaxone
- Tysabri
- Gelena

Case Presentations

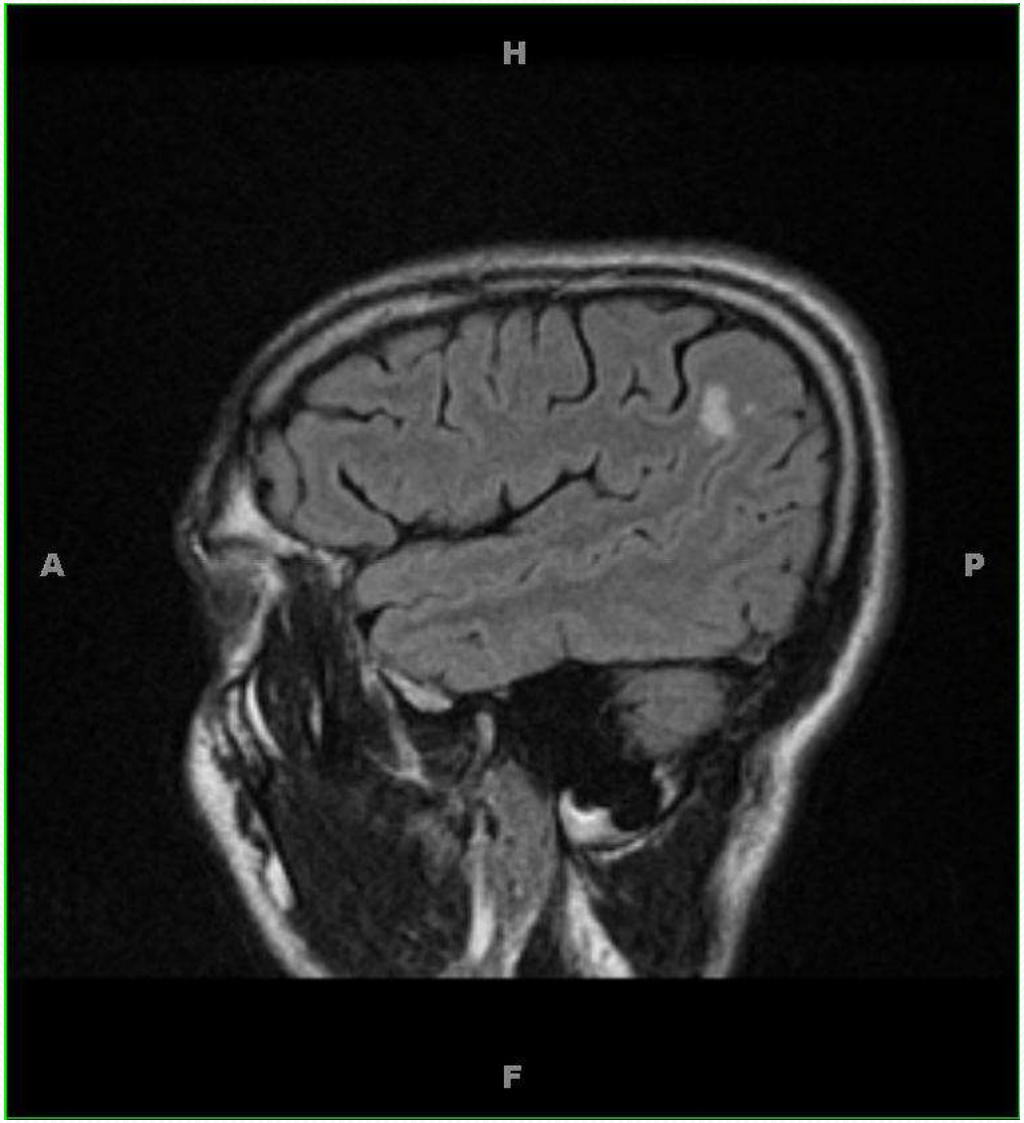
Case 1

- 45 year old Arabic male
- MS diagnosed 2006
- Has never taken MS platform medications
- Symptoms
  - Fatigue
  - Restless leg syndrome
  - Leg/arm weakness and paresthesias
  - Poor concentration

