

# Infectious mononucleosis (IM, mono)

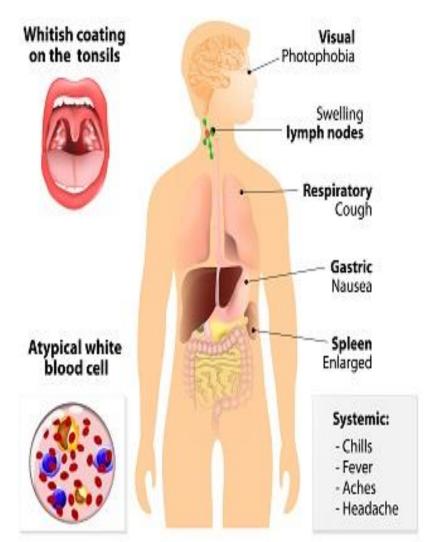
also known as mono, glandular fever, Pfeiffer's disease, Filatov's disease, and sometimes colloquially as the kissing disease is an infection usually caused by the Epstein–Barr virus (EBV).

Most people are infected by the virus as children, when the disease produces few or no symptoms.

In young adults, the disease often results in <u>fever</u>, sore throat, <u>enlarged lymph nodes</u> in the neck, and <u>tiredness</u>.

Most people recover in two to four weeks; however, feeling tired may last for months. The liver or spleen may also become swollen, and in less than one percent of cases splenic rupture may occur.

#### Mononucleosis



While usually caused by Epstein–Barr virus, also known as human herpesvirus 4, a member of the **Herpesviridae** family of **DNA**, a few other viruses may also cause the disease. It is primarily spread through saliva but can rarely be spread through semen or blood. Spread may occur by objects such as drinking glasses or toothbrushes or through a cough or sneeze. Those who are infected can spread the disease weeks before symptoms develop. Mono is primarily diagnosed based on the symptoms and can be confirmed with blood tests for specific antibodies. Another typical finding is increased blood lymphocytes of which more than 10% are atypical. The monospot test is not recommended for general use due to poor accuracy.

There is no <u>vaccine</u> for EBV, but infection can be prevented by not sharing personal items or saliva with an infected person.

Mono generally improves without any specific treatment.

Symptoms may be reduced by drinking enough fluids, getting sufficient rest, and taking pain medications such as paracetamol (acetaminophen) and ibuprofen.

- Mono most commonly affects those between the ages of 15 to 24 years in the <u>developed world</u>.
- In the <u>developing world</u>, people are more often infected in early childhood when there are fewer symptoms.
- In those between 16 and 20 it is the cause of about 8% of sore throats.
- Nearly 95% of people have had an EBV infection by the time they are adults.
- The disease occurs equally at all times of the year.
- Mononucleosis was first described in the 1920s and colloquially known as "the kissing disease".



The characteristic symptomatology of infectious mononucleosis does not appear to have been reported until the late nineteenth century. In 1885, the renowned Russian pediatrician Nil Filatov reported an infectious process he called "idiopathic denitis" exhibiting symptoms that correspond to infectious mononucleosis, and in 1889 a German balneologist and pediatrician, Emil Pfeiffer,

independently reported similar cases

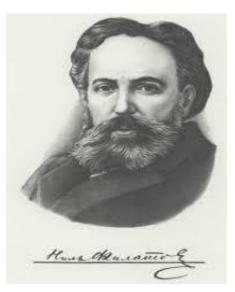
(some of lesser severity) that tended to

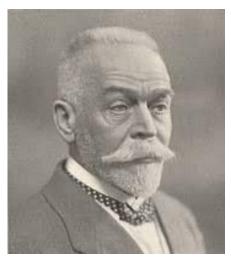
cluster in families, for which he coined

the term Drüsen fieber ("glandular

fever").

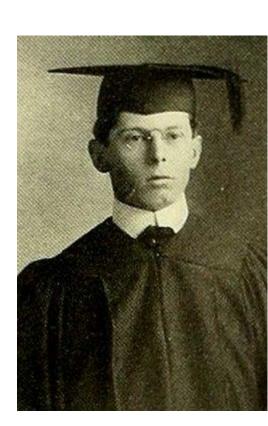






The word *mononucleosis* has several <u>senses</u>. It can refer to any <u>monocytosis</u> (excessive numbers of circulating <u>monocytes</u>), but today it usually is used in its narrower sense of infectious mononucleosis, which is caused by EBV and of which monocytosis is a finding.

