

Measles (Rubeola)

Disease Agent:

- Measles Virus (MV)

Disease Agent Characteristics:

- Family: *Paramyxoviridae*; Genus: *Morbillivirus*
- Closely related to canine distemper virus and rinderpest virus
- Morphology: enveloped, pleomorphic spheres 100-300 nm diameter. Virions have an inner helical nucleocapsid that is a coiled helix of protein and RNA. Envelope has hemagglutinin and fusion glycoprotein spikes.
- Nucleic acid: nonsegmented, single-stranded, negative-sense RNA virus. The 15.9-kb genome encodes at least eight structural proteins.
- Easily destroyed by light, high temperatures, UV radiation or disinfectants; persists for up to 2 hours outside the body depending on temperature and humidity.
- Strains can be differentiated by genome sequence to distinguish vaccine from wild-type virus and to evaluate the origin of imported cases.

Disease Name:

- Measles, rubeola, hard measles

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical
- Public perception and/or regulatory concern regarding blood safety: Absent
- Public concern regarding disease agent: Absent in nonendemic areas; high in endemic areas and during epidemics

Background:

- Measles is an acute infection caused by the measles virus that is among the most contagious of human pathogens. It usually infects children. Up to 90% of exposed susceptible individuals will develop disease. Infection confers lifelong immunity.
- Endemic measles was largely eliminated from the US in the decades following the introduction of live, attenuated vaccine in 1963, but cases imported from outside the US continue to be identified and small outbreaks resulting from imported index cases can occur, particularly where there are concentrations of unimmunized individuals.
 - Infants <12 months and persons with certain immune deficiency states respond poorly to immunization, and are at high risk for measles complications if infected. They are dependent on high population measles, mumps, rubella vaccine (MMR) coverage (>90%) for protection due to herd immunity, under which condition epidemic spread is not sustained.

- Measles containment has become a growing problem in the US due to the lack of familiarity of most physicians with clinical measles. This results in failure to suspect and recognize the disease and immediately implement stringent control measures. This is especially important in health care settings where individuals at high risk for measles complications congregate.

Common Human Exposure Routes:

- Airborne by droplet spread, direct contact with nasal or throat secretions of infected persons.
 - Less common by contact with articles freshly soiled by nose and throat secretions since the virus can persist in the environment for about 2 hours.
 - Infectious droplet nuclei (respiratory secretions plus virion) remain suspended in the air for several hours, especially in low relative humidity.
 - The virus is present in respiratory secretions from about 4 days before until 4 days after the onset of the measles skin rash.

Likelihood of Secondary Transmission:

- Clinical attack rates are approximately 90% among susceptible exposed persons.
- If immunization rates are maintained at or above 95%, sustained community outbreaks are largely prevented by herd immunity.

At-Risk Populations:

- In the US, persons born after 1956 who have no reliable history of measles, and who have not received the recommended 2-dose vaccine regimen are considered susceptible.
- People born in 1956 and before in the US are generally considered to have had measles.

Vectors and Reservoir Involved:

- Humans are the only natural host.

Blood Phase:

- There is a primary cell-associated viremia arising from amplification of MV in regional lymph nodes of the respiratory tract 2-3 days after infection and before the onset of symptoms that seeds distant tissues. This is followed in 5-7 days by secondary viremia.
- The secondary viremia is associated with the rather nonspecific prodromal symptoms (i.e., preceding the rash), peaks at the onset of the classic rash, and persists for a week or longer after the rash.
- The primary cell involved in cell-associated viremia appears to be the monocyte, but could include other cell types.

Survival/Persistence in Blood Products:

- Unknown

Transmission by Blood Transfusion:

- Has not been described; however, the existence of cell-associated viremia and the detection of viral RNA by RT-PCR raises a theoretical concern.

Cases/Frequency in Population:

- During 2001-2008 there were a median of 56 cases (37-140) in the US. This is the highest number for this period since 1996.
- Increases of measles incidence in areas frequently visited by US residents and from which travel is increasingly common have raised concern that the potential for the introduction of measles to the US is rising.
 - In the first 19 weeks of 2011, 118 cases were reported, of which 105 (89%) were associated with 46 importations from other countries: 34 involved US residents travelling abroad and 12 were related to foreign visitors to the US. Of the 118 cases, 47 resulted in hospitalization.
 - The most frequent sources of importation were countries in the WHO European Region and the South-East Asia Region. France, the source of most of the European importations, had reported approximately 10,000 cases during the first 4 months of 2011.
 - Unvaccinated persons accounted for 105/118 cases (89%).
 - The largest of the 9 US outbreaks in 2011 involved 21 persons in a population refusing vaccination because of concerns about safety of the MMR vaccine; concerns about vaccine safety have not been confirmed.
- If increasing numbers of children remain unvaccinated, and if immunocompromised persons accumulate in the population who cannot be vaccinated, the population of susceptibles may increase and more sustained outbreaks than have been seen in recent years will be possible.

