

# Measles

**Measles** (lat. *morbilli*, diminutive of *morbus*; in czech **spalničky**, in slovakian **osýpky**) is a **highly contagious viral childhood rash disease**. It mainly affects preschool children, most often in late winter and spring.<sup>[1]</sup> They are caused by *Morbillivirus*, which is almost 100% infectious in susceptible individuals and is able to cause epidemics. The only natural host for this virus is humans. The measles disease takes place in 2 stages. The first phase has a picture of a **febrile respiratory disease with cough and conjunctivitis**, in the oral cavity there are typical gray **Koplik's stains**. The second phase is characterized by the sowing of a **deep red rash**. The patient is **deliberately and very ill** all the time. There is no specific antiviral treatment.<sup>[2]</sup>

Measles are **especially dangerous due to their complications** from secondary bacterial infections. Measles are among the leading causes of death in childhood worldwide, especially in the least developed countries. The cause of death in young children is most often **pneumonia**, in older children **encephalitis**.<sup>[3]</sup>

**Vaccination** against measles has existed since the 1960s, which has been a part of compulsory vaccination in the Czech Republic since 1969. In the pre-vaccination period, measles affected almost everyone during childhood. Vaccination has significantly reduced the incidence of measles in Europe, but the disease often breaks out here, due to its high infectivity.<sup>[4]</sup> There have been several epidemics in the Czech Republic recently, in 2014, 2017 and 2018 due to imported diseases. The problem begins to be a decrease in vaccination due to postponement or refusal of vaccination.<sup>[2][5]</sup>

## Etiology and epidemiology

Measles is **single-stranded RNA virus** of the genus *Morbillivirus* in the family *Paramyxoviridae*. The only natural host is humans, so worldwide eradication is theoretically possible. The entire genome of the virus was sequenced, so when measles breaks out, it is possible to identify the source of the infection by geographical distribution.<sup>[4]</sup> Despite genetic variations, *Morbillivirus* is considered monotypic - a virus with a single antigenic type (or single serotype). Based on gene analysis of 450 nucleotides of N protein, 8 types (clades A - H) and 24 subtypes (subclades A, B1-3, C1-2, D1-11, E, F, G1-3, H1-2). Since 2012, the occurrence of genotypes D4, D8 and B3 has been proven in the Czech Republic. Genotypes D4 and D8 have long dominated Europe, genotype B3 was originally typical of Africa and the Eastern Mediterranean, but it became the cause of Czech epidemics in 2014 and 2017.<sup>[2]}</sup>

Measles are **an extremely easily transmitted** disease. It is estimated that 90% of non-immune people become infected upon contact with an infected individual. The virus is transmitted by **droplets during coughing or sneezing** of a sick person, ie in the prodromal phase of the disease, which lasts 2-4 days. Droplets with the virus can remain in the air for several hours and the virus is infectious on the surfaces for up to 2 hours. Infected people are **already infectious about 5 days before the rash and only 4 days after**.<sup>[4]</sup> The disease leaves a lifelong immunity.

The virus penetrates the body **through the airway epithelium**. **2-3 days** after exposure, **primary viremia** occurs with virus replication at the site of entry (inoculation) and in distant reticuloendothelial tissues. **Intensive secondary viremia** occurs **between days 5 and 7**. For 4-7 days, the virus replicates in the skin, conjunctiva, respiratory tract and internal organs. The formation of huge multinucleated Warthin-Finkelday cells can be observed microscopically.<sup>[4]</sup>

**After birth, babies are protected by maternal antibodies**, if the mother is immune to measles. This passive immunity gradually disappears during the second half of the first year of life. Infants with partial passive immunity may experience a milder and shorter form of measles and remain immune.<sup>[4]</sup>

Measles **is a particular risk for young children who have not yet been vaccinated**. Furthermore, individuals in whom vaccination did not lead to the formation of antibodies (primary vaccine failure) and those who were not vaccinated for medical, religious or other reasons.<sup>[4]</sup> **Globally, it is one of the leading causes of child death**, especially in developing countries.

