

# Infectious Mononucleosis

## Background

### 1. Definition

- Clinical syndrome typically characterized by fever, pharyngitis, lymphadenopathy and atypical lymphocytosis
- Caused by Epstein-Barr Virus (EBV)

## Pathophysiology

### 1. Pathology of disease

- EBV (herpes virus)

### 2. Incidence, prevalence

- Affects 6-8 per 1000 per year aged 10-19 years
- Most common in populations with many adults (military/college) affecting 11-48 persons per 1000
- By adulthood 90-95% have antibodies to EBV, so new infection in this age group uncommon
- Incidence of clinical infection is much higher in whites than blacks (30x)

### 3. Risk factors

- Transmission most commonly through exposure to saliva with incubation period of 4-8 wks
- Virus may shed in saliva for many weeks and may periodically be shed in oropharynx for decades once infected with EBV

### 4. Morbidity / mortality

- Mortality rate estimated to be 1 per 3000 cases
- Splenomegaly
  - Present in over 50% with mononucleosis
  - Risk of splenic rupture estimated to be 0.1%<sup>2</sup>
    - 50% are spontaneous, most likely to occur between day 4-21 of illness
    - Refrain from vigorous physical activity for at least 4 weeks
    - Risk of rupture may be increased in contact sports, weightlifting or rowing<sup>3</sup>
- Other rare complications
  - Airway compromise (supraglottic or glottic obstruction)
  - Neurologic syndromes
    - Meningitis, encephalitis, Guillain-Barre syndrome, cranial nerve palsies, mononeuropathies, transverse myelitis, peripheral neuritis, optic neuritis
  - These manifestations tend to occur 2-4 weeks or more after initial symptom onset
  - Hematologic abnormalities (including hemolytic anemia, thrombocytopenia, aplastic anemia)
  - Others: pneumonia, myocarditis, pancreatitis, glomerulonephritis
- Some evidence that IM in adolescents and young adults may be a risk factor for developing multiple sclerosis<sup>4</sup>

## Diagnosis

### 1. History

- In a series of 500 patients with confirmed IM:<sup>5</sup>
  - Lymphadenopathy was present in 100%
  - Fever in 98%
  - Pharyngitis in 85%
- Syndrome often heralded by malaise, headache, and low grade fever before development of more specific symptoms
- Fatigue-can be pronounced and prolonged
- Older patients are less likely to have sore throat and lymphadenopathy and more likely to have hepatomegaly and jaundice<sup>6</sup>

### 2. Physical exam

- Febrile
- Lymphadenopathy
  - Posterior > anterior (cervical)
  - Cervical, axillary, inguinal (lymphadenopathy may become more generalized, which distinguishes IM from other etiologies)<sup>7</sup>
- Pharyngitis
  - White or gray-green exudates
  - Swollen tonsils
  - Palatal petechiae
- Splenomegaly
- Skin
  - Occasionally generalized maculopapular, urticarial or petechial rash
  - Rash more common following treatment with ampicillin or amoxicillin
    - Also described with azithromycin, levofloxacin, cephalexin

### 3. Diagnostic tests

- Suspect IM in febrile pts with sore throat & splenomegaly, palatal petechiae, or posterior cervical, axillary or inguinal adenopathy
    - Absence of cervical adenopathy and fatigue is most helpful in dismissing the diagnosis<sup>8</sup>
  - Laboratory evaluation
    - Accepted testing strategy
      - WBC plus Heterophile test in presence of clinical suspicion
    - Peripheral blood smear
      - Elevated WBC
        - >20% atypical lymphocytes, or
        - >50% lymphocytes with >10% atypical lymphocytes<sup>8</sup>
    - Heterophile antibodies (**Monospot Test**)
      - Relatively specific, somewhat insensitive for mononucleosis
      - If negative, return visit in 5-7 days; if no clinical improvement repeat test as false negative rates highest in first week of symptoms<sup>8</sup>
- Specific immunologic tests for EBV
- Anti-VCA (viral capsid antigen) IgM
    - Expensive but can be useful when diagnosis is important (urgent return to sports) or in doubt

