Measles (Rubeola) Disease Report
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Etiological Agent
- **Measles Virus**: Measles virus (MeV) is a member of the genus *Morbillivirus* of the family *Paramyxoviridae*. (1)

Transmission
- **Direct Contact / Airborne**: Measles is well known as a contagious, infectious disease; 90% of susceptible persons with close contact to a measles patient typically develop measles infection. The virus is transmitted by direct contact with infectious droplets but can also infect via non direct contact. MeV can also be spread through the air when an infected person breathes, coughs, or sneezes. Airborne, the measles virus is capable of infection for up to two hours after an infected person exits the area. (2)

Reservoirs
- **Humans**: Measles is a human disease. There is no known animal reservoir. (3)

Microorganism General Characteristics
- **Single stranded RNA virus**: “Measles virus is a negative-sense, single stranded RNA virus. It consists of a helical nucleocapsid, 100-300 nm in diameter, surrounded by an envelope. The envelope is lined by matrix proteins and carries transmembrane hemagglutinin and fusion glycoproteins which are the virulence factors.” (4)

Identification Key Tests
- **Laboratory Confirmation**: Measles-specific IgM antibody and measles RNA detection by real-time polymerase chain reaction (RT-PCR) are typical methods used to confirm measles infection. In suspected patients, serum samples and throat swab (or nasopharyngeal swab) should be collected at first contact. (2)
- The CDC uses assays in their reference lab specific for measles serologic testing of IgM and IgG. The assays use a recombinant measles nucleoprotein (NP) antigen in the EIA (enzyme immunoassay). (5)
- Urine samples may also detect the measles virus. (2)
- Molecular Analysis can also be completed. Genotyping is used to map the transmission pathways of measles viruses. The genetic data can help to link or unlink cases and can suggest a source for imported cases. “Genotyping is the only way to distinguish between wild-type measles virus infection and a rash caused by a recent measles vaccination.” (2)
- Occasionally false positive IgM results are produced. No assay is 100% specific. When warranted, the CDC provides additional serological testing to aid in confirmation of diagnosis. (5)

Signs and Symptoms of Disease
- Prodromal fever. Can be as high as 105° Fahrenheit. (1)
- Cough. (6) (1)
- Coryza (runny nose). (1)
- Conjunctivitis (red eyes). (6)
- Sore throat. (1)
- Red or reddish brown rash. (7) (8)
- Koplik spots. (7) (8)
- 1 to 2 days prior to the rash development, Koplik spots may appear. They are typically white in color and a sand type appearance. The spots can be found in the lining of the cheeks, roof of mouth and inside the lips. (9)
- 3 to 5 days following symptoms, a rash typically develops. Flat red spots alone or with small raised bumps on top become visible on the face at the hairline and spread downward towards the feet. The spots may spread and join together. In addition, when the rash appears, a person’s fever can rise to more than 104° Fahrenheit. After a few days, the rash will fade once the fever subsides. (8)

Historical Information
• **900 CE**: A Persian physician described smallpox and measles in a written publication trying to differentiate between the two diseases. (10)
• **1657-1757**: During this period, measles is noted to make an appearance in colonies of the U.S with deaths reported. (10)
• **1757**: A Scottish physician showed measles can be caused by an infectious agent in the blood of humans. (11)
• **1861**: The Civil War saw its fair share of measles outbreaks and secondary infections resulting in casualties on both sides of the war. (10)
• **1912**: Measles (if contracted in the US) must now be reported by healthcare providers and laboratories. (11)
• **1920**: Per MMWR (Morbidity and Mortality Weekly Report) this year 469,924 measles cases were reported, and 7575 patients died. (13)
• **1954**: John Enders and Dr Thomas Peebles were successful in isolating measles virus from an infected thirteen year old patient named David Edmonston. (11)
• **1958-1962**: 503,282 measles cases and 432 measles-associated deaths were reported on average over this five year period. (13)
• **1963**: “Edmonston-B strain” of the Measles virus is developed by John Enders and team to become a vaccine and is licensed within the United States. (11)
• **1968**: Maurice Hilleman PhD and his team develop and improve the current measles vaccine by making a weaker, more attenuated strain renamed “Moraten”. This vaccine was widely distributed and continues to be the only measles vaccine used within the United States since 1968. (11)
• **1971**: First MMR (Measles Mumps Rubella) combination trivalent vaccine is licensed in the US. (10)
• **1978**: Center for Disease Control declares goals to eliminate measles in the US by 1982. (11)
• **1981**: Reported US measles cases were not eliminated completely, but greatly reduced (80%) compared to 1980. Vaccine coverage is credited for this achievement. (11)
• **1986**: NCVIA (National Childhood Vaccine Injury Act) is passed by US Congress to address growing public concerns of adverse reactions following vaccine administration. NVICP (National Vaccine Injury Compensation Program) was also included in the NCVIA to allow compensation to individuals for table injury and non- table injury claims. Measles (MMR), Mumps (MMR, MR, M) is listed as a compensable vaccine. (14) (15)
• **1988**: Measles, mumps, rubella or any of its components are listed on the Vaccine Injury Table with illness, injury, disability, and conditions covered including death. The timeframe in which the symptom, significant aggravation, or manifestation of onset may occur is also established. (16)
• **1989**: “Measles outbreaks among vaccinated school-aged children prompted the Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAP) to recommend a second dose of MMR vaccine for all children. Following widespread implementation of this recommendation and improvements in first-dose MMR vaccine coverage, reported measles cases declined further.” (11)
• **2000**: Measles confirmed “eliminated” per the US. No cases reported within one year. (11)
• **2005**: MMRV (Measles, Mumps, Rubella, Varicella/ ProQuad) vaccine approved by FDA and marketed as an alternative to monovalent vaccines and MMR alone. (17)
• **2007**: WHO/UNICEF reports that efforts to achieve a reduction in measles mortality were very successful and had reduced measles mortality by 60%, from an estimated 873,000 deaths in 1999 to 345,000 deaths in 2005. (18)
• **2010**: A paper published in a journal called Virology investigated divergence times suggesting MeV possibly came from a non human species and was responsible for the infectious disease around the 11th to 12th century. (12)
• **2011-2013**: Per the CDC, collectively 464 measles cases were reported in the US. (19)
• **2014-2016**: According to the Centers for Disease Control, 2014 saw the biggest increase in multiple states of measles cases (667 confirmed) reported since the CDC declared measles eliminated in 2000 from the US. Multiple outbreaks have occurred worldwide during this time. (20)