Case 1

Physical exam

- CN: Normal
- Motor: 5/5 upper/lower strength, mild increased tone of legs
- Cerebellar: Intact
- Sensory: Normal proprioception, decreased vibratory to level of DIP, no agraphesthesia or astereogonosis, negative rhomberg and retropulsion
- DTR: 2+ upper, 3+ knees/ankles bilateral, downward toes bilaterally
- Gait: Normal gait and easily runs down the hall
- Cognition: Normal MMSE
- General: Appears fatigued and anxious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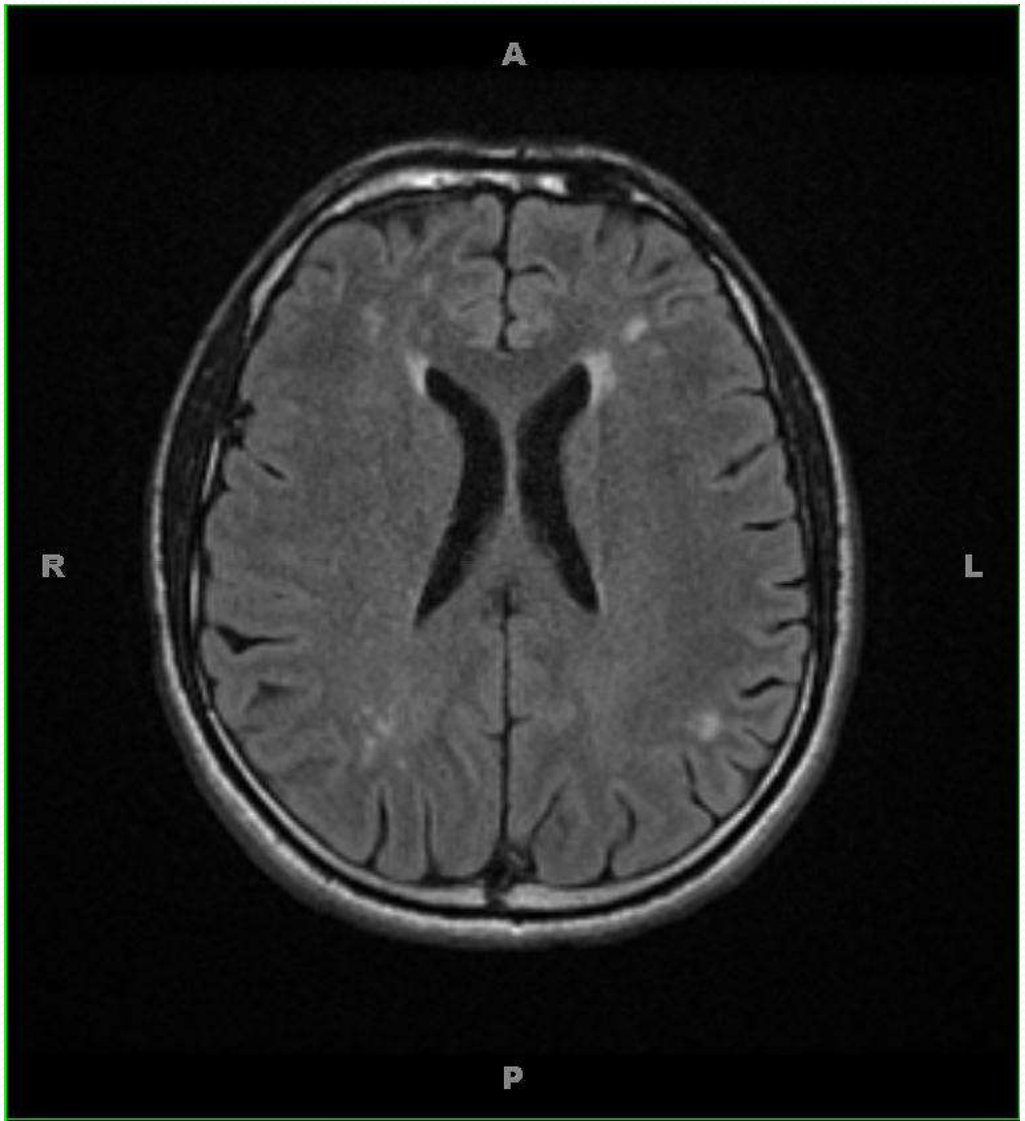
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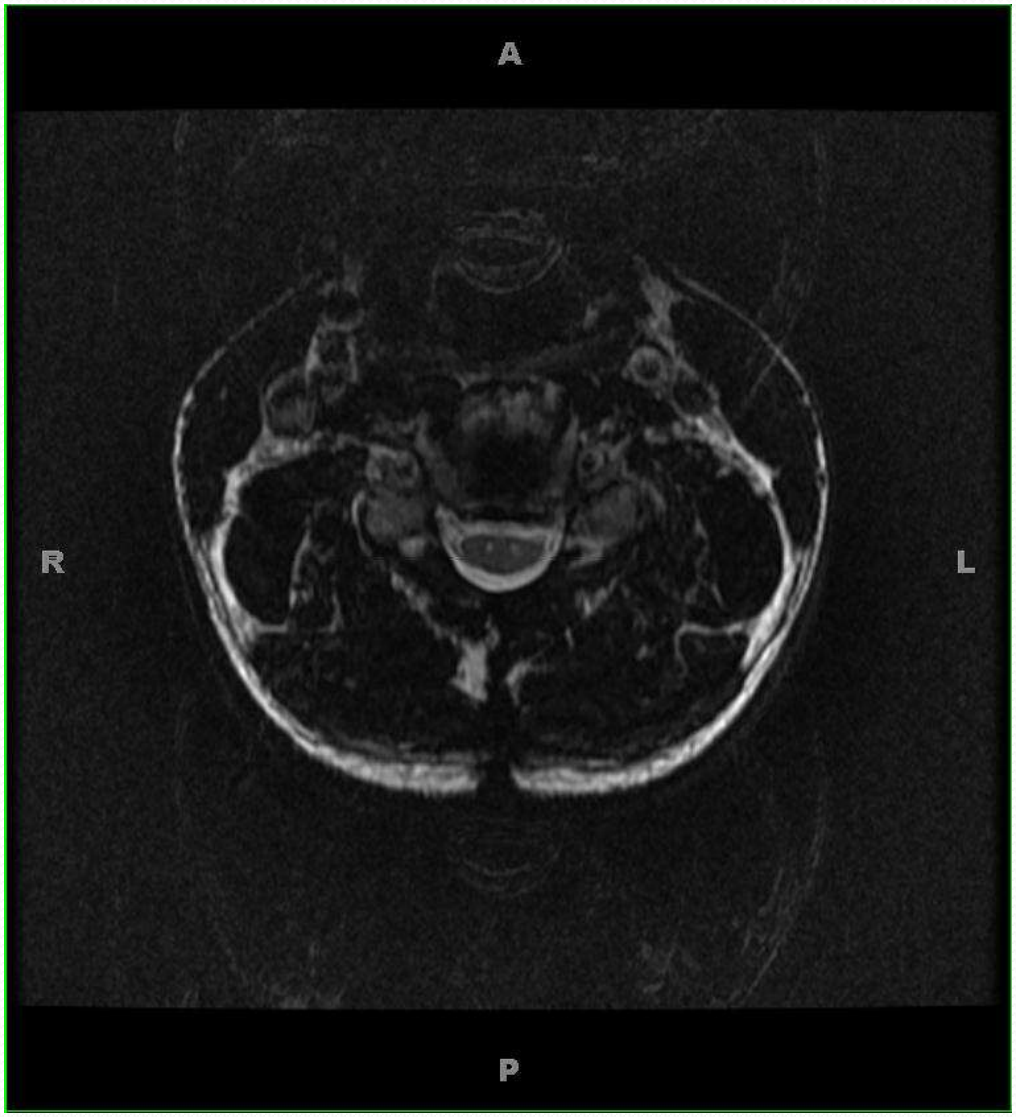
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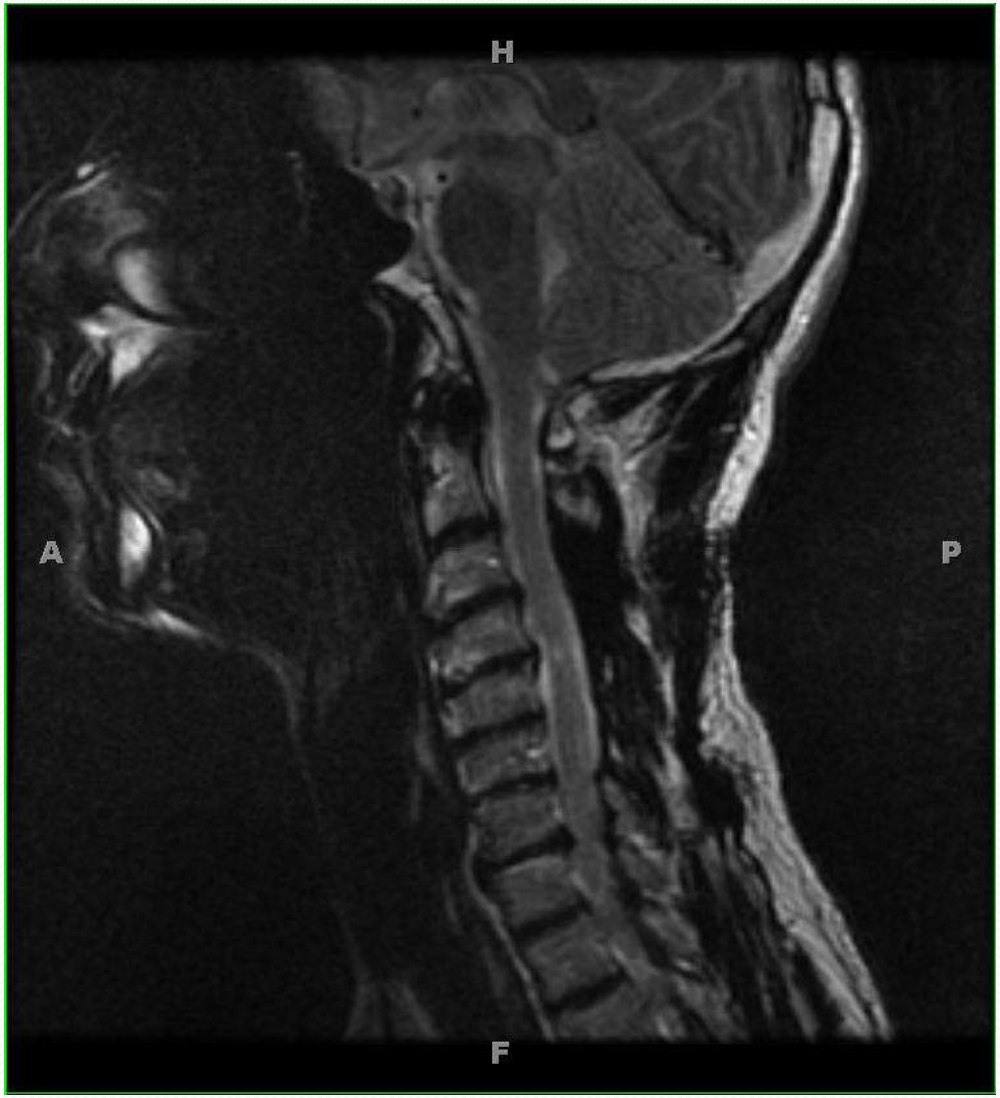
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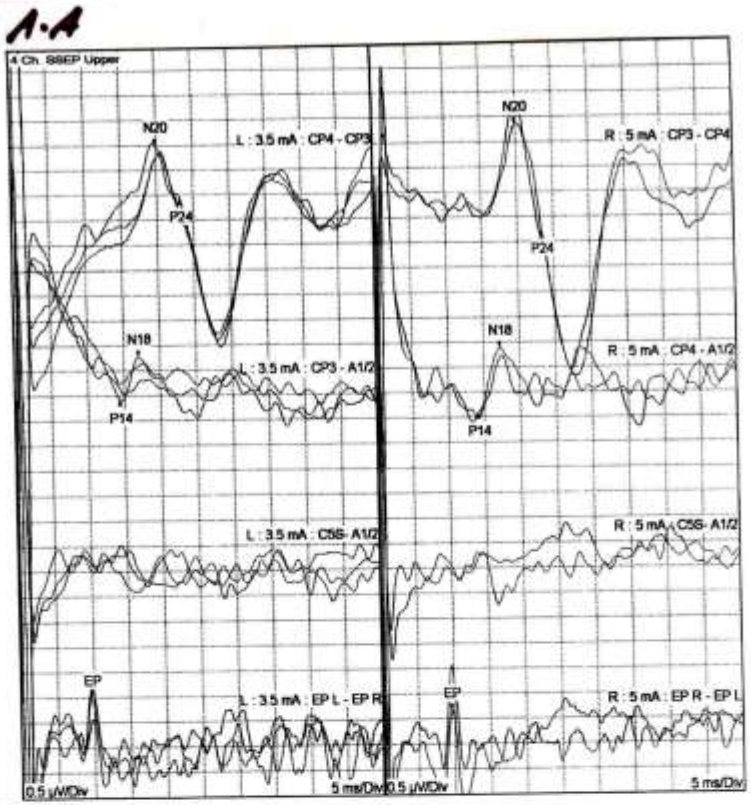
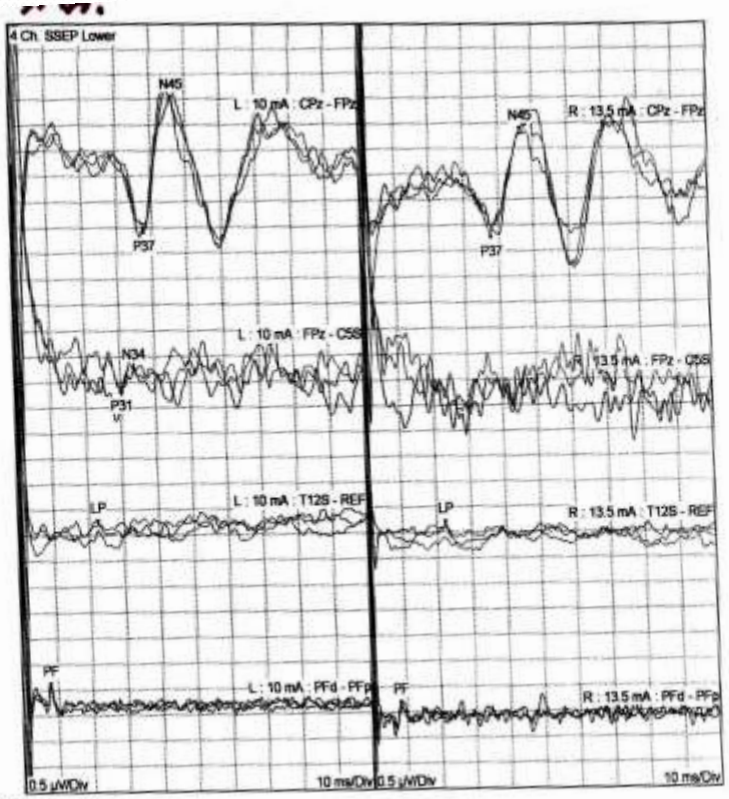


