

Fatigue Update  
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**F**atigue is an extremely common symptom with many possible causes. New medications have been introduced which treat multiple causes of fatigue effectively, raising awareness and manageability of the condition.

- I. Fatigue as a 'sixth sense'
  - a. Physical effort
  - b. Mental effort
  
- II. Excessive sleepiness
  - a. Increased sleep drive
  - b. Sleep disruption
  - c. Circadian misalignment
  - d. Accumulated sleep debt
  - e. Functional impairment
    - i. Impact on activities of daily living
    - ii. Decreased concentration
    - iii. Makes concomitant conditions worse, e.g., diabetic control
  
- III. Diagnostic workup
  - a. History
    - i. Frequency of fatigue or sleepiness
    - ii. Degree of impairment
    - iii. Situational contributors
    - iv. Epworth Sleepiness Scale
  - b. Differential Diagnosis
    - i. Narcolepsy
      1. Irresistible sleep attacks
      2. Cataplexy
      3. Hypnagogic hallucinations
      4. Sleep paralysis
      5. Disrupted night time sleep
    - ii. Idiopathic hypersomnolence
      1. Neurogenic fatigue
      2. Fatigue related to multiple sclerosis
      3. Fatigue related to Binswanger's disease
    - iii. Sleep-disordered breathing
      1. Obstructive sleep apnea syndrome

- 2. Upper airway resistance syndrome
  - iv. Sleep-movement disorders
    - 1. Periodic limb movements of sleep
    - 2. REM behavior disorder
- c. Physical examination
- d. Neurological examination
- e. Laboratories
  - i. Polysomnography
  - ii. Actigraphy
  - iii. For narcolepsy
    - 1. Decreased hypocretin levels in CSF
    - 2. Positive HLA-DR2

#### IV. Pharmacological Therapy of Fatigue

- a. Stimulants
  - i. Methylphenidate (Ritalin, et al.)
  - ii. Dextroamphetamine (Dexedrine)
  - iii. Mixed amphetamine salts (Adderall, Adderall XR)
  - iv. Pemoline (Cylert) – watch for hepatotoxicity!
  - v. Amantadine (Symmetrel) – nausea, sleep disruption
  - vi. Venlafaxine (Effexor XR) – avoid plain or generic Effexor
- b. Modafinil (Provigil)
  - i. Not a stimulant, works specifically in the hypothalamus and prefrontal cortex
  - ii. Approved for narcolepsy
  - iii. Approved for obstructive sleep apnea
  - iv. Approved for shift work sleep disorder
  - v. Dosing up to 1000 mg daily in divided doses is effective and safe.