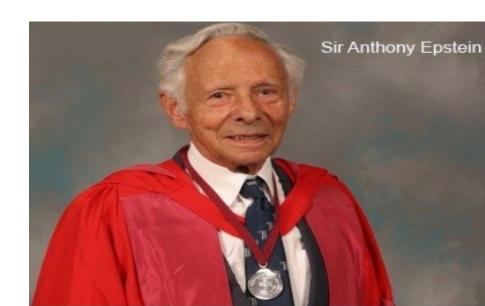
The term "infectious mononucleosis" was coined in 1920 by Thomas Peck
Sprunt and Frank Alexander Evans in a classic clinical description of the disease published in the <u>Bulletin of the Johns</u>
<u>Hopkins Hospital</u>, entitled "Mononuclear leukocytosis in reaction to acute infection (infectious mononucleosis)".



The Epstein–Barr virus was first identified in <u>Burkitt's</u> <u>lymphoma</u> cells by <u>Michael Anthony Epstein</u> and <u>Yvonne</u> <u>Barr</u> at the <u>University of Bristol</u> in 1964.

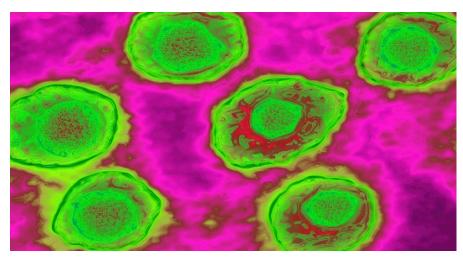
The link with infectious mononucleosis was uncovered in 1967 by Werner and Gertrude Henle at the <u>Children's Hospital of Philadelphia</u>, after a laboratory technician handling the virus contracted the disease: comparison of serum samples collected from the technician before and after the onset revealed development of <u>antibodies</u> to the virus.





# **Etiology**

## an EBV, belong to Herpes viruses, type IV

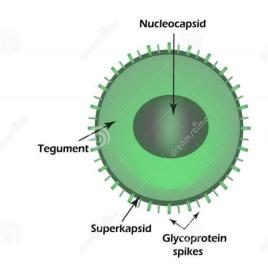


#### Diseases associated with **Epstein-Barr virus** Hodgkin's Multiple sclerosis lymphoma Hepatitis Herpes Gastric Burkitt's cancer lymphoma Nasopharyngeal Inflammatory bowel disease cancers

# Structure and genome

The virus is about 122–180 nm in diameter and is composed of a double helix of deoxyribonucleic acid (DNA) which contains about 172,000 base pairs and 85 genes. The DNA is surrounded by a protein nucleocapsid, which is surrounded by a tegument made of protein, which in turn is surrounded by an envelope containing both lipids and surface projections of glycoproteins, which are essential to infection of the host cell.

The structure of the Epstein-Barr virus



# **Epidemiology:**

Source of infection

are patients with symptomatic and asymptomatic forms, EBV- carriers

Mechanism of transmission is droplet, rarer is contact.

The virus *is transmitted* primarily through saliva during speaking, breathing, coughing, especially during kisses, hand-to-hand contacts.

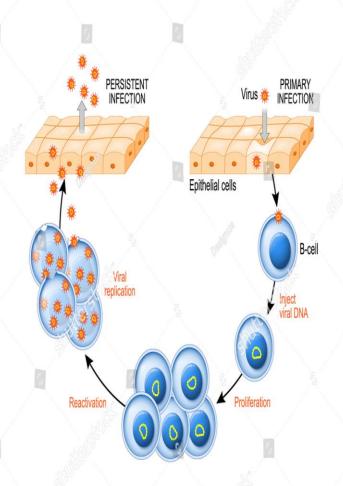
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The transmission of EBV through blood product transfusions has been well documented.