4 Ch. SSEP Upper

Trial	N20 (ms)	P24 (ms)	N18 (ms)	P14 (ms)	N13 (ms)	EP (ms)	N13-N20 (ms)	N20-P24 (µV)
Norm	<22.1							
Trial2 - L	19.9	23.2	17.0	14.4	0.0	9.7	0.0	1.10
Trial5 - R	19.9	23.4	17.3	14.1	0.0	9.6	0.0	2.13
L-R Norm	<1.0	<1.0	<1.0	<1.0	<1.0	<.5		<50
L-R	0.0	0.2	0.3	0.3	0.0	0.1	0.0	1.03

Patient Complaints:
45 yr old male w/hx of MS since 2006. Pt w/numbness, tingling and weakness in upper and lower extremities

RM: 514-1



4 Ch. SSEP Lower

Trial	P37 (ms)	N45 (ms)	P31 (ms)	N34 (ms)	LP (ms)	PF (ms)	LP-P31 (ms)	P31-P37 (ms)
Norm	<43.5							
Trial1 - L	37.7	46.1	30.0	33.9	22.7	8.0	7.3	7.7
Trial5 - R	37.7	46.4	0.0	0.0	22.5	8.3	0.0	0.0
L-R Norm	<1.5	<1.5	<1.5	<1.5	<1.5	<.5		
L-R	0.0	0.3	30.0	33.9	0.2	0.3	7.3	7.7

Patient Complaints:
45 yr old male w/hx of MS since 2006. Pt w/numbness, tingling and weakness in upper and lower extremities

RM: 514-1

Case 2

- 42 year old white male
- 5 day history of numbness and paresthesias of feet, lower legs, buttocks, hands and lips, and legs feel heavy.
- Since hospitalization, progressive paresthesias to level of T8, neurogenic bladder, neurogenic bowel.

Case 2

Physical Exam

CN: Normal

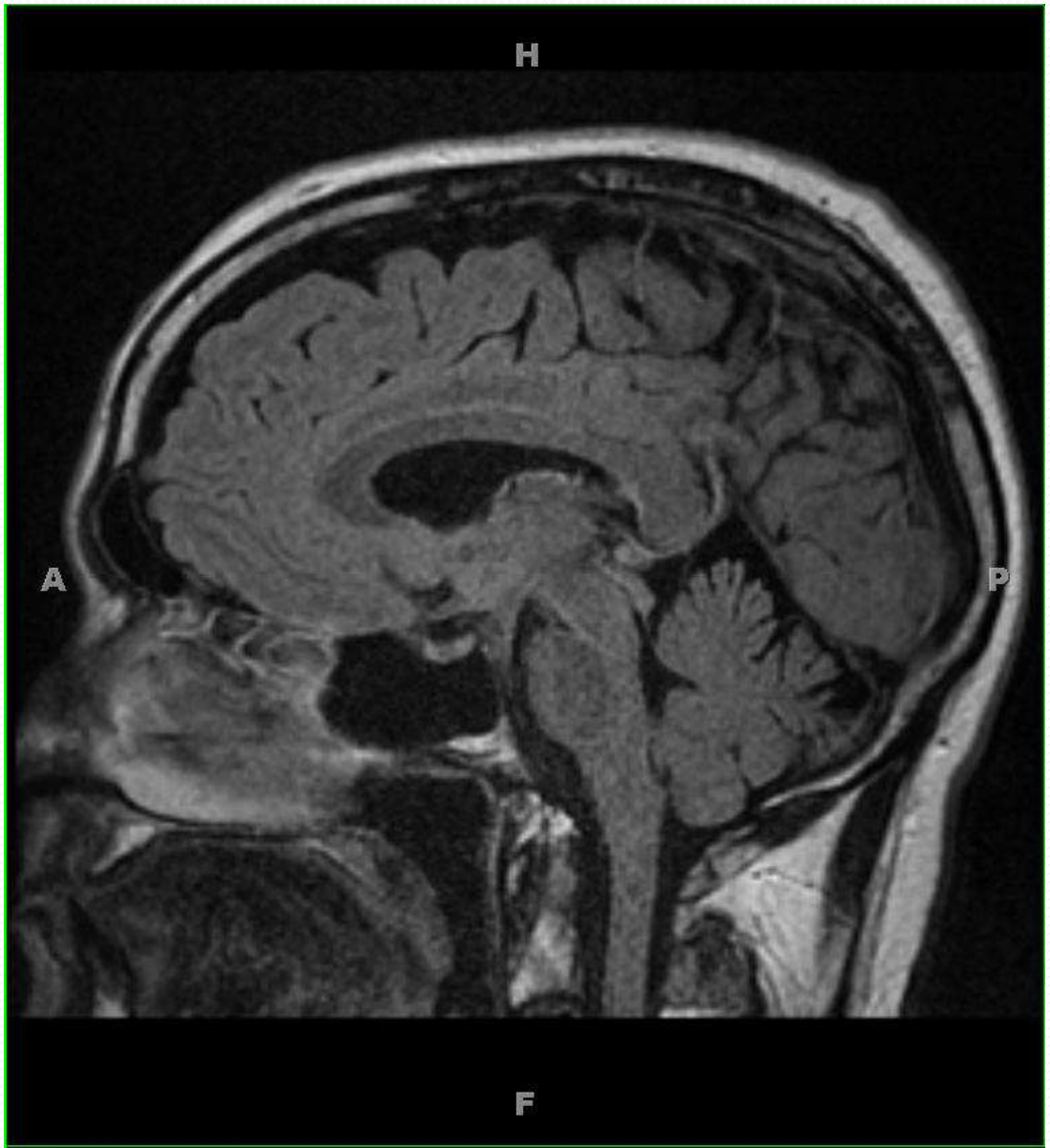
Motor: 5/5 upper and lower

Sensory: T8 sensory level, proprioception to level of ankle, decreased vibration to the DIP, no agraphesthesia or astereognosis, negative Rhomberg, positive retopulsion

