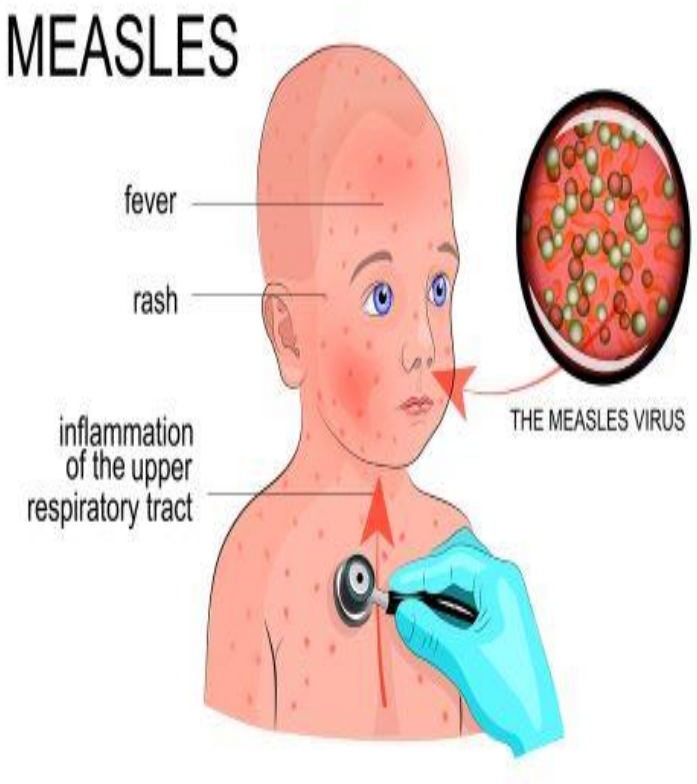
Measles

Measles (rubeola)

is a highly contagious, acute, exanthematous respiratory disease with a characteristic clinical picture and a pathognomonic enanthem: Koplik's spots, an eruption on the buccal mucous membranes



Abu Becr, an Arab physician known as Rhazes from Baghdad, called the disease measles as hasbah ("eruption" in Arabic) and considered it a type of smallpox.

According to Rhazes, measles epidemics are reported since the 6th century.

In European literature, the disease was called "morbilli", in contrast to il morbo - plague.

Sanvages in 1763 defined morbilli as measles, but named the disease rubeola, setting in motion the confusion over the definitions of the two diseases, measles and rubella, which can be seen in the occasional name "measles rubella".

In the study of measles, 3 main periods can be distinguished:

1) Before antibiotic therapy;

2) When using antibiotic therapy;

3) With the introduction of active immunization

Global Surge in Measles Cases

Number of reported measles cases across the world

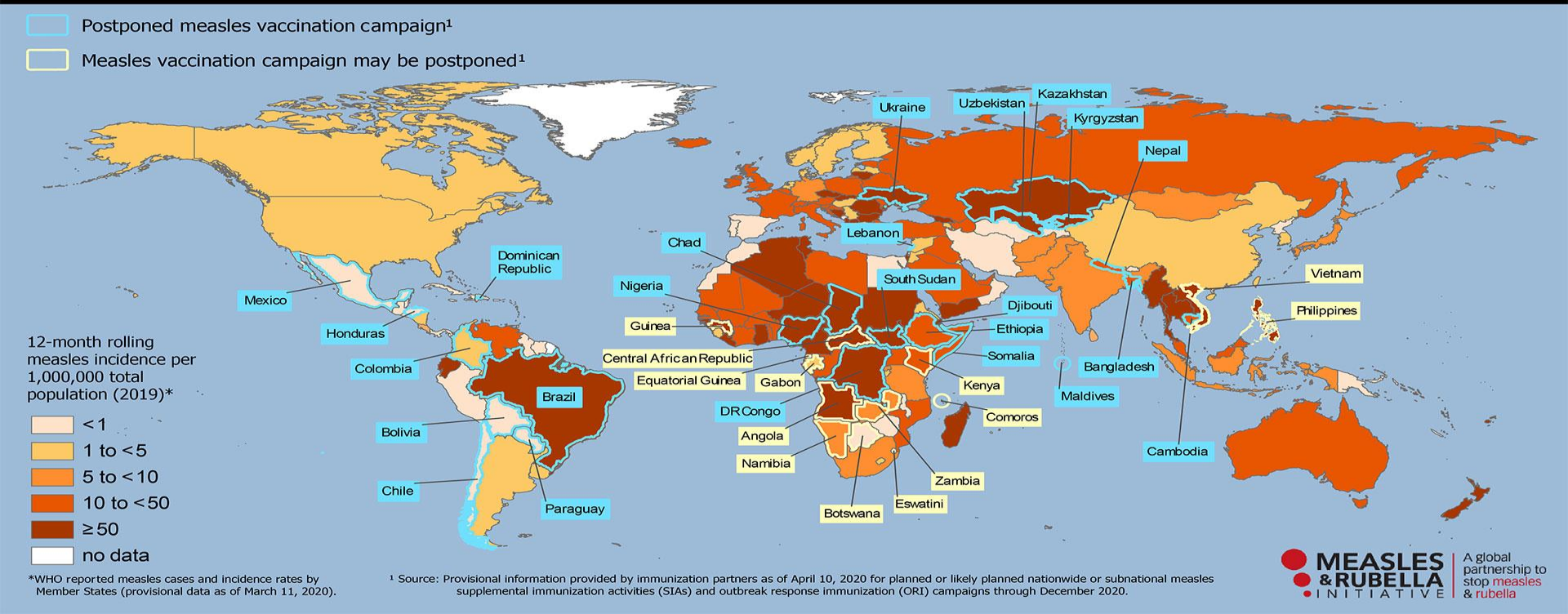
2000	2010	2016	2019
853,479	343,806	132,490	869,770

Estimated total measles cases including those unreported was 9,828,400 in 2019 with an estimated death toll of 207,500

Sources: World Health Organization, U.S. Centers for Disease Control and Prevention

As COVID-19 continues to spread globally, over 117 million children in 37 countries may miss out on receiving life-saving measles vaccines. Measles immunization campaigns in 24 countries have already been delayed; more will be postponed.

More than 117 million children at-risk of missing out on measles vaccines, as COVID-19 surges



*WHO reported measles cases and incidence rates by Member States (provisional data as of March 11, 2020).

[1] Source: Provisional information provided by immunization partners as of April 10, 2020 for planned or likely planned nationwide or subnational measles supplemental immunization activities (SIAs) and outbreak response immunization (ORI) campaigns through December 2020.

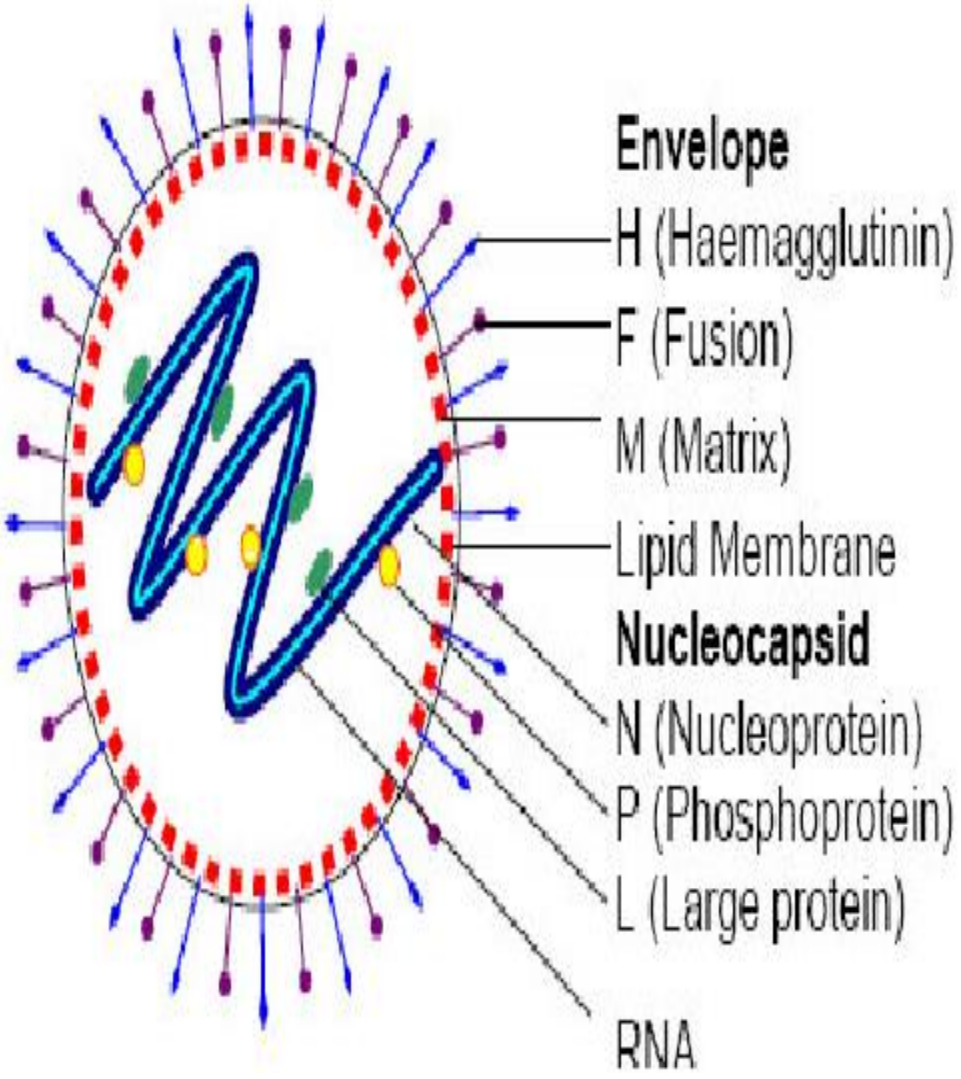
MEASLES & RUBELLA INITIATIVE | A global partnership to stop measles & rubella

In a number of countries, measles still ranks first in the overall infectious morbidity of the population.

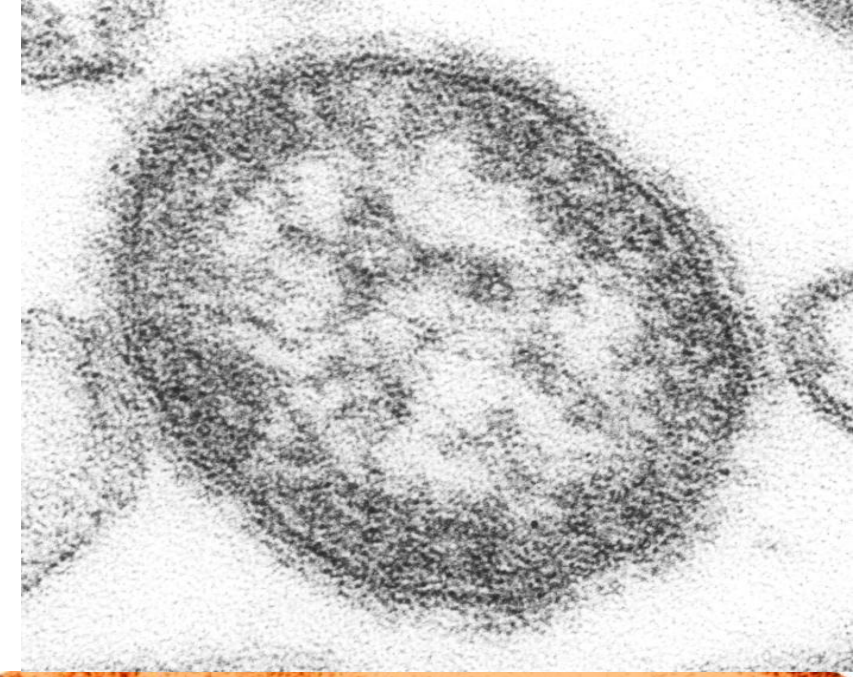
According to WHO, up to 30 million cases of measles are registered annually in the world.