A total of 40 people died of measles in Europe in 2016 and 2017.<sup>[6]</sup> Most measles deaths (more than 95%) are reported from low-income and poorly accessible healthcare countries.<sup>[7]</sup> WHO aims to eradicate the measles virus, which it wants to achieve by better vaccination in countries where the vaccine is poorly available for many reasons.

## Clinical picture

1. incubation period 10-12 days;
2. prodromal period;
3. rash phase.

### Prodromal period

Fever, conjunctivitis, rhinitis, cough, bronchiolitis, weakness, muscle and joint pain, loss of appetite and characteristic **Koplik's spots** (gray macules) on the buccal mucosa of the oral cavity are usually present. They appear at the end of the prodromal stage, 1-2 days before the rash and are pathognomonic for measles, they may resemble thrush.<sup>[4][2]</sup>

## Exanthema phase

**Erythematous maculopapular rash** (deep red, irregular). It develops 2-4 days after the onset of fever (ie about 14 days after infection) and **spreads from head to body for 3-4 days** (starting on the auricle and on the head, then changes to the face, neck and torso, until on the lower limbs). It gradually disappears within 3-4 days in the same order as it appeared. The rash at an early stage turns white when pressed, but not later. It lasts a total of 6-8 days. The skin often peels off after the exanthema has disappeared.

During sowing, temperatures exceed 39 ° C and react little to antipyretics. Respiratory symptoms such as runny nose and cough persist - dry irritant (laryngotracheal). The infection can spread to the lower respiratory tract such as spastic bronchitis, bronchiolitis or pneumonia. Conjunctivitis persists (mucopurulent, bilateral, with marked secretion).<sup>[4][1][2]</sup>

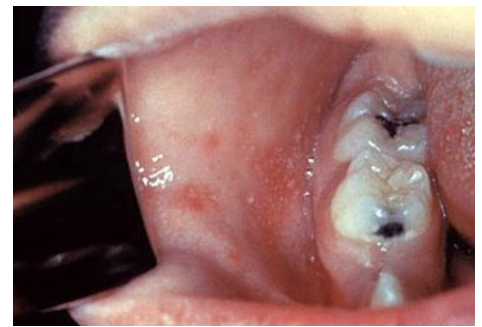
During the prodromal and exanthematous phases, the patient is very ill, confined, often dehydrated, apathetic, sleeping. Fever can last up to 9 days.<sup>[2]</sup>

## Complications

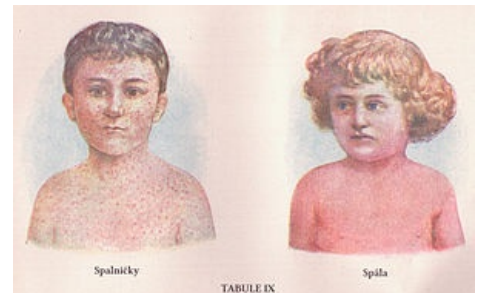
The most serious course is in children under 5 years of age and in immunocompromised individuals - in children with malnutrition, lacking especially in vitamin A, or in children weakened by HIV/AIDS or other diseases.<sup>[7]</sup> Deaths are mainly due to secondary bacterial infections. Complications are more likely to occur if the fever does not subside within 1-2 days after the onset of the rash.