DTR's: Absent

Cerebellar: Intact upper and lower

Gait: Appears minimally ataxic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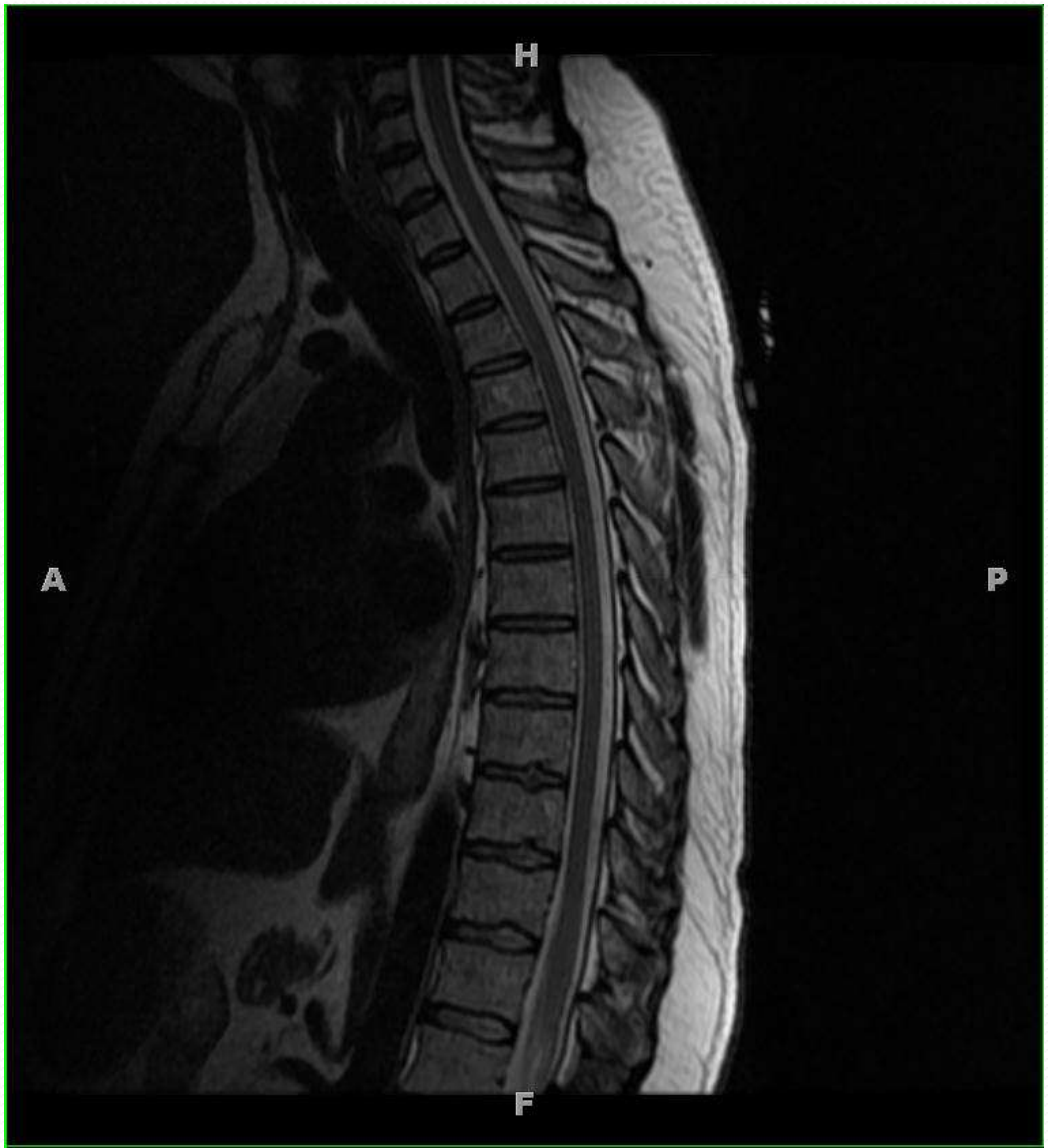
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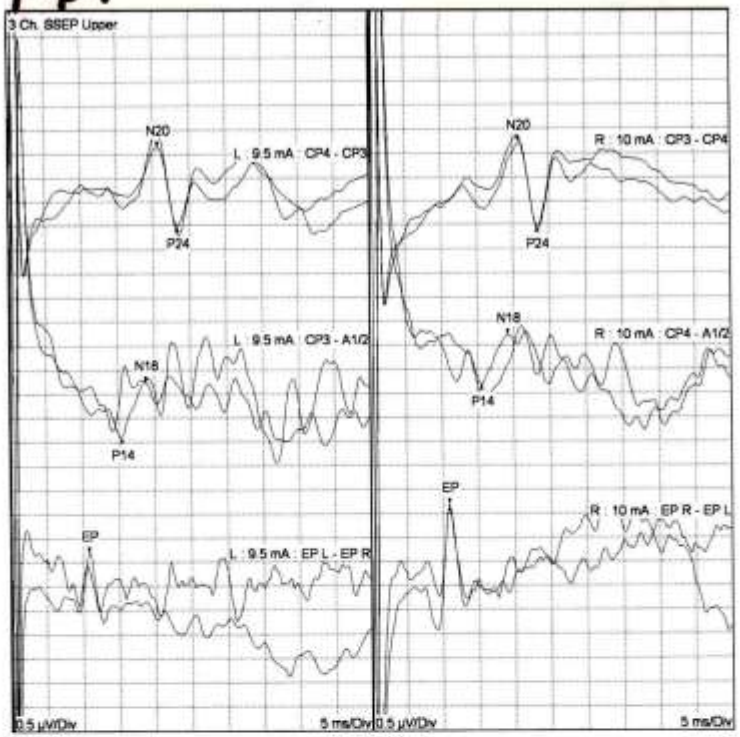
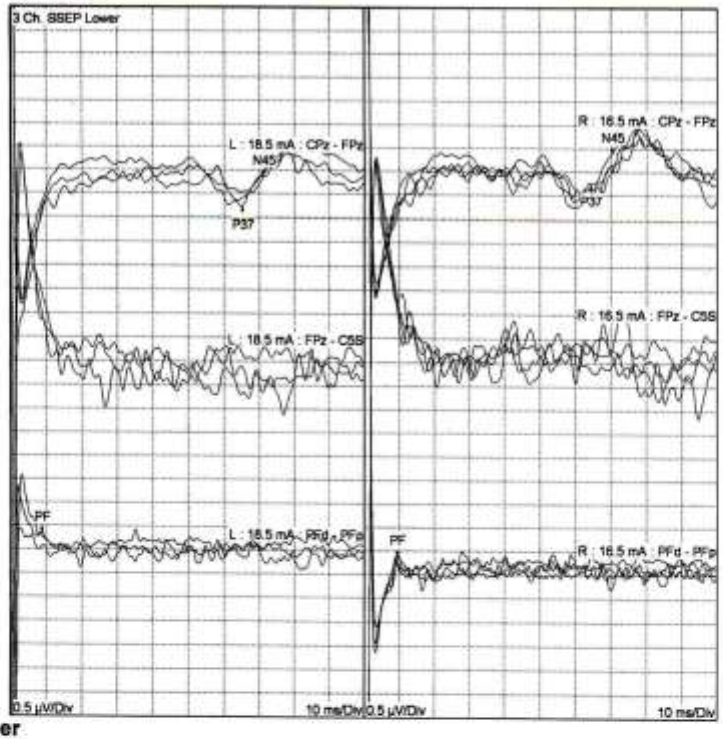


3 Ch. SSEP Upper

Trial	N20 (ms)	P24 (ms)	P14 (ms)	N18 (ms)	EP (ms)	EP-P14 (ms)	P14-N20 (ms)	N20-P24 (µV)
Norm	<22.1							
Trial1 - R	20.9	23.4	15.5	19.2	10.9	4.6	5.4	1.76
Avg - L	20.7	23.4	15.5	18.8	10.9	4.6	5.2	1.66
L-R Norm	<1.0	<1.0	<1.0	<1.0	<.5			<50
L-R	0.2	0.0	0.0	0.4	0.0	0.0	0.2	0.10

Patient Complaints:
Weakness in hands and feet for the past 5 days, numbness/tingling

F.P.



3 Ch. SSEP Lower

Trial	P37 (ms)	N45 (ms)	P31 (ms)	N34 (ms)	PF (ms)	P31-P37 (ms)	P37-N45 (µV)
Norm	<43.5						
Trial3 - L	65.3	71.1	0.0	0.0	8.9	0.0	0.62
Trial7 - R	64.4	70.3	0.0	0.0	9.5	0.0	0.64
L-R Norm	<1.5	<1.5	<1.5	<1.5	<.5		
L-R	0.9	0.8	0.0	0.0	0.6	0.0	0.02

Patient Complaints:
Weakness in hands and feet for the past 5 days, numbness/tingling

