Multiple Sclerosis

History of Presenting Illness: Initial symptoms in order of frequency
- Weakness
- Sensory Loss
- Paresthesia
- Optic Neuritis
- Diplopia
- Ataxia
- Vertigo
- Bladder urge incontinence
- Paroxysmal Symptoms
  - (brief attacks of paraesthesia + spasm and tonic contraction)
    - Lhermitte’s sign (electric shock on neck flexion)
- Pain
- Dementia
- Visual loss
- Facial palsy
- Impotence

Differential Diagnoses
- Systemic Lupus
- Sjogrens syndrome
- Behcets disease
- Paraneoplastic effect
- sarcoidosis
- Lyme disease
- Systemic Lupus
- Sjogrens syndrome
- Behcets disease
- Paraneoplastic effect
- sarcoidosis
- Subacute combined degeneration
- Multiple emboli → stroke
- Acute encephalomyelitis
- Neurosyphilis

Pertinent Findings on History
AIM is to exclude the diagnosis of every other disease on the list above; not easy
The review of systems should concentrate on the evidence of bladder, kidney, lung, or skin infection and irritative or obstructive bladder symptoms.

Classic MS symptoms
- Sensory loss (ie, paresthesias) usually is an early complaint.
- Motor (eg, muscle cramping secondary to spasticity) spinal cord symptoms
- autonomic (eg, bladder, bowel, sexual dysfunction) spinal cord symptoms
- Cerebellar symptoms (eg, Charcot triad of dysarthria, ataxia, tremor) may occur.
- fatigue (which occurs in 70% of cases)
- Dizziness
- Subjective difficulties with attention span, concentration, memory, and judgment may be noted any time during the disease course.
- About 50% of patients with MS have impairment, usually mild, in information processing on neuropsychological testing.
- Depression is common, but euphoria is less common.
- Over the course of the disease, 5-10% of patients develop an overt psychiatric disorder (eg, manic depression, paranoia, major depression) or dementia.
- Eye symptoms, including diplopia on lateral gaze, occur in 33% of patients.
- Trigeminal neuralgia may occur.

Family History:
Consider asking about ethnic background. The Norse cultures suffer most (except Eskimos, who are paradoxically immune.) Also, the risk seems to be associated entirely with childhood years spent in a temperate climate.
**Optic neuritis** = the initial presentation of 15% of patients with MS.

!! Fifty percent of all patients who present with ON have MS !!

Isolated episodes of ON, even if they are recurrent, do not represent MS.

= Acute onset (minutes or hours) of
  - single eye visual blurring,
  - decreased acuity (ie, usually scotoma),
  - decreased color perception,
  - discomfort of the moving eye

3 phenomena of optic neuritis:
1. **Phosphenes**: flashes of light when you move your eyes
2. **Uhthoff phenomenon**: eye symptoms made worse by HEAT
3. **Pulfrich effect**: rate of transmission between the optic nerves are unequal, thus a sense of disorientation in traffic

!! BILATERAL OPTIC NEURITIS IS RARE !!

**Findings on Examination**

:focus on long white matter tracts:

**Eye: Optic neuritis**

- funduscopes results are usually normal: UNLESS your pt is a chronic sufferer, in which case expect **OPTIC NERVE ATROPHY**: a pale and useless-looking optic disk
  
  "The patient sees nothing and the doctor sees nothing."

- **Light Reaction**: afferent pupillary defect (i.e cant see thus cant react) may be seen in the affected eye.

- **Visual acuity** usually is impaired (ie, subtle to total blindness).

- **internuclear ophthalmoplegia (INO)** = classic finding; a lesion in the median longitudinal fasciculus (MLF) resulting in
  - a weakness in adduction of the ipsilateral eye
  - nystagmus on abduction of the contralateral eye,
  - an incomplete or slow abduction of the ipsilateral eye upon lateral gaze,
  - complete preservation of convergence.

- abnormal pupillary responses,

- **acquired pendular nystagmus**: rapid, small amplitude pendular oscillations of the eyes in the primary position resembling quivering jelly. Patients frequently complain of oscillopsia (subjective jumping/jerking of objects in the field of vision), which impairs visual performance

  - loss of smooth eye pursuit.

  YOU HAVE TO FIND ONE OF THESE SIGNS TO EVEN CONSIDER A DIAGNOSIS OF MS

**Spinal Cord Symptoms**

= indicative of upper motor neuron dysfunction, as long white matter highways is what the SC is all about

- **Sphincter paralysis** = bladder, bowel, and sexual dysautonomies.

- Paralysis

- Spasticity

- hyperreflexia

- Decreased joint position and vibration sense

- Decreased pain and temperature (less common)

**Cerebellar symptoms:**

- Disequilibrium,

- truncal or limb ataxia,

- scanning (ie, monotonous) speech,

- intention tremor,

- saccadic dysmetria

**Lhermitte sign:** Neck flexion results in an electric shocklike feeling in the torso or extremities
Tests and Investigations

**Visually Evoked Potentials**

The individual visual evoked potentials with the major scotoma superimposed (grey-shaded area).