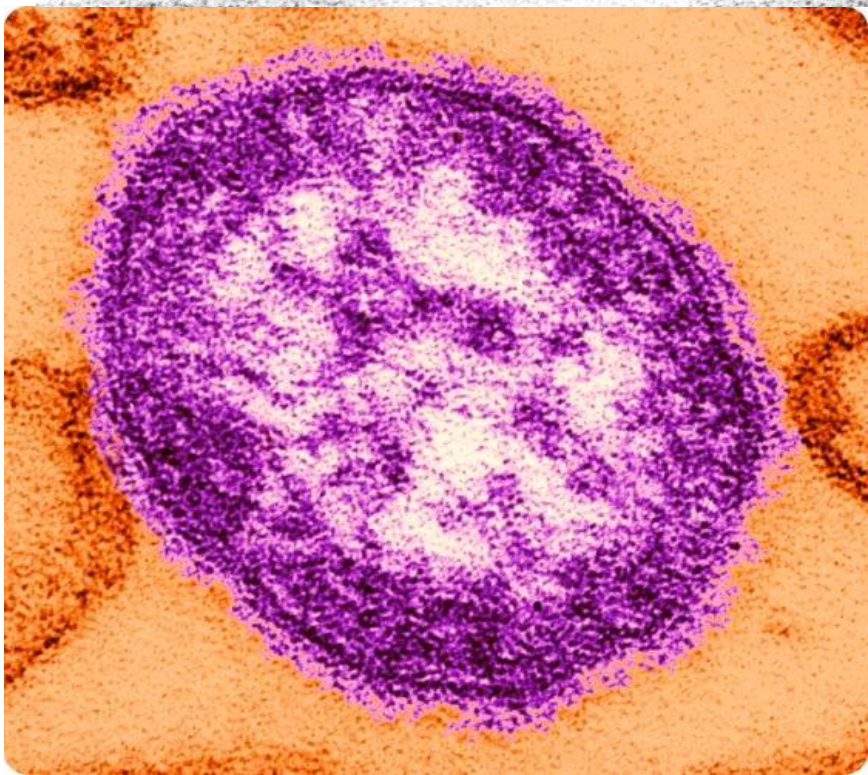
Measles virus is the only member of the genus Morbillivirus that infects humans. There is only one antigenic type.

Virions—pleomorphic spheres with a diameter of 100–250 nm—consist of six proteins.The inner capsid is composed of RNA and three proteins. The outer envelope consists of a matrix protein bearing short surface-glycoprotein projections or peplomers, one a hemagglutinin (H) and the other a fusion (F) protein. Sequencing of the single-stranded genome makes it possible to distinguish vaccine-type from wild-type virus. The genetic variability of wild-type virus (23 genotypes identified) permits identification of strains endemic within a given locale where measles cases have occurred. The cellular receptors for measles virus are the CD46 and CD150 molecules expressed on many human cells.



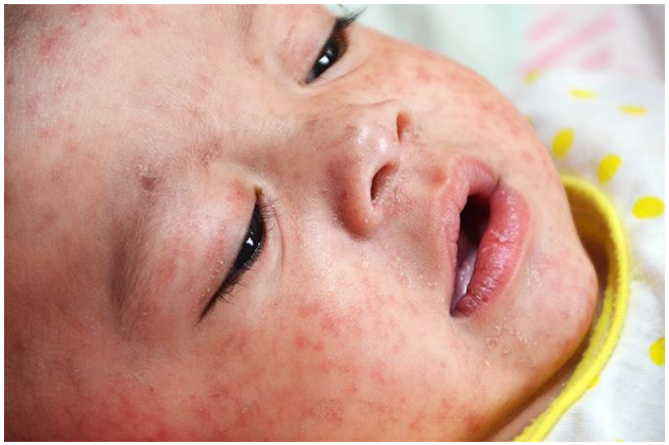
In cell culture, the measles virus produces a characteristic cytopathic effect with the formation of giant cells and/or syncytia, or forms granular bodies of inclusions in cytoplasm and nucleus.





The measles virus is not resistant to physical and chemical factors and persists in the external environment for no more than 30 minutes, but it can be transported by air currents together with droplets of mucus over considerable distances; sensitive to sunlight and ultraviolet rays, easily inactivated by ether, formalin. Resistant to antibiotics

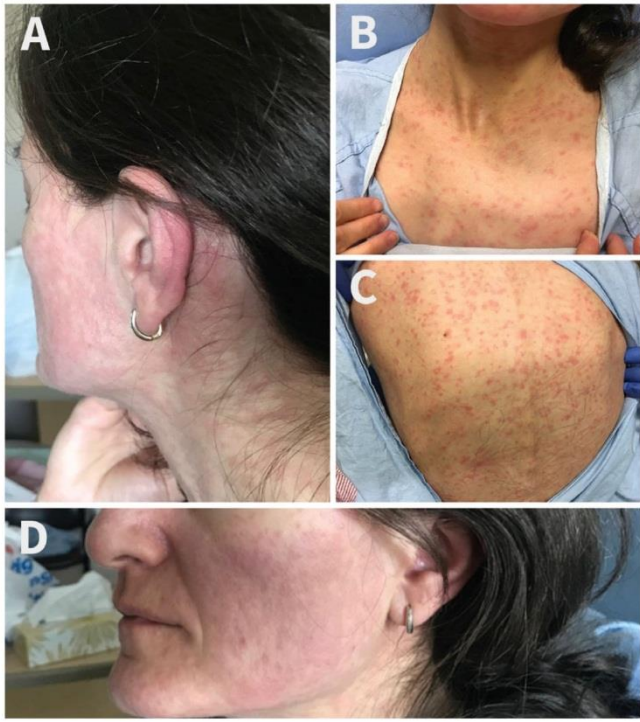
EPIDEMIOLOGY



Measles can affect people of any age, but more often sick children aged 1 to 5 years.

Children under 3 months of age usually do not get sick.

Not only children are susceptible to measles, but also adults who have not had it.



The source of infection in measles is a sick person. Measles is an airborne virus that is spread by direct contact with droplets from respiratory secretions of infected persons. It is one of the most communicable of the infectious diseases, most infectious during the late prodromal phase of the illness, when cough is at its peak.

The susceptibility of humans to measles is very high.

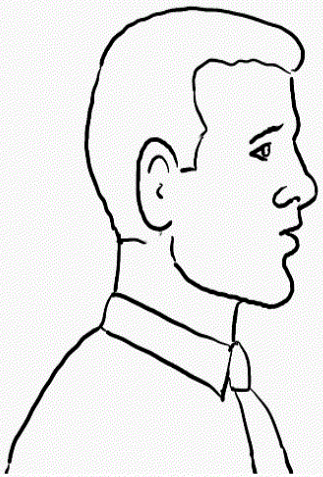
EPIDEMIOLOGY

Temporal pattern
Primarily late winter and spring

Patients are contagious from 1 or 2 days before symptom onset until 4 days after the rash appears. Infectivity peaks during the prodromal phase.

The mean intervals from infection to symptom onset and rash appearance are 10 and 14 days, respectively.

From the 5th day of the rash, the patient is already considered non-infectious and his isolation can be terminated.



The high contagiousness of the patient in the catarrhal period is associated with the abundant release of the virus from the nasopharynx and conjunctiva, when coughing, sneezing, talking.

Measles convalescents are epidemiologically safe.

PATHOGENESIS

- Measles virus invades the respiratory epithelium and spreads via the bloodstream to the reticuloendothelial system, from which it infects white blood cells, thereby establishing infection of the skin, respiratory tract, and other organs.
- Both viremia and viruria develop.

- Multinucleated giant cells with inclusion bodies in the nucleus and cytoplasm (Warthin-Finkeldey cells) are found in respiratory and lymphoid tissues and are pathognomonic for measles.
- Direct invasion of T lymphocytes and increased levels of suppressive cytokines (e.g., interleukin 4) may play a role in the temporary depression of cellular immunity
that accompanies and transiently follows measles.

- The major infected cell in the blood is the monocyte. Infection of the entire respiratory tract accounts for the characteristic cough and coryza of measles and for the less frequent manifestations of croup, bronchiolitis, and pneumonia.

- Generalized damage to the respiratory tract, with loss of cilia, predisposes to secondary bacterial infections such as pneumonia and otitis media.

Clinical Features

Four Stages of Infection

Stage 1: Incubation

Incubation Period: 6-21 days (~13 Days)

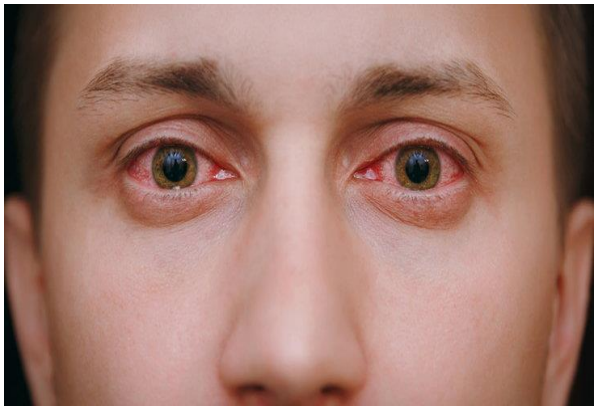
Stage 2: Prodrome

Occurs for 2 to 4 days (up to 8 days)

Fever, malaise, anorexia

“3 Cs”

Conjunctivitis (non-purulent), Coryza, Cough



Stage 3: Exanthem

- **Koplik sports prior to exanthem**

- **Maculopapular rash ~2-4 days after fever**
  - **Macules = Flat skin lesion less than 1 sm in diameter**
  - **Papules =Raised skin lession less than 1 sm in diameters**

- **Blanchable at first, then non-blanchable**
- **Starts on face, then spreads down to neck, trunk, upper extremities, then lower extremities**
- **“Head-to-toe”**

Stage 3 (Continued):

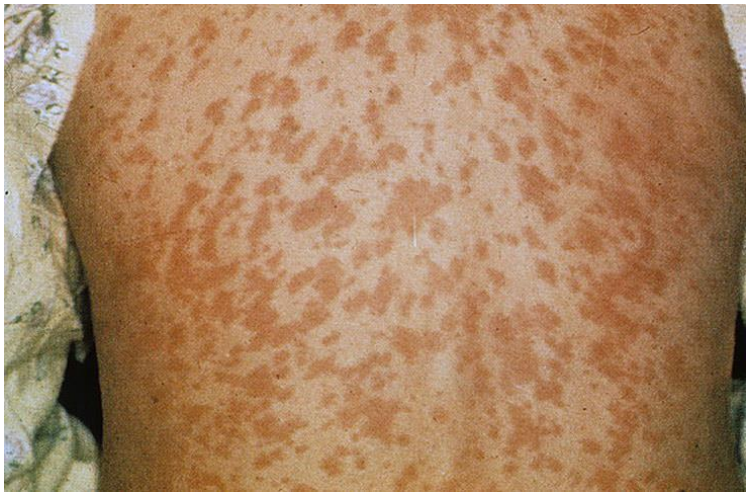
- ❑ **Other Findings:**
  - ✓ **Lymphadenopathy**
  - ✓ **Pharyngitis**
  - ✓ **Splenomegaly**
  - ✓ **Diarrhea**

Continuation of prodromal symptoms

"4 Cs" of Measles:

Conjunctivitis, Coryza, Cough, C(K)oplik spots

- **Rash darkens to brown in color at 3-4 days post-eruption**
- **Rash fades (from head-to-toe) then desquamates**

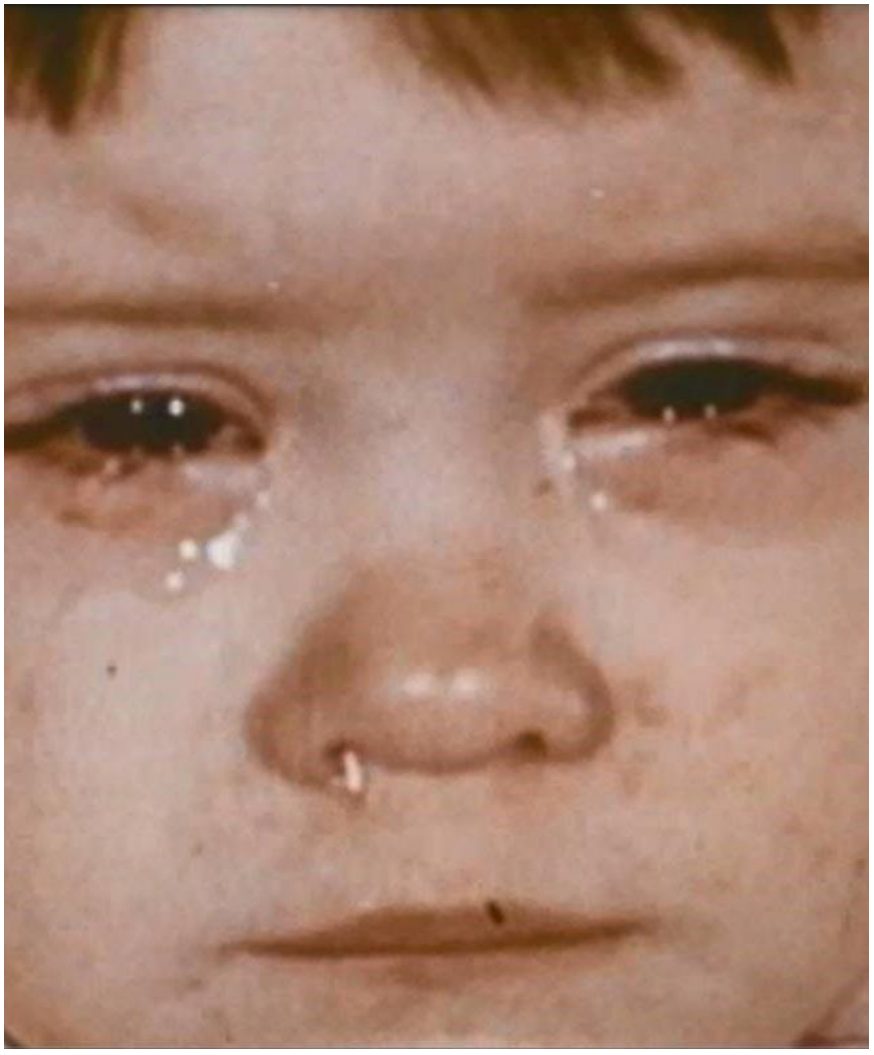


Stage 4: Recovery

- **Improvement in symptoms ~ 48 hours of rash occurs**
- **May have post-infectionus symptoms**