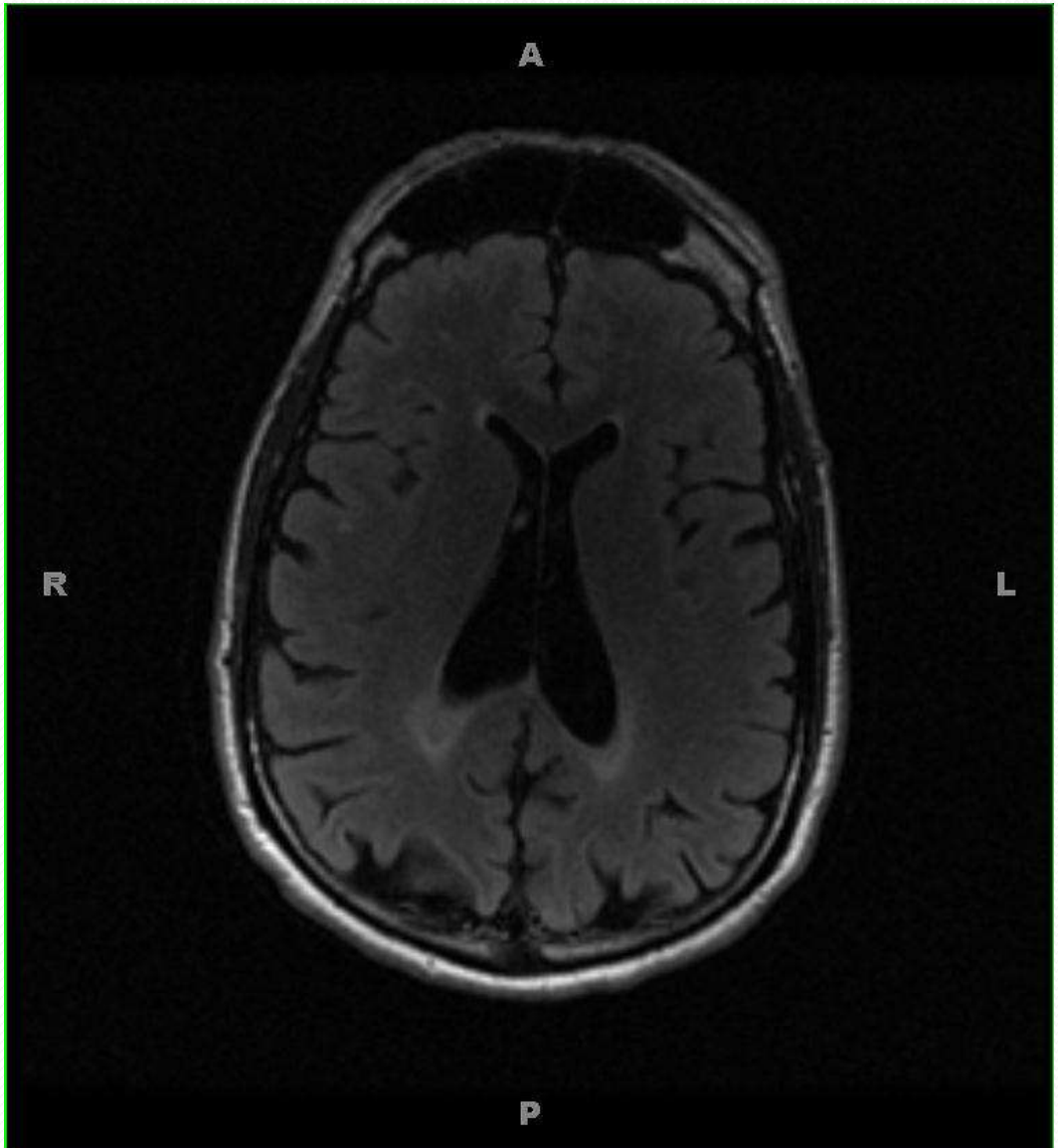
Case 3

- 51 year old white male with MS for 6 years
- Takes Rebif q Monday, Wednesday and Friday
- Symptoms
  - Fatigue - severe
  - Arm/Leg weakness, paresthesias,
  - Neurogenic bladder/bowel
  - Restless leg syndrome
  - Sexual dysfunction

