Measles (Rubeola)

One of the most infectious childhood diseases known. Humans are the natural host. Caused by measles v. typical paramyxovirus; envelope spikes containing H+ Fusion protein (hemolysins) with no neuramindase activity.

In culture, produces characteristic intranuclear inclusion bodies and syncytial giant cells.

One serotype, protection after infection is lifelong.

Measles cases occur throughout the year in temperate climate. Epidemics tend to occur in late winter and early spring.

Transmission:

Measles virus transmitted through respiratory droplets but this virus can also infect via the eye and multiply in the conjunctivae. Viremia following primary local multiplication results in widespread distribution to many organs. Hematogenous transplacental transmission when occur during pregnancy.

Pathogenesis & Immunity:

Virus infects URT cell lining where it multiplies locally, the infection then spreads to the regional lymphoid tissues &then multiply there (primary Viremia).

Secondary Viremia seeds the epithelial surfaces of the body including skin, respiratory tract, conjunctiva where focal replication occurs. Virus replicates in certain lymphocytes which aid in dissemination throughout the body.

Skin rash: due to *cytotoxic T cells attacking the measles virus-infected vascular endothelial cells in the skin

**Antibody-mediated vasculitis( so that specific antibodies coincide with appearance of rash)

Virus shedding from infected person start 4 days prior to and 4 days after the appearance of rash.

Both neutralizing antibodies- IgG & cell mediated Immunity are involved during viremic stage of measles.

Clinical findings:

1- **Incubation period:** 8-12 days may lasts up to 3 wks in adults.
2- **Prodromal phase:** last for (2-4 days) this phase is characterized by high grade fever, running nose, dry cough, sore throat, conjunctivitis (virus may be excreted during this phase) in tears, nasal secretions, urine and blood.
3- **Koplik’s spots** - raised bright red macules or ulcer with white centers on the buccal mucosa opposite the lower molar (It’s a valuable diagnostic sign) and it appears 2 days before the rash.

4- **Eruption phase**: (last for 5-8 days) a characteristic light pink, discrete maculopapules that coalesce to form blotches, rash appear on face to the chest, the trunk and then proceeds gradually down the limbs. Rash become brownish in 5-10 days.

The disease is more extensive in this stage with generalized virus infection in lymphoid tissues and skin, it’s more severe in malnourished children, AIDS & TB.

Modified Measles: occur in partially immune persons, such as infant with residual maternal antibodies. I.P is prolonged, diminished prodromal symptoms, koplik’s spots are usually absent and rash is mild.

**Complications**

1- **bronchopneumonia** (giant cell pneumonia, croup & bronchitis)

2- **Otitis media** (with or without secondary bacterial infections)

3- **Conjunctivitis** and corneal ulcer

4- **Encephalitis** ~ 1:1000 cases, 10% mortality rate, 40% with permanent sequelae (deafness & MR)

5- **Subacute sclerosing pan encephalitis (SSPE)** a rare late and fatal complication of measles with incidence of about 1:300,000 cases occurs several years after measles, slow viral (conventional) infection in which the virus multiplies in the brain, resulting in neurodegenerative disease. It’s usually fatal within 1-3 years after onset.

There are a large amount of viral Ag within the inclusion bodies in infected brain cells, there is no mature v. particle (v. lacks M protein). This is because the immune response unable to deal with this viral infection due to immune modulation of the expressed viral Ag on cell surface; or due to presence of defective virus particles. Patient with SSPE exhibit high titers of measles Ab in CSF & serum with titer 10-100 fold higher than those seen in typical convalescent sera.

6- **progressive measles inclusion body encephalitis**.

7- **Measles in pregnant** women resulting in stillbirth
8-Atypical measles following taken a killed vaccine, Occurs only in adult; infrequent

**Characteristics of Measles**

1. The virus is spread by breathing in virus-containing droplets or by touching contaminated surfaces.
2. The virus grows in cells in the back of the throat and lungs. Symptoms appear after 10 to 12 days.
3. Infected person has a fever lasting two to four days, followed by a cough, runny nose and red, watery eyes.
4. A rash, lasting five to six days, appears about the face and head, spreading through the torso to the hands and feet.
5. The virus can be transmitted from four days prior to and four days after the appearance of the rash.

*Sources: Centers for Disease Control World Health Organization*

---

**Diagnosis:**

1. Clinical
2. Lab. Diagnosis:

   a. Specimens: nasopharyngeal swab or washing, blood, conjunctival secretions, urine.
   b. Cell culture isolation: Monkey or human kidney cells

   CPE: multinucleated giant cells, intranuclear or intracytoplasmic inclusion bodies.

