Infectious mononucleosis

Infectious mononucleosis (also known as "mono" or the "kissing disease") is a disease caused by primary Epstein-Barr virus (EBV) infection. It is clinically similar to streptococcal pharyngitis, because of its similar manifestations such as fever, sore throat, lymphadenopathy and hepatosplenomegaly, but unlike pharyngitis, **it does not respond to antibiotic therapy**. It is one of the relatively common diseases in the Czech Republic (2–2.5 thousand cases per year). [1]

Infectious mononucleosis syndrome is a much less common disease (in about 20% of cases of infectious mononucleosis) and is caused by **cytomegalovirus** (CMV), or rarely by adenoviruses, HIV, HHV-6, or Toxoplasma gondii.[2][3]

Epidemiology

The source of the infection is a **sick person** or a **healthy carrier**. People in the convalescent stage can also be healthy carriers as EBV remains in the body in a **latent form** throughout one's life and can be reactivated (as with other herpes infections). The population is infected in early age, and children under 2 years of age usually have no symptoms. The highest incidence is in adolescence and young adults between **15 to 24 years of age**. Infectious mononucleosis is almost non-existent in adults over 40 years.

Pathogenesis

EBV is **transmitted through saliva** via intimate contact (kissing, shared food) or by blood transfusion. The incubation period is between **4 days to 4 weeks.**[1] The virus infects the **epithelium of the pharynx**. From there, it enters **B-lymphocytes** and causes polyclonal activation of B cells, so that B-lymphocytes begin to produce antibodies. Subsequently, the virus travels to all of the organs, which causes the **activation of cellular immunity** (**cytotoxic T-lymphocytes and NK-cells**) and thus suppresses the infection in the body. If cellular immunity is not activated, uncontrollable severe to fatal lymphoproliferative disorder (**X-linked lymphoproliferative syndrome**, "XLP") may develop.[2]

The acute phase of the disease is terminated by **activated suppressor T cells**, which appear in the peripheral blood as **atypical lymphocytes** (also known as "Pfeiffer's cells").[4] Some of the infected B-lymphocytes can still survive and become the source of late salivary excretion of the virus. The patient acquires **long-term immunity**.

Clinical picture

The onset may be sudden or gradual with **prodromal symptoms** such as headache or abdominal pain, sore throat, myalgia, nausea, loss of appetite, fatigue, sweating, fever (in 90% of children; may reach up to 40 °C and last from 10 to 14 days). However, a **typical triad** is present:

- **pseudomembranous angina** (hypertrophic tonsils with bilateral coating)
- **cervical lymphadenopathy** (in 90% of cases; submandibular lymph nodes, cervical lymph nodes, occipital nodes and sometimes also axillary or inguinal ones are enlarged),
- **hepatosplenomegaly** (hepatomegaly is present in 1/3 cases, splenomegaly in almost 1/2 cases – being most visible in the 2nd week).

The following may also appear:

- **petechiae** (a rash of many tiny red spots) (*Holzel's sign*) in 25-60% of cases,
- **swelling of the eyelids** (*Bass symptom*) in 1/3 cases,
- **rash of various natures**,
- **subicterus**,
- **rhinophonia**,
- **bad breath** (*foetor ex ore*).

The disease subsides within **2 to 4 weeks**, but fatigue, weakness and loss of appetite can persist for several months.[2]

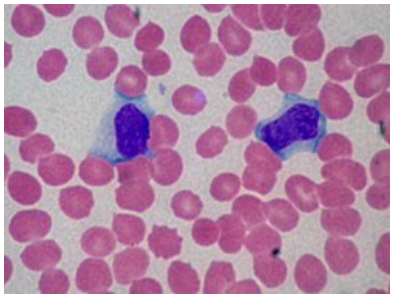
Diagnostics

- **A complete blood count**: leukocytosis with lymphocytosis and monocytosis with large atypical lymphocytes, neutropenia and mild thrombocytopenia.
- **Liver function tests**: elevation of **aminotransferases** and **L-lactate dehydrogenase** (usually 2-3 times higher than the upper limit of the normal value, sometimes it may be up to 10 times).
- **CRP** can be increased, depending on the presence of **bacterial superinfection**.
- The diagnosis consists of detection of **heterophile antibodies** (Paul-Bunnel test – which often appears negative among young children; OCH-Ericson test) and specific antibodies by ELISA (VCA – viral-capsid

antigen, EA - early antigen, EBNA – Epstein-Barr nuclear antigen), or eventually by PCR.
- Primary infection: increase in IgM and IgG against VCA, then EA, but Ig against EBNA is missing.
- Latency: positive Ig against EBNA.
- Reactivation of infection: IgG against VCA, EBNA, EA and sometimes IgM against VCA.

Complications

- Airway obstruction caused by tonsillar hypertrophy and lymphadenopathy.
- **Hematological**: autoimmune hemolytic anemia, mild thrombocytopenia without bleeding, rarely aplastic anemia.
- **Neurological**: serous meningitis and meningoencephalitis, polyradiculoneuritis, cerebellitis, Guillain-Barré syndrome.
- **Pulmonary**: interstitial pneumonia.
- **A ruptured spleen**: most often in 2nd or 3rd week of the illness; manifestations: abdominal pain and symptoms of hemorrhagic shock.
- **Rare**: myocarditis, pericarditis, acute acalculous cholecystitis, chorioretinitis, rhabdomyolysis.
- **Duncan's syndrome**: fatal course of primary EBV infection in boys with primary immunodeficiency (X-linked lymphoproliferative syndrome)[2].



