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# Know More About Measles

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**Abstract**

Measles is a highly contagious viral disease.Measles (Rubeola) is endemic throughout the world. Measles is probably the most infectious of the common fevers. Measles is relatively the disease of humans and assumably evolved from animals morbillivirus.Phylogenetically measles virus is more closely related to rinderpest virus ,a pathogen of cattle. More than 1 million children a year die from measles.Measles is not just a little rash.Measles is a serious disease.Measles affects all age groups.One attack confers a high degree of immunity.The disease has a characteristic tendency to epidemicity every second year so that in Great Britain and North America there are "Measles years",usually commencing in the autumn which alternate with years in which a limited number of cases occur.Measles Is an ideal virus for eradication through vaccination.Measles remains a leading cause of vaccine preventable childhood mortality.

**Keywords**: Rubeola, Haemagglutinin (HA), catarrh, Koplik's spots, Real-time RT-PCR, vaccines

## Introduction

Measles, also known as rubeola, is a preventable, highly contagious, acute febrile viral illness. (1)

It is the main cause of mortality and morbidity (2)

The structural proteins are nucleoprotein, phosphoprotein, matrix, fusion, haemagglutinin (HA), and large protein. The HA protein is responsible for virus attachment to the host cell.(3)

Four days after the rash develops, progress cough, conjunctivitis, and coryza.(4)

Cellular immune responses are essential for recovery as demonstrated by elevated Th1 dependent plasma interferon-gamma levels during the acute phase, and subsequent elevation of Th2 dependent interleukin 4, interleukin 10, and interleukin 13 levels.(5)

The rash appears first on the face and spreading become generalized.(6,7) infection control measures includes isolation form the mainstay of therapy (8)

Measles complications should be identified early and initiate appropriate therapy (9)

Measles is seen in every country in the world (10)

Annual measles outbreaks typically occur in late winter (11)

Countries in which the measles vaccine is widely used have experienced a marked decrease of disease (12)

After MV infection, the recovery of immunity occurs (13)

The monocomponent is used in most African countries including Russia (14)

The combined mumps, measles, rubella (MMR) vaccine is used instead in the rest of Europe and North America (15)

**History**

Measles is a highly contagious viral illness.Disease was described by the Persian physicianRhazes in the 10th century. The first systematic description of measles, and its distinction from smallpox and chickenpox, is credited to the Persian physician Muhammad ibn Zakariya al-Razi.Enders and Peebles isolated the measles virus in human and monkey kidney tissue in 1945. Merck, Maurice Hilleman developed the first successful vaccine (16) Licensed vaccines to prevent the disease became available in 1963.(17)

**Structure**

Measles is caused by a single-stranded, enveloped RNA virus with 1 serotype. It is classified as a member of the genus Morbillivirus in the Paramyxoviridae family. Humans are the only natural hosts of measles virus..It is spherical virus.It is pleomorphic.Size 120-250nm in diameter.The MV core consists of the RNA genome and nucleocapsid proteins surrounded by a lipid envelope derived from host-cell membranes, which contains hemagglutinin (H) and fusion (F) glycoproteins.The measles virus resembles the parainfluenza and respiratory syncytial viruses.However it has no neuraminidase.

**Properties**

Measles agglutinates monkey erythrocytes at 37 degrees C.,but does not elute and interacts with a distinct cell receptor.Measles virus also causes hemolysis ,and this activity can be separated from that of the hemagglutinin.

**Animal susceptibility**

The virus can be isolated from blood or throat washings of a patient during the first 24 hours after the onset of fever.The experimental disease has been produced in monkeys.They develop fever,catarrh,Koplik's spots,and papular rash.The virus has been grown in chick embryos; in cell cultures human,monkey and dog kidney tissue;and in continuous celllines.In cell cultures,multinucleated syncytial giant cells form by fusion of mono nucleated ones and other cells become spindle shaped in course of their degeneration.Measles virus is unstable after it is released from cells.

**Symptoms**

After 2-3 days,few tiny white spots like salt grains appear in the mouth.After 1-2 days rash appears first behind ears and on the neck,and then on the face and body. The rash spreads from the head to the trunk to the lower extremities. Patients are considered to be contagious from 4 days before to 4 days after the rash appears.

**Transmission**

The virus enters into the respiratory tract.Virus infects epithelium of the nasopharynx.It grows silently for some days in lymphoid tissue, and spread between immune cells, MV takes advantage of the signaling lymphocytic activation molecule (SLAM; also known as CD150), which is expressed on alveolar macrophages and dendritic cells as well as in activated lymphocytes .

In respiratory tract secretions, the amounts of cell-free MV are low compared to other respiratory viruses.When multiplication has continued to the point when many infected cells break open,the virus floods into circulation and causes prodromal illness.