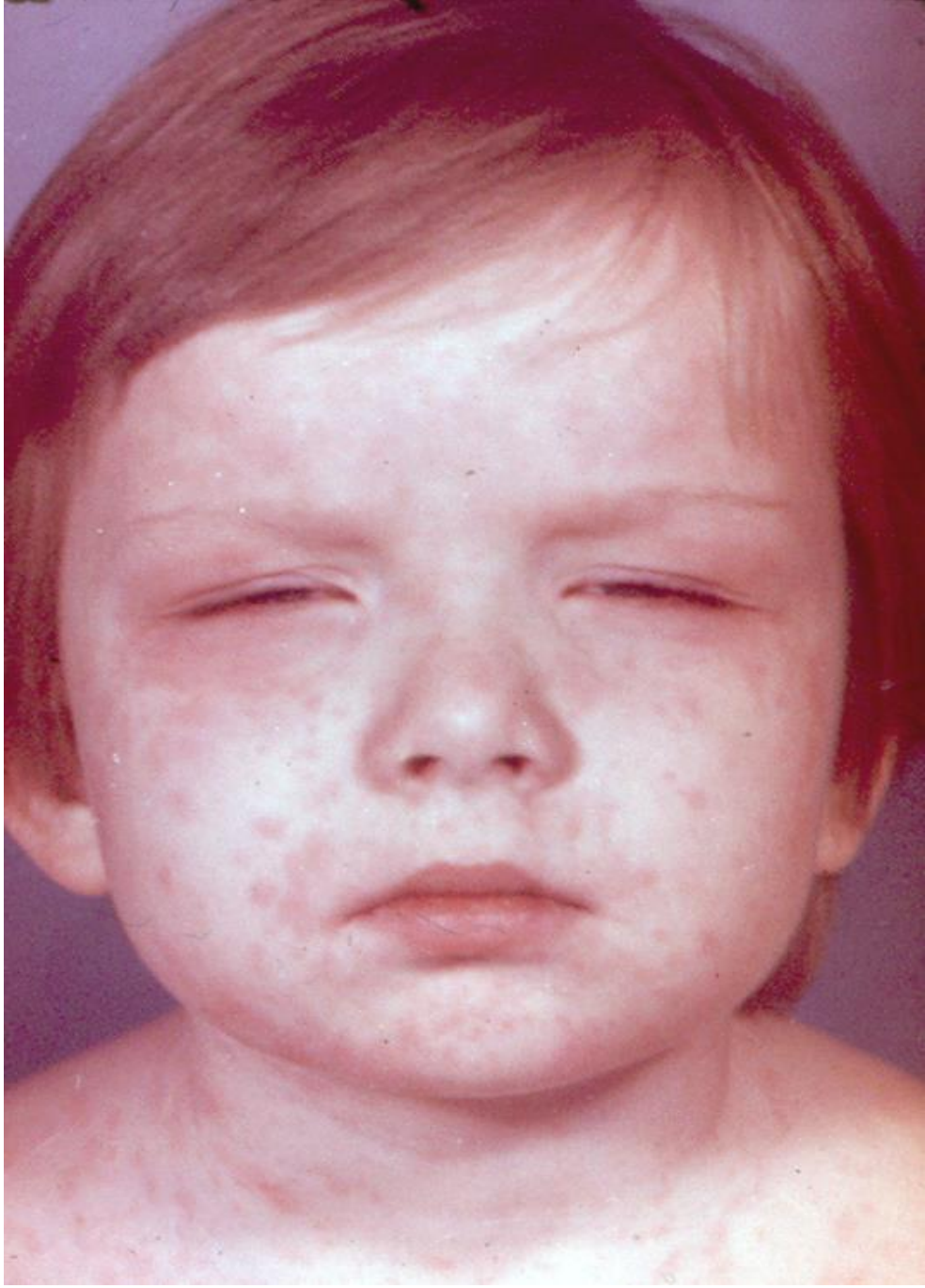
CLINICAL MANIFESTATIONS

Measles begins with a 2- to 4-day respiratory prodrome of malaise, cough, coryza, conjunctivitis with lacrimation, nasal discharge, and increasing fever [with temperatures as high as 40.6°C (105°F), probably reflecting secondary viremia]. At this stage of the illness, in which the rash has not yet developed, influenza may be suspected.



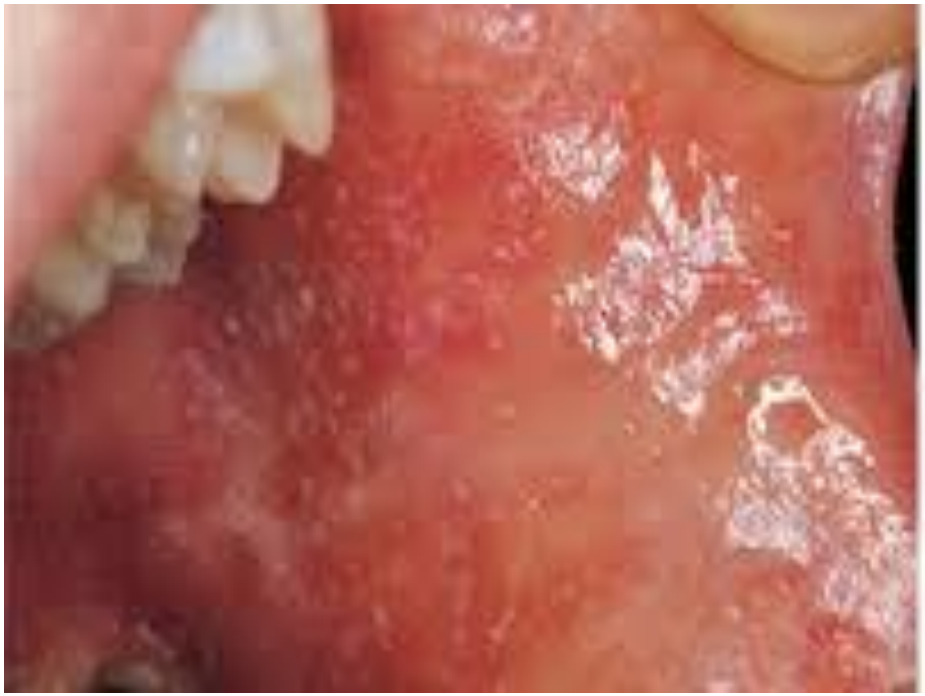
Young child with moderate illness: runny nose, teary eyes caused by measles infection.

Conjunctivitis develops, accompanied by lacrimation and photophobia, which can be so severe that **blepharospasm** occurs - closing of the eyelids. The eyelids swell



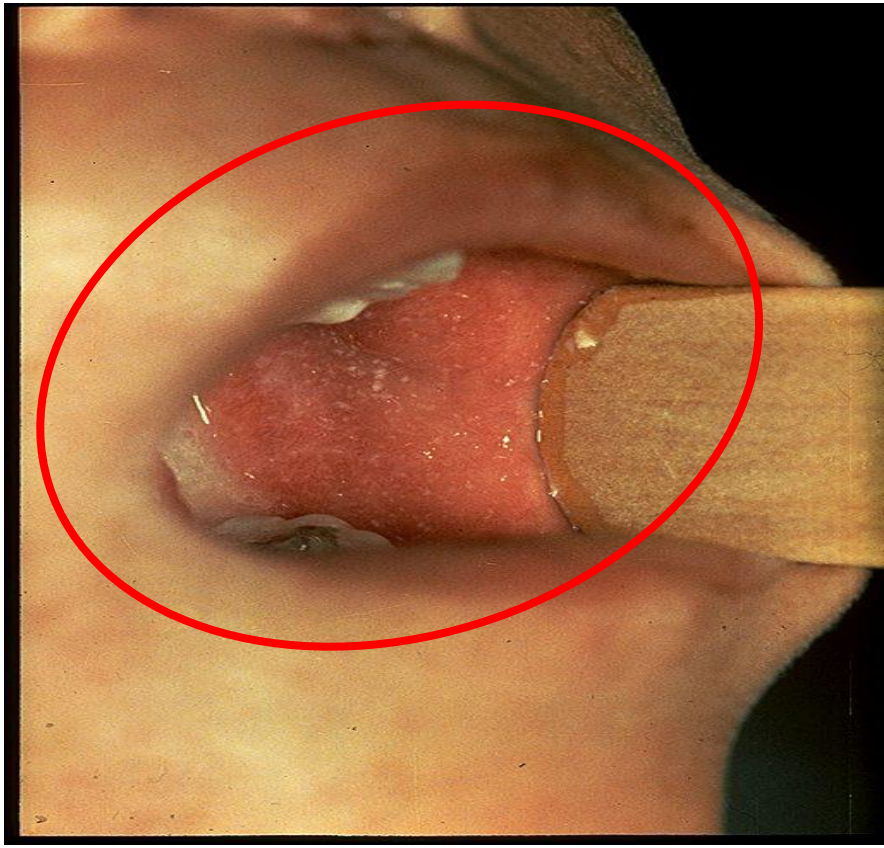
blepharospasm

Just before rash onset, Koplik's spots appear as 1- to 2-mm blue-white spots on a bright red background. Without adequate illumination for examination, they may be overlooked. Koplik's spots are typically located on the buccal mucosa, alongside the second molars, and may be extensive; they are not associated with any other infectious disease. The spots wane after the onset of rash and soon disappear. The entire buccal and inner labial mucosa may be inflamed, and the lips may be reddened.

