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Measles

- Measles is a highly contagious viral illness that occurs worldwide.
- The infection is characterized by fever, malaise, cough, coryza, and conjunctivitis, followed by exanthem.
- Following exposure, approximately 90 percent of susceptible individuals 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.
- Patients being evaluated for measles should be isolated.

- **Stages of infection**
- Classic measles infection in immunocompetent patients consists of the following clinical stages: incubation, prodrome, exanthem, and recovery.
- 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. 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 day 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 two weeks after measles. The occurrence of fever beyond the third to fourth day of rash suggests a measles-associated complication

Clinical variants

- Clinical variants include modified measles and atypical measles.

- 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.
- **Diagnosis** :

- The diagnosis of measles should be considered in a patient presenting with a febrile rash illness and clinically compatible symptoms. The approach to diagnosis differs depending on the regional prevalence of measles.
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- In regions of low measles prevalence, cases of suspected or confirmed measles should be reported to the local health authorities, who provide guidance on specimen collection for diagnosis as well as infection control interventions.

- In general, it is useful to obtain three samples from patients with suspected measles infection: a serum sample for measles immunoglobulin (Ig)M, a throat or nasopharyngeal swab for viral culture, and a urine sample for viral culture.
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- In the setting of diagnostic uncertainty, the diagnosis may be confirmed by evaluation of paired acute and convalescent sera for anti-measles virus IgG; at least fourfold increase in anti-measles antibody titer is indicative of infection.

- In countries with high measles prevalence, the World Health Organization uses serum IgM as the standard test to confirm the diagnosis of measles.

- However, the anti-measles IgM assay should be interpreted with caution as false-positive and false-negative results have been reported.

- **DIFFERENTIAL DIAGNOSIS**

- The differential diagnosis of measles depends on the clinical stage.
- Dengue fever may be mistaken for measles during the prodromal period or after the appearance of exanthem and should be considered in the setting of relevant epidemiologic exposure. Dengue may be diagnosed via serologic testing.

- During the prodromal period, the differential diagnosis includes:
- Common respiratory viruses of childhood – These include rhinoviruses, parainfluenza, influenza, adenovirus, and respiratory syncytial virus infections.
- Fever due to measles infection is typically more pronounced than fever due to other respiratory viruses; these may be distinguished via nasal swab for polymerase chain reaction .

- Fordyce spots – Koplik spots can be mistaken for Fordyce spots (tiny yellow-white granules sometimes found on the buccal or lip mucosa resulting from benign ectopic sebaceous glands.

- Unlike Koplik spots, Fordyce spots do not occur on an erythematous mucosal background .

- Once an exanthem has appeared, the differential diagnosis includes :

- Viral causes of rash in children

- varicella, roseola (human herpesvirus 6 infection), erythema infectiosum (parvovirus B19 infection), enterovirus (hand-foot-and-mouth disease), and rubella.
- Measles can usually be distinguished clinically by the characteristic progression of the rash, its subsequent brownish coloration, blanching on pressure, and other clinical manifestations (especially coryza and conjunctivitis) .

- Group A *Streptococcus* infection – Manifestations of group A *Streptococcus* (GAS) that resemble measles include scarlet fever and toxic shock syndrome.
- Scarlet fever is diagnosed based on clinical manifestations including rash (coarse, sandpaper-like, erythematous, blanching) in association with pharyngitis.
- Toxic shock syndrome is based on isolation of GAS from a normally sterile site (or for a probable case, if GAS is isolated from a nonsterile site), together with hypotension and organ system dysfunction.

- Drug eruption – An exanthematous drug eruption can resemble the rash associated with measles; it may be distinguished based on history of recent drug exposure and resolution of the rash after drug withdrawal.

- Meningococcemia – Clinical manifestations of meningococcemia may include petechial rash in association with fever, nausea, vomiting, headache, altered mental status, and hemodynamic instability. The diagnosis is established via culture.

