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INFECTIOUS MONONUCLEOSIS IN THE PEDIATRIC POPULATION: PATHOGENESIS, DIAGNOSTICS, AND RECOVERY KINETICS. A LITERATURE REVIEW

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ABSTRACT

Background: Infectious Mononucleosis (IM) is a multisystem viral illness primarily caused by the Epstein-Barr virus (EBV). While typically self-limiting, its clinical course in pediatric and adolescent patients can lead to severe organomegaly such as hepato/splenomegaly or debilitating post-infectious fatigue.

Objective: This paper reviews current clinical standards, diagnostic markers, and recovery kinetics, focusing on the transition from acute infection to long-term convalescence.

Results: Differential diagnosis remains critical to avoid antibiotic-induced complications. Recent longitudinal data indicate that acute illness severity is the primary predictor of chronic fatigue, while systemic inflammatory markers often fail to correlate with long-term symptoms.

Conclusion: Management should prioritize early identification of high-risk cases and a gradual, "pacing" approach to recovery.

KEYWORDS

Mononucleosis, Lymphadenopathy, Chronic Fatigue, EBV

CITATION

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1. Introduction

Infectious Mononucleosis (IM), colloquially known as "glandular fever," is a clinical syndrome most commonly caused by the Epstein-Barr virus (EBV) (approx. 90% of cases). However, mononucleosis-like syndromes can also be induced by CMV, HIV, HHV-6, HHV-7, or *Toxoplasma gondii* [1, 2, 5].

Primary EBV infection in preschool children is often asymptomatic or mild, whereas in adolescents, it presents with the full clinical triad (fever, pharyngitis, lymphadenopathy) in approximately 50% of cases [10, 12]. Given EBV's oncogenic potential—including associations with Burkitt lymphoma and nasopharyngeal carcinoma—understanding its acute pathogenesis and long-term impact on the pediatric immune system is vital [9]. Although those are the most common ones, virus has its impact in pathogenesis of Hodgkin lymphoma, NK-cell leukemia, extranodal NK/T-cell lymphoma nasal type.

2. Pathogenesis and Clinical Presentation

EBV is transmitted via saliva or contact with contaminated objects. The incubation period lasts 30–50 days, and patients remain contagious for six months post-infection [1, 4]. This is very troubling especially in young athletes, who share bathrooms and common objects or play contact sports, because illness can be spread easily among the team and lead to long term inability to train.

2.1. Acute Phase Symptoms

The clinical presentation typically follows a prodromal phase of 1–2 weeks characterized by malaise and myalgia [8].

- Pharyngotonsillitis: High fever, significant tonsillar exudates, and erythematous pharynx. Enanthema and bad breath may also be one of the symptoms.

- Lymphadenopathy (95%): Lymphadenopathy is concomitant symptom in 95% of cases in adult population. Importance of knowledge of how mononucleosis-like nodes present themselves should be highlighted. Nodules have inflammatory features, such as: enlargement of the nodule >2cm, mobility,

tenderness, not matted, elasticity [7]. Fluctuant node would suggest abscess formation (pus collection) and be considered as secondary infection of the node, which is why close observation is required. Lymphadenopathy can last up to 6 months.

- Splenomegaly occurs in approximately 50% of cases and carries a risk of rupture, necessitating the avoidance of strenuous activity during the first month of illness [1, 3].
- Enlargement of the spleen manifests itself in 50% cases, mostly in 2nd week of illness. Spleen is touchy and fragile, that is why the stomach examination should be performed with caution. Splenomegaly typically resolves within approximately two weeks. Although spleen rupture is rare complication it is extremely dangerous, so patients need to avoid sports and hardcore physical activity.
- In 50% of cases hepatitis can present itself with pain under right rib, hepatomegaly, sclera, and last up to 4 weeks.

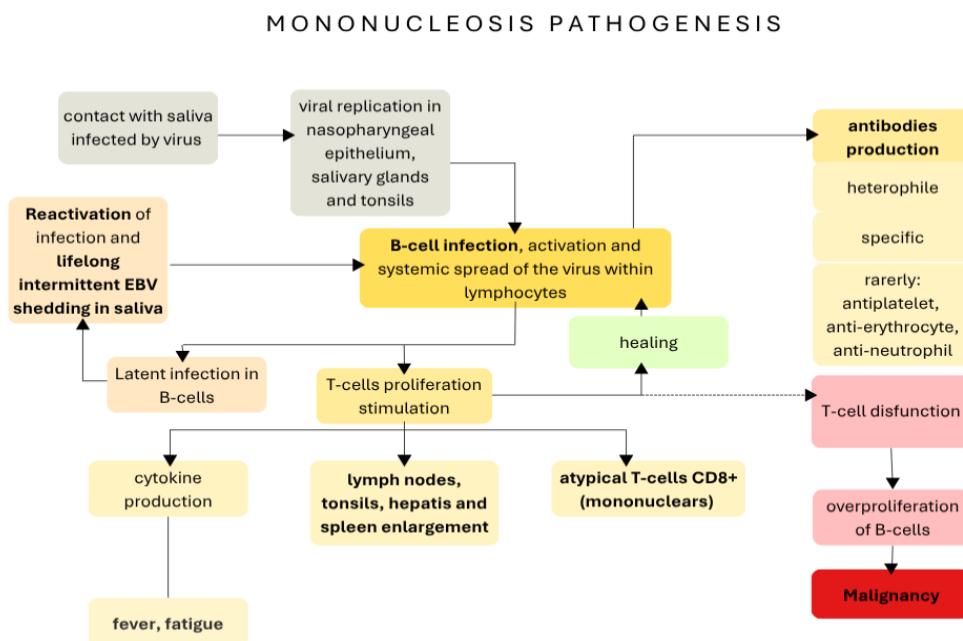


Fig. 1. Mononucleosis pathogenesis.