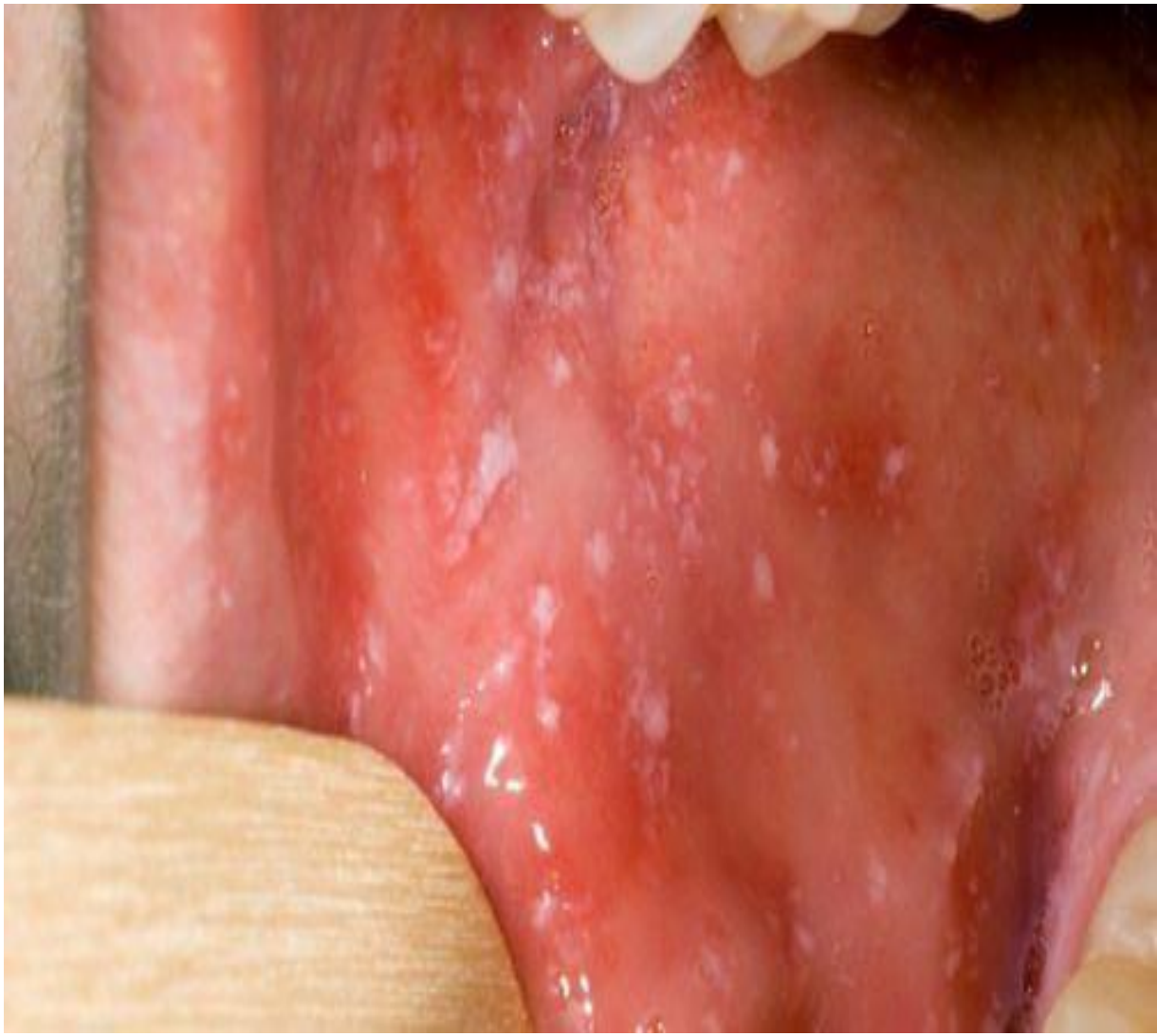


Koplik's spots

The origin of the spots is similar to the genesis of a skin rash and is a consequence of the hematogenous introduction of the virus. The epithelium of the mucosa undergoes degeneration and partial necrosis followed by irregular keratinization, as well as necrosis and keratinization deprive the epithelial layer of transparency, then the underlying vascular network ceases to shine through, which gives the spots a whitish color.



- **White, gray spots on erythematous base "Grains of salt"**



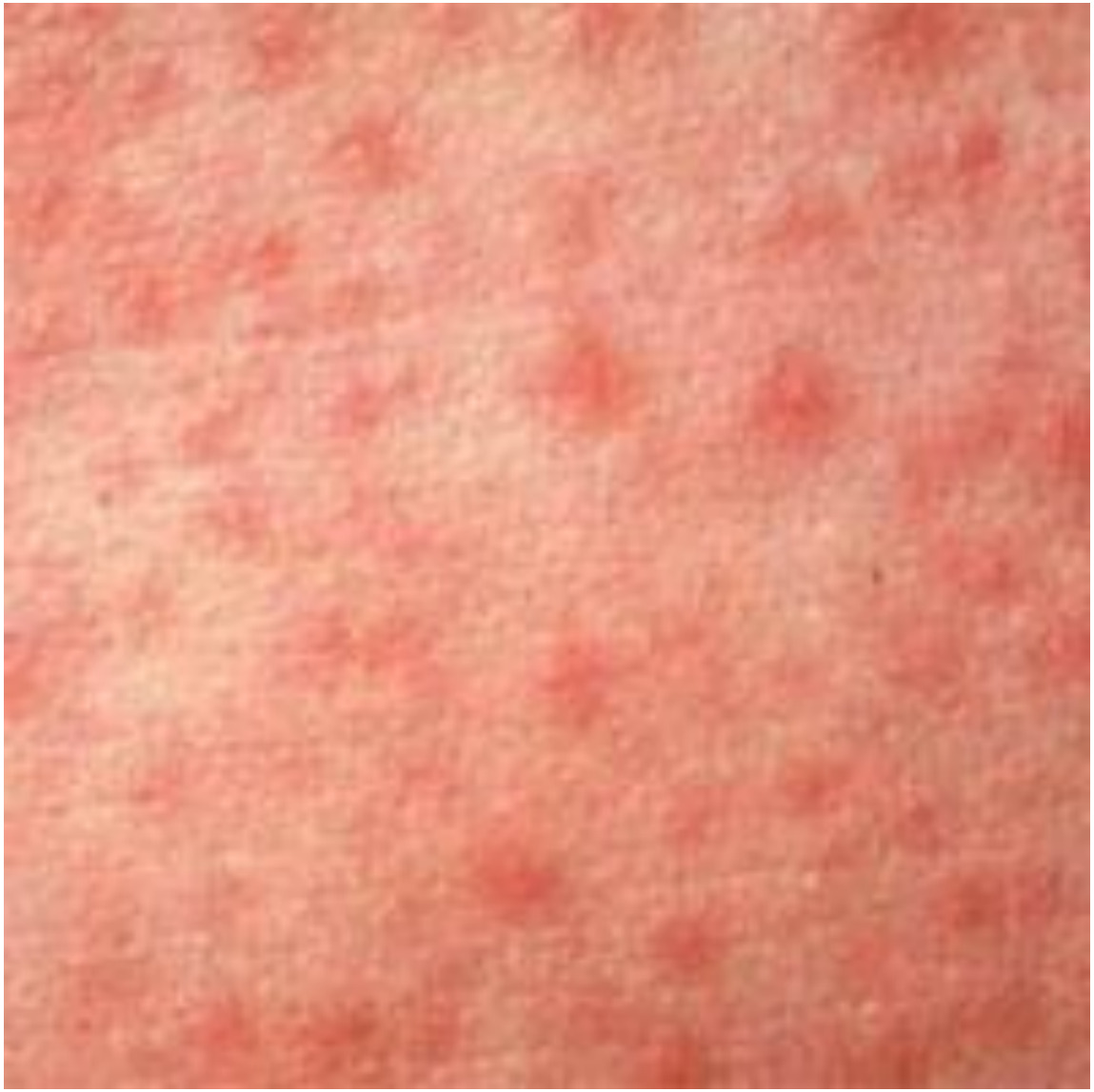
- **Occurs 48 hours prior to exanthem**
- **Last upwards of 72 hours**

The characteristic erythematous, nonpruritic, maculopapular rash of measles begins at the hairline and behind the ears, spreads down the trunk and limbs to include the palms and soles, and often becomes confluent. At this time, the patient is at the most severe point of the illness.

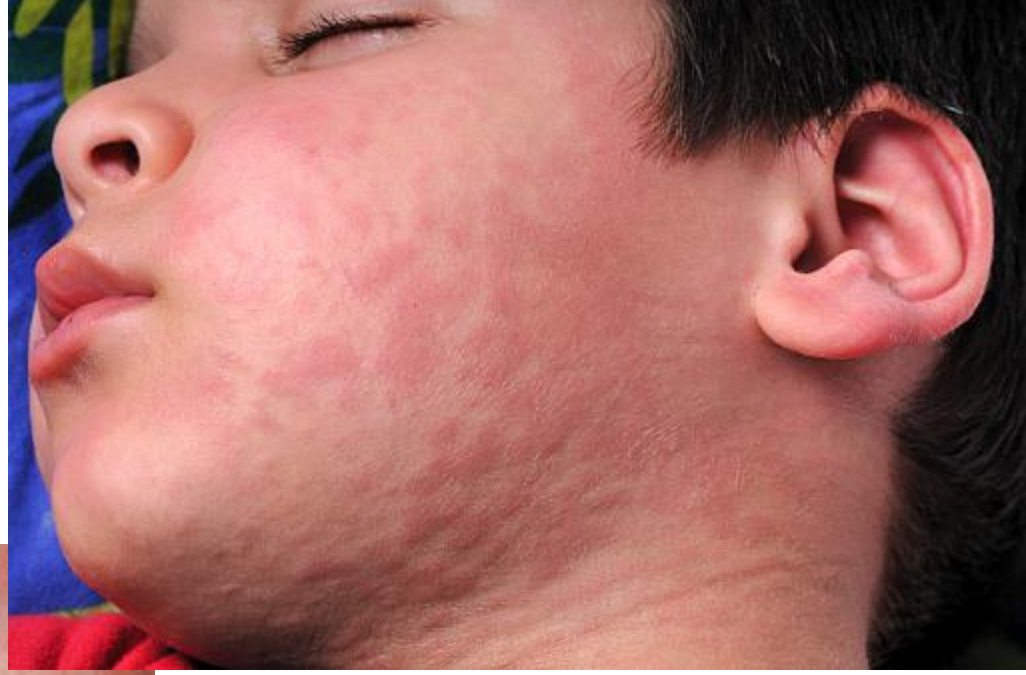
By the fourth day, the rash begins to fade in the order in which it appeared.

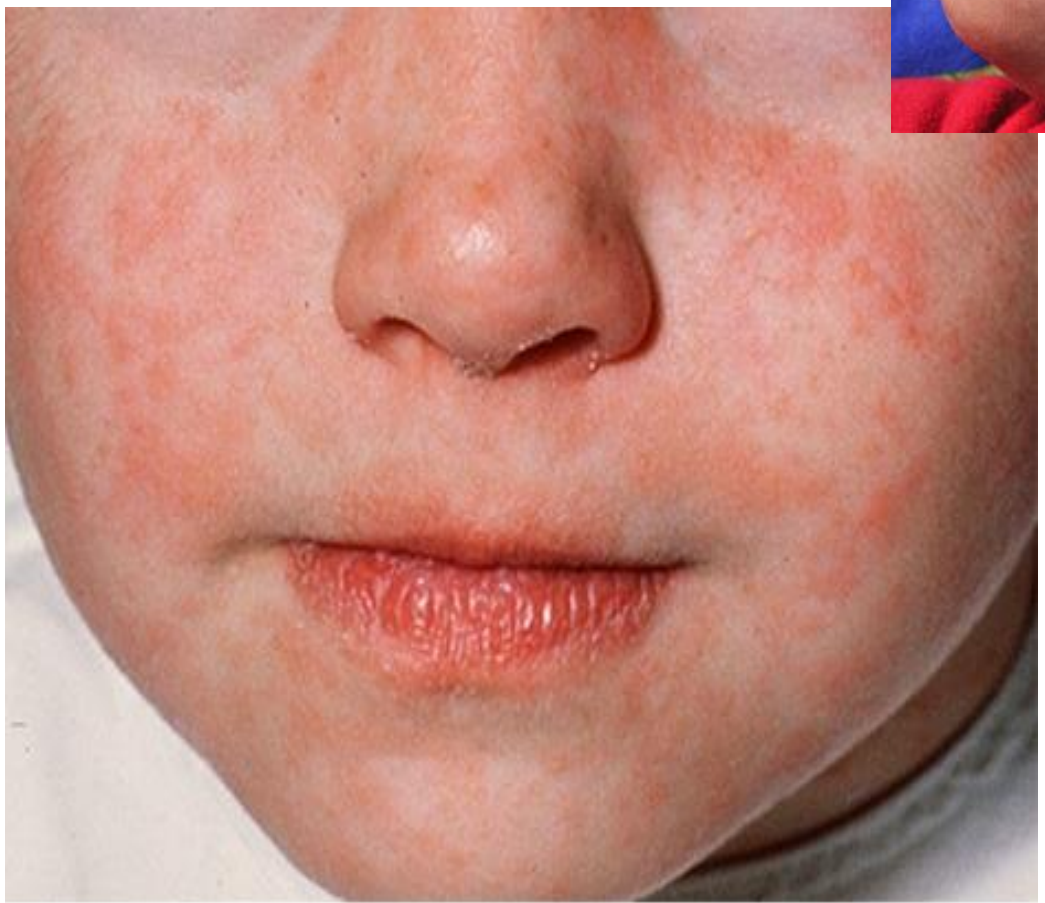
Brownish discoloration of the skin and desquamation may occur later.

