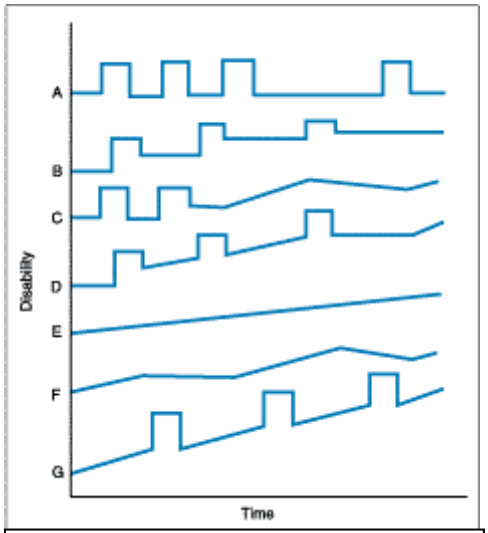
Multiple Sclerosis

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



Clinical patterns of MS. A, B, relapsing-remitting; C, D, secondary progressive; E, F, primary progressive; G, progressive relapsing.

Differential Diagnoses

Systemic Lupus
Sjogrens syndrome
Behcets disease
Paraneoplastic effect
sarcoidosis
Lyme disease
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 abut 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

- **funduscopy** 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 dysautonomias.
- **Paralysis**
- **Spasticity**
- **hyperreflexia**
- **Decreased joint position and vibration sense**
- **Decreased pain and temperature (less common)**

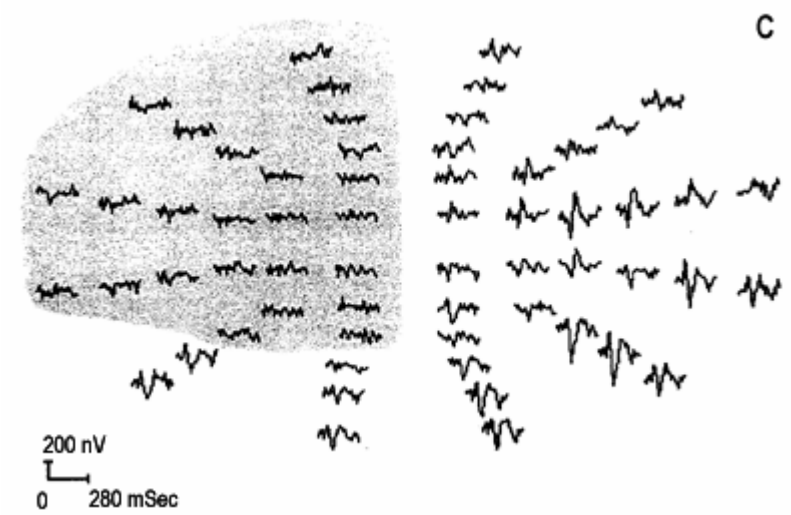
Cerebellar symptoms:

- **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**

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*

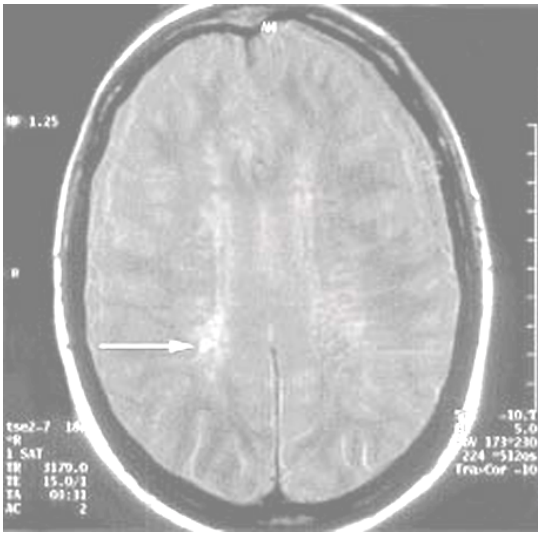
A blood test used to diagnose syphilis. Neurosyphilis has many manifestations, and can mimic MS in many ways; however it is not as common in civilised countries as it is in Calcutta or London

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 treatmentn to prior infection, begins 1-2 weeks after event, occus 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 respecially 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:

Immunochemistry

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 MULIPLE 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.