2.2. The Post-Antibiotic Exanthem

A hallmark diagnostic challenge in IM is the maculopapular rash that occurs in up to 70–100% of patients treated with semi-synthetic penicillins (e.g., amoxicillin) [1, 5, 12]. This generalized exanthem is not an allergy but an immune-mediated reaction, serving as a late clinical indicator of an underlying viral etiology.

3. Post-Infectious Fatigue and Recovery Kinetics

While the acute phase typically resolves within 2–4 weeks, "post-infectious asthenia" can persist for months [4, 6]. Complications during the course of infectious mononucleosis occur relatively rarely. These include splenic rupture (occurring primarily during the 2nd-3rd week of the illness), thrombocytopenia, hemolytic anemia, encephalitis, myocarditis, pancreatitis, or orchitis, and parenchymal liver damage (hepatitis). Conversely, bacterial superinfections are encountered quite frequently. The feeling of fatigue and weakness (post-infectious asthenia) may persist for up to eight weeks following the disease.

3.1. Predictors of Chronicity

Landmark research by Hickie et al. (2006) established that post-infective fatigue is a discrete biological entity rather than a psychological manifestation. In adolescents, the severity of the acute illness (e.g., total days spent in bed) and the presence of autonomic symptoms are the most reliable predictors of Chronic Fatigue Syndrome (CFS) at 6 and 12 months post-infection (Katz et al., 2016).

3.2. Pathophysiological Insights

Contrary to traditional inflammatory models, Cameron et al. (2014) demonstrated that peripheral cytokine levels (IL-6, TNF- α) do not remain elevated in patients with chronic fatigue. This suggests that long-term recovery depends more on localized neuroinflammation or mitochondrial metabolic restoration than on ongoing systemic "cytokine storms."

4. Diagnostics and Differential Diagnosis

Diagnosis is primarily clinical, supported by characteristic laboratory findings.

- Complete Blood Count (CBC): Essential for detecting lymphocytosis and atypical lymphocytes (mononuclears). CBC is also critical for the differential diagnosis of Acute Lymphoblastic Leukemia (ALL) [1, 5].
- Serology: Detection of VCA IgM/IgG and EBNA antibodies is the gold standard for staging the infection [10].
- Ultrasonography: Used to monitor hepatosplenomegaly and rule out complications such as splenic rupture or parenchymal liver damage [11].
- Transaminases (ALT, AST) may also be elevated and normalized after 14 days.

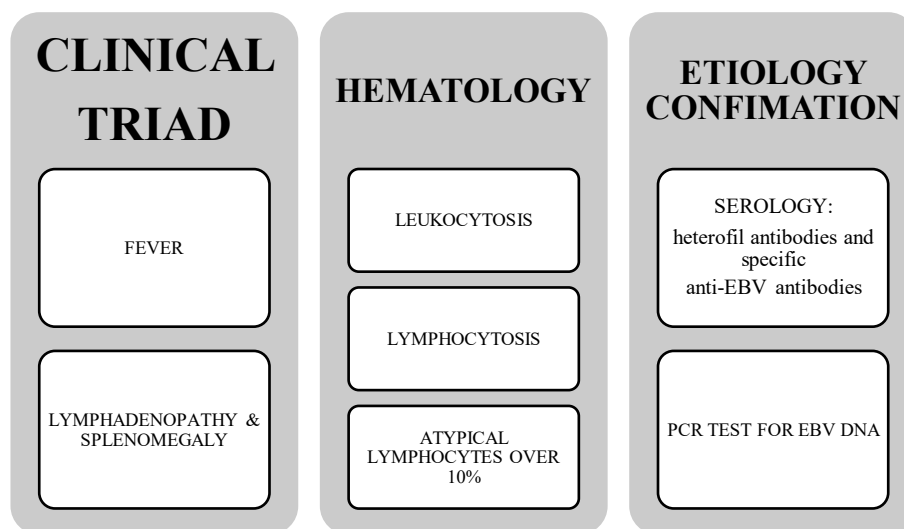


Fig. 2. Mononucleosis diagnosis.

5. Management Strategies

Treatment remains largely supportive, focusing on hydration and fever management [1, 12]:

1. Pharmacotherapy: Corticosteroids are used judiciously, reserved for severe airway obstruction or hematological complications (e.g., thrombocytopenia), only after malignancy has been ruled out [3, 11].
2. Activity Management: Modern guidelines (NICE 2021) suggest pacing—a gradual, symptom-contingent return to activity—to prevent Post-Exertional Malaise (PEM), particularly in adolescents.

6. Conclusions

1. Diagnostic Vigilance: IM should always be considered in pediatric pharyngitis to prevent the administration of penicillins and subsequent avoidable complications.
2. Prognostic Assessment: Clinicians should closely monitor patients with high acute illness severity, as they represent a high-risk group for long-term functional impairment.
3. Biological Monitoring: While IM is often self-limiting, monitoring organomegaly and liver function is necessary to prevent dangerous, though rare, complications.
4. Holistic Convalescence: Recovery protocols should include school accommodations and cognitive monitoring for adolescents experiencing "brain fog" or prolonged fatigue.

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