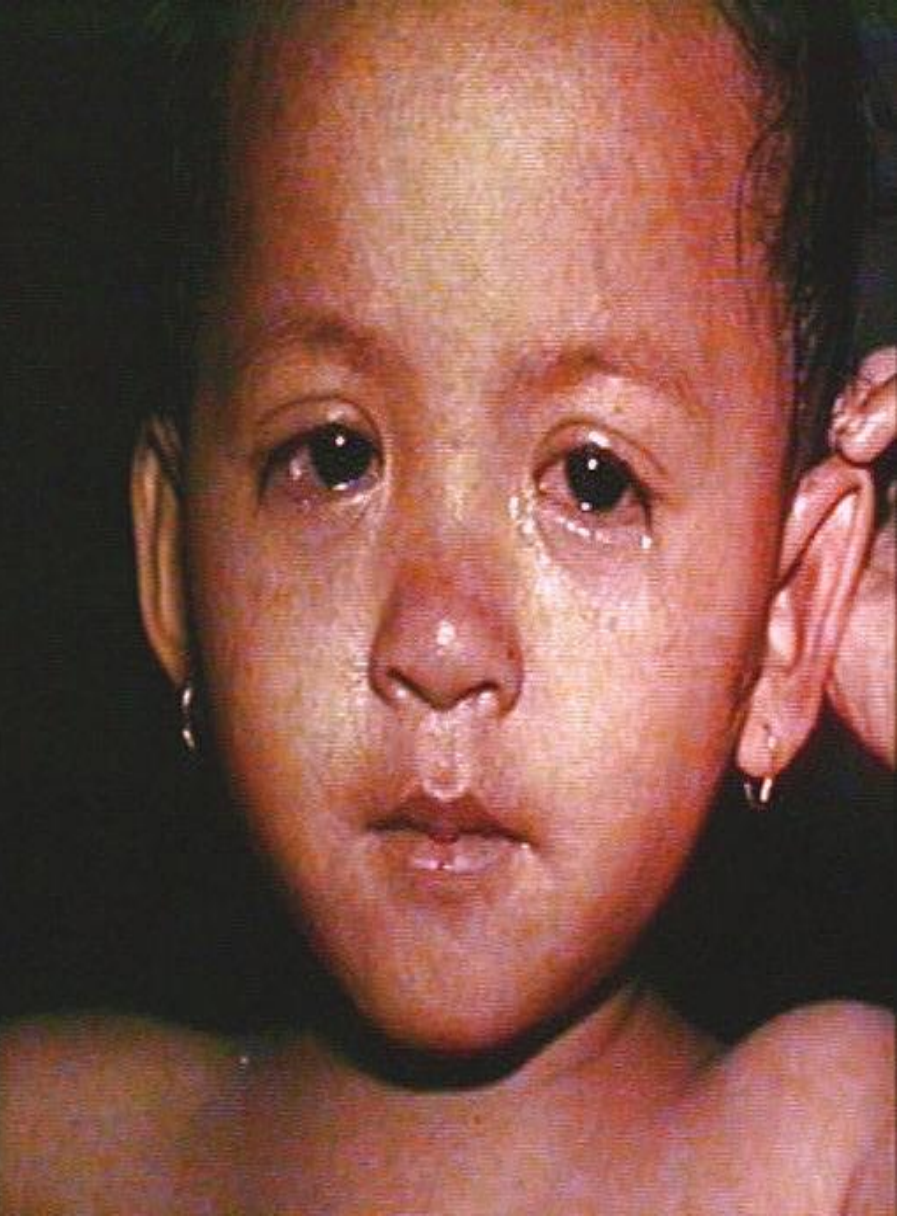
Fever usually resolves by the fourth or fifth day after the onset of rash; prolonged fever suggests a complication of measles.

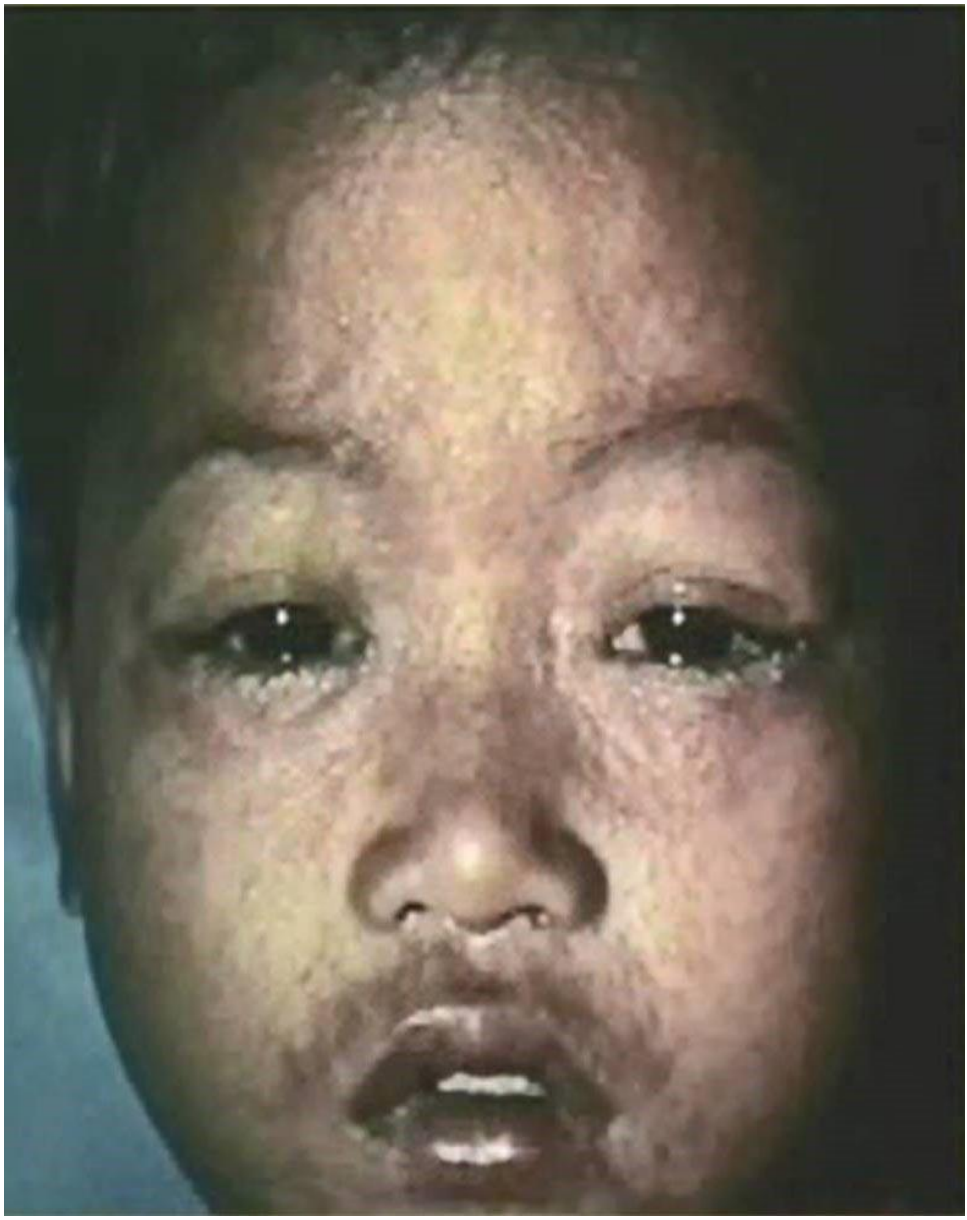


maculopapular rash

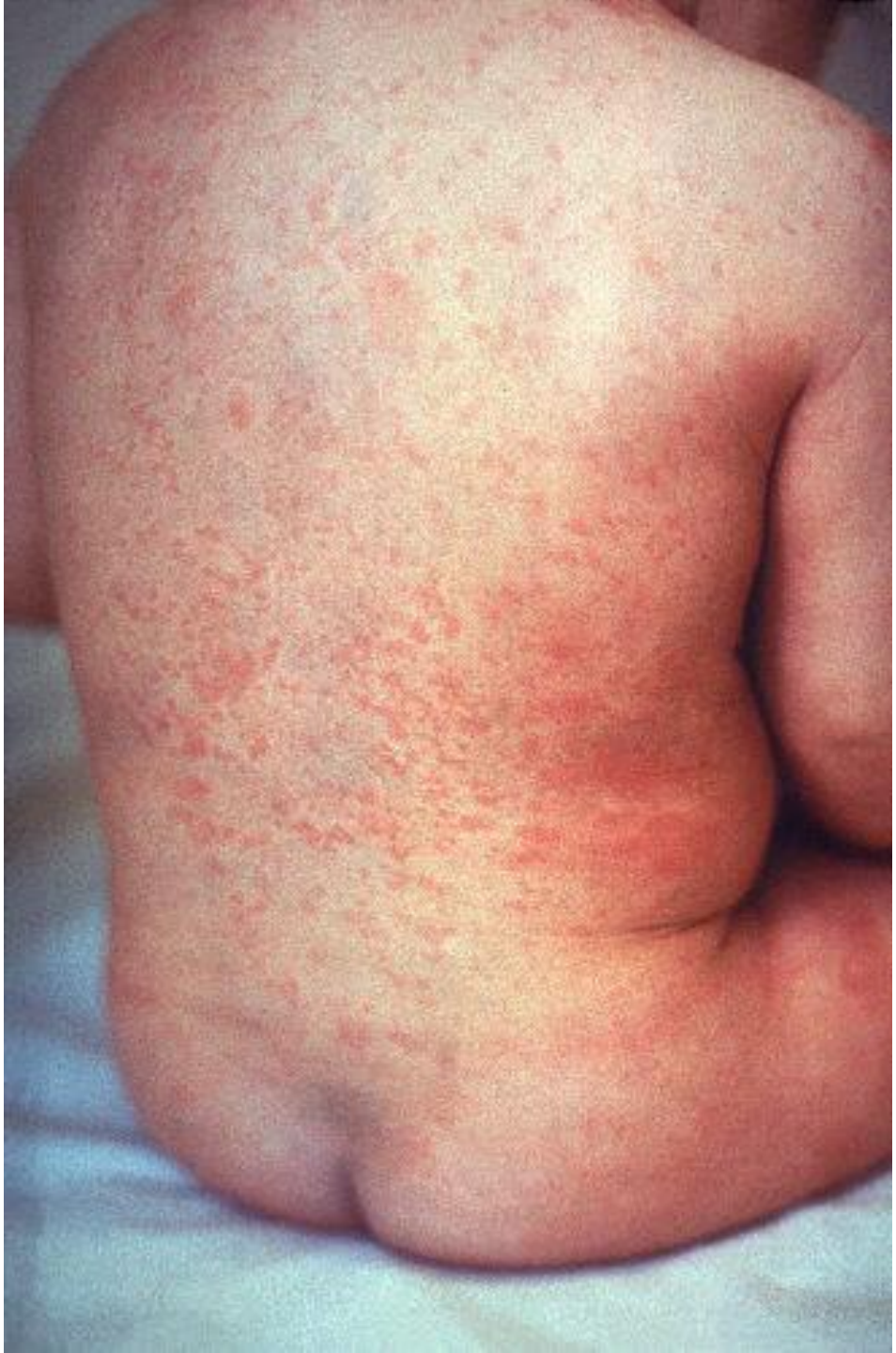


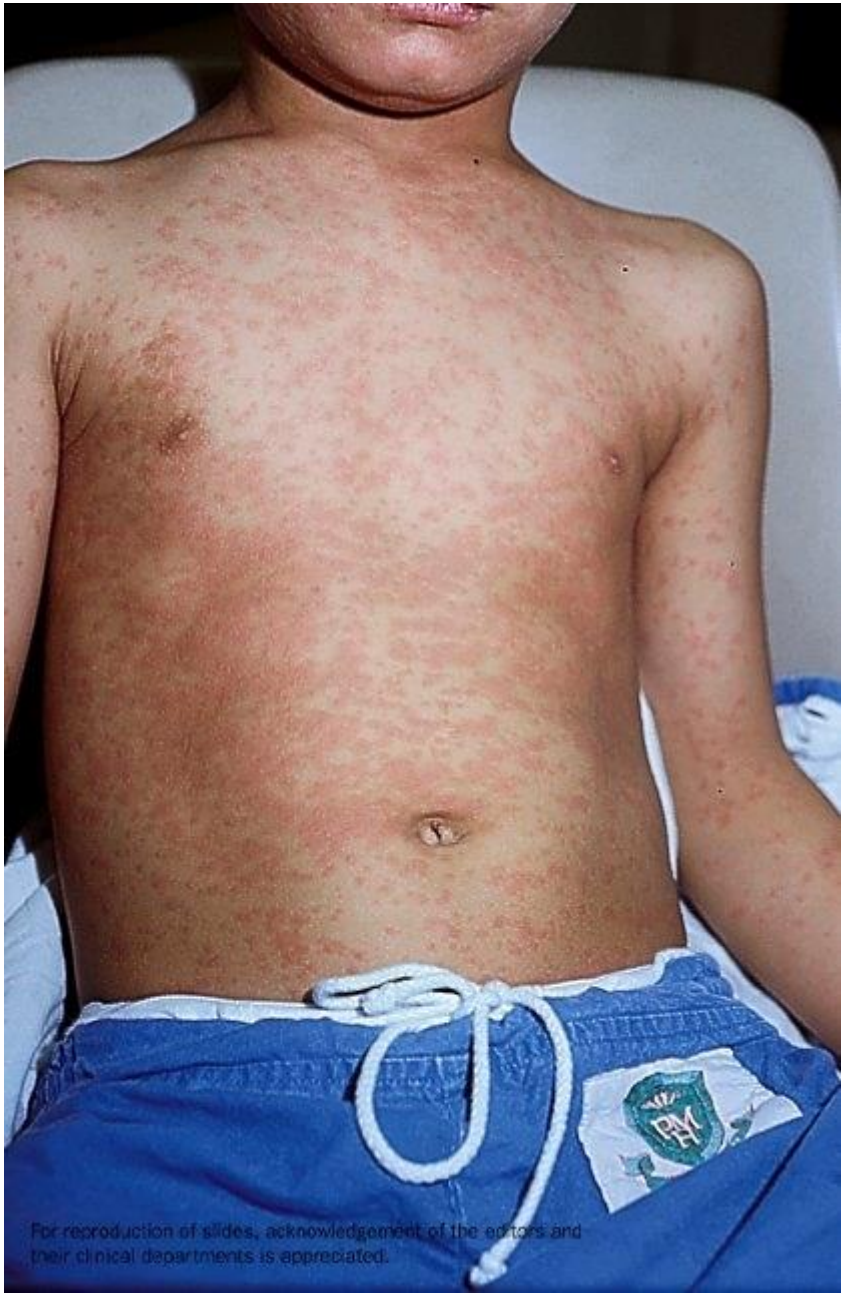






Young, dark-skinned childs with watery eyes, runny nose, and raised rash.

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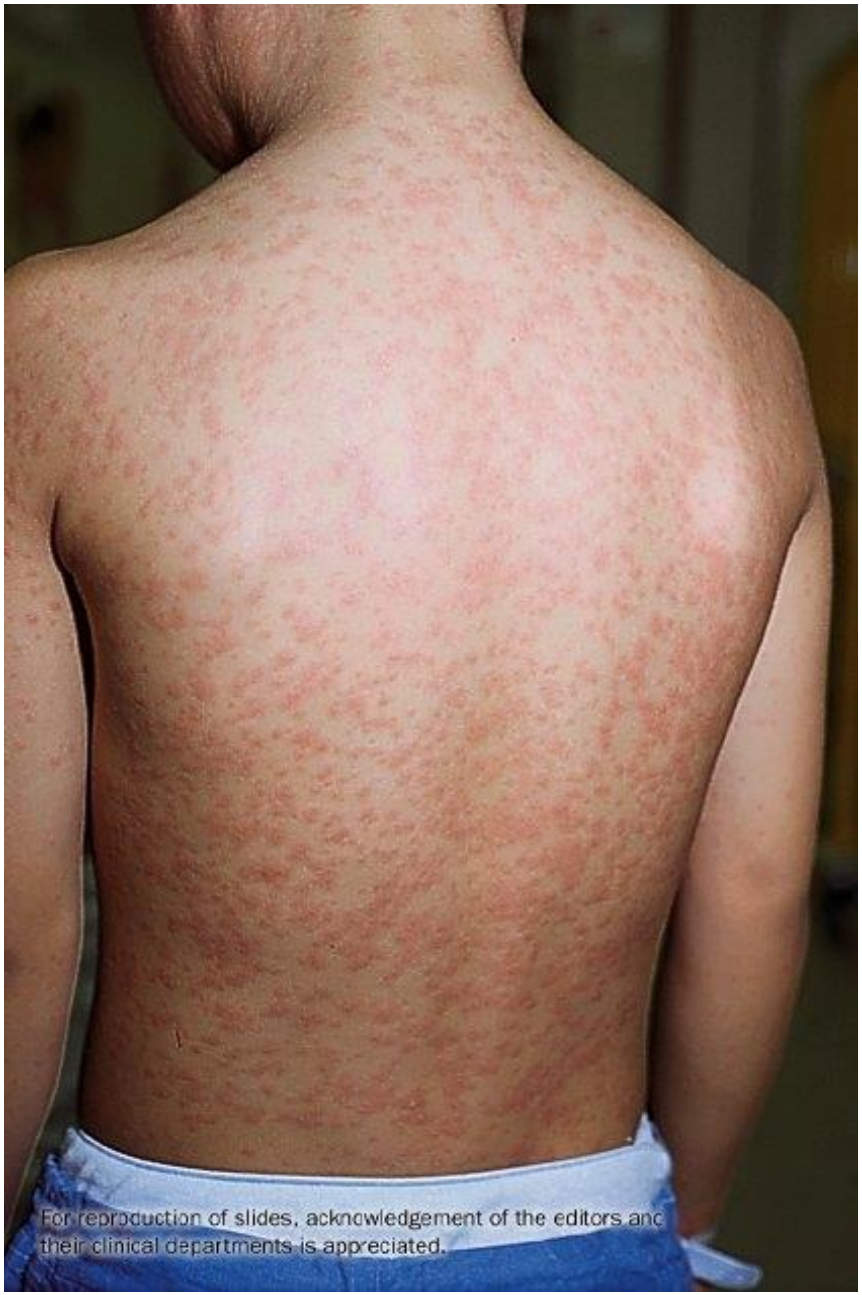
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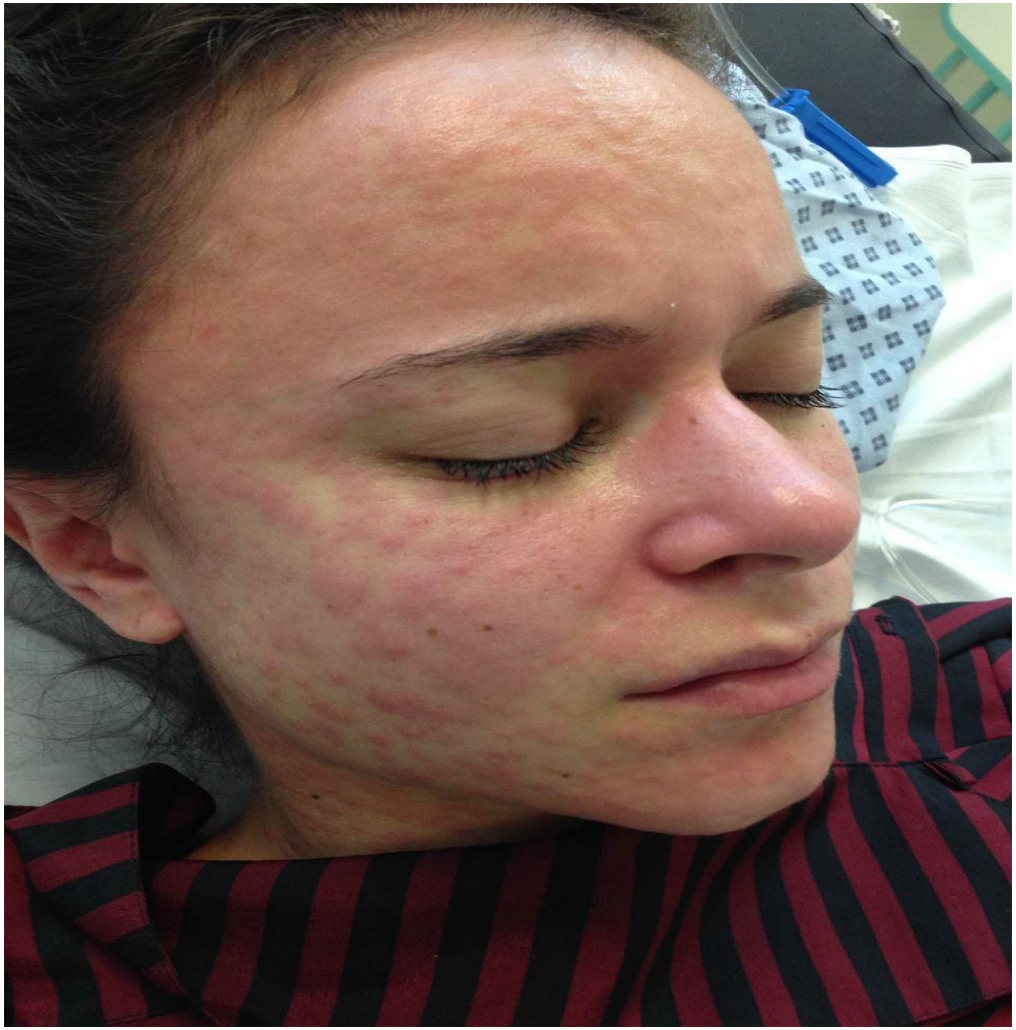
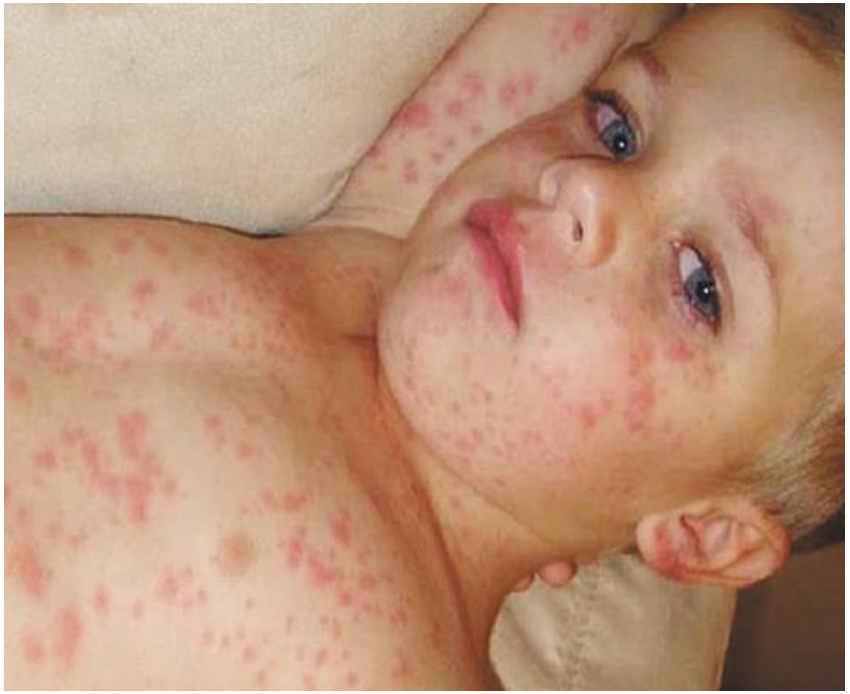
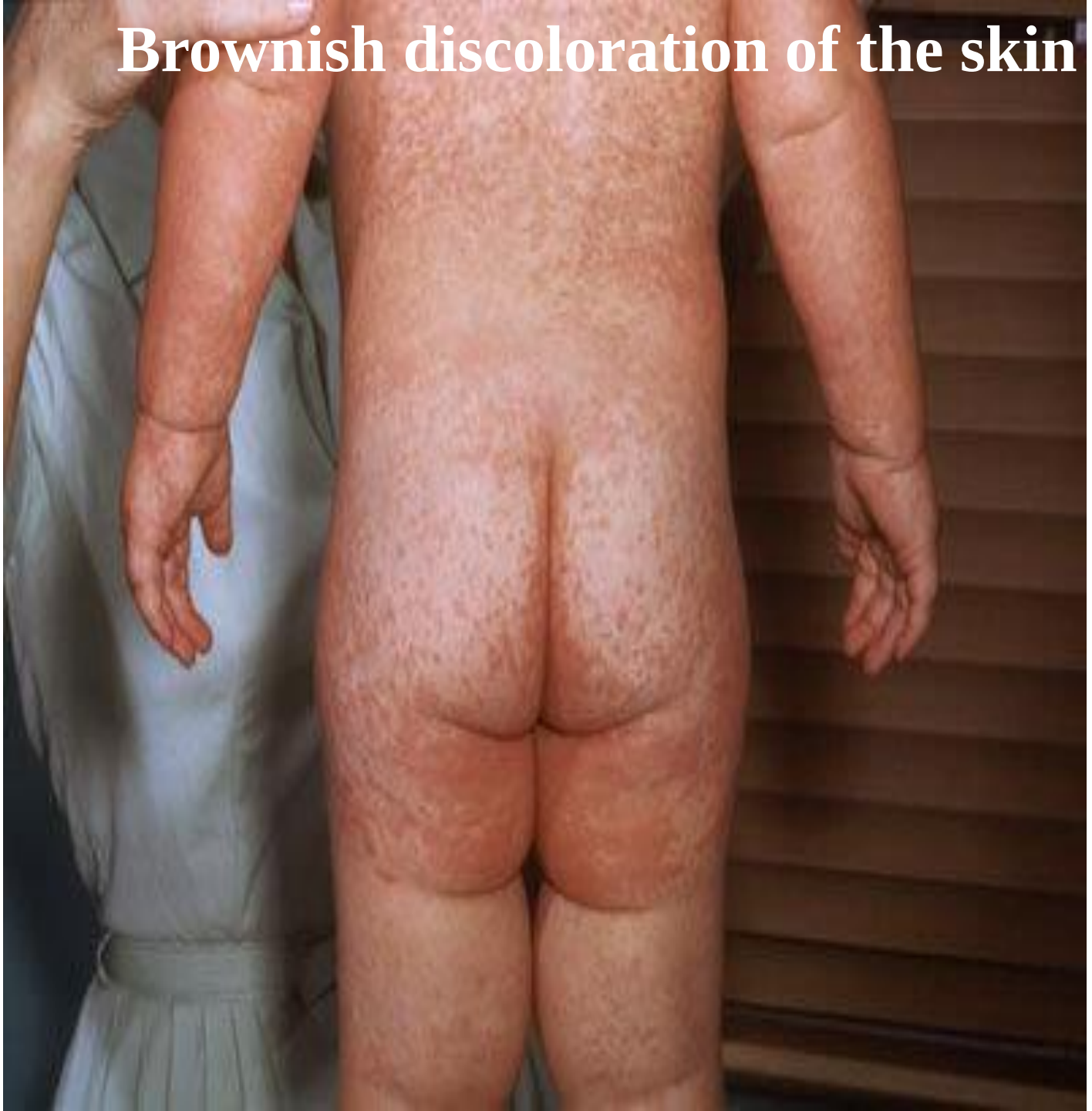
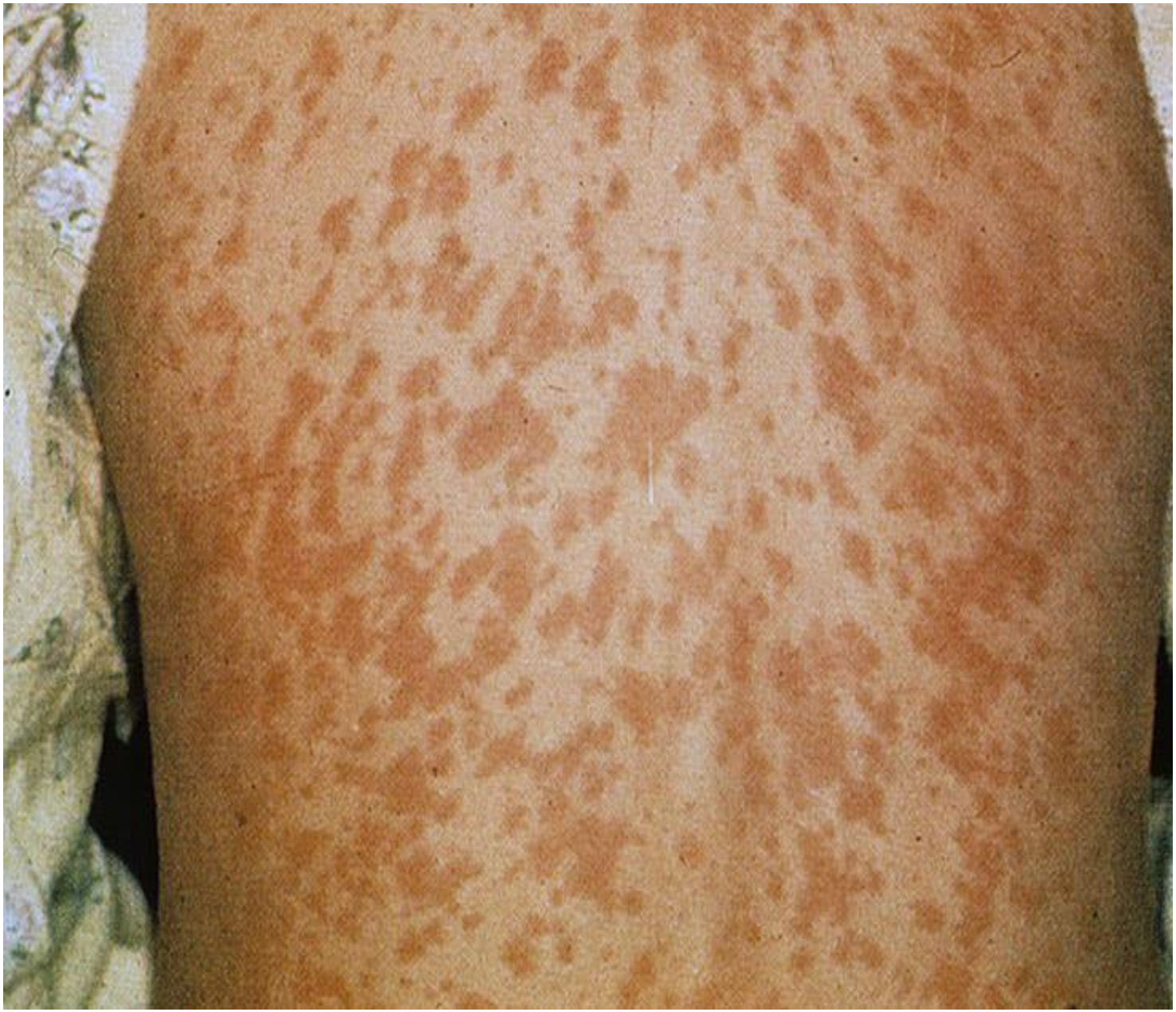




