PRESENTED BY

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Herpes virus 4.

Infectious mononucleosis and Epstein–Barr virus

Kissing 'due to its transmission by oral secretions/ formation of granulomatous hypertrophic tonsils 'kissing tonsils'.

Infectious mononucleosis (IM) is a clinical syndrome characterised by: *It is a syndrome caused mostly by EBV , however Approximately 10% of cases are caused by cytomegalovirus (CMV).*

- Pharyngitis
- cervical lymphadenopathy
- fever and
- lymphocytosis

That's why it is known as glandular fever 'LAP+ fever'.

Also called as glandular fever. It is most often caused by Epstein–Barr virus (EBV) but other infections can produce a similar clinical syndrome like:

- Cytomegalovirus *HV3.*
- Human herpesvirus-6 or 7
- HIV-1 primary infection and
- Toxoplasmosis.*Chlamydia.*

EBV is a gamma herpesvirus. In developing countries, subclinical infection in childhood is virtually universal. In developed countries, primary infection may be delayed until adolescence or early adult life. Under these circumstances, about

50% of infections result in typical IM. The virus is usually acquired from asymptomatic excreters via saliva, either by droplet infection or environmental contamination in childhood, or by kissing among adolescents and adults.

Clinical features

About 6 weeks.

EBV infection has a prolonged but undetermined incubation period, followed in some cases by a prodrome of fever, headache and malaise. This is followed by IM with severe pharyngitis, which may include tonsillar exudates and non-tender anterior and posterior cervical lymphadenopathy. Palatal petechiae, periorbital oedema, splenomegaly, inguinal or axillary lymphadenopathy, and macular, petechial or erythema multiforme rashes may occur. In most cases, fever resolves over 2 weeks, and fatigue and other abnormalities settle over a further few weeks.

especially posterior. *severe cases, lead to airway obstruction*

Difficulty in breathing and swallowing.

Pathophysiology

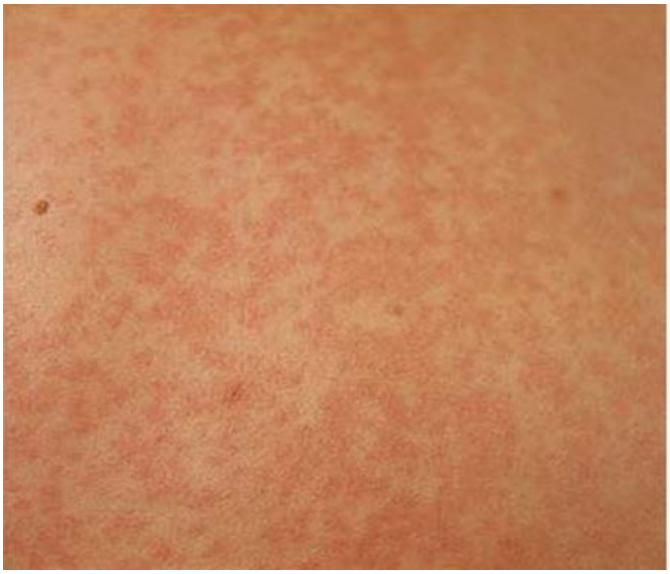
EBV infects **B lymphocytes** in mucosal epithelium (e.g., oropharynx, cervix) via the **CD21 receptor** → infected B lymphocytes induce a humoral (B-cell) as well as a cellular (T-cell) immune response → an increased concentration of **atypical lymphocytes** in the bloodstream, which are **CD8+ cytotoxic T cells** that fight infected B lymphocytes

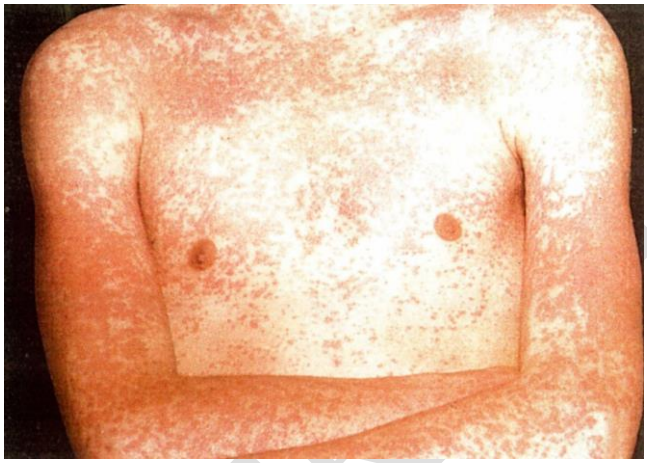
Complications

Maculopapular rash (similar appearance to measles): 1)~ 5–15% caused by the infection itself. 2)Most commonly caused by antibiotic use (e.g., aminopenicillins).

Common

- Severe pharyngeal oedema
- Antibiotic-induced rash (80–90% with ampicillin)





- Hepatitis (80%) ***Mild elevation of aminotransferase is a common but nonspecific finding.***
- Prolonged post-viral fatigue (10%)
- Jaundice (< 10%)

Uncommon

❖ Neurological ***Guillain-Barré syndrome. Multiple sclerosis.***

- Cranial nerve palsies
- Polyneuritis
- Transverse myelitis
- Meningoencephalitis

❖ Haematological

- Haemolytic anaemia

- **Hematologic system**
  - **Hemophagocytic lymphohistiocytosis** (HLH): a life-threatening hematologic disorder involving pancytopenia and severe inflammation due to increased activity of cytotoxic T cells and macrophages [22]
    - Other secondary causes: malignancy (e.g., colon cancer) [23]
    - Clinical features: fever, hepatosplenomegaly, weight loss
    - Laboratory findings: pancytopenia, ↑ serum ferritin, cholestasis
    - Bone marrow biopsy: phagocytosis of hematopoietic cells
  - Autoimmune hemolytic anemia, thrombocytopenia
  - TTP, HUS
  - DIC