- EBNA (Epstein-Barr Nuclear Antigen)
  - Detectable at 6-8 weeks after onset of symptoms
  - If positive in patient with acute symptoms, prior infection is suspected (SOR:C)<sup>8</sup>

#### LFTs

- Elevated hepatic transaminases occur in approx half of patients<sup>9</sup>

#### Rapid Strep Test

- 3-30% of patients with mononucleosis have been reported to have concurrent GABHS pharyngitis; consider testing patients with mono and treating if positive (avoiding ampicillin and amoxicillin due to rash) (SOR:C)<sup>8</sup>

## Differential Diagnosis

### 1. Key DDx

- Heterophile-negative conditions with a clinical presentation similar to IM can be grouped into 3 principal categories:<sup>10</sup>
  - Non-EBV viral etiologies (Viral pharyngitis):
    - Human herpesvirus 6
    - Rhinovirus/ Coronavirus (common cold)
    - Adenovirus
    - Influenza
    - Herpes virus
    - Enteroviruses
    - CMV
    - Coxsackie virus
      - Hand-foot-mouth dz
      - Herpangina
    - Rubella
    - Acute retroviral syndrome (manifestation of HIV infection)
  - Bacterial infections (Bacterial pharyngitis):
    - Group A streptococcus
    - Chlamydia
    - N. gonorrhoeae
    - Diphtheria
  - Protozoal causes:
    - Toxoplasma gondii

### 2. Extensive DDx

- Mycoplasma
- Candida
  - Esp. in immunocompromised pts
- Kawasaki dz
- Peritonsillar abscess
- Hepatitis
- Lymphoma

## Treatment

- ### 1. Acute treatment supportive:
- Analgesics
  - Adequate hydration

- Throat sprays or lozenges
  - Treat GABHS if present (SOR:C)<sup>8</sup>
    - Avoid ampicillin or amoxicillin due to possible rash
2. Further management:
- Acyclovir provides no significant or consistent benefit (SOR:A)<sup>11</sup>
  - Steroids controversial
    - Consider for significant airway edema or impending airway obstruction (SOR:C)<sup>8</sup>
    - Cochrane review found there was insufficient evidence to recommend steroid treatment for symptom control in mononucleosis (SOR:A)<sup>12</sup>
  - Enforced bed rest may slow recovery of function
3. Long-term care
- Risk of splenic rupture
    - Refrain from vigorous physical activity for at least 4 weeks

### Follow-up

1. Return to office:
  - As indicated for repeat Monospot testing (5-7 days) or for persisting symptoms (fatigue, etc.)
2. Refer to specialist:
  - Not indicated unless complication develops (neurologic, hematologic, etc.)
3. Admit to hospital:
  - Not indicated unless complication develops (splenic rupture, etc.)

### Prognosis

1. Majority of patients recover completely in 4-8 weeks without any sequelae
2. Prospective series of 150 patients with confirmed IM revealed the following:<sup>14</sup>
  - Fatigue persisted in 28% at 1 month, 21% at 2 months, and 13% at 6 months
  - Cervical adenopathy persisted in 55% at 1 month, 39% at 2 months, and 29% at 6 months
  - Pharyngitis persisted in 47% at 1 month, 21% at 2 months, and 25% at 6 months
3. Association between EBV and chronic fatigue syndrome remains uncertain

### Prevention

1. To reduce risk of splenic rupture, athletes should refrain from vigorous physical activity for at least 4 weeks

### Patient Education

1. Educational handout from the American Academy of Family Physicians
  - <http://familydoctor.org/online/famdocen/home/common/infections/common/viral/077.html>

### References

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### **Evidence-based Inquiry**

1. Can we prevent splenic rupture for patients with infectious mononucleosis?
2. What test is the best for diagnosing infectious mononucleosis?
3. When should an athlete with infectious mononucleosis return to sports?

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