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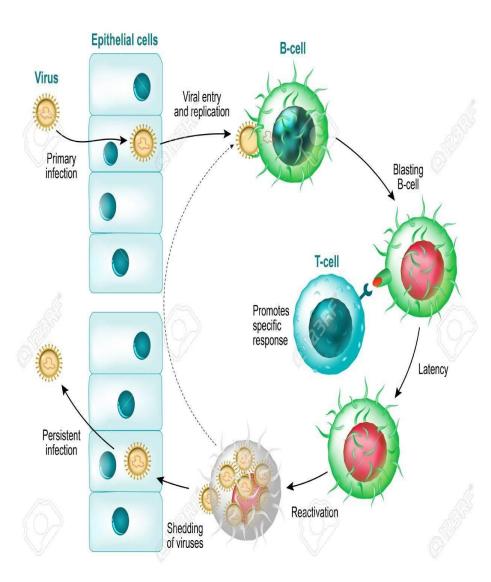
Susceptibility - any age, disease is low contagious, more frequent up to 15 years, in boys

# Epstein-Barr virus life cycle



## The EBV replication cycle





# Pathogenesis:

1. Inoculation of the virus into upper respiratory tract mucous membranes.

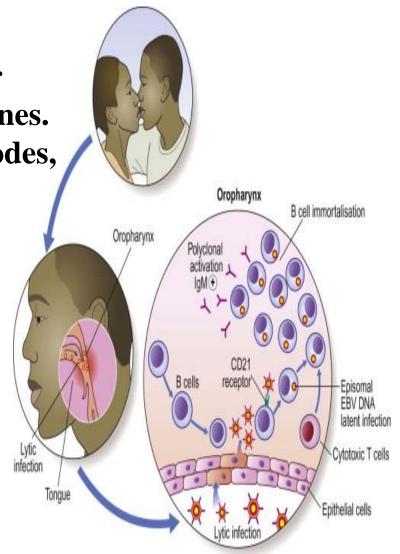
2. Diffusion by lymph to the lymph nodes,

spleen, liver.

3. Lymphoprolipherative syndrome.

4. Bacterial complications.

5. Persistence of the virus (even 16 months or more).



# Clinical criteria

## Incubation period

is 10-15 days (may be longer-2 month).

**Beginning** is acute from fever, intoxication

(headache, myalgia, arthralgias, malaise).

Fever usually febrile from 3 days till 3 weeks

# Symptoms of MONO

extreme fatigue

1

swollen tonsils

sore throat

2

headache

fever



skin rash

#### Tonsilopharyngitis,

which may be exudative (follicular, lacunar) in case of secondary bacterial infection, lymphoid follicles hyperplasia (on the back pharyngeal wall).

#### Adenoiditis, posterior rhinitis

(appearance of the patient is typical – breathing with open mouth, absence of nasal discharge, usually snore is present).

#### Generalized lymphadenopathy

with previous enlargement of cervical and occipital lymph nodes.

#### Hepatosplenomegaly

is the sign of lymphoproliferative syndrome.

#### Maculopapular rashes,

wich may confluence with erythema development, sometimes hemorrhagic elements with later skin pigmentation may occur as a sign of hypersensitivity in case of amoxicillin, ampicillin treatment (in 70-80%).

In the young childhood patient in 25% of cases "spontaneous" rashes can develop.





# Other signs:

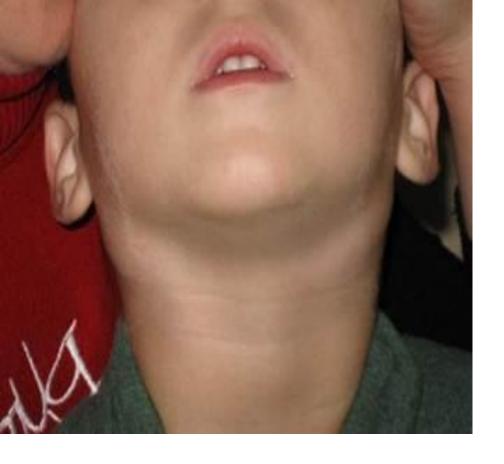
hepatitis (jaundice form of infectious mononucleosis); toxic myocarditis diarrhea.