Case 3

Physical Exam

- CN: Intact
- Motor: 5/5 of upper extremities, 4/5 of L lower extremity, 3/5 of R hip flexion/extension, knee flexion/extension, 2/5 foot flexion/extension. Increased tone of R lower extremity.
- DTR's: 2/4 of upper extremities, 2/4 knees, 3/4 ankles, bilateral babinski's
- Cerebellar: Intact upper and lower extremities
- Gait: Spastic gait, R foot drop, circumducts with R leg
- General appearance: Appears fatigued, leans to L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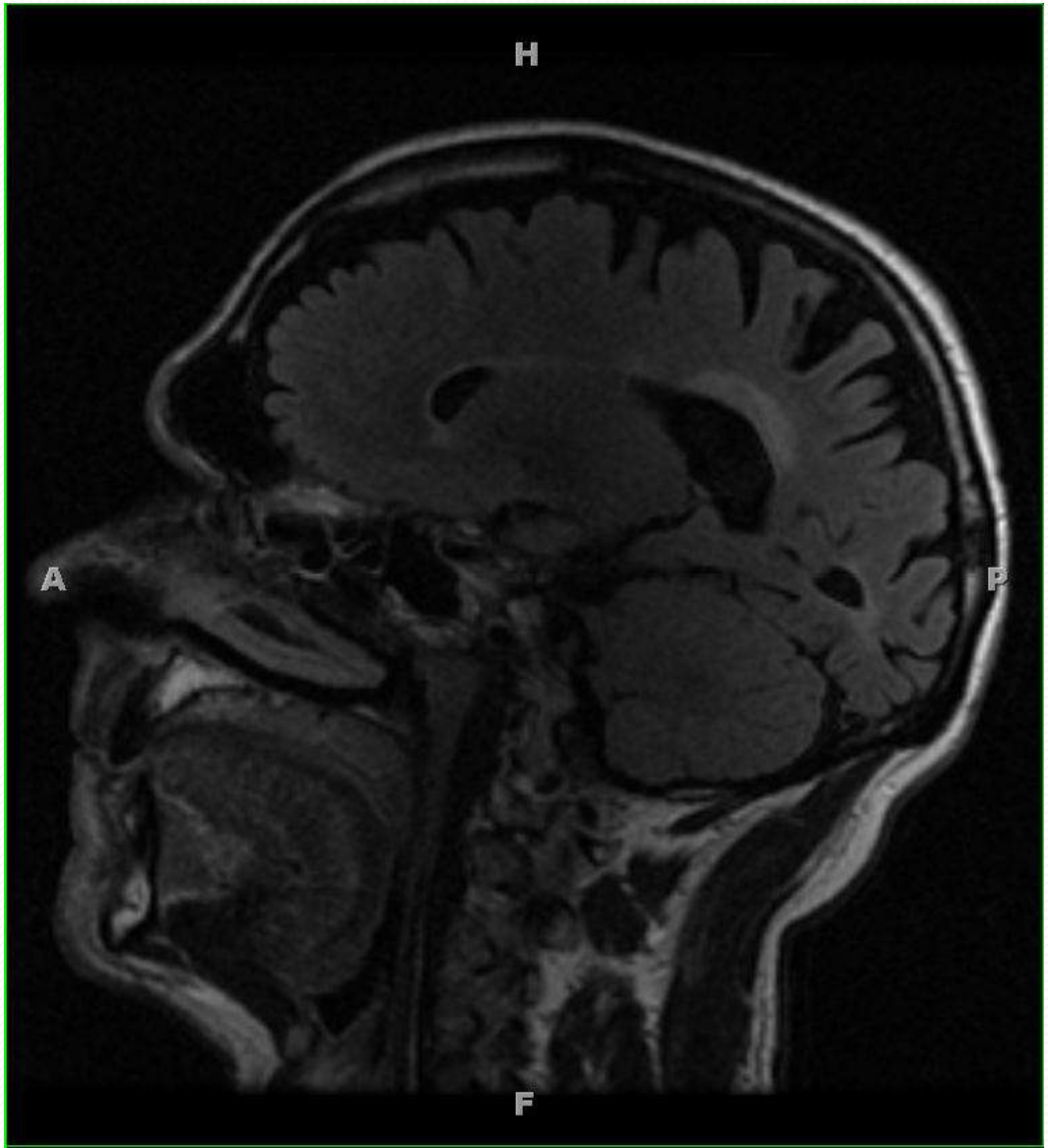
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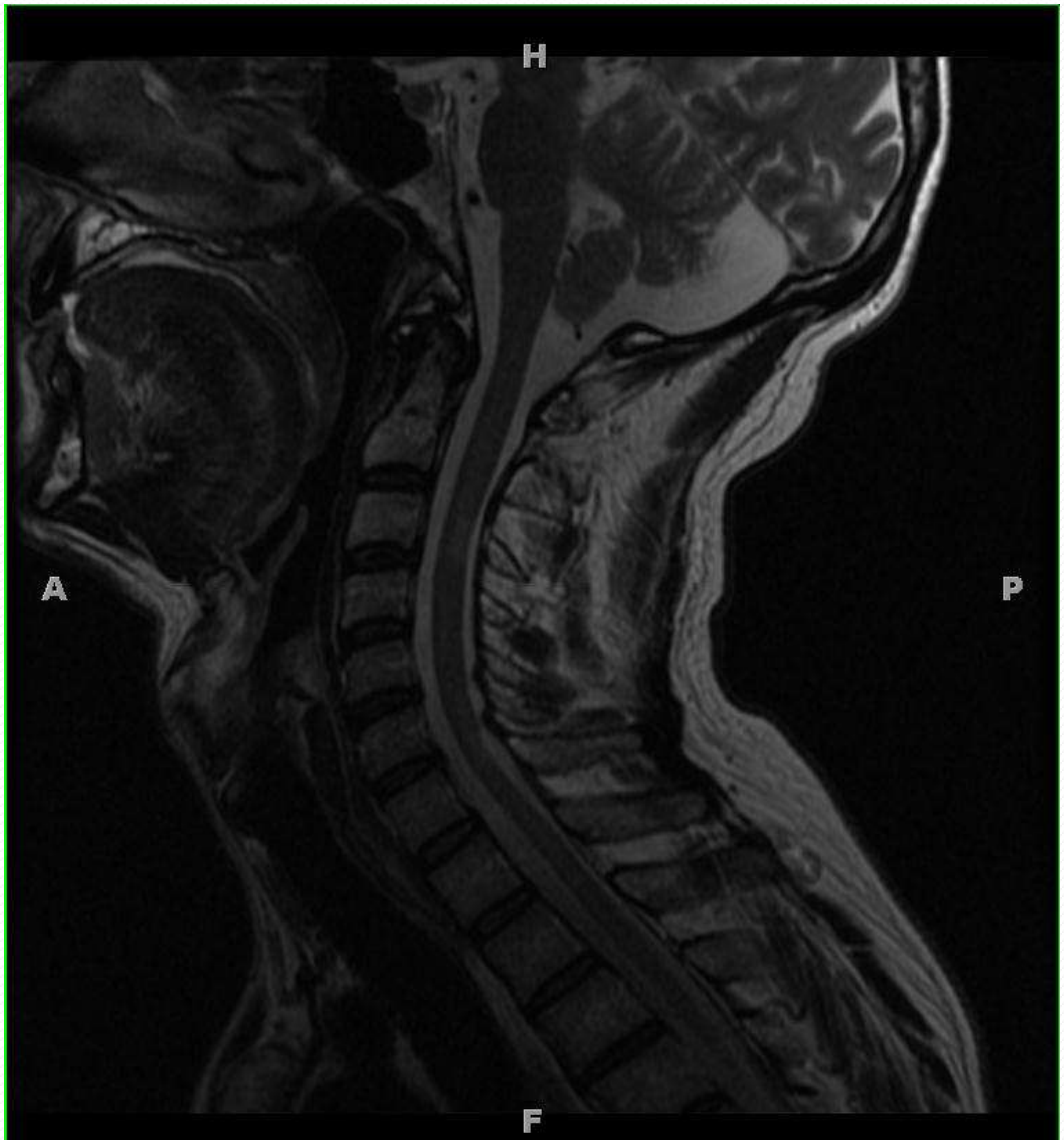
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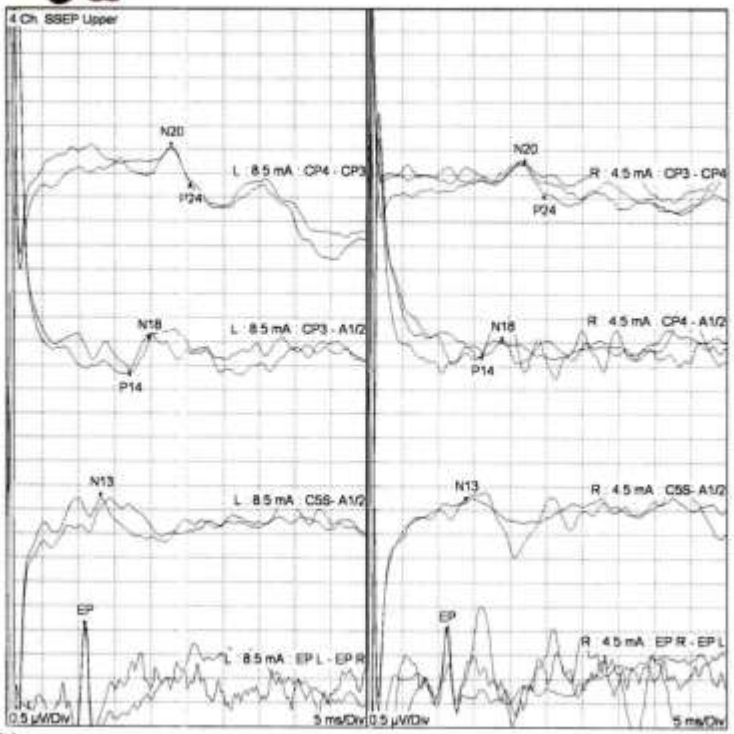
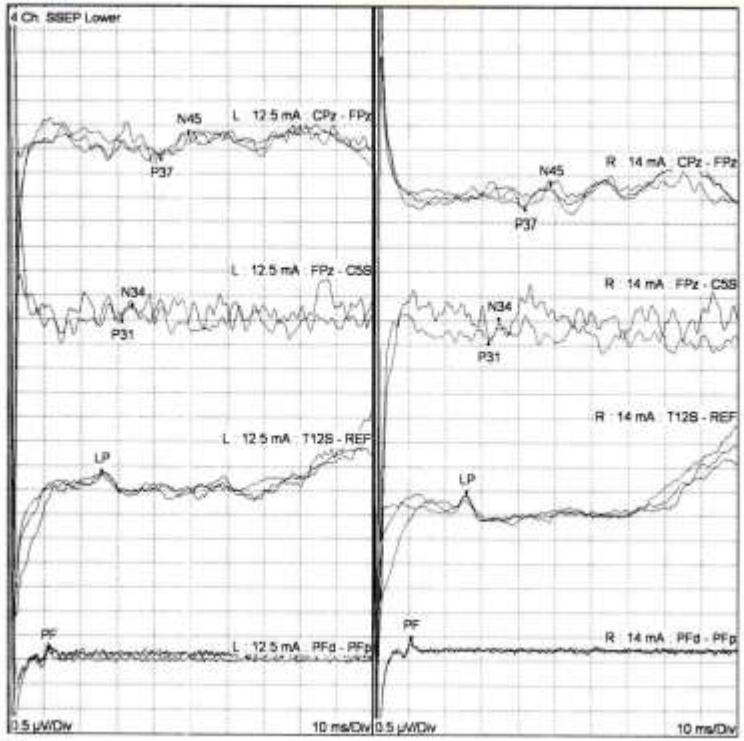


4 Ch. SSEP Upper

Trial	N20 (ms)	P24 (ms)	N18 (ms)	P14 (ms)	N13 (ms)	EP (ms)	N13-N20 (ms)	N20-P24 (µV)
Norm	<22.1							
Trial7 - R	22.0	24.6	18.9	16.1	13.9	11.3	8.1	0.59
Trial15 - L	22.8	25.4	19.7	17.1	13.1	10.9	9.7	0.71
L-R Norm	<1.0	<1.0	<1.0	<1.0	<1.0	<.5		<50
L-R	0.8	0.8	0.8	1.0	0.8	0.4	1.6	0.12

Patient Complaints:
51 yr old male with hx MS for aprox 6 yrs,

JQ



4 Ch. SSEP Lower

Trial	P37 (ms)	N45 (ms)	P31 (ms)	N34 (ms)	LP (ms)	PF (ms)	LP-P31 (ms)	P31-P37 (ms)
Norm	<43.5							
Trial1 - L	41.9	49.4	31.3	34.1	25.6	11.3	5.7	10.6
Trial5 - R	41.9	48.9	31.9	34.7	25.9	10.8	6.0	10.0
L-R Norm	<1.5	<1.5	<1.5	<1.5	<1.5	<.5		
L-R	0.0	0.5	0.6	0.6	0.3	0.5	0.3	0.6

