A synonym of infectious mononucleosis is the “kissing disease”. This term contains also the main method of transmission of Pfeiffer’s glandular fever: the kissing. Nearly all people will get infected with the responsible Epstein-Barr virus in the course of their lives. Read the following article for the pathogenesis, symptomatology, diagnosis, and treatment of infectious mononucleosis.
Infectious mononucleosis is a viral infectious disease caused by the pathogen Epstein-Barr virus (EBV). It is associated with fever, angina, pharyngitis, and lymphadenopathy. EBV belongs to the group of human herpes viruses.

Description and synonyms: infectious mononucleosis (*Mononucleosis infectiosa*), Pfeiffer’s disease, Pfeiffer’s glandular fever, mono, “kissing disease”

Epidemiology of Infectious Mononucleosis

> 95% of people worldwide will be infected with EBV during their lifetimes.

Infectious mononucleosis was first described in 1920. It occurs more frequently in spring and autumn. Children and adolescents aged 15–19 years are affected most often. EBV seroprevalence is dependent on age, socioeconomic status, ethnicity, and gender.

In the United States, infectious mononucleosis is a common cause of viral pharyngitis, especially among young adults.

- **Note**: People who are older than 30 years are almost 100% infected with EBV.

Etiology and Pathogenesis of Infectious Mononucleosis

Pathogenesis of infectious mononucleosis

EBV belongs to the human herpesviruses (HHV): HHV 4. The human pathogenic enveloped double-stranded DNA virus was first discovered in 1964 by M. Epstein and Y. Barr from the B lymphocytes of a patient with Burkitt lymphoma.

EBV has an exceptionally high species specificity; the virus replicates almost exclusively in human epithelial cells of the oropharynx and in B lymphocytes.

Transmission of Pfeiffer’s glandular fever

The disease is transmitted mainly via contact with body secretions, primarily oropharyngeal secretions. Other common methods of transmission include:

- Droplet infection
- Smear infection, especially in children by parents, playmates, etc.
- Contact infection, especially in adolescents by infected saliva during **kissing** (“kissing disease”)

**Note**: No vertical transmission occurs during pregnancy. EBV transmission from blood
transfusions or transplants is rare. The virus spreads from the mouth throughout the body and infects CD-21-positive epithelia in nasopharyngeal space and B lymphocytes, which infiltrate tissues. Immortalization of B lymphocytes occurs, then a strong increase of EBV. In primary infection, only a small number of viral proteins are likely to be expressed, resulting in an initially less pronounced immune response and a lack of clinical symptoms.

With an insufficient immune response, the immune system can destroy the affected B lymphocytes. However, complete elimination of all virus cells never occurs, resulting in lifelong virus persistence.

Incubation period of Pfeiffer’s glandular fever

The incubation period is 10–14 days for adolescents and approximately 50 days for adults.

Symptoms and Clinical Signs of Infectious Mononucleosis

The prodromal stage is usually asymptomatic, especially in children younger than 10 years.

Symptoms of acute mononucleosis

Typical symptoms of symptomatic mononucleosis include the following:

Classic triad:
Fever

- Tonsillitis
- Cervical lymphadenopathy

Other symptoms:

- Weakness and fatigue
- Headaches
- Limb pain
- Typical petechiae at the transition from hard to soft palate
- Halitosis
- Hepatosplenomegaly with jaundice
- Generalized lymph node swelling
- Very long convalescence period

Note: Younger patients (younger than 10 years) have milder symptoms. Older patients (older than 30 years) often lack classic symptoms.
In **Hoagland syndrome**, a maximum manifestation of infectious mononucleosis occurs. Patients suffer from impaired nasal breathing, periorbital edema, and swollen upper eyelids.

**Symptoms of chronic mononucleosis**

Rarely, persistent viral replication can lead to chronic mononucleosis. Affected patients suffer from fever, fatigue, weight loss, lymphadenopathy, cytopenia, interstitial pneumonia, and hepatitis. Lymphoma and death also may occur.