Reactive lymphocytes in peripheral blood in infectious mononucleosis

Therapy

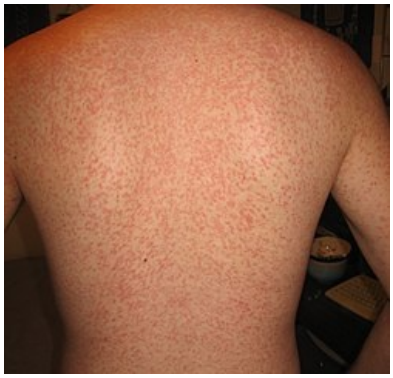
Treatment is symptomatic. Resting, liver disease diet, hepatoprotectants, vitamins, antipyretics, neck compresses, and gargling are recommended.

- **Antibiotics** are indicated only in case of **superinfection** (presumed or proven).
- **Corticosteroids** in case of an abnormal throat finding and swallowing problems, difficulties with breathing, etc...

After undergoing infectious mononucleosis, a **six-month follow-up** is recommended (general health condition, complete blood count, liver tests).[2][5]

- The disease is reported, but isolation is not necessary.
- **Prophylaxis and prevention do not exist**.

⚠ In the administration of **aminopenicillin antibiotics**, in 90–100% of cases, a noticeable **red maculopapular rash**, sometimes even of a hemorrhagic nature, is present.[2]



Exanthema as a response to aminopenicillins in infectious mononucleosis

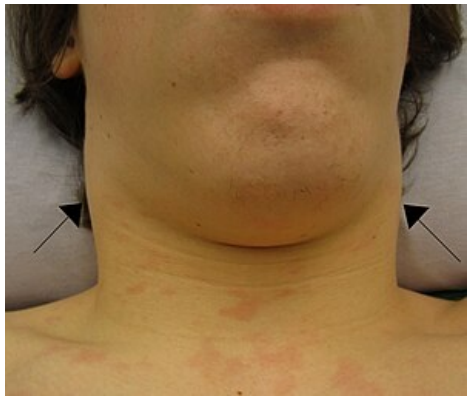
Infectious mononucleosis syndrome

Infectious mononucleosis syndrome is a disease that is clinically **very similar to infectious mononucleosis**, but does not meet all laboratory criteria and is characterized by a lack of heterophile antibodies. Clinically, it manifests as cervical lymphadenopathy followed by other symptoms that are less common (such as throat-related findings, hepatosplenomegaly).

Causative agents

- human Cytomegalovirus,
- rarely HIV, rubeola virus, adenoviruses, Toxoplasma gondii, HHV-6 and HHV-7 .

Source, transmission and incubation period depend on the **causative agent**. We determine the diagnosis based upon lymphadenopathy, atypical lymphocytes in peripheral blood, increase in aminotransferases enzymes in the blood without increase in lactate dehydrogenase at the same time and serological evidence of the causative agent. The prognosis is good, we are able to treat the symptoms (rest and liver disease diet).[6]



Cervical lymphadenopathy in infectious mononucleosis (marked by arrows)

⚠ The differentiation of etiological agents is not very significant, except for the recognition of **primary HIV infection**, which has a crucial importance for the patient and his surroundings.

Comparison of infectious mononucleosis and IM syndrome

CRITERIA	Infectious mononucleosis	Infectious mononucleosis syndrome
Agens	EBV (Epstein-Barr virus)	**CMV**, HIV, rubeola, toxoplasma
Lymphadenopathy	✔	✔
Atypical lymphocytes	✔	✔
Aminotransferases	elevated	elevated
L-lactate dehydrogenase	**elevated**	normal
Heterophile antibodies	**elevated**	×
Hepatic syndrome	✔	could be present
Throat-related findings	✔	could be present

References

Related articles

- Herpesviridae • EBV

External links

- Infekční mononukleóza (článek z časopisu Pediatrie pro praxi) (http://www.pediatriepropraxi.cz/pdfs/ped/2005/05/05.pdf)
- H. Ambrožová: Infekční mononukleóza (http://www.solen.sk/index.php?page=pdf_view&pdf_id=1867&magazine_id=4)
- H. Ambrožová: Infekční mononukleóza (http://www.solen.sk/index.php?page=pdf_view&pdf_id=1867&magazine_id=4)

Citations

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2. AMBROŽOVÁ, H. Infekční mononukleóza. *Pediatrie pro praxi* [online]. 2005, vol. 6, no. 5, p. 244-246, Available from <www.pediatriepropraxi.cz>. ISSN 1803-5264.
3. Havlík J, et al, Infekční nemoci, 2. vyd., Galén 2002; 144–145.
4. MUNTAU, Ania Carolina. *Pediatrie.* 4. edition. Praha : Grada, 2009. pp. 188-190. ISBN 978-80-247-2525-3.
5. HRODEK, Otto – VAVŘINEC, Jan, et al. *Pediatrie.* 1. edition. Praha : Galén, 2002. pp. 619-621. ISBN 80-7262-178-5.
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