Approximately 85% of clinically definite MS patients have abnormal VEPs.

SOMETHING VERY SIMILAR can be done for somatic sensations and hearing.

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**Full Blood Count**

Should be NORMAL;

if white cells are increased, you may be looking at a case of meningitis or brain abscess

**VDRL: Venereal Disease Research Laboratory test**

A blood test used to diagnose syphilis. Neurosyphilis has many manifestations, and can mimic MS in many ways; however it is not as common in civilised countries as it is in Calcutta or London

**ESR**

Hopefully NOT ELEVATED

This is done to rule out infection and various nasty rare illnesses which cause raised ESR such as

- **Acute Disseminated Encephalomyelitis**
  - Immune-mediated encephalitis (IME), ADE, allergic treatment to prior infection, begins 1-2 weeks after event, occurs after viral infection or vaccination, affects corpus callosum and white matter (above and below tent), self-limited; steroids may help

- **Meningitis**

- **Wegener's granulomatosis**
  - Sinuses, mucoperiosteal thickening, may destroy bone and cartilage, lungs, necrotizing granulomata, multiple round nodules (2 mm - 9 cm), may cavitate, kidneys, glomerulonephritis most likely to be necrosis of capillary tuft, generalised necrotizing vasculitis of arteries and veins, auto-immune: basement membrane, almost always involves lungs, M = F, 30-50 years of age, symptoms: cough, haemoptysis, fever, wt loss, multiple especially infections, treatment: cytotoxins, immunosuppression

**MRI with Gadolinium Contrast**

- If there was a gold standard for MS diagnosis, MRI would be it.
- The MRI findings are gadolinium-absorbing lesions over the white matter tracts in the brain, where the BBB is broken and acute inflammation is taking place.
- This may not pick up small lesions during a period of remission, because some of them re-myelinate.

The signature lesions are the "periventricular high signal areas", or "Dawson’s Fingers"!

Acute disseminated encephalomyelitis may be radiographically indistinguishable from MS. BEWARE!!

**CSF:**

**Imunochemistry**

selective increase in immunoglobulin G with oligoclonal bands; ..and maybe elevated protein in acute phase

**Microscopy**

Up to 50 mononuclear cells on cell count (lymphocytes dominate)

**Culture**

Hopefully nothing; however this excludes meningitis and encephalitis
How is this diagnosis made? ...BY EXCLUSION!!

To call it MS, you must..
- Find objective CNS abnormalities, eg. big scotoma
- These abnormalities are due to white matter tract destruction, eg. corticospinal tracts, dorsal column tracts, cerebellar pathways, medial longitudinal fasciculus or optic nerve problems
- Must have at least two sites where this is occurring (four if you involve MRI)
- Symptoms must last at least 1 day, and occur at least 1 month apart
- OR: 6 months of progressive decline with increased CSF IgG
- That IgG has to be OLIGOCLonal with 2 or more bands
- The patient must be between 15 and 60 years old
- After all that,

ITS MULTIPLE SCLEROSIS IF YOU CANT FIND A BETTER EXPLANATION

Disease Definition

Multiple sclerosis (MS) is an idiopathic inflammatory demyelinating disease of the CNS. MS is characterized by
(1) a relapsing-remitting or progressive course and
(2) a pathologic triad of CNS inflammation, demyelination, and gliosis (scarring). Lesions of MS are classically said to be disseminated in time and space.

Management

ACUTE:
Hit them with steroids right away if you suspect an acute lesion in progress:
DRUG ‘O’ CHOICE: IV infusion Methylprednisolone 3-5days
Mechanisms of action same as for Cortisol (but more potent (5x anti-inflammatory) and does not stimulate Na retention. Decreases inflammation by suppressing migration of polymorphonuclear leukocytes and reversing increased capillary permeability.

NO LONG TERM BENEFIT but duration of attack is reduced

LONG TERM:
Aim is to slow progression and delay onset of SUSTAINED PROGRESSION DRUGS which do this include:
- INTERFERON BETA 1a
- INTERVERON BETA 1b
  IFNs have nasty side effects such as
  - Injection site reactions;
  - Flu-like symptoms;
  - CNS disturbances incl. depression and suicidal ideation;
  - Leucopenia;
  - Menstrual disturbances
  - Elevated hepatic enzymes;
  - Hypersensitivity reactions;
  - COPAXONE (glatiramer acetate)
is practically the same except side-effects are nicer, eg. no menstrual disorders or depression.
The mechanism is unknown, but it seems to decrease the frequency of relapses
- MARIJUANA: although anecdotally patients report improvements in ataxia and spasticity, this management option is not supported by world literature and thus cannot be recommended with a straight face.