- Thrombocytopenia

❖ Renal

- Abnormalities on urinalysis
- Interstitial nephritis

❖ Cardiac

- Myocarditis
- ECG abnormalities
- Pericarditis

❖ Rare

- Ruptured spleen
- Respiratory obstruction
- Agranulocytosis
- X-linked lymphoproliferative syndrome
- EBV-associated malignancy
- Nasopharyngeal carcinoma
- Burkitt's lymphoma
- Hodgkin lymphoma (certain subtypes only)

non-Hodgkin lymphoma

- Primary CNS lymphoma***In immunocompromised.***

Post-transplantation.

• Lymphoproliferative disease in immunocompromised

Death is rare but can occur due to:

- ❖ respiratory obstruction,
- ❖ haemorrhage from splenic rupture, thrombocytopenia or
- ❖ encephalitis.

The diagnosis of EBV infection outside the usual age in adolescence and young adulthood is more challenging. In children under 10 years the illness is mild and short-lived, but in adults over 30 years of age it can be severe and prolonged.

often absent. EBV may present with jaundice, In both groups, pharyngeal symptoms are as a or with a complication.

PUO

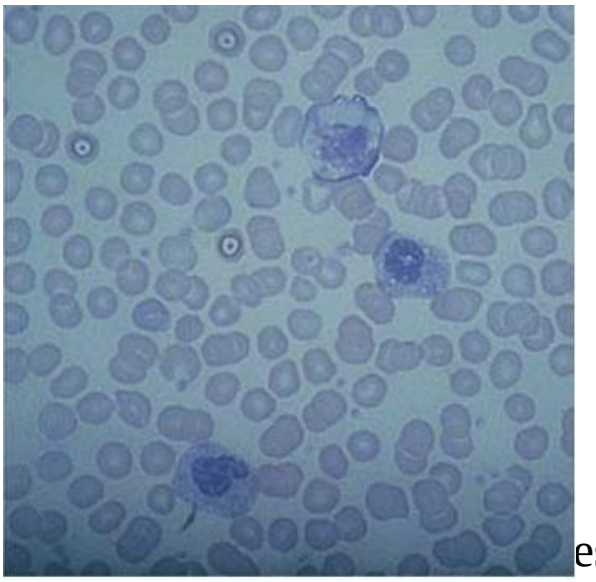
Investigations

Absolute lymphocyte count > 4 x 109/L
> 50% lymphocytes
> 10% atypical lymphocytes

CBC and blood film, atypical lymphocytes are common in EBV infection but also occur in other causes of IM, acute retroviral syndrome with HIV infection, viral hepatitis, mumps and rubella. They are also a feature of dengue, malaria and other geographically restricted infections .

Imaging [3][8]

- Imaging is not routinely recommended.
- Ultrasonography shows splenomegaly in almost all patients and is therefore unnecessary. [8]
- CT abdomen with contrast is recommended for patients with clinical features of splenic rupture.



esent during the acute illness and convalescence, which is detected by the Paul–Bunnell or 'Monospot' test. Sometimes antibody production is delayed, so an initially negative test should be repeated. However, many children and 10% of adolescents with IM do not produce heterophile antibody at any stage. Specific EBV serology confirms the diagnosis. Acute infection is characterised by IgM antibodies against the viral capsid, antibodies to EBV early antigen and the initial absence of antibodies to EBV nuclear antigen (anti-EBNA). Seroconversion of anti-EBNA at approximately 1 month after the initial illness may confirm the diagnosis in retrospect. CNS infections may be diagnosed by detection of viral DNA in CSF.

EBV nuclear antigen antibodies are detectable ≥ 6 weeks after symptom onset and may persist for life.

Interpretation of VCA serology for EBV [3][6]

	anti-VCA IgM	anti-VCA IgG	anti-EBNA IgG
Acute infection (0–6 weeks)	↑	↑ (titers peak at 2 weeks)	Undetectable
Past infection (≥ 6 weeks)	Undetectable	↑	↑

Management

Treatment is largely symptomatic. If a throat culture yields a β-haemolytic streptococcus, penicillin should be given. Administration of ampicillin or amoxicillin in this condition commonly causes an itchy macular rash and should be avoided. When pharyngeal oedema is severe, a short course of glucocorticoids, e.g. prednisolone 30 mg daily for 5 days, may help. Current antiviral drugs are not active against EBV. Return to work or school is governed by physical fitness rather than laboratory tests; contact sports should be avoided until splenomegaly has resolved because of the danger of splenic rupture. Unfortunately, about 10% of patients with IM suffer a chronic relapsing syndrome.

Differential diagnoses

- Mononucleosis-like syndromes [18]
  - Streptococcal pharyngitis, tonsillitis
  - **Acute HIV infection**
  - Viral hepatitis
  - Toxoplasmosis
- Diphtheria
- Acute leukemia
- Chronic fatigue syndrome

Tonsillitis is an important differential diagnosis that is often treated with aminopenicillins (e.g., ampicillin). However, if given to a patient with infectious mononucleosis, the patient often develops a maculopapular rash after 2–10 days. [7][8]

In patients with fatigue lasting > 6 months, in whom EBV was not confirmed, consider alternative diagnoses (e.g., chronic fatigue syndrome). [9]