KESANS: International Journal of Health and Science
e-ISSN: 2808-7178, p-ISSN: 2808-7380
Web: http://kesans.rifainstitute.com/index.php/kesans/index

Overview of Measles

Nian Sarawarastri
Faculty of Medicine, Tadulako University-Palu, Indonesia
niansara94@gmail.com

Article Information
Submitted: **30 November 2023**
Accepted: **04 December 2023**
Online Publish: **20 December 2023**

Abstrak
Rubeola, also known as measles, that can lead to serious complications and death and one of the world's most contagious viral diseases. Immunisation against measles started in the 1960s and has dramatically reduced the incidence of measles. The virus, which produces a distinct rash that appears within days of exposure, can spread quickly, and can produce severe complications. Treatment is mainly symptomatic, preventing and controlling dehydration, providing adequate nutrition, and infection control measures. Vaccination is the most effective way to prevent measles virus infection.
Keywords: ***Virus; Measles; Rubeola;***

How to Cite	**Nian Sarawarastri/Overview of Measles, Vol. 3, No. 3, 2023**
DOI	https://doi.org/10.54543/kesans.v3i3.264
e-ISSN/p-ISSN	**2808-7178 / 2808-7380**
Published by	**Rifa'Isntitute**

Introduction

Rubeola, also known as measles (MV), that can lead to serious complications and death and one of the world's most contagious viral diseases. It is caused by a virus that is transmitted via person-to-person contact as well as airborne spread. and it is estimated that 90% of non-immune people exposed to an infective individual will contract the disease (Krawiec & Hinson, 2020), (Gasta�aduy et al., 2021)

Immunisation against measles started in the 1960s and has dramatically reduced the incidence of measles. But despite overall high immunisation coverage, measles continues to cause frequent outbreaks. During the first half of 2019, over 182 countries reported more than 300,000 measles cases; greater than double the number from the same period in 2018. Globally, measles remains a leading cause of childhood deaths and an estimated 140 000 children die each year from complications caused by the disease (Dunn et al., 2020)

The virus, which produces a distinct rash that appears within days of exposure, can spread quickly and can produce severe complications. Common complications of measles include otitis media and diarrhea, but more serious complications can also occur and include pneumonia, encephalitis, and subacute sclerosing panencephalitis, a slowly progressive neurologic sequela of measles that is universally fatal (Blakely et al., 2020), (Gasta�aduy et al., 2021)

Epidemiologi

Measles is the one of leading causes of death among children worldwide, despite the availability of a safe and effective vaccine. Between 2000 and 2017, the global annual incidence of reported measles cases declined by 83%, from 145 to 25 cases per million population. In 2017, an estimated 109,000 deaths occurred due to measles globally, down from 545,000 in 2000. Cumulatively over this period, compared to no measles vaccination, measles vaccination prevented about 1 million deaths. The recent increase in measles cases in the United States and other industrialized countries is part of a global upsurge in reported measles cases that began in 2018 and continued into 2019 (Peter M. Strebel, MB, Ch. B., MPH, and Walter A. Orenstein, 2019)

Countries with the highest reported cases include Madagascar, Ukraine, India, Brazil, the Philippines, Venezuela, Thailand, Kazakhstan, Nigeria, and Pakistan. While most cases worldwide occur in countries with weak healthcare systems, vaccine hesitancy has emerged as a risk factor for measles outbreaks. The World Health Organization (WHO) has identified vaccine hesitancy as one of the 10 greatest global health threats in 2019. The Americas are the only region verified as measles-endemic-free. Unfortunately, this achievement is temporary as local measles outbreaks sporadically occur throughout the U.S. due to incoming travellers bringing the virus from other countries and spreading it to subpopulations with inadequate or no vaccination. The measles outbreak that began in Venezuela in 2017 continues, indicating a resurgence of endemic measles transmission in the Americas (Dunn et al., 2020), (Peter M. Strebel, MB, Ch. B., MPH, and Walter A. Orenstein, 2019)

Pathogenesis

The highly contagious measles virus is transmitted through aerosols and droplets. Measles enters the upper or lower respiratory tract by infecting CD150+ cells or binding to dendritic cells (DCs) expressing DC-SIGN+ or alveolar macrophages. Infected cells migrate to bronchus-associated lymphoid tissue or drain to lymph nodes to spread the infection further to susceptible lymphocytes. Infected CD150+ lymphocytes, mostly CD4+ memory T cells, disseminate the infection systemically through both the bloodstream and the lymphatic system. Infection of respiratory epithelial cells from the basolateral side, combined with epithelial damage, leads to the release of infectious measles virus particles into the respiratory tract lumen. Infection of myeloid and lymphoid dermal cells is followed by the spread of infection among epidermal keratinocytes in a nektin-4-dependent manner. MV-specific lymphocytes then begin to develop to clear the infection (Laksono et al., 2020)