**Virulence Factors**
- Portal of entry = Respiratory mucous membranes. (21)
- Attachment = Humagglutinin (H) protein found on the surface of the virus and Fusion (F) protein. Both interact in order to establish attachment and fusion of the viral envelope with the host cellular receptors. (M) protein is also involved in viral assembly. (21)
• MeV quickly spreads to the lymph system and enters the bloodstream where multiple organ systems can then be infected. Complications from measles virus have been reported in every organ including Respiratory, Gastrointestinal, Neurological (including Central Nervous System), and Ocular systems. The most common cause of long term sequelae is encephalitis.  

• Immune suppression occurs long enough to evade immune defenses allowing measles virus to establish itself. As the disease progresses, destruction of tissue can cause significant neutropenia and secondary bacterial infections which can also be deadly.  

• Age can affect the rate of complications and underlying conditions resulting in mild, modified and atypical MeV.

Control and Treatment

• 4 days before to 4 days after the measles rash appears patients are considered to be infectious. Once confirmed, prompt isolation is highly recommended and treatment for MeV is mainly supportive.

• Post exposure prophylaxis is available (typically best if given within 72 hours) to those exposed to MeV but cannot show immunity to measles in the form of MMR vaccination. Immunoglobulin (IG) administered via IM or IV can also be given within 6 days of exposure to select patients.

• WHO (World Health Organization) recommends supplementing Vitamin A (dosing age dependent) to help reduce complications. Also antibiotic therapies for secondary infections can help with reduction in measles associated deaths in developing countries.

• Factors that affect measles morbidity and mortality include sex, age, crowding, immunosuppression, malnutrition and Vitamin A deficiency.

Prevention and Vaccines

• Prevention of measles virus infection is possible with a measles-containing vaccine. In the United States, the Centers for Disease Control are advised by ACIP (Advisory Committee on Immunization Practices) and a recommended vaccine schedule is published annually.

• Monovalent measles vaccine is no longer available in the US and has been replaced with two combination vaccines. Currently MMR (Measles Mumps Rubella II by Merck and Co., Inc.) and quadrivalent vaccine ProQuad (Measles, Mumps, Rubella, Varicella by Merck and Co., Inc.) are recommended to prevent measles infection. Both are administered subcutaneously and are indicated for patients twelve months or older. However, certain circumstances may allow for earlier administration of the vaccine depending on the choice of combination vaccine selected and the condition of the patient.

• For prevention of measles infection, one dose of either MMR or MMRV is recommended for preschool aged children (12-15 months old) and adults not at high risk for exposure and transmission. Two doses are recommended for school age children (Kindergarten through 12 years) and adults in a high risk setting. MMRV (ProQuad) is not licensed for anyone under the age of 12 months.

Local Current Outbreaks/Cases

• In 1958 measles incidence peaked at 85,862 cases in the state of Texas. As measles vaccines were introduced, these cases dropped considerably to 99.9%. Measles exposure resulting in outbreaks in the US and Texas since 2000 have primarily occurred due to people exposed during travel to countries where measles is considered endemic.

• 2013 records indicate 27 cases of measles infection were reported statewide with a decrease in 2014 to 10 cases. No deaths have been reported since 2000 per the Texas Department of State Health Services database for Measles.

Global Current Outbreaks/Cases

• In 2015 the United States reported a large measles outbreak over multiple states that were traced back to an amusement park in California. Further investigation suggested one of the cases had recently traveled internationally and became infected with the measles virus. Detection of the measles virus was implemented immediately but identification of the source is still unknown. However, “Analysis by the Centers for Disease Control showed that the measles virus type in this outbreak (B3) was identical to the virus type that caused the large measles outbreak in the Philippines in 2014.”

• While measles cases have declined considerably in the United States, measles and deaths globally are still reported. Measles outbreaks can occur especially where gaps in vaccination programs exist. WHO (the World Health Organization) supports changes in policies and practices in order to ensure high access and coverage of life saving vaccines. In 2001 multiple organizations joined together to form the Measles and Rubella Initiative. A program credited with preventing 17.1 million measles cases.
In 2014, the Americas and Western Pacific regions saw increased numbers of reported cases due in part to large outbreaks in China, the Philippines and Viet Nam. In Angola, Ethiopia, India, the Russian Federation and Somalia large outbreaks also occurred although the overall number of cases declined in some regions. Per WHO in 2014, approximately 114, 900 people died globally from measles and the majority of the cases were children under the age of five. (26) [27]

“Despite the welcome reduction in measles deaths, this highly-infectious disease continues to take a terrible toll on the lives of children around the world,” said Dr Seth Berkley, CEO of Gavi, the Vaccine Alliance. “A coordinated approach that puts stronger routine immunization at its core will be central to getting measles under control and securing further reductions in mortality from this vaccine-preventable disease.” [27]

References


