

## **Multiple Sclerosis: Some Basics Worth Understanding**

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### **Course Objectives:**

1. Attendees will learn the biology of multiple sclerosis, including criteria for diagnosis and classification
  2. Attendees will learn the ocular effects of MS, including EOM disorders and OCT findings
  3. A review of currently available disease-modifying drugs (DMD) will be presented
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- I. What is MS? An autoimmune disease of the CNS characterized by demyelination of the white matter resulting in numbness, weakness, loss of muscle coordination and problems with vision, speech and bladder control.
    - a. Multiple sites of CNS involvement
    - b. Multiple attacks over time
    - c. RRMS versus CPMS
  - II. Clinically Isolated Syndrome (CIS) The original demyelinating event is referred to as CIS. Common presentations include
    - a. retrobulbar optic neuritis
    - b. transverse myelitis (ascending numbness from the feet up through the torso or hands to arms; balance problems; partial or complete paralysis; L'Hermitte's sign; bladder and sexual dysfunction)
    - c. brainstem syndromes (e.g. internuclear ophthalmoplegia)
  - III. Diagnosis of MS
    - a. MRI of brain and spine (T2 weighted FLAIR; T1 weighted with gadolinium contrast)
      - number of lesions predicts conversion to MS and progression of disability
    - b. Blood tests to rule out mimetics (B12, ESR, Lyme titer, ANA, RF, anticardiolipin, TSH)
    - c. Lumbar puncture with CSF analysis (oligoclonal bands demonstrate B-lymphocyte infiltration of the CNS; elevated IgG index)
    - d. Evoked potential (visual, auditory, somatosensory) to detect multifocal process
    - e. OCT – emerging evidence
      - Meta-analysis shows significant RNFL thinning in patients with MS and no Hx of optic neuritis when compared to age matched controls
      - RNFL loss more pronounced in pts with optic neuritis (Lancet Neurol. 2010 Sep;9(9):921-32.)
  - IV. Risk Factors

- a. Female
- b. 25-40 years of age at initial event
- c. vitamin D deficiency
- d. inheritance: 3-4% chance of developing MS in offspring or siblings (30% in identical twins)
- e. Disability from MS: EDSS

#### V. Ocular complications

- a. Retrobulbar optic neuritis: sudden loss of vision in one or both eyes (20/40 to NLP); pain on eye movement; color desaturation; visual field defects; recovery over days to weeks
- b. INO: loss of adduction with intact convergence; diplopia on lateral gaze; bilateral INO is pathognomonic of MS

#### VI. Disease Modifying Drugs (DMDs) and side effects

- a. Interferon B
  - 1. B 1a IM (Avonex®)
  - 2. B 1a SC (Rebif®)
  - 3. B 1b (Betaseron®)
- b. Glatiramer acetate (Copaxone®)
- c. These 3 DMDs demonstrate fairly equivalent reduction in event relapses and reduction in risk for disability progression; evidence of long-term benefit is accumulating.
- d. Adverse Rxns: Depression; Injection site reactions; flu-like symptoms; elevated liver function tests
- e. 50% of patients discontinue initial DMD because of AEs
- f. Managing AEs: patient education; prophylax anti-depressants with interferons; rotate injection sites and warm medication to room temperature; dose reduction or discontinuation of drug

#### VII. Second Line Agents and side effects

- a. Natalizumab (Tysabri®): humanized monoclonal antibody against the cellular adhesion molecule  $\alpha$ 4-integrin; risk of progressive multifocal leukoencephalopathy (PML)
- b. Mitoxantrone (Novantrone®): anti-cancer drug; cumulative cardiac toxicity; 1:133 chance of developing leukemia

#### VIII. New Drugs and What's On the Horizon

- a. Oral agents – goal is equivalent or superior efficacy – example: Fingolimod (Gilenya®): prevents egress of T cells from lymph nodes and auto-aggressive lymphocytic infiltration of CNS; 0.5-1.6% incidence of cystoid macular edema; superior reduction in relapses when compared head to head with IFB-1 $\alpha$

**b. teriflunomide (Aubagio®): prevents mitosis of activated T lymphocytes; less effective than interferon B at preventing relapses**

**b. Monoclonal antibodies: IV infusion – example:**

**Alemtuzumab: significantly superior reduction in relapse rates and disability score progression when compared with IFB-1a; significant rates of thyroid dysfunction**

#### **IX. A Few Alternative Naturopathic Treatments**

**a. LDN (low dose naltrexone)**

**b. Estriol**

**c. Dietary strategies – ‘leaky gut syndrome’ associated with MS (intestinal permeability syndrome)**

- **Best Bet Diet: avoidance of dairy, gluten, refined sugar, eggs, yeast; individualized dietary intake based on food allergy testing**
- **Swank Diet: eliminate saturated fat and minimize PUFA, grains**