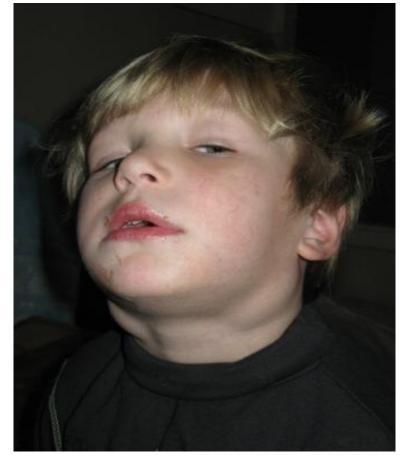






Tonsilopharyngitis



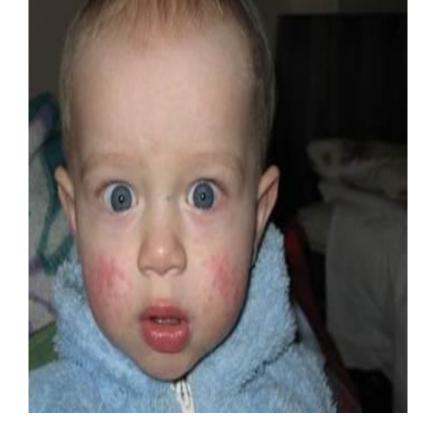


Generalized lymphadenopathy with previous enlargement of cervical lymph nodes





Hepatosplenomegaly



Maculopapular rashes











## **Epstein Barr Virus Rash**







## Classification

### Form: - typical

- atypical: erased (mild)
  - asymptomatic (subclinical) mild
- visceral *severe* (heart, kidneys, adrenal glands, CNS damage)

### Severity (for typical forms): - mild

- -moderate
- severe

### Course - uncomplicated

- complicated
- prolonged

## Infectious mononucleosis Severity Criteria

Sign	Mild	Moderate	Severe
Toxic syndrome	absent, mild	Moderate	Expressed
Body t°	Up to 38 °C	38,5-39 °C	More than 40 °C
Lymph nodes damage	mild, cervical predominantly	marked, cervical especially, visible	conglomerates, neck disfiguration, neck subcutaneous tissue swelling
Nasal breathing	Some labored	Labored, "snoring" in sleep	Absent, snoring, opened mouth, puffy face
Throat damage	Catarrhal tonsillitis	tonsils hyperplasia 1st- 2nd degree, considerable exudates	tonsils hyperplasia 3 <sup>rd</sup> degree, large membranous exudates
Hepato- splenomegaly (outcome from the rib arch)	Up to 2-3 cm	3-4 cm	4-5 cm and more, jaundice
Atypical mononuclear cells number	Up to 30 %	20-50 %	More than 50 %
Cough	Rare	Often	Often
Rashes	Rare	Often	Hemorrhagic in 1/3, nasal bleeding
Dyspepsia	Rare	Present abdominal pain, vomiting	abdominal pain, several vomiting
Heart changes "toxic- infectious heart"	Not typical	Rare	Often

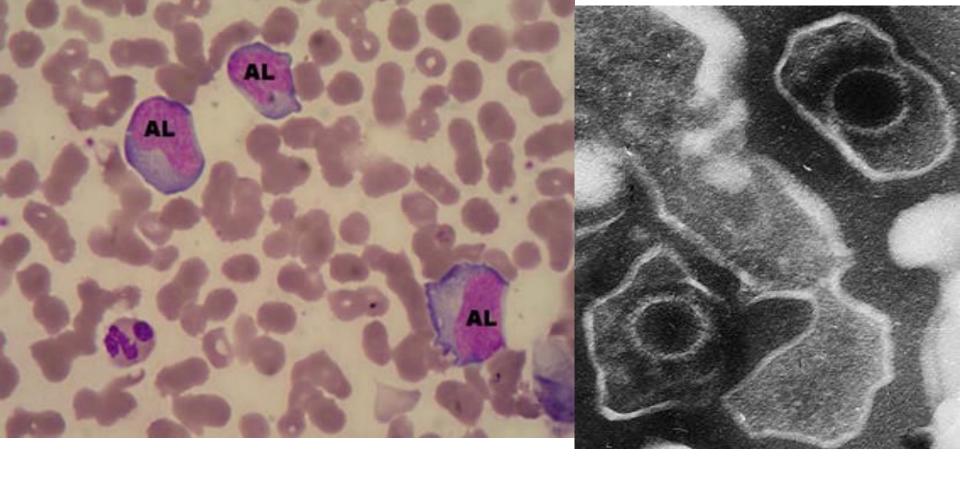
# Complications, which may occur (rare):

- 1. Respiratory tract pneumonia, airway obstructions.
- 2. Neurological seizures, meningitis, encephalitis, peripheral facial nerve paralysis, Gillian Barrette syndrome.
- 3. *Hematological* thrombocytopenia, hemolytic anemia.
- 4. *Infectious* recurrent tonsilopharyngitis.
- 5. **Renal** glomerulonephritis.
- 6. **Genital** orchitis.
- 7. *Spleen rupture* (is lethal).