**Sequence of events**

Virus infects epithelium of the nasopharynx---------It replicates in nasopharynx and regional lymph node----------After 2-4 days primary viremia occurs, with subsequent infection of the reticulo endothelial system----------Following further viral replication in reticulo endothelial system----------After 5 -7days secondary viremia occurs, with spread to epithelial surface of skin, mouth, respiratory tract and conjunctiva ----

**Immunity**

Since one attack confers lifelong immunity.Most people suffer from measles in childhood,and a mother who has had the disease confers passive immunity on her infant for the first six months of life. Measles is very severe with a high mortality in many tropical countries. Cell mediated immunity plays a major role for recovery and



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protection. Although IgG antibody may play a role in neutralizing the virus, the role of IgA antibody is not sure. MV infection results in a short-lived immune suppression,and susceptibility to infections.(18)

The virus replicates in lymphoid tissues,like BALT and gut associated lymphoid tissues (GALT), and instigated by proliferation of lymphocytes. CD11c+ DCs and follicular DCs are present within to maintain the structure of these tissues (19,20)

The presence and interaction of CD150+ lymphocytes in these tissues consequently makes them the perfect site for MV infection and amplification (21)

BALT and GALT increase immunity against mucosal pathogens that are present in entry portals for opportunistic infections. MV infection leads to lymphopenia, in which the number of T- and B-cells, both circulating and lymphoid tissue homing, decreases extensively (22)

The infection induces the clearance of MV-infected cells by cytotoxic T-cells and subsequently a lifelong measles-specific immune response (23)

A Th1 cytokine profile, with elevations in peripheral blood gamma interferon (IFN-γ) and interleukin-2 (IL-2), is present during the measles prodrome.(24).

Innate responses are not well defined with evidence primarily of inflammasome (IL-1β, IL-18) and NF-κB (IL-6), rather than type I IFN pathway activation, but these responses do not prevent virus replication and dissemination (25)

Clearance is dependent on the adaptive immune response. The maculopapular rash that appears 10–14 days after infection is a manifestation of the cellular immune response to infection with lymphocyte infiltration into sites of virus replication in skin epithelial cells (26)

Although antibody is likely to contribute, MeV-specific T cell responses are required for virus clearance (27,28)

**Pathogenesis**

Measles commences in much the same way as a common cold.There is an acute febrile onset,with a nasal catarrh,Dry cough,runny nose,body pains,headache,sore throat,watering of mouth,discomfort,fatigue,loss of appetite,diarrhea,light sensitivity,inflammation of lymph nodes and Koplik spots.Measles is an acute viral respiratory illness. It is characterized by a prodrome of fever (as high as 105°F) and malaise, cough, coryza, and conjunctivitis a pathognomonic en anthem (Koplik spots) followed by a maculopapular rash external icon.The rash usually appears about 14 days after a person is exposed.At this stage,a diagnosis of measles may be made from the presence of Koplik's spots on the mucous membrane of mouth.There are small white spots surrounded by a narrow zone of inflammation.Though often numerous on the side of the cheeks, they may be sparse and confined to the region around the opening of the parotid duct.The disease is highly infectious during the catarrh stage and the child is miserable and irritable.

**Measles skin rash**

After 3 or 4 days,the Koplik's spots disappear and dark red macular rash develops. The rash seen first at the back of the ears and at the junction of forehead and hair.With a few hours there is invasion of the whole skin,and there is usually some accentuation of fever.As the spots rapidly become more numerous they fuse to form the characteristic blotchy appearance of measles.The face is ordinarily the most densely covered area.When the rash is fully erupted,usually 2or 3 days,it tends to deepen in colour and then fade into a faint brown stain followed by a fine desquamation of the skin.The fever subsides and rash fades.

**Complications of Measles**

Mainly due to secondary bacterial infections by Beta haemolytic streptococci otitis media

Lower respiratory tract infection - **bronchopneumonia** - very severe with high mortality

Giant cell pneumonia – a complication in children with immunodeficiency and may be due to unchecked viral replication

**Acute encephalitis**

Symptoms appear few days after the rash -Second bout of fever with drowsiness or convulsions

Survivors may show permanent mental changes - Psychosis or personality change or physical disabilities



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**Subacute sclerosing panencephalitis (SSPE) –**

It is rare and late complications of measles infection

Characterized by progressive mental deterioration, involuntary movements, muscular rigidity and coma – invariably fatal

The main complication of the eye is conjunctivitis, occasionally associated with keratitis, secondary to bacterial or viral infections (e.g., HSV or adenovirus), which rarely can lead to permanent scarring and blindness

**Laboratory diagnosis**

Measles is a recurrent health problem in both advanced and developed countries.Most cases are diagnosed clinically.In atypical cases or to differentiate it from Rubella laboratory tests are useful.

**Microscopy:**

Demonstration of multi nucleated giant cells( Warthin Finkeldey cells are found in lymphoid tissue of patients) in Giemsa stained smear of nasal secretion for early diagnosis, even before rash appears. Demonstration of virus in nasal secretion by direct immunofluorescence test.