Patient Complaints:
51 yr old male with hx MS for aprox 6 yrs,

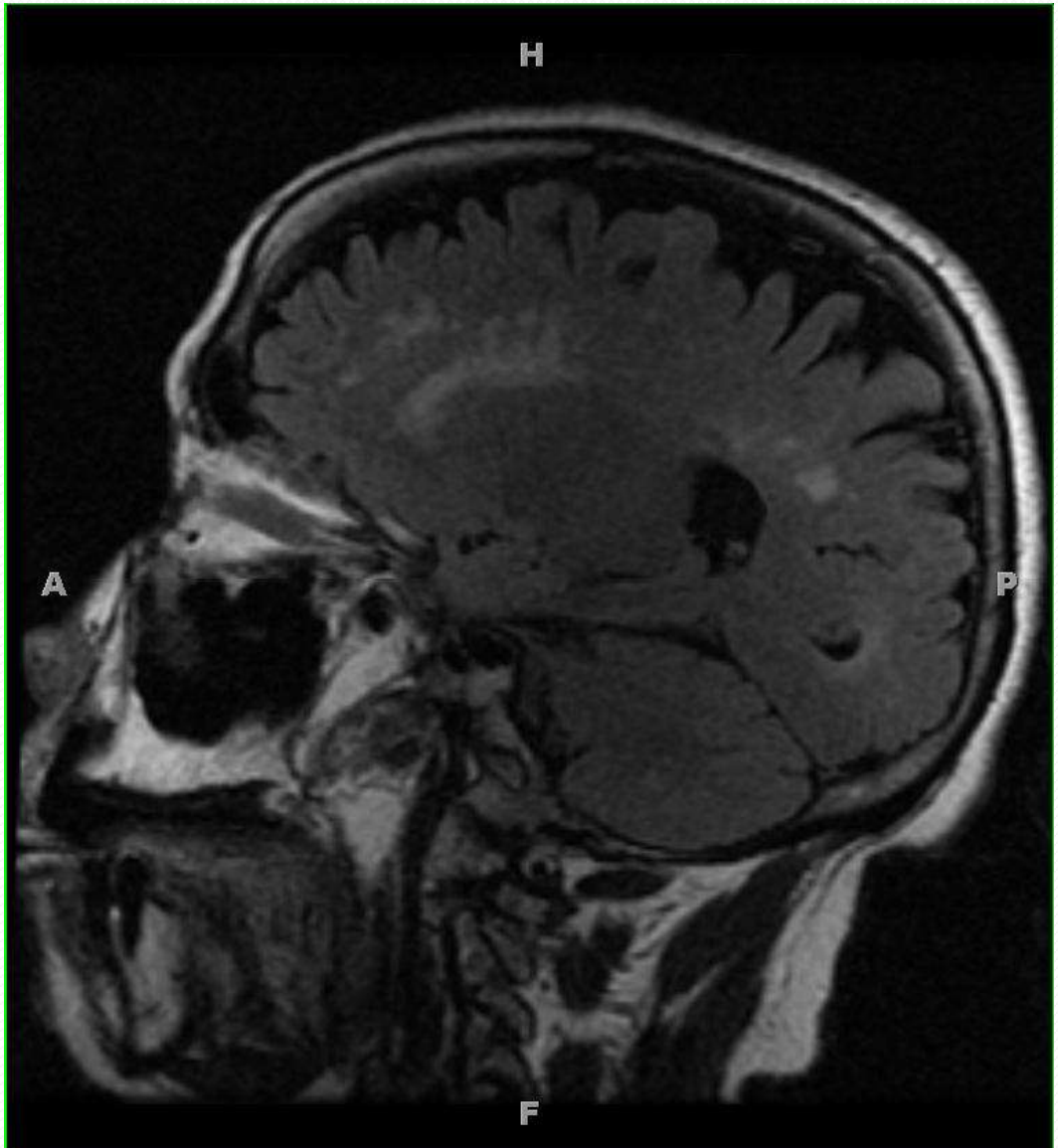
Case 4

- 57 year old black female
- MS diagnosed 2001
- Unable to tolerate interferon platform medications or Copaxone; taking methotrexate
- Symptoms:
  - Fatigue
  - Bilateral leg weakness/paresthesias
  - Generalized severe pain
  - Worsening balance, falls