Capillary skin hyperaemia leads to the recruitment of MV-specific lymphocytes and activated macrophages to the infected skin area. Along with edema, this process results in the emergence of erythematous and morbilliform skin rash. Following recovery, the partial loss of lymphocytes is covered by the expansion of newly generated cells. The skin rash disappears, and the epidermis becomes free from infection. Patients are protected from clinical measles for life. However, due to the loss of previously existing lymphocytes and plasma cells, as well as pre-existing antibodies, patients become vulnerable to other infectious diseases, especially respiratory infections. A schematic representation of lymphopenia and changes in lymphocyte population composition before and after measles (Laksono et al., 2020)

The lymphotropic nature of measles virus (MV) leads to infection and depletion of pre-existing CD150+ lymphocytes. However, long-term loss is compensated by the rapid formation of MV-specific cells and the expansion of new cells due to a homeostatic response. The types of cells infected by MV vary over time. Myeloid cells act as the initial target and 'Trojan horses,' carrying the virus to CD150+ cells in lymphoid tissues. Lymphocytes play a key role in systemic spread, while respiratory epithelial cells are crucial for virus transmission. Myeloid and dermal lymphoid cells, as well as epidermal keratinocytes, are responsible for the appearance of skin rash. Most MV-infected cells are cleared by specific MV-immune cells, but some lymphocytes still retain MV RNA long after recovering from measles (Laksono et al., 2020)

In addition to its impact on the immune system, Measles Virus (MeV) also has a direct cytopathic effect on infected cells. MeV induces the formation of syncytia, where infected cells merge to form giant, multinucleated cells. This process can cause tissue damage and contribute to the development of MeV-related complications such as encephalitis (Nwalozie et al., 2023)

Clinical manifestation

Measles is an acute viral infection typically characterized by fever, cough, coryza, and conjunctivitis, followed by a maculopapular rash. The incubation period of measles varies from 7 to 21 days, with a median of 13 days. The prodromal phase lasts for 2 to 4 days. The prodromal illness caused by measles is marked by increasing fever, anorexia, malaise, and the classic triad of three "C's": coryza (runny nose), cough, and conjunctivitis (red and watery eyes). Photophobia, periorbital edema, and myalgia can also occur, resembling influenza virus infection. One to two days before the onset of the rash, small 1 to 3 mm whitish-blue papules with a "grain of sand or rice" appearance on an erythematous base, known as Koplik spots, appear on the buccal mucosa opposite the first molar but can also occur on the soft palate and vaginal mucosa. This is a pathognomonic sign. Clinical diagnosis can be established: The combination of a widespread maculopapular rash, fever (≥38 °C), and cough, coryza, or conjunctivitis has high sensitivity (75–90%), but its specificity is low (Nwalozie et al., 2023), (Misin et al., 2020), (Leung et al., 2018)

Measles can also cause life-threatening complications that affect systems such as the respiratory and central nervous systems. Pneumonia is the most common complication of measles and is responsible for most measles deaths. It can be caused by a direct viral infection of the lungs or a secondary bacterial infection. Children under the age of five and adults over the age of 20 have a higher risk of developing pneumonia after measles infection (Nwalozie et al., 2023), (Schoini et al., 2019)

Diagnosis

Measles should be suspected if the following symptoms are present: fever ≥101°F (38.3°C); a characteristic erythematous maculopapular (non-vesicular) rash with an evolving pattern developing on the face and behind the ears 3-4 days after the onset of fever. From here, the disease spreads to the extremities, becoming more confluent over time, spreading in a cephalocaudal direction from the face downwards and lasting for 3 days or more; and at least one of the three "C's": coryza, cough, or conjunctivitis. Suspicion should be very high in individuals who lack measles immunity if there is a history of measles exposure, travel to endemic areas (e.g., Africa, the Western Pacific, and Southeast Asia), or during a measles outbreak. If present, Koplik spots are pathognomonic. Diagnosis may be challenging in areas with a low incidence of measles (Leung et al., 2018), (Graber et al., 2020)