**Culture**

**Isolation of virus-**

The virus can be isolated in cell culture from secretions of nose, throat, conjunctiva and blood during prodromal phase and upto 2 days after the rash appears.

The specimen is inoculated on primary human or monkey kidney cell culture or human amnion. Growth take one to two weeks.

Growth are characterized by multi nucleate synctium formation with acidophilic nuclear and cytoplasmic inclusions.

**CPE (cytopathic effects)**

the cytopathic effect of measles virus is characteristic formation of large multinucleate giant cells or syncytial masses in which many vacuoles give lace work appearance.After continued passage of the virus in human amnion cells ,the nature of cytopathic effects alters,and in addition to giant cells,increasing numbers of refractile stellate cells appear..Variation of the constituents of the culture medium may modify the cytopathic lesions.With glutamine deficiency,for example more giant cells are formed,but when the glutamine is restored the number of giant cells is diminished,the appearance of cytopathic effect is delayed.The most constant feature of cells infected with measles virus is the late appearance of Cowdry type A eosinophilic intranuclear inclusions.Subsequently,the virus may be propagated in primary human amnion orHEp2 cells with greater yields.

**Serological tests**

ELISA for detection of IgM in a single specimen of serum drawn between the 1 and 2 weeks after the onset of rash is confirmatory. Serum antibodies appear a few days after the onset of rash,reach a peak about 10 days later and decline slowly there after,but a detectable level remains indefinitely.Antibodies are most conveniently estimated by the complement fixation method but neutralization and haemagglutination-inhibition techniques may also be employed.

A real-time reverse transcription-PCR (RT-PCR) method specific for genotype A measles virus (MeV) (MeVA RT-quantitative PCR [RT-qPCR]) that can identify measles vaccine strains rapidly, and without the need for sequencing to determine the genotype was developed.The new assay was able to detect RNA from five currently used vaccine strains, AIK-C, CAM-70, EdmonstonZagreb, Moraten, and Shanghai-191. The MeVA RT-qPCR assay has been used successfully for measles surveillance in reference laboratories, and it could be readily deployed to national and subnational laboratories on a wide scale (29)

**Treatment**

Vitamin A should be administered immediately on diagnosis and repeated the next day.Measles is so infectious and susceptibility to it so high that there is no point in isolating cases to control the spread of the infection in the population.Hospital patients with measles ,however should be isolated to protect them from the risk of crosws-infection from patient ill with other disease.The patient should be isolated if possible and excluded from school for ten days from the appearence of rash.Most cases of measles ,inspite of high temperature,remains uncomplicated,and



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antibiotics should be prescribed only for unequivocal bacterial complications.

**Vaccination**

The vaccine protects against three diseases: measles, mumps, and rubella. CDC recommends children get two doses of MMR vaccine, Measles vaccine is extremely stable between −70°C and −20°C. Live measles vaccine has been administered successfully in combination or in conjunction with a variety of immunizing agents, such as yellow fever vaccine, poliovirus vaccine, diphtheria and tetanus toxoids and whole-cell pertussis vaccine (DTP), meningococcal vaccine, hepatitis B vaccine, and smallpox vaccine.

First dose of MMR vaccine should be given on or after the first birthday.

Second dose of MMR vaccine should be given routinely at age 4 through 6 years.

Contra indicated in pregnant and immunocompromised individuals

Vaccination in childhood with a live attenuated virus gives immunity that should be boosted at 4-6 years of age.

**Prognosis**

Most persons with measles recover and develop long term protective immunity to reinfection. Measles case fatality proportions vary with the average age of infection, the nutrition and immunological status of population, measles vaccine coverage and access to health care. Among previously vaccinated persons who do become infected, disease is less severe and mortality rates are significantly lower. The number of measles cases declined in European Union/European Economic Area countries and the United Kingdom in 2020.

**Prophylaxis**

Measles is so infectious and susceptibility to it so high that there is no point in isolating cases to control the spread of the infection in the population. Hospital patients with measles, however, should be isolated to protect them from the risk of cross-infection from patients ill with other disease.

**Control**

Community outbreaks of measles often inundate hospitals with cases. These cases may lead to nosocomial outbreaks if hospitals are not prepared to admit measles patients under airborne isolation precautions or if healthcare workers are unvaccinated.Measles has caused a high number of fatalities. Measles virus (MV) eradication is biologically, and operationally possible. Live attenuated measles virus vaccine effectively prevents measles. Prior to introduction of vaccine,500,000 cases of measles occurred annually in USA and over 300 developed encephalitis. Following, mass immunization the number greatly declined. The measles virus usually spreads when someone comes into contact with droplets from another person that contains the virus. A case of measles without complications usually lasts about 14 days and most people make a full recover. Antibodies are made by the immune system to protect against an infection. An immunization is the best protection against measles. A person who receives the recommended two doses of a measles vaccine has 99 per cent immunity against measles infection**.**

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