Case 4

Physical Exam

- General appearance: Appears fatigued and painful, leans to the L sitting in the chair.
- CN: Intact
- Motor: 5/5 with exception of 4/5 of L grasp, 3/5 of bilateral hip flexion/extension, 4/5 knee flexion/extension and foot flexion/extension. Increased tone of bilateral legs. Drift downward of L arm.
- Cerebellar: Bilateral finger to nose and finger to finger past-pointing.
- Sensory: Decreased vibration to wrist bilaterally, absent proprioception to at ankles and normal at ankles bilaterally. Agraphesthesia of bilateral hands. Extinction with double simultaneous stimulation of face>arm>leg bilaterally.
- DTR's: ¾ upper extremities, knees; 4/4 with clonus at ankles; bilateral babinski's
- Gait: Labored with rolling walker, spastic gait, bilateral foot drop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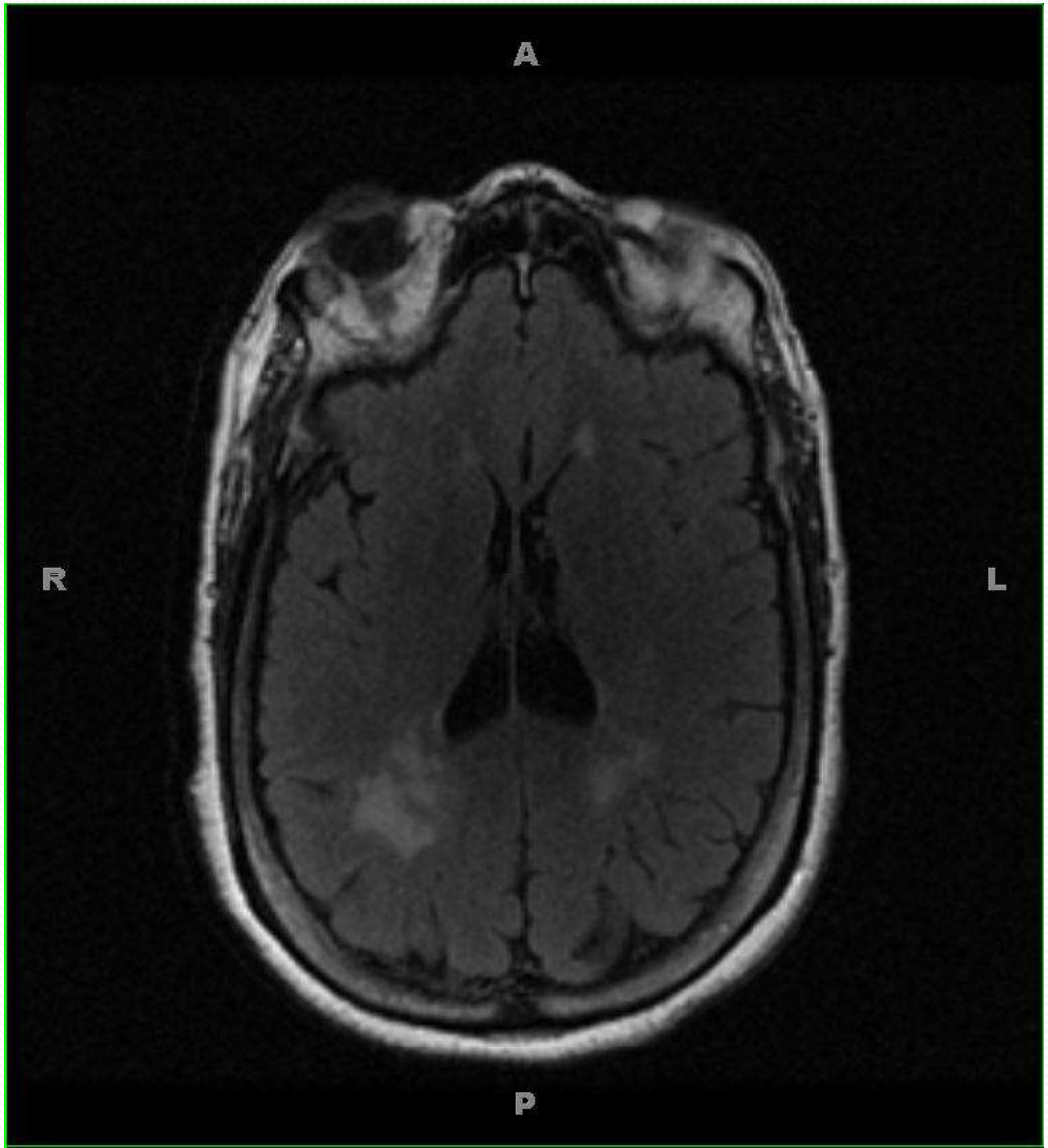
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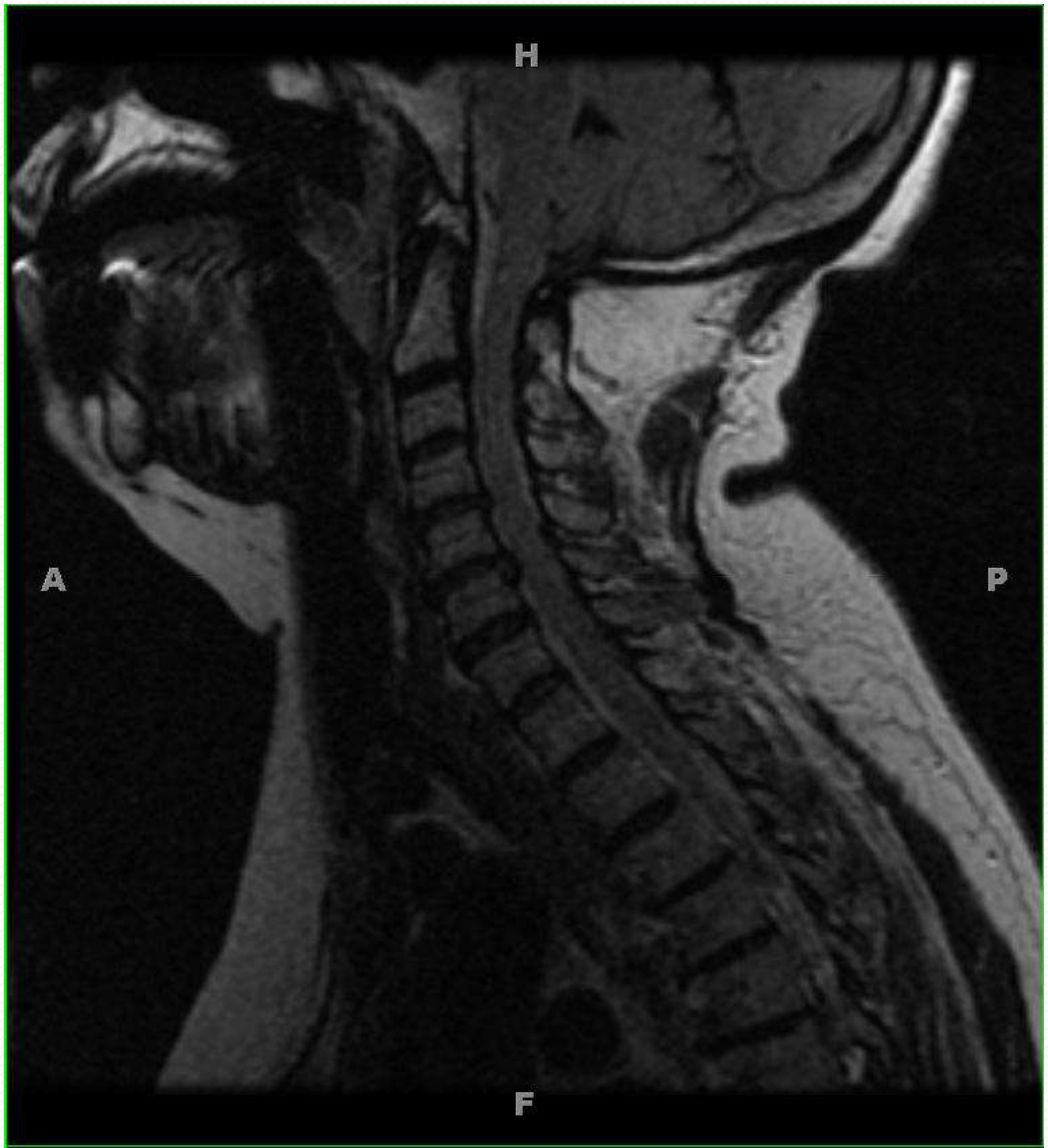
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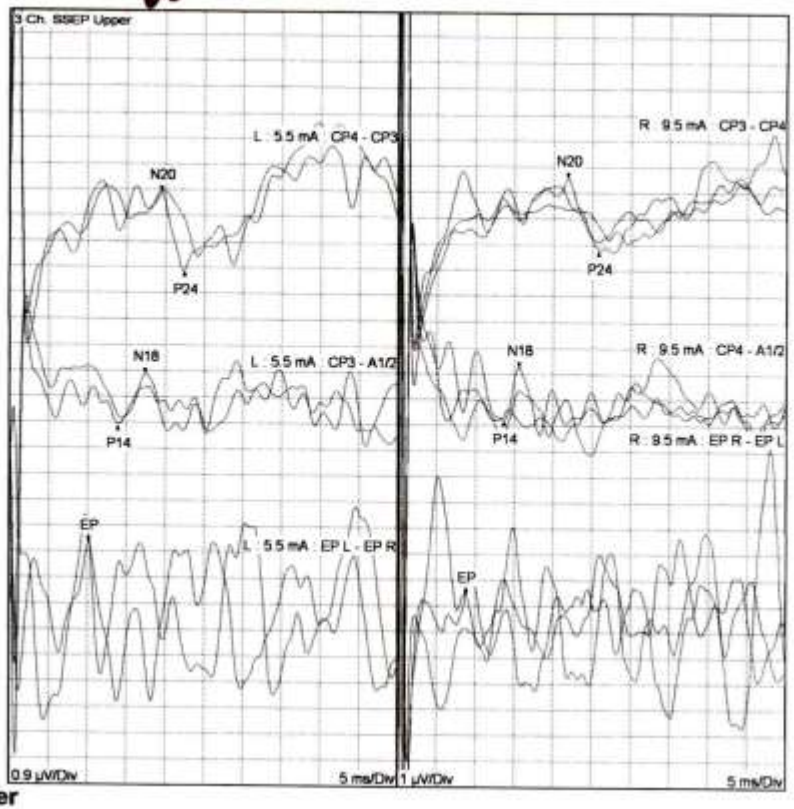
W.M.

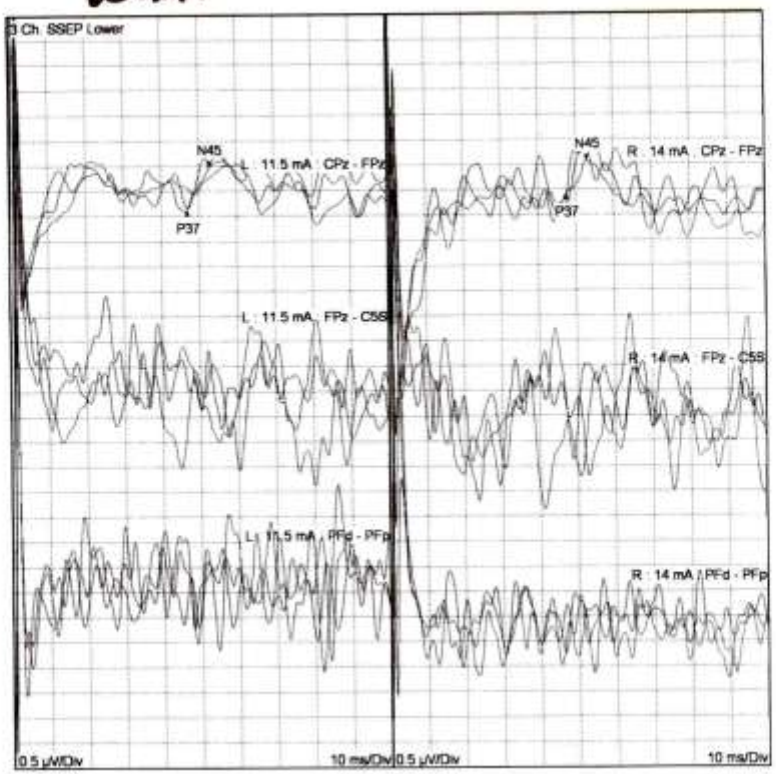


3 Ch. SSEP Upper

Trial	N20 (ms)	P24 (ms)	P14 (ms)	N18 (ms)	EP (ms)	EP-P14 (ms)	P14-N20 (ms)	N20-P24 (µV)
Norm	<22.1							
Trial1 - L	19.5	22.5	13.9	17.4	10.2	3.7	5.6	2.71
Trial3 - R	21.9	25.9	13.7	15.6	8.8	4.9	8.2	2.75
L-R Norm	<1.0	<1.0	<1.0	<1.0	<.5			<50
L-R	2.4	3.4	0.2	1.8	1.4	1.2	2.6	0.04

Patient Complaints:
Weakness, increased numbness, MS
stim median nerve - no sedation pt constant tremors

W.H.



3 Ch. SSEP Lower

Trial	P37 (ms)	N45 (ms)	P31 (ms)	N34 (ms)	PF (ms)	P31-P37 (ms)	P37-N45 (µV)
Norm	<43.5						
Trial2 - L	47.0	52.8	0.0	0.0	0.0	0.0	0.84
Avg - R	47.5	53.0	0.0	0.0	0.0	0.0	0.65
L-R Norm	<1.5	<1.5	<1.5	<1.5	<.5		
L-R	0.5	0.2	0.0	0.0	0.0	0.0	0.19

Patient Complaints:
Weakness, increased numbness, MS
no sedation pt constant tremors