Incubation Period:

- Average is 10 days, with a range of 7-18 days from exposure to onset of fever. It is usually 14 days until rash appears; rarely, as long as 19-21 days. Immune serum globulin, used for postexposure prophylaxis when exposure of a susceptible individual is recognized, may prolong the incubation period.

Likelihood of Clinical Disease:

- Asymptomatic primary infection is very unusual.
- Infections are more severe in infants, the immunocompromised (including those with HIV infection), adults and the elderly.

Primary Disease Symptoms:

- Prodromal fever, conjunctivitis, coryza, cough, and small spots with pale centers on an erythematous base on the buccal mucosa (Koplik spots).

- A characteristic red, blotchy rash appears on the third to seventh day; the rash begins on the face, then becomes generalized, lasts 4-7 days, and sometimes ends in brawny desquamation.
- Complications may result from viral replication or bacterial superinfection, and include otitis media, pneumonia, laryngotracheobronchitis (croup), diarrhea, and encephalitis.

Severity of Clinical Disease:

- The disease is more severe in infants and adults than in children, and in those with compromised immunity.
- The severe complications are encephalitis and pneumonia.
- In approximately 1/10,000 individuals who recover from measles infections, subacute sclerosing panencephalitis (SSPE) develops an average of 7 years later; in >50% of SSPE cases, measles was diagnosed at ≤ 2 years of age. SSPE is a chronic, lethal, neurodegenerative illness.

Mortality:

- During a resurgence of measles during 1989-91 in the US, more than 100 deaths were reported from over 55,000 recognized cases.
- In the developing world, mortality rates of 3-5% and higher are seen.

Chronic Carriage:

- May be present in the brains of SSPE patients, where non-productive infection with mutated MV may be central to the pathogenesis.

Treatment Available/Efficacious:

- Supportive treatment only

Agent-Specific Screening Question(s):

- No specific question is in use.
- Not indicated because transfusion transmission has not been demonstrated.
- No sensitive or specific question is feasible given that the primary viremia of greatest interest occurs before the onset of symptoms.
- During focal outbreaks, exclusion of unimmunized donors with no reliable history of measles who have had potential exposure may be feasible.

Laboratory Test(s) available:

- No FDA licensed blood donor screening test exists.
- Serological assays, especially EIA, for IgM and IgG are the mainstays for diagnosis when there is clinical suspicion of measles and during outbreaks. IgM antibodies generally appear within about 3 days of the rash and persist for at least 4 weeks.
- RT-PCR of respiratory secretions is used routinely for diagnostic purposes.
- Virus isolation in clinical cases is encouraged to provide samples for genotyping.

Currently Recommended Donor Deferral Period:

- No FDA Guidance or AABB Standard exists.
- In outbreak settings, prudent practice would be deferral of exposed potential donors for a period exceeding the longest incubation period for the infection, which would be >21 days from last exposure.
- Recipients of MMR vaccine are currently deferred for 14 days after immunization.
- Recipients of prophylactic immune serum globulin should be deferred for at least six months which will allow clearance of passively acquired antibodies (i.e., anti-HBc) that might be detected in required blood donor screening tests.

Impact on Blood Availability:

- Agent-specific screening question(s); Not applicable
- Laboratory test(s) available: Not applicable

Impact on Blood Safety:

- Agent-specific screening question(s); Not applicable
- Laboratory test(s) available: Not applicable

Leukoreduction Efficacy:

- Unknown

Pathogen Reduction Efficacy for Plasma Derivatives:

- Multiple pathogen reduction steps used in the fractionation process have been shown to be robust in removal of enveloped viruses.

Other Prevention Measures:

- Age appropriate immunization using licensed vaccines
 - Blood collection facilities may want to consider the implementation of requirements for mandatory dem-

onstration of measles immunity or vaccination similar to those in hospitals if the incidence of importations and small outbreaks increases.

- Appropriate isolation of cases and contacts
- Vaccine administered within 72 hours of exposure of susceptibles may prevent or modify illness.
- Immune serum globulin given within 6 days of exposure may prevent or modify illness.

Suggested Reading:

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