Clinical suspicion should be confirmed through laboratory testing. Testing serum immunoglobulin (Ig)M antibodies against measles is the fastest method and is highly beneficial during outbreaks. Serum IgM is detectable from 4 days after the onset of the rash to at least 30 days after the onset. Negative IgM tests obtained within the first 72 hours should be repeated. In the United States and other countries with high vaccination rates, both serology and polymerase chain reaction (PCR) are recommended. PCR samples can be taken from blood, urine, throat, and nasopharynx. Confirmation studies with IgG can also be obtained by collecting two samples with an interval of 10 to 30 days. A fourfold increase in IgG can help differentiate between acute and convalescent sera. All specimens should be sent to the state public health laboratory or the CDC (Graber et al., 2020)

IgM ELISA is the gold standard detection test for confirming measles cases. However, real-time RT-PCR should be introduced and used to complement laboratory diagnosis, especially in pre-elimination and/or elimination settings if needed (Cui et al., 2018)

Management

The primarily treatment is symptomatic and consists of the use of antipyretics, prevention and control of dehydration, adequate nutrition, and infection control measures. If there is a bacterial infection, it should be treated with appropriate antibiotics. The World Health

Organization recommends vitamin A supplementation for all children diagnosed with measles, as it has been proven to reduce mortality and the risk of complications such as pneumonia and diarrhea. A systematic review in 2017 indicated that vitamin A supplementation is associated with a significant decrease in mortality and morbidity in children with measles. It is recommended to administer vitamin A to all children with acute measles orally, once a day, for 2 consecutive days, with age-appropriate doses (50,000 IU, 100,000 IU, and 200,000 IU for infants under 6 months, infants aged 6 to 11 months, and children over 12 months). For children with clinical evidence of vitamin A deficiency, the third age-appropriate dose is recommended 2 to 4 weeks later (Gasta�aduy et al., 2021), (Nwalozie et al., 2023), (Leung et al., 2018)

Most treatments are generally aimed at preventing or treating infections such as pneumonia, which is often found in infected patients. Antibiotics are commonly used to treat complications associated with bacterial superinfection (Ferren et al., 2019)

Serum immunoglobulin

Since the 1940s, intramuscular immunoglobulin serum injections have been reported to provide protection of up to 79% in unvaccinated individuals who had close contact with measles-infected patients. Recently, the effectiveness of immunoglobulin serum as post-exposure prophylaxis is estimated to be between 50% and 69% during the measles outbreak in 2014 in British Columbia, Canada. However, these estimates are highly controversial due to many other factors that may contribute to preventing the onset of the disease (Ferren et al., 2019)

Ribavirin, IFN-α, Isoprinosin

Ribavirin is an antiviral medication with broad antiviral activity, initially used for the treatment of HCV (Hepatitis C Virus). It is a nucleoside analog derived from guanosine, and its primary in vivo antiviral activity is demonstrated by its incorporation as a mutagenic nucleoside by the virus's RNA polymerase. The use of ribavirin and immunoglobulin serum appears to reduce respiratory symptoms in patients infected with Measles Virus (MeV). However, as of now, there are no standard protocols and recommended doses for treating patients, and further research is needed to establish effective treatment guidelines (Ferren et al., 2019)

Vitamin A

Vitamin A deficiency is closely associated with measles complications, and vitamin A supplementation has been proven to reduce morbidity and mortality related to Measles Virus (MeV) infections in children. Vitamin A is especially used to prevent blindness due to MeV infection in children. Therefore, the World Health Organization (WHO) recommends the immediate administration of vitamin A to children infected with MeV with two repeated doses of 200,000 IU, primarily because vitamin A deficiency is a public health issue. Nevertheless, vitamin A is also recommended for administration in all severe cases, regardless of the patient's country or age. In cases of severe measles, the combination of vitamin A with ribavirin treatment can also reduce morbidity (Ferren et al., 2019)

Prevention

The prevention of measles virus involves a combination of measures, including vaccination, maintaining a high level of population immunity, and early identification and isolation of infected individuals. Vaccination is the most effective way to prevent measles virus infection and is recommended by the World Health Organization (WHO) as part of routine childhood immunization programs (Nwalozie et al., 2023)

The measles vaccine is a weakened live vaccine that is highly effective in preventing measles virus infection when administered in two doses. The first dose is recommended at the age of 12-15 months, followed by the second dose at the age of 4-6 years. Vaccination not only protects individuals from measles virus infection but also contributes to herd immunity, which is crucial for safeguarding vulnerable populations that cannot receive the vaccine, such as infants, pregnant women, and individuals with weakened immune systems (Nwalozie et al., 2023)