The most common complications:

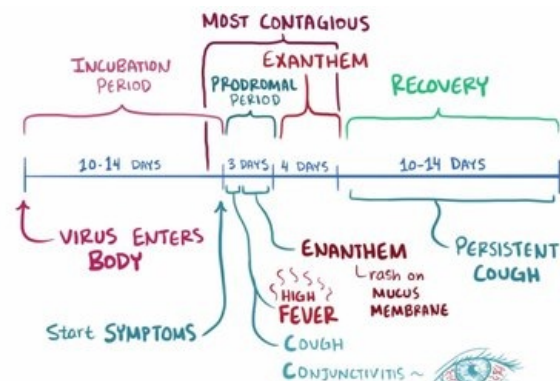
- **Otitis media** (7-9 %).
- **Pneumonia** (1-6 %) is either primary interstitial or secondary bacterial (causing 6 out of 10 measles deaths).
- **Gastroenteritis** with vomiting and diarrhea leading to dehydration (8%).
- Post-infectious **encephalitis** (1 in 1000 to 2000 cases)<sup>[4]</sup>. It manifests with temperature rise in convalescence, headache, impaired consciousness and often convulsions.<sup>[2]</sup> Mortality is up to 10%<sup>[1]</sup>.
- Bogaert's **subacute sclerosing panencephalitis** (1 in 100,000 cases). A rare but fatal degenerative disease of the central nervous system that develops several years after measles (on average after 7 years). More common in children who have had measles in the first 2 years of life.<sup>[4]</sup>



Koplik spots



Measles vs. Scarlet fever



Definition, pathogenesis, symptoms, complications, treatment.

Although measles in pregnancy is not associated with the risk of developmental defects such as rubella, they are increasing the risk of the possibility of miscarriage<sup>[8][9]</sup>, intrauterine death of the fetus<sup>[8][10]</sup> and the risk of having to induce preterm birth<sup>[8][9]</sup>. The mother is threatened by secondary complications such as pneumonia<sup>[9][8]</sup> and diarrhea<sup>[8]</sup>, which often lead to hospitalization<sup>[9]</sup>.

## Diagnostics

### Typical clinical picture

Acute erythematous rash with fever, preceded by cough, rhinitis, conjunctivitis and photophobia.<sup>[4]</sup> Koplik stains. Difficult to distinguish other Infectious exanthematous diseases in childhood caused by rubella, parvovirus B19, HHV-6 and dengue fever.<sup>[4]</sup> Morbiliform rash can occur in burns, in adults with rubella, in enterovirus and adenovirus diseases or toxoallergic rashes, especially drug rash.<sup>[11]</sup>

### Laboratory card

- **Direct identification** from nasopharyngeal swab, urine or cerebrospinal fluid.
  - Isolation of measles virus from clinical material - collection into a viral transport medium that protects the virus from degradation; is not routinely used.
  - **Detection of measles virus RNA by PCR** - by the 3rd to 4th day after rash sowing, the presence of

RNA virus can be detected in more than 80% of positive cases; allows genotyping of measles strain.

- **Serological evidence:** detection of IgM antibodies, seroconversion or significant increase of IgG antibodies in paired serum.
  - Detection of IgM antibodies in prime-infected patients is positive in the 3rd to 4th day after rash only in 60-70% of patients.
  - In vaccinees, serological detection is difficult - IgM antibodies are often not produced due to the rapid rise of pre-existing IgG antibodies. Likewise, there is sometimes no significant increase in IgG antibodies when examining a paired serum sample.
- Detection of measles virus antigen by direct immunofluorescence in a clinical specimen using measles-specific monoclonal antibodies. It is not used in routine diagnostics.<sup>[2]</sup>

Sampling for direct detection of infectious agents should be performed no later than day 5 (ideally day 3) from the start of clinical manifestation of the disease, especially in vaccinated patients. Due to the rapid rise of IgG antibodies, they soon become neutralized by the virus.<sup>[2]</sup>

### Laboratory finding

Blood count: leukopenia, lymphopenia.

Liver tests: elevated Transaminases.<sup>[1]</sup>

Diferenciální diagnostika spalniček a zarděnek

CRITERION	Measles	Rubella
Incubation period	ø 10 days	ø 18 days
Temperature	febril	subfebril
Exanthem	raised, merging, deep red	flat, non-blending, pink (up to mauve)
sowing	behind the ears → nape → torso and limbs	face → torso and limbs
Swelling of the nodes	submandibular	nuchal
A typical symptom	<b>Koplik's spots</b> (gray macules; buccal mucosa in the stool area)	<b>Forscheimer stains</b> (enanthema / petechiae on the palate)
Fetal damage	no	yes

## Treatment

There is no specific antiviral therapy, only **symptomatic** treatment (hydration, antipyretics). We start antibiotic treatment in case of bacterial superinfection (if the fever persists for more than 2 days after sowing the rash).