- Rocky Mountain spotted fever – Clinical manifestations of Rocky Mountain spotted fever include fever, headache, and maculopapular rash in the setting of tick exposure.
- The rash typically begins on the extremities and subsequently spreads to the trunk. The diagnosis is established via serology or skin biopsy.

- Infectious mononucleosis

- Typical features of infectious mononucleosis include fever, pharyngitis, adenopathy, and fatigue. A generalized rash (maculopapular, urticarial, or petechial) is occasionally seen; a maculopapular rash often occurs following administration of certain antibiotics.

- *Mycoplasma pneumoniae*

- Clinical manifestations of *M. pneumoniae* infection include respiratory tract infection, which may occur in association with a mild erythematous maculopapular or vesicular rash. The diagnosis can be difficult to establish and most treatment is empiric.

- Immunoglobulin A vasculitis (IgAV ; Henoch-Schönlein purpura [HSP])

- Clinical manifestations of IgAV (HSP) include palpable purpura, arthritis, abdominal pain, and renal disease. The diagnosis is based on clinical manifestations and/or biopsy.

- Kawasaki disease

- Clinical manifestations of Kawasaki disease include fever and mucocutaneous involvement including conjunctivitis, erythema of the lips and oral mucosa, rash, and cervical lymphadenopathy. The diagnosis is based on clinical criteria .

Complications

- Complications of measles include secondary infections such as diarrhea and pneumonia.
- Complications of measles among immunocompromised individuals include giant cell pneumonia and measles inclusion body encephalitis.
- Groups at increased risk for complications of measles include immunocompromised hosts, pregnant women, individuals with vitamin A deficiency or poor nutritional status, and individuals at the extremes of age.
- Neurologic syndromes following measles virus infection include acute disseminated encephalomyelitis (ADEM) and subacute sclerosing panencephalitis (SSPE).
- ADEM is a demyelinating disease that presents during the recovery phase of measles infection and is thought to be caused by a postinfectious autoimmune response.
- SSPE is a progressive degenerative disease of the central nervous system that generally occurs 7 to 10 years after natural measles infection;
- Its pathogenesis may involve persistent infection with a genetic variant of measles virus within the central nervous system.

Treatment

- The treatment of measles is largely supportive; in some cases, vitamin A and/or ribavirin may be beneficial.

- Supportive care − Supportive therapy includes antipyretics, fluids, and treatment of bacterial superinfections and other complications.

- Role of vitamin A − For children with severe measles, we suggest administration of vitamin A .

- In addition, for children in resource-limited settings with measles (regardless of severity), we suggest administration of vitamin A .
- Dosing of vitamin A consists of oral administration once daily for two days, as follows :
- Infants <6 months of age − 50,000 international units
- Infants 6 to 11 months of age − 100,000 international units
- Children ≥12 months − 200,000 international units.

- For children with clinical signs and symptoms of severe vitamin A deficiency (such as xerophthalmia, keratitis, keratoconjunctivitis, corneal ulceration, or Bitot spots), a third dose of vitamin A should be administered four to six weeks later.

- Role of ribavirin − For patients <12 months with measles pneumonia, patients ≥12 months with measles pneumonia requiring ventilatory support, and immunosuppressed patients with measles, we suggest treatment with ribavirin .

PREVENTION

- **Measles, mumps, and rubella vaccination**
- Vaccination has led to interruption of measles virus transmission in the developed world and affords protection to unvaccinated individuals via herd immunity.

- To disrupt broad transmission, herd immunity must be maintained above 85 to 95 percent .

- **Infection control**
- In the inpatient setting, airborne transmission precautions are indicated for four days after the onset of rash in otherwise healthy patients and for the duration of illness in immunocompromised patients.

- Susceptible individuals should not enter the room of patients with suspected or confirmed measles.
- Exposed susceptible individuals should be excluded from work from day 5 through day 21 after exposure. If the case is confirmed, even those who were vaccinated within 72 hours should be excluded.

