Multiple Sclerosis
HIHIM 400

Patterns of MS
- Relapsing - remitting
  - Attacks with complete/incomplete recovery
  - Stable between attacks
- Secondary - progressive
  - Initially relapsing, remitting
  - Then progression +/- attacks
- Progressive - relapsing
  - Initial gradual deterioration
  - Subsequent episodes
- Primary progressive
  - Gradual decline
  - No attacks

Clinical Manifestations
- Demographic
  - Female
  - Women make up to 70%-75% MS patients
  - Young age
  - Onset before age 16: 5% of cases
  - Peak onset post puberty, early 20's
  - Relapsing MS 28-30 years
- Symptoms
  - Recent onset
  - Frequently progressive
  - Coming on over 1- several days
  - Very acute symptoms possible

The MS Event
- Attack/relapse/exacerbation
  - Acute episode of CNS dysfunction
  - Lasting at least 24 hours
  - In absence of fever or metabolic derangement
  - All events within 30 days are unitary

MS Symptoms

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<tr>
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Clinical Manifestations
- Motor
  - Weakness, spasticity, ataxia
  - Rarely radicular
    - Lesion ant. hom, root entry zone
    - Painful
    - Atrophy
- Somatosensory
  - 1st sx. in 45% patients
  - Includes visual
  - Any anatomic distribution
  - Any combination
    - Loss pain, temp., light touch, vbn, position
  - Positive sx. common
    - Paresthesiae, hyperpathia, allodynia, dysesthesias
**Nonspecific Associated Features That Suggest MS**
- Excessive unexplained fatigue
- Temperature sensitivity
- Hot, humid weather
- Relatively recent symptoms
- History of Lhermitte's sign
- History of bandlike sensation around the waist
- Uhthoff's phenomenon
  - e.g., blurry vision with exercise or heat exposure

**Clinical Manifestations**
- Fatigue
  - One of the most important causes of disability
  - Several sources
    - Handicap fatigue
    - Increased effort to perform routine tasks
    - Secondary fatigue
      - Depression, sleep disturbances, medication side-effects, other conditions
    - Systemic fatigue
      - Chronic lack of energy, tiredness, malaise
      - Etiology unknown

**Clinical Manifestations**
- Cognitive Disturbances
  - Common, frequently overlooked
  - Estimated 50-75%
  - Most common
    - Impaired attention, slow info processing, short term memory loss, reduced visuospatial skills, impaired executive function
    - Impaired driving skills
    - Important impact QoL, ADL
    - Can occur independent
    - of disease course
    - other manifestations

**MRI in MS**
- Brain lesions
  - Character
    - Large > 3 mm
    - Ovoid
    - Oriented perpendicular to ventricles
    - Enhancing
      - Open-ring enhancement
      - Multifocal homogeneous
  - Location
    - Multiple white matter
    - Brainstem, infratentorial
    - Juxtacortical
    - Corpus callosum
    - Pointing away
    - Moth eaten
    - Enlarged atrophy

**Evoked Potentials**
- Visual evoked potentials
  - Not auditory or somatosensory
  - May point to subclinical involvement of optic nerve
    - Quality control issues

**Principal Differential Diagnosis of Multiple Sclerosis**
- Infection
  - Lyme, Syphilis, Progressive Multifocal Leukenoesphalopathy, HIV, HTLV-1
- Inflammatory
  - SLE, Sjogren syndrome, vasculitis, Sarcoidosis, Behcet's disease
- Metabolic
  - B12 deficiency, lysosomal disorders, adrenoleukodystrophy, mitochondrial disorders, other genetic diseases
- Neoplastic
  - CNS lymphoma
- Spine disease
  - Vascular malformations, degenerative spine disease
Cerebrospinal Fluid

- Useful, not diagnostic
- Other conditions
  - Chronic CNS infections, viral syndromes, neuropathies
- Immunoglobulin abnormalities
  - Production of immunoglobulin
    - By plasma or B cells in CNS
  - Oligoclonal bands of immunoglobulin (IgG) (OCB)
  - In CSF, not serum
  - Isoelectric focusing technique
- Elevated IgG index
- Ratio of IgG/protein in serum and CSF
  - \[ \text{index} = \frac{\text{CSF IgG}}{\text{CSF albumin}} \times \frac{\text{serum IgG}}{\text{serum albumin}} \]

MRI in MS

- Spinal cord lesions
  - Character
    - Asymptomatic lesions
    - Focal T2 hyperintense lesions
    - Diffuse T2 hyperintense lesions
    - Asymmetric involvement
    - Multiple scattered lesions
  - Location
    - Cervical and thoracic
    - Especially midcervical
    - Lateral, dorsal cord

Paroxysmal Symptoms in MS

- Trigeminal neuralgia (and others)
- Tonic "seizures"
- Paroxysmal dysarthria
- Hemifacial spasm
- Paroxysmal itching
- Abrupt loss of muscle tone
- Paroxysmal aphasia
- Paroxysmal kinesogenic choreoathetosis
- Lhermitte’s sign