   Identification: IF or hemadsorption

   c. Serology: ELISA, HI and NT. IgM (appear 1-2 wks after the onset of rash = recent infection) and IgG (4 fold rise in ab titer between acute and convalescent phase indicate acute infection)

   d. Ag and nucleic acid detection; detection of viral RNA by using RT-PCR.

**Treatment & Prevention**
No antiviral drug, only supportive treatment; the use of vitamin A is useful to prevent blindness due to measles.

**Live attenuated vaccine**, Trivalent live attenuated vaccine (MMR) usually given to 15 months of age

**Killed vaccines** should not be used

**Human Immunoglobulin** given to modify the disease if given early in incubation period to unimmunized pt., neonates and pregnant women.

**Ribavirin**; measles is susceptible in vitro to this drug with not proved clinical benefit.

**Genus Henipavirus(zoonotic paramyxoviruses)**

Two zoonotic paramyxoviruses were recognized in late 1990s with disease out breaks in Australasia. Both are of public health concern because their high mortality, wide host range &ability to jump species barrier and classified as Biosafety level 4 pathogen. Animal reservoir is the fruit bat (flying fox).

1-**Nipah virus**: an out break of severe encephalitis was recognized in 250 cases in Malaysia (1998-1999) with mortality rate more than 35%.

Few survivors had persistent neurological deficits and 10% with late onset encephalitis develop months- years after initial attack.

**Transmission of the disease**: is through direct transmission from pig to humans.

2-**Hendra virus**: equine virus cause horse fatalities and few human deaths in Australia.

   No available vaccine for both viruses.

**Rubella (German measles)**

   3 days rash

Togavirus family

Composed of one piece of ss-RNA

Icosahedral nucleocapsid

Lipoprotein envelope,H-spikes

+ve strand RNA(-ve virion polymerase)

Single antigenic type

Humans are the natural host
**Transmission**

- Respiratory droplets
- Transplacental

**Pathogenesis**

Initial replication occurs in RT.: Nasopharax & cervical LN then after 5-7 days virus spreads via bl. to internal organs & skin

Skin Rash: due to Ab-Ag mediated vasculitis

Rubella v. Infections confer Lifelong immunity

**Clinical Findings**

- **Rubella (post natal rubella)**

**I.P:** 12 days or longer

**Prodromal period:** fever & malaise at the same time **Morphilliform rash** start on the face then down to extremities (lasts 3 days)

Post auricular lymphadeopathy is characteristic

Poly arthritis (due to immune complex deposit)

**Lab. Diagnosis:**

- **Clinical** diagnosis is unreliable because many viral infections share the same clinical features.

- **Specimens:** nasopharangeal swab, throat swab 3 days after symptoms appear

- **Cell culture:** Monkey kidney or baby hamster

- **Identification:** IF or Nt

- **Serology:** specific IgM detection using ELISA, IF, HAI & CFT

  - **Congenital rubella syndrome**

Maternal Viremia associated with rubella infection during pregnancy may result in infection of the placenta and fetus.

* Teratogenic virus; 25% of infections are subclinical.

* Rubella infection of non-immune women during 1st trimester (transplacental transmission) leads to the following consequences:
1- **Fetal loss**: Abortion, intra uterine death or still birth. If **survive**, fetus might have
2- **Transient effects**: growth retardation, failure to thrive, HSM, TCP, osteitis & meningoencephalitis
3- **Permanent manifestations**: Congenital malformations from maternal viremia and fetal infection are recognized at birth or during 1st year of life; baby may born with:

   - **Heart**: patent ductus arteriosus
   - **Eye**: cataract, total or partial blindness
   - **Brain**: deafness & mental retardation

4- **Developmental abnormalities**: become obvious during childhood (pre-school-school age) & adolescence including mental retardation, psychiatric disorders & abnormal behavioral manifestations.

   Asymptomatic baby; may shed virus for many months

**Lab. Diagnosis:**

**Newborn infant**: *IgM in cord blood= CRS*

   *Isolation of v. in pharyngeal secretions & other body fluids (CSF, urine, rectal swab)*

**Pregnant**: IgM indicate recent infection

4–fold rise in ab titer between acute and convalescent-phase in HA & ELISA tests

1:8 or greater IgG titer= immunity & protection to fetus

**Treatment & Prevention**

No antiviral therapy

Live attenuated vaccine: induces respiratory IgA

- **Measles Mumps Rubella vaccine (MMR)**: given to

   - **Boys and girls** at age *13-15 months*

   - **Girls** aged 10-14 yrs.

   **4-5 years before school entry**

Non-immunized women: sero-ve, not pregnant & should be warned to not to be pregnant at least 3-months after vaccination.

Immune serum globulin (IG) = 1st trimester pregnant women, does not protect fetus but can decrease disease severity.
Termination of pregnancy if sure?!