- In the outpatient setting, patients with febrile rash illness should be escorted to a separate waiting area or placed immediately in a private room, preferably at negative pressure relative to other patient care areas.

- Both patients and staff should wear appropriate masks/respirators (masks for patients to prevent generation of droplets, and respirators for staff to filter airborne particles, regardless of immunity status).

- If not admitted, patients should be told to remain in isolation at home through four days after rash onset.

- Measles virus can remain suspended in the air for up to two hours; therefore, the room occupied by a suspect case should not be used for two hours after the patient's departure.

Rubella

- Rubella is typically characterized by rash, fever, and lymphadenopathy, although subclinical or asymptomatic infection is common.

- The rash is usually an erythematous, discrete maculopapular exanthem that begins on the face and spreads caudally; palms and soles are spared. It usually lasts for three to eight days.

- Rubella infection during pregnancy can lead to fetal death, premature delivery, and a myriad of congenital abnormalities.

- The most common manifestations of congenital rubella syndrome are hearing loss, developmental delay, growth retardation, and cardiac and ophthalmic defects.

- Rubella is acquired through the inhalation of large particle aerosols of infectious secretions with initial infection of nasopharyngeal cells and subsequent viremia and spread to other body sites.

- Infected individuals may shed virus and are potentially contagious for one to two weeks before the infection becomes clinically apparent.

- Maternal-fetal transmission occurs via hematogenous spread and varies with gestational age.
- In the first trimester, fetal infection rates as high as 81 percent have been observed, dropping to 25 percent in the late second trimester and increasing again in the third trimester from 35 percent at 27 to 30 weeks to nearly 100 percent for fetuses exposed beyond 36 weeks.
- **Prenatal diagnosis,** reverse transcription-nested PCR assay has been used in small studies where it detects rubella virus in chorionic villous samples (CVS) and amniotic fluid samples of affected pregnancies.
- Vaccination prior to pregnancy is the primary strategy to prevent rubella during pregnancy

- Rubella-specific immunoglobulin (Ig)M serology as the initial diagnostic test due to its availability and low cost.

- Real-time reverse transcriptase-polymerase chain reaction is an alternative diagnostic modality that can be detected from a throat swab, nasal swab, or urine specimen when false-negative or false-positive IgM results are of concern.

- Differential diagnosis includes scarlet fever, parvovirus B19, roseola (human herpes virus 6 and 7-associated disease), rash-associated enteroviral infections, infectious mononucleosis, measles, toxoplasmosis, as well as noninfectious skin diseases and drug reactions.

- Management of infected individuals consists of supportive care. No specific therapy exists for rubella.

- Individuals with postnatal rubella should remain in isolation for seven days after the onset of the rash.

- Hospitalized or institutionalized patients should be placed on droplet precautions and only individuals who are known to be immune to rubella virus should care for infected individuals.

Postexposure management

- For individuals exposed to rubella, management depends on immune status.

- No precautions are necessary if the person is immune.

- For nonimmune individuals, isolation from infected individuals is recommended for seven days after onset of rash in the infected individual.
- In cases of an outbreak, avoidance of the outbreak setting is recommended for 23 days after the onset of rash in the last reported case.

- Specifically, Ig is not routinely recommended for postexposure prophylaxis.

- Although some evidence suggests that intramuscular or intravenous Ig may reduce the risk of clinically evident rubella after exposure , it has not been demonstrated to prevent asymptomatic infection, viremia, or CRS.

- Cases of CRS have been identified in infants of individuals who received Ig shortly following an exposure during pregnancy .

- Furthermore, Ig administration makes the subsequent diagnosis of rubella more challenging; since virus-specific IgG seroconversion would reflect receipt of exogenous Ig, the diagnosis would have to rely only on virus-specific IgM testing, which may be associated with false-positive results.