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Clinical Manifestations

- Visual symptoms, afferent
  - Almost any pattern, related to location
  - Optic neuritis
    - Central etiologies
    - Medial occipital
  - Visual blindness
    - Vast majority have excellent return by 6 months
  - Frequent pain
  - Worsen on eye movement
Optic Neuritis
Risk of Subsequent MS

- Higher Risk
  - Young adult (26-40 years)
  - Venous sheathing
  - Female sex
  - History of minor neurologic symptoms
  - Brain MRI lesions
  - CSF oligoclonal bands or intrathecal IgG production

- Lower Risk
  - Age < 10
  - Macular star/exudates
  - Retinal or disc hemorrhage
  - Retinal disc edema
  - No brain MRI lesions
  - Normal CSF

Clinical Manifestations

- Visual symptoms, efferent
  - Any eye movement abnormality
  - INO
    - Internuclear ophthalmoplegia
    - Adductor weakness
    - Abduction nystagmus
  - In young adult strongly suggests MS

- Nystagmus
  - Many types

Clinical Manifestations

- Other Brain Stem Structures
  - Facial weakness
  - Vertigo
  - Loss of hearing, taste
  - Dysthria, dysphagia
  - Bulbar muscles
    - Weakness, ataxia, spasticity

Clinical Manifestations

- Psychiatric Disturbances
  - Depression
    - Also up to 75% of patients
    - Major depression less frequent
    - Suicide: 16% of adult MS deaths
  - Risk factors
    - PH major depression, anxiety, alcohol abuse
  - Emotional incontinence
    - Frontal lobe involvement

Clinical Manifestations

- Bladder dysfunction; the importance of urodynamic studies
  - Urgency, frequency, nocturia
  - Failure to store: detrusor hyperactivity
  - Failure to empty: detrusor-sphincter dyssynergia
  - Poor detrusor contraction
  - Incontinence, increased residual vol., nocturia
  - Both
    - Combined
      - Detrusor hyperactivity
      - Detrusor-sphincter dyssynergia
    - Incontinence
      - Detrusor hyperactivity or
      - Overflow
    - Symptoms may not be accurate indicator of urodynamic pathology
**Pain Syndromes in MS**
- Primary pain
  - Neuropathic
    - Trigeminal neuralgia
    - Other neuralgias
  - Dysesthetic pain
  - Most often burning (legs)
  - Other dysesthesias
  - Radicular pain
  - Tonic seizures
  - Spasticity
  - Flexor spasms
  - Extensor spasms
- Secondary pain
  - Low back pain
  - Osteoporosis with fractures

**Neurologic Syndromes Likely for MS**
- Optic neuritis
  - Unilateral eye involvement
  - Retrobulbar rather than papillitis
  - Eye pain
  - Partial vision loss, with at least some recovery
- No retinal exudates, disc hemorrhages, macular star
- 10 years follow-up: 36% develop MS
  - MINI normal: risk 20%
  - 20 years follow-up: 70% develop MS

**Neurologic Syndromes Likely for MS**
- Transverse Myelitis
  - Incomplete
  - Sensory > motor
  - Associated
    - Lhermitte's sign
    - Bandlike abdominal or chest pressure
- Internuclear Ophthalmoplegia
- Trigeminal Neuralgia
- Hemifacial Spasm

**Neurologic Syndromes Likely for MS**
- Paroxysmal symptoms
  - Last seconds to minutes
  - Occur multiple times daily
- Tonic spasms
- Dysarthria, ataxia
- Hemiparesis, hypesthesia
- Polysymptomatic Syndrome Without Mental Status Changes

**Clues to a Misdiagnosis; MS**
- Historical
  - No dissemination
  - Onset < 10 yrs. or > 55 yrs.
  - Genetic red flags
    - +ve FH
    - However about 20% of MS patients have FH
    - Early-age onset
    - Unexplained non-CNS disease
  - Progressive course starting before age 35
  - Localized disease
**Clues to a Misdiagnosis; MS**

- **MRI**
  - Normal
  - Normalized IgG index
  - Cell count > 50 wbc/cubic mm.
  - Protein > 100 mg/dl

- **Brain**
  - Normal
  - Small lesions < 3 mm.
  - Subcortical location (internal capsule)
  - Prominent infratentorial involvement
  - Prominent grey matter involvement (basal ganglia)
  - Symmetric, confluent hemispheric white matter involvement
  - Heterogeneous
  - Severe cerebellar/brain stem atrophy
  - No callosal/periventricular lesions

- **Spinal cord**
  - Large lesion, multiple segments (>2)
  - Severe swelling
  - Full thickness lesions
  - Leptomeningeal enhancement
  - T1 hypointense lesions

- **CSF**
  - Normal
  - Disappearance of oligoclonal bands
  - Normalization of IgG index
  - Cell count > 50 wbc/cubic mm.
  - Protein > 100 mg/dl

**MS Diagnosis; 1 Final Slide**

- Manifestations due to CNS
  - Slowing or failure of transmission
  - Mostly damage of white matter tracts
  - Recent appreciation of axon/grey matter involvement
- Diagnosis based on clinical and laboratory evidence of
  - Dissemination in time
  - Dissemination in space
- Recent appreciation of role of MRI in assisting diagnosis
- In-office pattern recognition
  - Appropriate demographic
  - Appropriate clinical event