In addition to vaccination, early identification and isolation of infected individuals are also crucial to prevent the spread of the measles virus. Infected individuals should be isolated for at least four days after the onset of the rash to prevent transmission to others. Healthcare providers should be vigilant in identifying suspected cases of measles and promptly report them to public health authorities to prevent outbreaks (Nwalozie et al., 2023)

Prognosis

The prognosis for measles is generally good, with infections sometimes resulting in fatalities. The CDC reports that the mortality rate for children due to measles infection in the United States is 0.1-0.2%. However, many complications and lingering symptoms can occur, and measles is a leading cause of blindness in children in developing countries

Complication

Measles can weaken the immune system, making the body more susceptible to other infections such as middle ear infection, throat inflammation, bronchitis, pneumonia, or gastrointestinal infection (stomach and intestines). Measles can also lead to serious complications such as encephalitis (inflammation of the brain) and Subacute Sclerosing Panencephalitis (SSPE). Infants, toddlers, and adults are at higher risk of complications, and individuals with weakened immune systems are more likely to experience complications. Measles can also cause premature birth and miscarriage in pregnant women

Conclusion

In conclusion, measles, also known as rubeola, remains a significant global health concern despite the availability of a safe and effective vaccine. While immunization efforts have led to a substantial decline in reported cases, the disease persists and continues to cause outbreaks, especially in regions with weak healthcare systems and instances of vaccine hesitancy. The highly contagious nature of the measles virus and its potential to cause severe complications, including pneumonia and encephalitis, underscore the importance of vaccination as a preventive measure.

The pathogenesis of measles involves the virus's ability to exploit the respiratory and lymphatic systems, leading to widespread infection and the characteristic symptoms of fever, cough, and rash. The clinical manifestation of measles includes distinctive features such as Koplik spots and a maculopapular rash. Diagnosis relies on clinical suspicion and laboratory testing, with IgM ELISA being a standard method.

Management of measles is primarily symptomatic, focusing on supportive care, prevention of dehydration, and control of secondary bacterial infections. Vitamin A supplementation has proven beneficial in reducing mortality and complications, particularly in children. Immunoglobulin serum and antiviral medications like ribavirin show promise in managing respiratory symptoms, but further research is needed for standardization.

Prevention remains the cornerstone of measles control, with vaccination being the most effective strategy. The two-dose measles vaccine has not only reduced individual susceptibility but also contributed to herd immunity, protecting vulnerable populations. Early identification and isolation of infected individuals play a crucial role in preventing the spread of the virus. Despite the generally good prognosis, measles can lead to fatal outcomes and severe complications, emphasizing the importance of continued public health efforts to control and eliminate this highly contagious viral disease.

Reference

Blakely, K. K. Baker, N. (2020). Measles�What�s Old Is New Again. *Nursing for Women's Health*, *24*(1), 45–51.

Cui, A. Xu, W. (2018). Importance of real-time RT-PCR to supplement the laboratory diagnosis in the measles elimination program in China. *PLoS One*, *13*(11), e0208161.

Dunn, J. J. Harvala, H. (2020). Measles is back�considerations for laboratory diagnosis. *Journal of Clinical Virology*, *128*, 104430.

Ferren, M. Mathieu, C. (2019). Measles encephalitis: towards new therapeutics. *Viruses*, *11*(11), 1017.

Gasta�aduy, P. A. Patel, M. (2021). Measles in the 21st century: progress toward achieving and sustaining elimination. *The Journal of Infectious Diseases*, *224*(Supplement_4), S420–S428.

Graber, E. M. A. Gibbs, M. A. (2020). An update and review of measles for emergency physicians. *The Journal of Emergency Medicine*, *58*(4), 610–615.

Krawiec, C., & Hinson, J. W. (2020). *Rubeola (Measles)*.

Laksono, B. M. de Swart, R. L. (2020). Measles pathogenesis, immune suppression and animal models. *Current Opinion in Virology*, *41*, 31–37.

Leung, A. K. C. Sergi, C. M. (2018). Measles: a disease often forgotten but not gone. *Hong Kong Medical Journal*, *24*(5), 512.

Misin, A. Luzzati, R. (2020). Measles: an overview of a re-emerging disease in children and immunocompromised patients. *Microorganisms*, *8*(2), 276.

Nwalozie, R. Nnokam, B. A. (2023). Biology of Measles Virus: Epidemiology and Clinical Manifestations. *International Journal of Pathogen Research*, *12*(4), 1–10.

Peter M. Strebel, MB, Ch. B., MPH, and Walter A. Orenstein, M. (2019). Measles. *Vaccine*, *500*, 1200.

Schoini, P. Tzouvelekis, A. (2019). