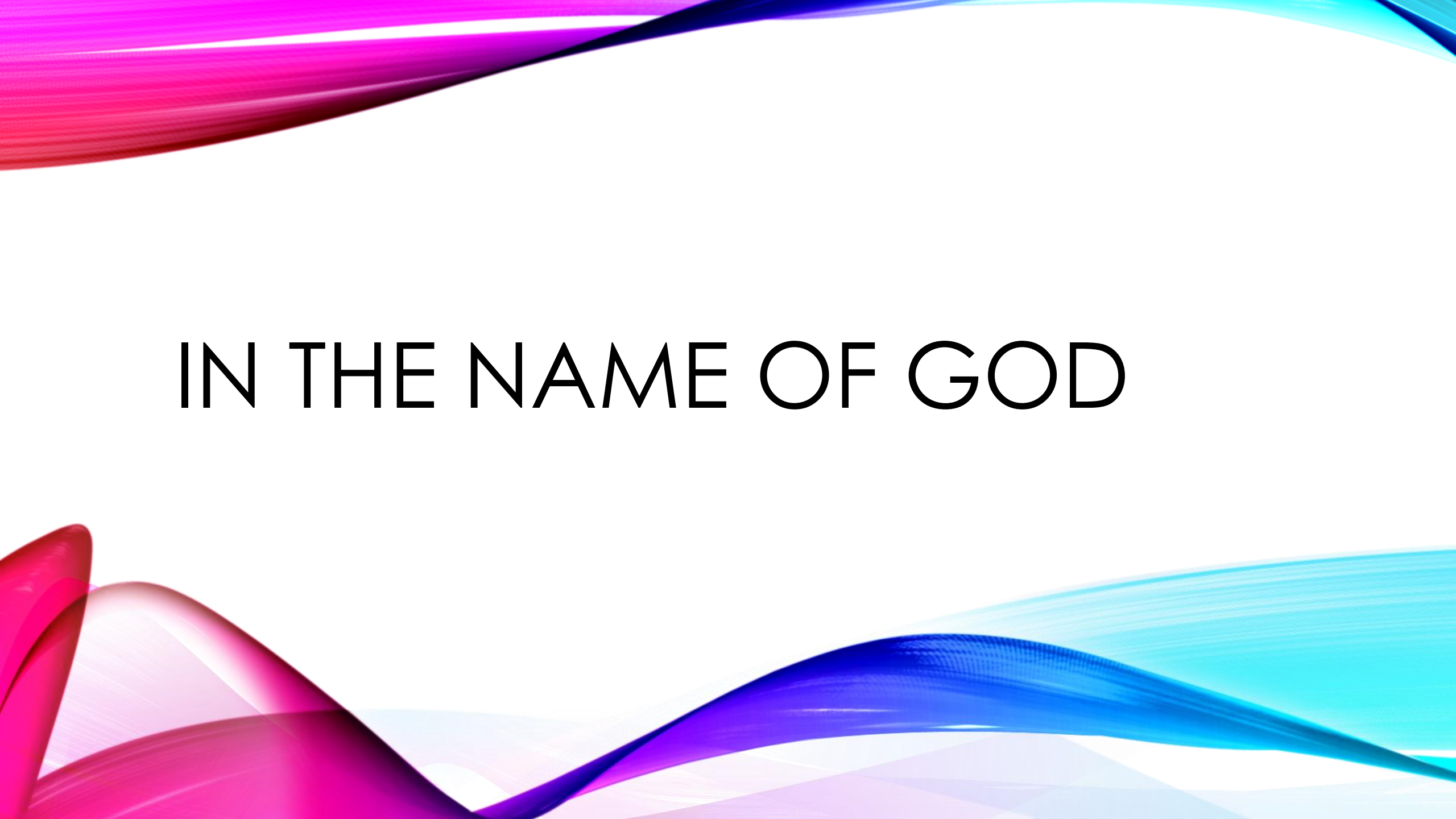




IN THE NAME OF GOD

Measles (Rubeola)



Dr.Khoshhal.PED



INTRODUCTION

- Measles is a highly contagious viral illness that occurs worldwide
- Causative agent is a Paramyxovirus.
- approximately 90 percent of susceptible individuals will develop measles.
- The period of contagiousness is estimated to be from five days before the appearance of the rash to four days afterward.
- The illness may be transmitted in public spaces, even in the absence of person-to-person contact.

- A vaccination level of 95% should be the minimum requirement, rather than the goal, for successful measles elimination

- Their analysis estimated that average MCV2 effectiveness was 96.4% in the general population under real world condition
- **Reported worldwide measles cases increased by 79% in the first 2 months of 2022, compared to the same period in 2021, as WHO and UNICEF warn conditions ripe for serious outbreaks of vaccine-preventable illnesses**
- As of April 2022, the agencies report 21 large and disruptive measles outbreaks around the world in the last 12 months. Most of the measles cases were reported in Africa and the East Mediterranean region.
- The current rate is <1 case per 1,000,000 population.



MEASLES (RUBEOLA)

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- Individuals at risk for measles include:
 - - Children too young to be vaccinated
 - - Unvaccinated children for any reasons
 - - Those who have not received a second dose of vaccine
 - - Cases of vaccine failure
 - • Natural measles infection leads to lifelong immunity

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- •Measles is highly contagious.(90%)
 - •The illness may be transmitted in public spaces, even in the absence of person-to-person contact.
 - • Measles virus can remain suspended in the air for up to two hours.
 - •Infectivity period: 5 days before the onset of rash to 4 days afterward. (start 1-2 days before prodrome)

MEASLES VIRUS INFECTION

CLINICAL SYNDROMES

- , •Classic measles infection in immunocompetent individuals
- •Modified measles infection in patients with pre-existing but incompletely protective anti-measles antibody
- •Atypical measles infection in patients immunized with the killed virus vaccine
- •Neurologic syndromes following measles infection, including acute disseminated encephalomyelitis and subacute sclerosing panencephalitis
- •Severe measles infection especially in immunocompetent individuals
- •Complications of measles including secondary infection, giant cell pneumonia, and measles inclusion body encephalitis

INCUBATION PERIOD

The incubation period for measles is 6 to 21 days (median 13 days)

; it begins after virus entry via the respiratory mucosa or conjunctivae. The virus replicates locally, spreads to regional lymphatic tissues, and is then thought to disseminate to other **reticuloendothelial sites via the bloodstream**, which is considered the first viremia

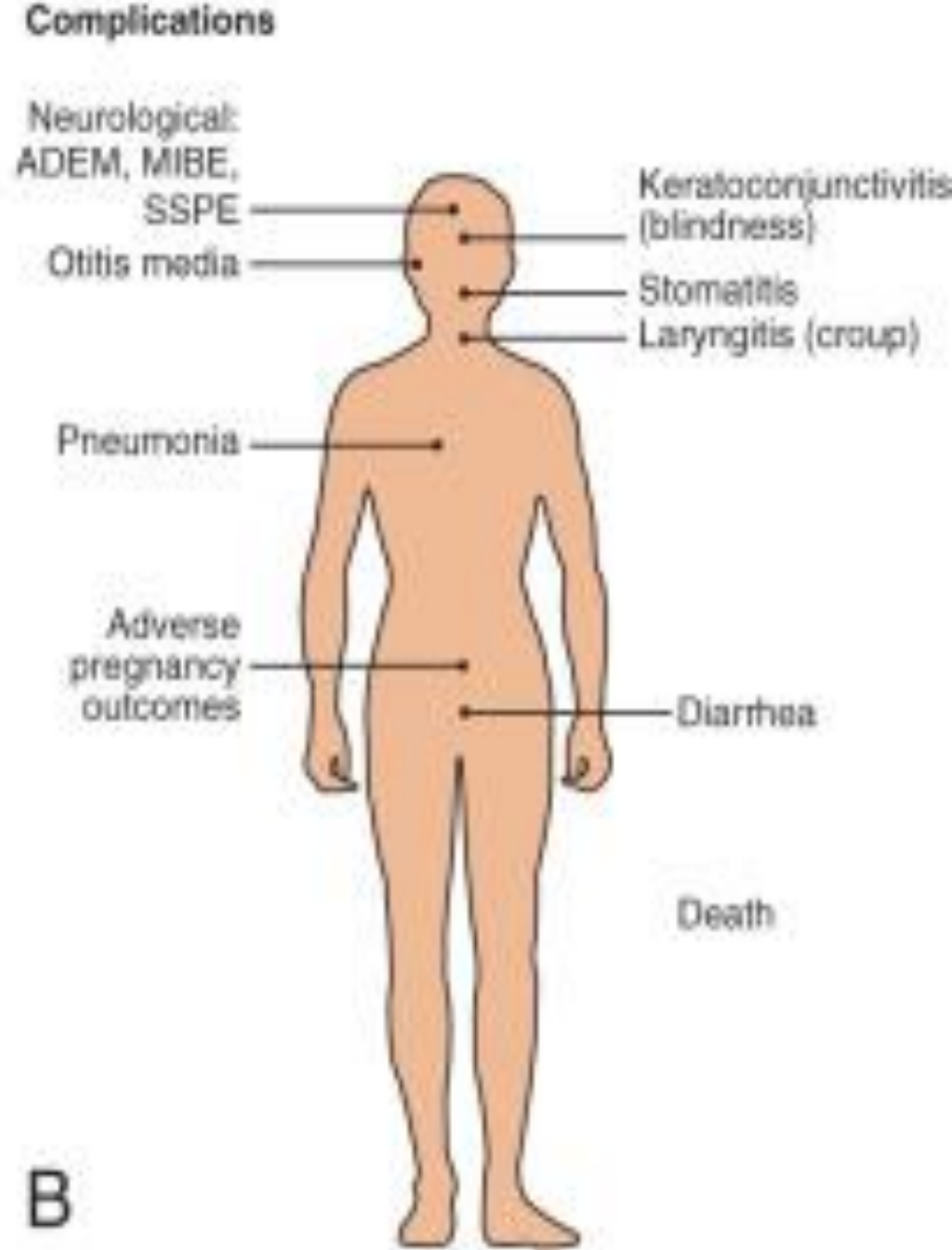
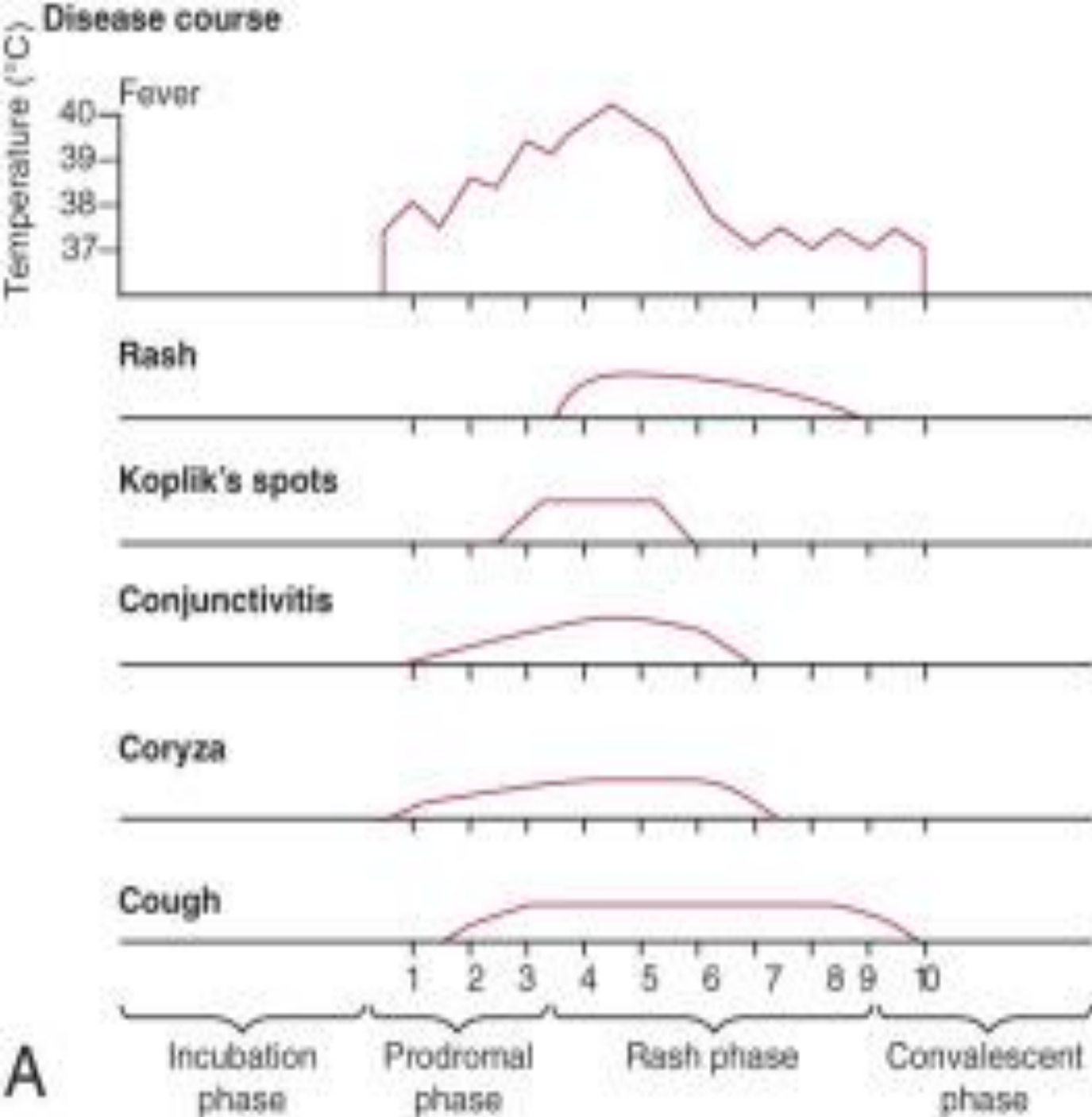
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asymptomatic during the incubation period, although some have been reported to experience **transient respiratory symptoms, fever, or rash**.

- The dissemination of measles virus due to viremia, with **associated infection of endothelial, epithelial, monocyte, and macrophage cells**, may explain the variety of clinical manifestations and complications that can occur with measles virus infection.
- **A second viremia occurs several days after the first, coinciding with the beginning of the prodromal phase with shedding of virus**

DISEASE COURSE

- incubation – The incubation is 6 to 21 days (median 13 days).
- •Prodrome – A two- to four-day prodrome phase is characterized by fever, malaise, and anorexia, followed by conjunctivitis, coryza, and cough. The severity of conjunctivitis is variable and may also be accompanied by lacrimation or photophobia. If present, Koplik spots, an enanthem considered pathognomonic for measles infection, typically occurs approximately 48 hours prior to the exanthem.
- •Exanthem – The characteristic exanthem arises approximately two to four days after onset of fever; it consists of a red maculopapular rash, which classically begins on the face and head and spreads downward. Early on, the lesions are blanching; in later stages, they are not. The rash resolves in five to six days, fading in the order it appeared.
- •Recovery – Cough may persist for one to two weeks after measles. The occurrence of fever beyond the third to fourth day of rash suggests a measles-associated complication.



KOPLIC SPOTS

Koplic Spots

- Appear approximately 48 hours prior to the rash.
- Generally last 12 to 72 hours



Exanthem

- •Erythematous maculopapular eruption.
- •Begins on the forehead (around the hairline), behind the ears, and on the upper neck.
- •Spreads downward to the torso and extremities.
- •The exanthem frequently becomes confluent on the face and upper trunk.
- •The rash fades over about 7 days cephalocaudally.
- •Often leaving a fine desquamation of skin.

Exanthem

- Other characteristic findings during the exanthematous phase include lymphadenopathy, high fever (peaking two to three days after appearance of rash), pronounced respiratory signs including pharyngitis, and nonpurulent conjunctivitis.
- Uncommonly, patients with severe measles develop generalized lymphadenopathy and splenomegaly .
- Clinical improvement typically ensues within 48 hours of the appearance of the rash. After three to four days, the rash darkens to a brownish color (and begins to fade,
- followed by fine desquamation in the more severely involved areas.
- The rash usually lasts six to seven days and fades in the order it appeared





- Blanching erythematous macules with some confluent areas on the trunk in a patient with measles



OTHER MANIFESTATIONS

- •Diarrhea and vomiting
- •Abdominal pain
- •Lymphadenopathy
- •Splenomegaly
- •Liver

Clinical manifestations of measles in immunocompromised

severe and desquamative; or purpuric rash.

- pneumonia (Giant cell pneumonia)

Encephalitis despite history of previous immunization.

LABORATORY FINDINGS

- Reduction in the total white blood cell count, with **lymphocytes** decreased more than neutrophils.
- absolute neutropenia has been known to occur.
- In measles not complicated by bacterial infection, the erythrocyte **sedimentation rate and C-reactive protein level** are usually normal.

RECOVERY AND IMMUNITY

- Cough may persist for one to two weeks after measles. The occurrence of fever beyond the third to fourth day of rash suggests a measles-associated complication.
- Both humoral and cellular measles-specific immunity are important for viral clearance and lasting protective immunity . Children with defects in humoral immunity, such as agammaglobulinemia, generally recover from measles, while individuals with T cell deficiencies often have severe measles infection and high mortality rates.
- Immunity after measles virus infection is thought to be lifelong, although there are rare reports of measles reinfection
- Measles virus infection is associated with immunosuppression that can persist



CLINICAL VARIANTS

- Modified measles occurs in patients with preexisting but incompletely protective anti-measles antibody.
- Atypical measles occurs in patients immunized with the killed virus vaccine administered between 1963 and 1967 in the United States who are subsequently exposed to wild-type measles virus

MODIFIED MEASLES

- Modified measles is an attenuated infection that occurs in individuals with pre-existing measles immunity (either via wild-type disease or vaccination). It is similar to classic measles except the clinical manifestations are generally milder and the incubation period is longer (17 to 21 days).
- Individuals with modified measles are not highly contagious .
- Transplacental transfer of anti-measles antibody from mother to infant Receipt of immunoglobulin.
- •Measles vaccination resulting in antibody titers lower than those considered seroprotective.
- •Prior history of measles

ATYPICAL MEASLES

- Atypical measles refers to measles virus infection among individuals immunized with the killed virus vaccine, which was used in the United States between 1963 and 1967; atypical measles is now rare. The killed virus vaccine sensitized the recipient to measles virus antigens without providing full protection.
- .
- individuals with atypical measles do not appear to transmit measles virus to others

ATYPICAL MEASLES

- Individuals with atypical measles develop high fever and headache 7 to 14 days after exposure to measles. Atypical measles is characterized by higher and more prolonged fever
- . A maculopapular rash develops two to three days later, beginning on the extremities (instead of the head as seen with typical measles) and spreading to the trunk. The rash may involve the palms and soles and tends to spare the upper chest, neck, and head
- . The rash may be vesicular, petechial, purpuric, or urticarial; it may have a hemorrhagic component.

ATYPICAL MEASLES

- A dry cough and pleuritic chest pain are often present; pneumonitis can be severe. Chest radiograph typically demonstrates bilateral pulmonary nodules and hilar lymphadenopathy .
- Atypical measles often results in severe illness; many individuals develop respiratory distress.
- Some individuals develop peripheral edema, hepatosplenomegaly, and/or neurologic symptoms such as paresthesias or hyperesthesias. Laboratory findings can include elevated serum aminotransferases.
- Atypical measles is associated with a characteristic antibody pattern: before or at the onset of the exanthem, the titer is usually $<1:5$ but, by day 10 of illness, the titer is typically $\geq 1:1280$. The height and rapidity of antibody titer rise is much higher than in primary natural measles infection

BLACK MEASLES

- **hemorrhagic measles** or **black measles**.
- hemorrhagic skin eruption and was **often fatal**.
- Keratitis, appearing as multiple punctate epithelial foci, resolved with recovery from the infection.
- Thrombocytopenia sometimes occurred following measles.

COMPLICATIONS

- One or more complications occur in approximately 30 percent of measles cases
- . The risk of complications is increased in resource-limited settings, where the case fatality rate is 4 to 10 percent.
- Groups at increased risk for complications of measles include
 - immunocompromised patients,
 - pregnant women,
 - individuals with vitamin A deficiency or poor nutritional status,
 - individuals at the extremes of age

COMPLICATIONS

- . Morbidity and mortality from measles are greatest in individuals younger than 5 yr of age (especially <1 yr of age) and older than 20 yr of age
- . In developing countries, higher case fatality rates have been associated with crowding,
- . Severe malnutrition in children results in a suboptimal immune response and higher morbidity and mortality with measles infection
- . Low serum retinol levels in children with measles
- patients with malignancy in whom measles develops, pneumonitis occurs in 58% and encephalitis occurs in 20%.

COMPLICATIONS

- •Acute otitis media (the most common).
- •Croup and bronchiolitis (in infants and toddlers)
- •Pneumonia (most common cause of death). giant cell pneumonia caused directly by the viral
- infection and superimposed bacterial Pneumonia. common bacterial pathogens are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Staphylococcus aureus*
- Sinusitis and mastoiditis
- Viral and/or bacterial tracheitis
- Neurologic: Encephalitis, ADEM, SSPE
- •Thrombocytopenia
- •Myocarditis
- •Appendicitis

IMMUNE SUPPRESSION AND SECONDARY INFECTION

Secondary and coinfections may include bacteremia, pneumonia, gastroenteritis and otitis media.

Pathogens involved include viruses (eg, parainfluenza virus and adenovirus), and bacteria (eg, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Streptococcus pyogenes*).

Tuberculosis reactivation in the setting of recent measles infection has also been described

T cell lymphopenia with depletion of T-dependent areas of lymph nodes and spleen, cutaneous anergy



GASTROINTESTINAL

- Diarrhea and vomiting are common symptoms associated with acute measles
- gingivostomatitis, gastroenteritis, hepatitis, mesenteric lymphadenitis, and appendicitis.
- In resource-limited settings, measles-induced stomatitis and diarrhea can lead to diminished nutritional status
- Dehydration is a common consequence, especially in young infants and children

PULMONARY

- Pneumonia is the **most common cause of measles-associated death in children**; it occurs in approximately 6 percent of cases]. Respiratory tract infections occur most frequently among patients <5 years and >20 years of age
- .. **giant cell pneumonia** caused directly by the viral infection or as superimposed bacterial infection.

bronchopneumonia, laryngotracheobronchitis (croup), and bronchiolitis

- development of **bronchiectasis**, which can predispose to recurrent respiratory infections
- Bacterial superinfection may occur in up to 5 percent of cases. measles-associated pneumonia, bacterial pathogens included *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Haemophilus influenzae*, and *Staphylococcus aureus*].
-

ENCEPHALITIS

- Encephalitis occurs in up to 1 -3 per 1000 measles cases.
- It usually appears within a few days of the rash, typically day 5 (range 1 to 14 days)
- symptoms may include fever, headache, vomiting, stiff neck, meningeal irritation,. seizures (56%), lethargy (46%), coma (28%), and irritability (26%)
- Acute measles encephalitis may also occur in the absence of rash
- Analysis of cerebrospinal fluid is notable for pleocytosis (predominantly lymphocytes), elevated protein concentration, and normal glucose concentration.
- Approximately 25 percent of children have neurodevelopmental sequelae
- rapidly progressive and fatal disease occurs in about 15 percent of cases

ACUTE DISSEMINATED ENCEPHALOMYELITIS

- ADEM presents during the recovery phase of measles, typically within two weeks of the exanthem ..
- Clinical manifestations more common in preschool- or school-age children. Encephalitis is a postinfectious, immunologically mediated process
- fever, headache, neck stiffness, seizures, and mental status changes such as confusion, somnolence, or coma
- Other manifestations may include ataxia, myoclonus, choreoathetosis, and signs of myelitis, such as paraplegia, quadriplegia, sensory loss, loss of bladder and bowel control, and back pain]. Analysis of cerebrospinal fluid generally demonstrates a lymphocytic pleocytosis and elevated protein concentration
- ADEM following measles infection is associated with a 10 to 20 percent mortality
- Residual neurologic abnormalities are common among survivors, including behavior disorders, cognitive deficits, and epilepsy and deafness

SSPE

- In general, patients with SSPE are ≤ 20 years and become ill 7 to 10 years after natural measles infection .
- Measles infection at an early age is a risk factor for SSPE; about half of patients with SSPE had measles before the age of two years . $M > F$
- the age of onset ranges from < 1 yr to < 30 yr, the illness is primarily one of children and adolescents.
- . The risk of SSPE after measles immunization is thought to be lower than after natural measles infection; according to the United States Centers for Disease Control and Prevention, the risk of SSPE following vaccination is $\leq 1/12$ the risk of SSPE following infection

SSPE STAGE

- Stage I – Stage I consists of insidious development of neurologic symptoms such as personality changes, lethargy, difficulty in school, and strange behavior. Stage I may last from weeks to years.
- Stage II – Stage II is characterized by **myoclonus**, worsening dementia, and long-tract motor or sensory disease. The patient eventually develops a highly characteristic form of myoclonus in which massive myoclonic jerks occur approximately every 5 to 10 seconds. **Stage II usually lasts 3 to 12 months.**
- Stages III and IV – Stages III and IV are characterized by further neurologic deterioration with eventual **flaccidity or decorticate rigidity** and symptoms and signs of autonomic dysfunction. Myoclonus is absent.
- Stage IV is **a vegetative state**. Death usually occurs during stage IV but is possible in any of the stages

SSPE

- The serum anti-measles antibody concentration is elevated, and cerebrospinal fluid analysis shows **elevated protein concentration and detectable anti-measles antibody**
- Electroencephalogram (EEG) during stage II may demonstrate bursts of high-voltage complexes (300 to 1500 microvolts) of two- to three-per-second delta waves (slow waves) and sharp waves. These complexes **last 0.5 to 3 seconds and occur every 3 to 20 seconds**
- These EEG findings are characteristic of SSPE and may be pathognomonic

SSPE

- The diagnosis of SSPE can be established through documentation of a compatible clinical course and at least 1 of the following supporting findings:
- (1) measles antibody detected in cerebrospinal fluid,
- (2) characteristic electroencephalographic findings
- (3) typical histologic findings in and/or isolation of virus or viral antigen from brain tissue obtained by biopsy or postmortem examination.



SSPE

- Clinical trials using **isoprinosine** with or without interferon suggest significant benefit (30–34% remission rate)
- **carbamazepine** is of significant benefit in the control of myoclonic jerks in the early stages of the illness.

SSPE

- Virtually all patients eventually succumb to SSPE. Most die within 1-3 yr of onset from infection or loss of autonomic control mechanisms.
- Prevention of SSPE depends on prevention of primary measles infection through vaccination.
- SSPE has been described in patients who have no history of measles infection and exposure only to the vaccine virus. However, wild-type virus, not vaccine virus, has been found in brain tissue of at least some of these patients,

suggesting that they had had subclinical measles previously.

DIFFERENTIAL DIAGNOSIS

- Rubella, adenovirus infection, enterovirus infection, and Epstein-Barr virus infection.
- Exanthem subitum (in infants) and erythema infectiosum (in older children).
- *Mycoplasma pneumoniae* and group A streptococcus
- . Kawasaki syndrome can cause many of the same findings as measles but lacks discrete intraoral lesions (Koplik spots) and a severe prodromal cough and typically leads to elevations of neutrophils and acute-phase reactants. In addition, the characteristic thrombocytosis of Kawasaki syndrome is absent in measles
- Drug eruptions may occasionally be mistaken for measles

DIAGNOSIS

- •Serologic confirmation is most conveniently made by detection of IgM in serum.
- • IgM appears 1-2 days after the onset of the rash and remains detectable for 1 mo.
- • If a serum IgM < 72 hr after onset of rash is negative, a second specimen should be obtained.
- •A 4-fold rise in IgG in acute and convalescent serum.
- •RT-PCR Molecular detection by polymerase chain reaction
- Viral isolation from blood, urine, or respiratory secretions can be accomplished by culture

TREATMENT

- •Management of measles is supportive.
- •Maintenance of hydration and oxygenation.
- •Antipyretics and vitamin A are indicated.
- •Airway humidification for patients with respiratory symptom specially croup is useful.
- •There is no specific antiviral therapy for measles.
- •Ribavirin

VITAMIN A THERAPY

- •Is indicated for all patients with measles once daily for 2 days at doses of :
- •200,000 IU for children ≥ 12 mo of age
- •100,000 IU for infants 6 mo -11 mo of age
- •50,000 IU for infants < 6 mo of age
- •In children with signs and symptoms of vitamin A deficiency, a 3rd dose is recommended 2 - 4 wk after the 2nd dose.

MMR VACCINE

- All children should get the MMR vaccine when they are 12 to 15 months old. Then they need a second shot when they are 4 to 6 years old.
- Some babies and children need to get the vaccine earlier than usual, if they:
 - Live in an area where there is a measles outbreak
 - Need to travel to an area where there is a measles outbreak



MMR ADDITIONAL DOSE

- For children who have not received 2 doses by 11-12 yr of age, a 2nd dose should be provided.
- Infants who receive a dose before 12 mo of age should be given 2 additional doses at 12-15 mo and 4-6 yr of age.
- Children who are traveling should be offered either primary measles immunization even as young as 6 mo or a 2nd dose even if <4 yr.



MMR

- Some older children and adults also need the MMR vaccine, such as:
- •Hospital or health care workers
- •Students who don't have written proof of 2 shots
- •People traveling outside the United States who don't have written proof of 1 shot

POSTEXPOSURE PROPHYLAXIS

- . The vaccine is effective in prevention or modification of measles if given within 72 hr of exposure. Ig may be given up to 6 days after exposure to prevent or modify infection.
- Immunocompetent children should receive 0.5 mL/kg (maximum dose in both cases is 15 mL/kg) intramuscularly (IM)
- . For severely immunocompromised children and pregnant woman without evidence of measles immunity, Ig intravenously is the recommended IG at 400 mg/kg.
- Ig is indicated for susceptible household contacts of measles patients, especially infants younger than 6 mo of age, pregnant women, and immunocompromised persons.

با تشکر
از توجه
شما