In hospitalized patients **isolation** (prevention of droplet transmission) is required by day 4 after rash. Exposed individuals can be immunized within 72 hours of exposure (post-exposure prophylaxis) because the incubation time of the vaccine virus is shorter than the incubation time of the wild-type virus.



<sup>[4]</sup>

## Prevention

The only effective prevention is vaccination. In the Czech Republic, measles vaccination is part of the Mandatory vaccination. Currently, a **vaccine with attenuated measles virus** is given in combination with 2 or 3 other viruses (rubella, mumps, or chickenpox virus such as MMR or MMRV) **between the ages of 13 and 18**. Revaccination to strengthen immunity is carried out **between the 5th and 6th year of age** (according to Vyhláška 355/2017 Sb. valid from 1.1.2018).

Evropské očkovací programy (<https://vaccine-schedule.ecdc.europa.eu/>) now recommend a 2-dose vaccination schedule with the first dose given during the second year of life and the second dose at a later age (this varies from country to country). Combination vaccines (MMR and MMRV) have the same efficacy as vaccines given individually. Vaccination of individuals who are already immune to one or more antigens in the combination vaccine (after previous vaccination or after a natural infection) does not lead to a higher incidence of side effects.<sup>[4]</sup> The measles vaccine is effective min. of 95% and a seroconversion rate approaching 100%. Primary vaccine failure (at the first dose) occurs in about 5% of people (or children over 12 months of age), but 95% of them experience seroconversion at the second dose. The most common cause of primary vaccine failure is the presence of maternal antibodies.

In the pre-vaccination period, measles was endemic in Europe and affected most people during childhood. The disease broke out regularly at 2-5 year intervals. After the age of 20, few people were susceptible. Vaccinations against measles began in the 1960s, dramatically changing the epidemiology of the disease. Measles are no longer an endemic disease in most European countries, but the disease often breaks out when the virus is imported from areas with low population immunity, usually from another European country. **There have been thousands of**

**confirmed measles cases per year in Europe** since 2001. The introduction of widespread vaccination of children against measles has led to a prolongation of the intervals between individual epidemics. During these intervals, susceptible individuals develop. Vaccine virus disease has not been demonstrated.<sup>[4]</sup>

**Measles meet the criteria for the possibility of disease eradication.** They do not have an animal reservoir or a reservoir in the environment, they can be reliably diagnosed, and the measles vaccine is effective and safe. The virus is transmitted over long distances, so it is necessary to eliminate the infection in all countries in order to eradicate it worldwide.<sup>[4]</sup>

## Links

### External links

- European Centre for Disease Prevention and Control (ECDC): Measles updates (<https://ecdc.europa.eu/en/measles>)
- DermNet Spalničky (<https://www.dermnetnz.org/viral/morbilli.html>),
- Pediatrie pro praxi: Spalničky – aktuální epidemiologická situace a klinické zkušenosti (2017) (<https://www.pediatriepropraxi.cz/pdfs/ped/2017/06/02.pdf>)
- Pediatrie pro praxi: Infekční exantémová onemocnění v dětském věku (2009) (<http://www.pediatriepropraxi.cz/pdfs/ped/2009/03/09.pdf>)
- Pediatrie pro praxi: Virové exantémy dětského věku (2008) (<http://www.pediatriepropraxi.cz/pdfs/ped/2008/06/03.pdf>)
- Pediatrie pro praxi: Spalničky – choroba stále ještě nevymýcená (2004) (<http://www.pediatriepropraxi.cz/pdfs/ped/2004/03/14.pdf>)

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