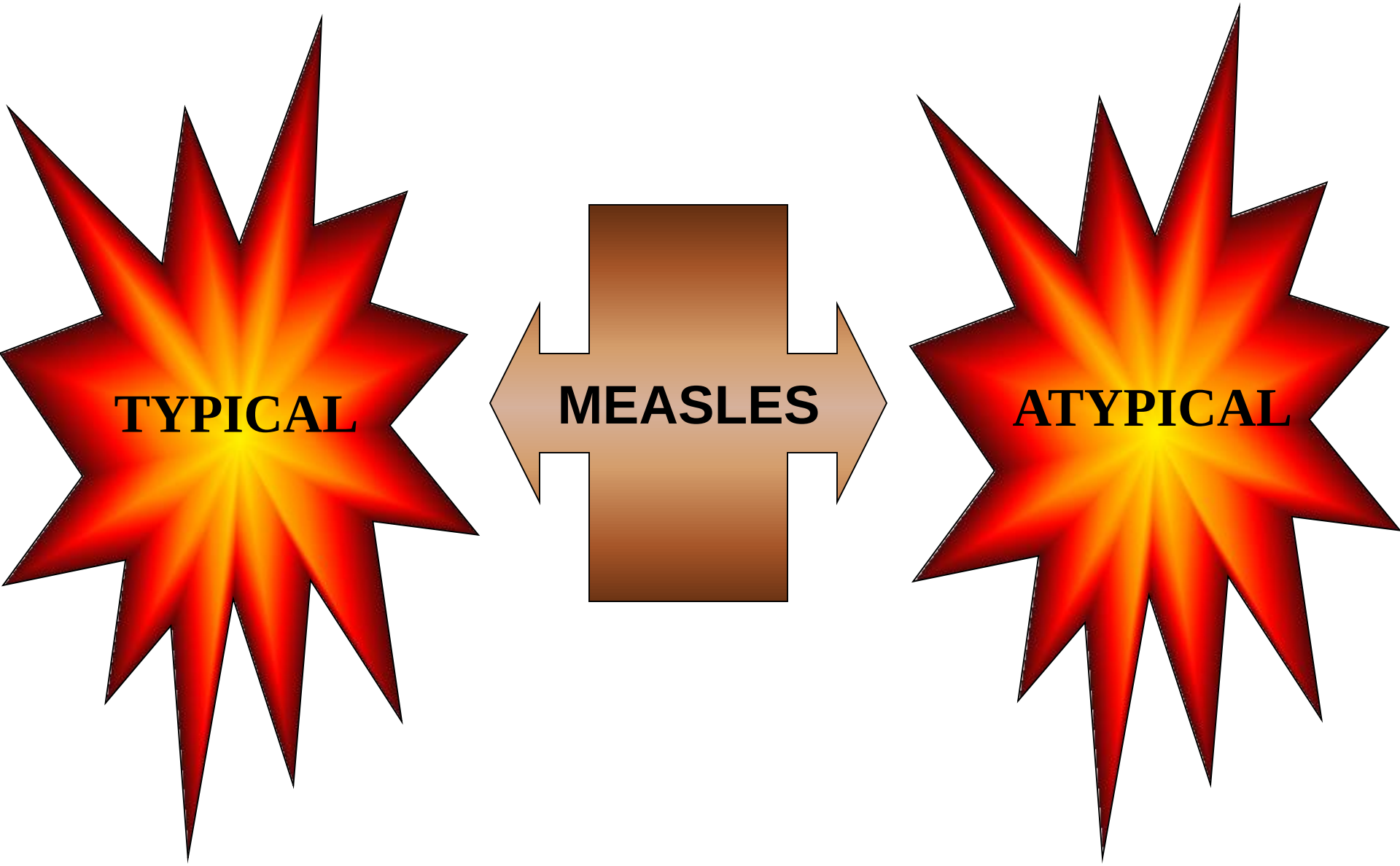
Lymphadenopathy, diarrhea, vomiting, and splenomegaly are common features.
The chest x-ray may be abnormal, even in uncomplicated measles, because of the propensity of measles virus to invade the respiratory tract.
The entire illness, which usually lasts ~10 days, tends to be more severe in adults than in children, with higher fever, more prominent rash, and a higher incidence of complications

Brownish discoloration of the skin

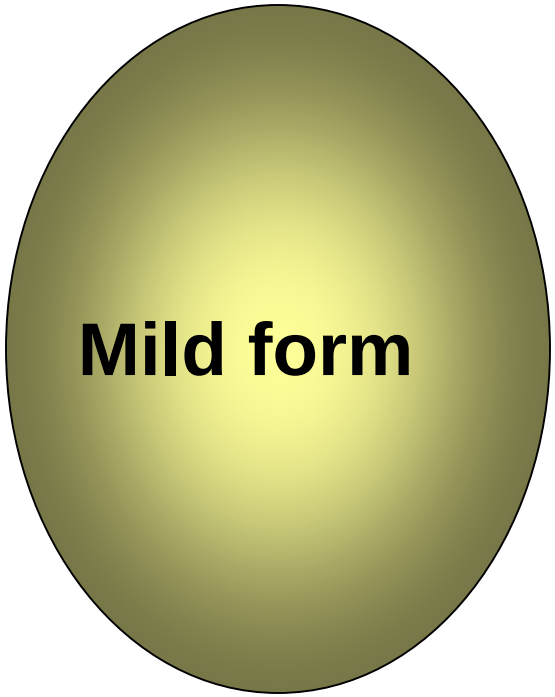


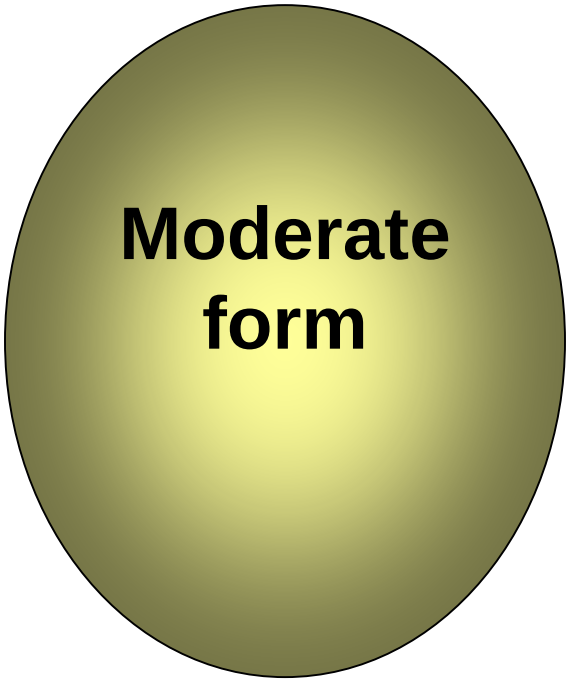


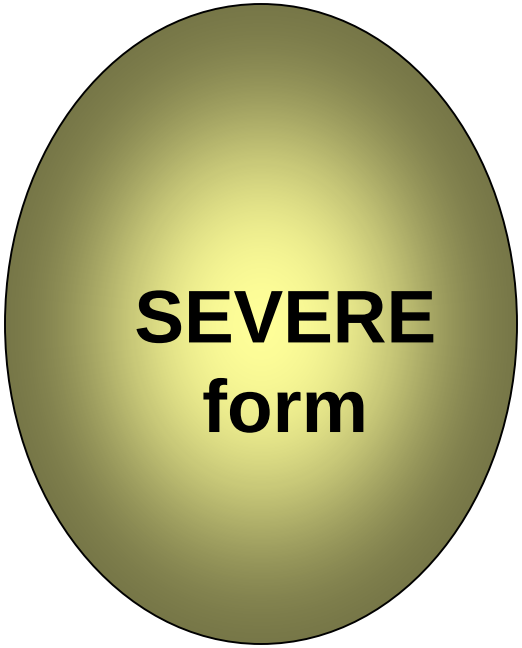
CLASSIFICATION OF CLINICAL FORMS



BY THE GRAVITY OF THE DISEASE



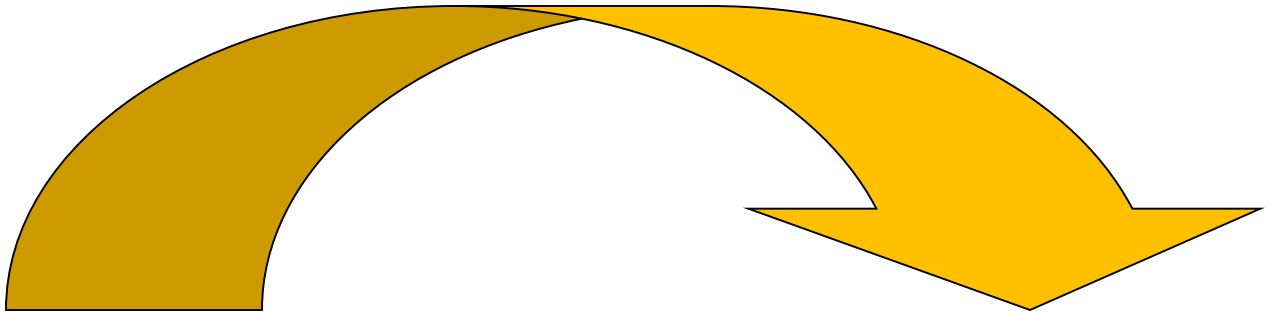




Criteria for the severity of the disease:

severity of toxication syndrome

the severity of local changes

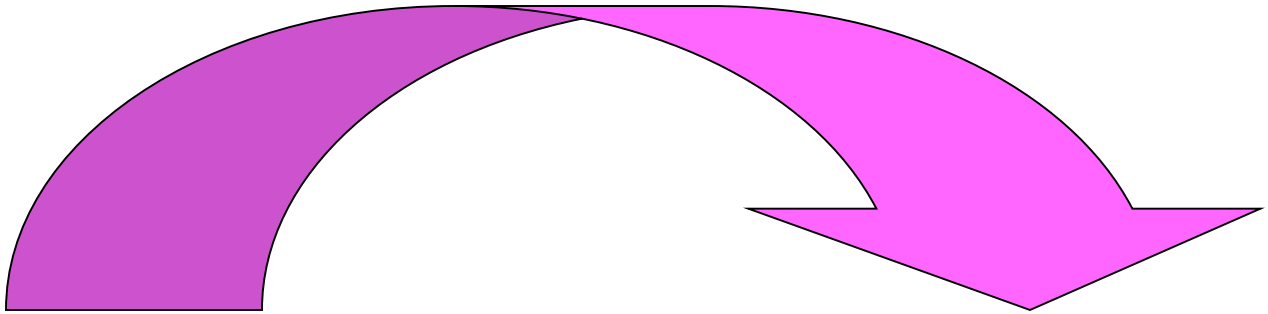


Mild form

characterized by moderately severe catarrhal symptoms, feverish reaction not higher than 37.5^{0}C and lasting no more than 3-4 days, 2-3 day period of rash. Spotted rash

Moderate form

Disorders of the general condition,
pronounced catarrhal period,
lasting 3-4 days, fever 38-39 ^{0} C for 4 days,
vomiting,
delirium,
period of rash lasting
no more than 4-5 days.
Rash profuse, bright



SEVERE form

severe symptoms of intoxication,
hyperemia,
damage to the nervous system with a disorder of consciousness,
convulsions,
repeated vomiting,
adynamia,
acute cardiovascular insufficiency.

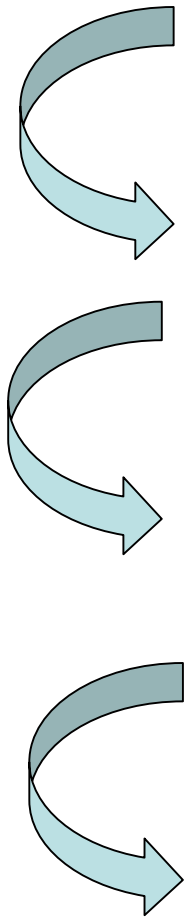
Milder forms of the illness with less intense symptoms and a milder rash, termed *modified measles*, may occur in individuals with preexisting partial immunity induced by active or passive vaccination.

These patients include infants <1 year of age who retain some proportion of passively acquired maternal antibodies.

On occasion, individuals with a history of immunization may develop modified measles.

COMPLICATIONS

The complications of measles can be divided into three groups, according to the site involved:



- the respiratory tract
- the central nervous system (CNS),
- the gastrointestinal tract

Respiratory tract involvement,

manifested

- as laryngitis,
- croup,
- or bronchitis,
- occurs in the majority of cases of uncomplicated measles.

In young children, otitis media is the most common complication.

❖ Pneumonia is a frequent reason for hospitalization, especially of adults.

The pneumonia is of viral origin in the majority of cases, but secondary bacterial infection (most commonly caused by streptococci, pneumococci, or staphylococci) also develops with some frequency. Primary giant-cell (Hecht's) pneumonia is most often documented in immunocompromised and/or malnourished patients.

COMPLICATIONS OF MEASLES

COMPLICATION	COMMENTS
Otitis media	Very common in infants with measles
Pneumonia	May be primary viral pneumonia or bacterial superinfection; frequent reason for hospitalization of adults; measles rash sometimes lacking in immunocompromised patients with measles pneumonia
Croup	Occasionally severe, requiring intubation in infants
Gastroenteritis	Diarrhea can be life threatening in infants
Cervical adenitis	Due to lymphoid hyperplasia as host response to virus; common
Acute encephalitis	May be mild to severe/fatal; occurs in 1 in 1000 cases of measles; cerebral and cerebellar forms; immune-mediated pathogenesis
Subacute sclerosing panencephalitis (SSPE)	In 1 in 100,000 cases of measles, usually when measles occurs in infancy; seen 5–10 years later

Gastrointestinal complications of measles include

gastroenteritis,
hepatitis,
appendicitis,
ileocolitis, and
mesenteric adenitis.
It is not uncommon to detect high levels of alanine and aspartate aminotransferases in the absence of gastrointestinal signs such as jaundice.

Rare complications

include

- ✓ **myocarditis,**
- ✓ **glomerulonephritis,**
- ✓ **and postinfectious thrombocytopenic purpura.**

Measles can exacerbate preexisting tuberculosis, presumably through virus-induced depression of cellular immunity.

Natural measles and immunization against measles can result in tuberculin skin-test anergy lasting for ~1 month.

MEASLES IN ADULTS

Measles is naturally a disease of childhood and, like many other viral infections, is more severe in adults than in children.

About 3% of young adults with measles develop primary viral pneumonia and require hospitalization.

Hepatitis and bronchospasm are more common among adults with measles than among children, and the rash is more severe and more confluent in adults.

Bacterial superinfection is more common among adults, more than one-third of whom develop respiratory complications such as otitis media, sinusitis, and pneumonia. Adults may develop measles because they were never immunized or (more rarely) because their vaccine-induced immunity has waned.

Very low titers of antibody to measles virus have been associated with lack of protection.

DIAGNOSTICS

CLINICAL AND EPIDEMIOLOGICAL METHOD

LABORATORY FINDINGS

lymphopenia
neutropenia

A specific diagnosis of measles can be made quickly by immunofluorescent staining of a smear of respiratory secretions for measles antigen; monoclonal antibodies conjugated to fluorescein are commercially available.

Secretions can be examined microscopically for multinucleated giant cells. Measles virus can be demonstrated by culture or polymerase chain reaction in respiratory secretions or urine.

A number of serologic tests are available.

A serologic diagnosis by enzyme immunoassay (EIA) cannot necessarily be made rapidly if acute- and convalescentphase serum specimens are examined. However, EIA measurement of specific IgM permits diagnosis on the basis of an acute-phase serum sample.

Specific IgM antibodies are detectable within 1–2 days after rash onset, and the IgG titer rises significantly after 10 days.

Atypical measles and SSPE are associated with extremely high levels of measles antibodies in blood and/or CSF.

DIFFERENTIAL DIAGNOSIS

Classic measles—with Koplik's spots, cough, coryza, conjunctivitis, and a rash beginning on the head—is easily diagnosed on clinical grounds. Modified measles is more difficult to diagnose because one or more characteristic signs or symptoms may be lacking. The differential diagnosis of measles includes Kawasaki disease, scarlet fever, infectious mononucleosis, toxoplasmosis, drug eruption, and *Mycoplasma pneumoniae* infection. In the differential diagnosis of measles, attention should be paid to the current epidemiology of the disease in the community and to the patient's history of measles vaccination and foreign travel.

ARVI (influenza, parainfluenza, adenovirus, rhinovirus)

ALLERGIC EXANTHEMS

RUBELLA

ENTEROVIRUS infection

PSEUDOTUBERCULOSIS

MENINGOCOCCAEMIA

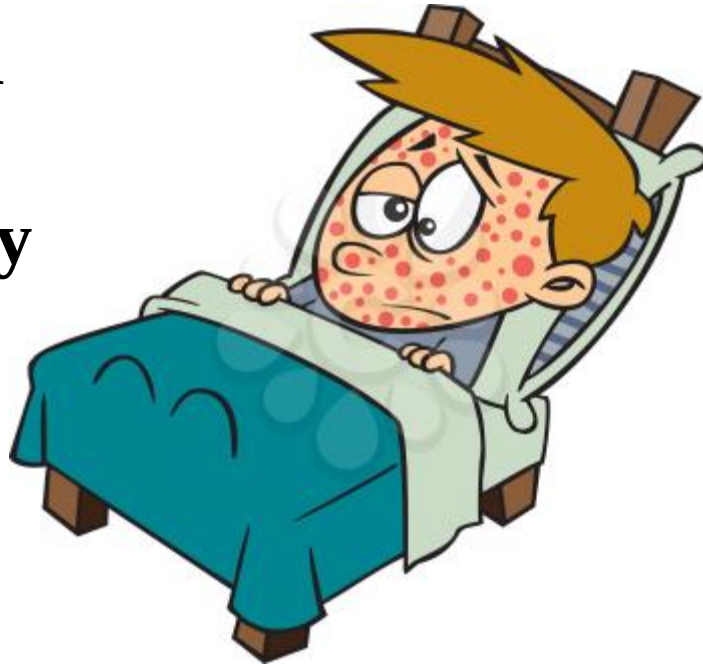
Therapy

Therapy for measles is largely supportive and symptom based.

Patients with otitis media and pneumonia should be given standard antibiotics.

Patients with encephalitis need supportive care, including observation for increased intracranial pressure.

Controlled trials suggest clinical benefit from high doses of vitamin A in severe or potentially severe measles, especially in children <2 years old who are or may be malnourished..



~~Measles vaccine has been available as the combination~~ vaccine measles-mumps-rubella (MMR);
this vaccine should be administered to children at 12–15 months of age. (Vaccination at 12 months is preferred for infants whose mothers were immunized against measles in childhood.)
A second dose of MMR vaccine is recommended for school-age children. MMR vaccine is likely to be supplanted by MMRV vaccine, which also covers varicella and was licensed by the U.S. Food and Drug Administration in 2005. MMRV vaccine is licensed only for children 1–13 years of age.