**Complications of Infectious Mononucleosis**

Rare severe Pfeiffer’s glandular fever progression

Severe courses of infectious mononucleosis occur rarely. In addition to autoimmune hemolytic anemia and thrombocytopenia, internal organs may be involved, leading to hepatitis, myocarditis, nephritis, interstitial pneumonia, and/or lymphocytic meningoencephalitis, among other conditions.

Distinctive splenomegaly can lead to a ruptured spleen. Other complications include **Guillain-Barré syndrome** and **Portillo’s syndrome**.
Portillo’s Syndrome

Portillo’s syndrome is an X-linked recessive inheritance disorder of the immune response against EBV in which no antibodies against antigens of EBV can be formed. The result is self-destruction of the immune system, which can lead to fatal progression (hepatitis, organ infiltration by cytotoxic lymphocytes, hemophagocytic syndrome).

EBV-associated tumors

- Nasopharyngeal carcinoma
- Hodgkin’s disease
- Burkitt’s lymphoma
- B-cell lymphoproliferative disorder

Diagnosis of Infectious Mononucleosis

Physical examination of Pfeiffer’s glandular fever

Infectious mononucleosis is accompanied by enlarged lymph nodes (cervical, axillary, and inguinal). Some patients have hepatosplenomegaly, characteristically crimson, swollen tonsils with typical dirty-gray membranes.

Laboratory tests for Pfeiffer’s glandular fever

Significant results for infectious mononucleosis are:

- Absolute and relative leukocytosis (> 4,000/ml and > 50% of leukocytes) with > 10% atypical large T cells (Pfeiffer cells, fibrocytes)
- Mild anemia, neutropenia, and thrombocytopenia
- Increased blood sedimentation rate (BSR)
- Increased C-reactive protein (CRP)
- Increased transaminases

Note: Cells are characterized by a basophilic vacuole in the cytoplasm and an eccentrically localized, subdivided nucleus.
Tests to detect Pfeiffer’s glandular fever

The gold standard to diagnose infectious mononucleosis is enzyme-linked immunosorbent assay (ELISA) via the detection of virus-specific immunoglobulin antibodies (against the viral capsid antigen). Infection is indicated by the detection of Epstein-Barr nuclear antigen immunoglobulin antibodies.

Paul-Bunnell test

The Paul-Bunnell test has low specificity and sensitivity. The rapid test characterizes mononucleosis but hardly plays a role in current diagnostics.

Histology of Pfeiffer’s glandular fever

Typical in infectious mononucleosis is polymorphic hyperplasia of the pulp. Propagation in lymph nodes and fast growth of blast cells/necrosis are seen in histological samples.

Differential Diagnoses of Infectious Mononucleosis

Pfeiffer’s glandular fever: pure clinical delimitation is difficult

Clinically, no distinction can be made among acute infections with EBV, cytomegalovirus (CMV), or human immunodeficiency virus (HIV). Differential diagnoses may include consideration of the following:

- Acute CMV, HIV, group A Streptococcus, toxoplasma infections
- Rare HHV-6, HHV-7, parvovirus B19, Bartonella infections
- Viral rhino-, corona-, adenovirus infections, which often occur on a seasonal basis and are accompanied by intensified cold symptoms
- Parainfluenza viruses: sudden myalgia/arthritis with fever and perhaps a mild case of tonsillitis
- Diphtheria
- Acute necrotizing ulcerative gingivitis (often accompanied by development of necrosis and dirty-gray pseudomembrane)
- Listeriosis: Listeria infection may be considered in the case of negative EBV results.

Treatment of Infectious Mononucleosis

Symptomatic treatment of Pfeiffer’s glandular fever
No specific antiviral therapy is currently available. **Treatment** of symptoms includes physical preservation, antipyretics and analgesics, nonsteroidal antirheumatics, and volume loading. Administration of penicillin or aminopenicillins can trigger exanthema formation.

No antiviral medications, such as acyclovir and valaciclovir, should be used in patients with adequate immune function.

**Prognosis of Infectious Mononucleosis**

**Best course of Pfeiffer’s glandular fever**

Prognosis of infectious mononucleosis is good in normal cases. In patients with cellular immunodeficiency and post-transplant patients, more severe courses may occur. Chronic infections are extremely rare.

**References**


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**Correct answers:** 1E, 2B, 3D

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