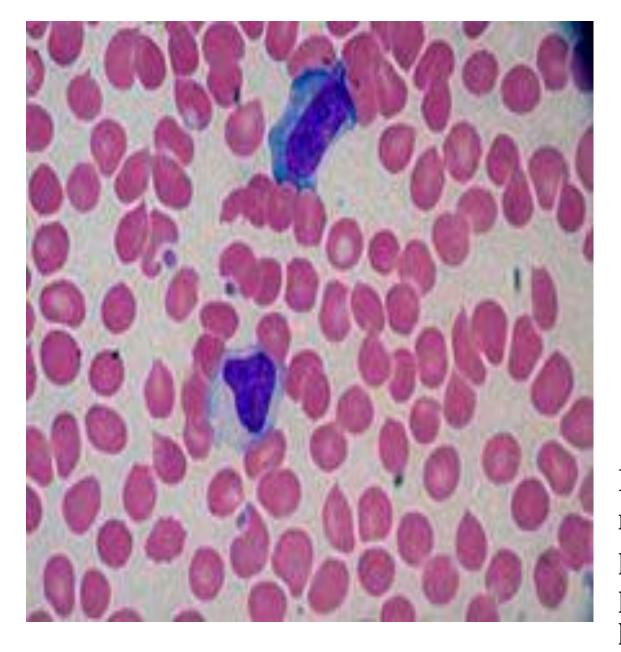


# Laboratory findings

- 1. *Blood analyses:* leucocytosis, even 15-30,000/mm3, lymphocytosis, monocytosis, appearing of atypical mononuclear cells (virocytes) more than 10%, ESR enlarges to 20-30mm/hour.
- 2. Heterophil agglutination test (is positive in 25-95% of preschool children, 53-94 young school children, and nearly 100% of older children).
- 3. *Immune-enzyme method* VCA IgM, EA IgM presence in the blood.
- 4. *PCR* (measuring of EBV nucleinic acid in the blood, saliva, lymphatic tissues).



atypical mononuclear cells



Infectious mononucleosis, peripheral smear, high power showing reactive lymphocytes





#### **Description**

Accutest® Rapid Mono test is an immunoassay for the Qualitative Detection of Infectious Mononucleosis Heterophile Antibodies in Whole Blood, Serum or Plasma. This test is intended for use as an aid in the diagnosis of infectious mononucleosis.

- •Results in minutes.
- •No age restrictions.
- (for whole blood

# Differential diagnosis

should be performed with 'mononucleosis like' syndrome caused of AIDS.

Another disease, which has similar features:

- ▲ diphtheria,
- **▲** adenoviral infection,
- ▲ acute leukemia,
- **▲** lymphogranulomathosis,
- ▲ viral hepatitis etc.



Infectious mononucleosis generally selflimiting, so only symptomatic and/or supportive treatments are used

## **Treatment**

- ■1. Reduction of activity and bed rest.
- 2. Special diet (diet N 5),
- Exclude heavy fats (like pork), spices, fried foods, "fast food""; avoid stimulators of gastrointestinal secretions, the diet must be rich by metionine, lecithin, and choline to stimulate synthesis of proteins and enzymes in the liver. Diet with normal value of proteins and vitamins, with restriction of fats and carbohydrates is administered, also restrict salt.
- Foods boiled, steamed and baked are recommended; food taking 5 times daily

- 3. Control of fever and myalgia (when the temperature is more than 38.5-39°C); in children before 2 mo and in case of perinatal CNS damage, seizures in the history, severe heart diseases when the temperature is up to 38°C with acetaminophen (paracetamol 10-15 mg/kg not often than every 4 hours (not more than 5 times per day) or ibuprophen 10 mg/kg per dose, not often than every 6 hours. Aspirin is contraindicated for children before 12 years.
- 4. *Antihistamines* (in average doses) pipolphen, suprastin, claritin, cetirizin.
- 5. Corticosteroids in severe cases 1-2 mg/kg/day prednisone for 3-5 days.

6. In case of secondary bacterial complications macrolides (erythromycin 30-50 mg/kg/day, azythromycin 10 mg/kg/day, clarythromycin) or cefalosporins (cefalexin 50 mg/kg/day, cefuroxim 50 mg/kg/day, cephasolin 100 mg/kg/day), Ampicillin and other semisynthetic penicillins are contraindicated!

The administration of oral acyclovir does not significantly alter the course of clinical illness from placebo.

# **Prophylaxis:**

is nonspecific, includes disinfecting; Isolation of the patient, hospitalization of children younger 1 year, in case of severe forms.

A quarantine is not imposed.

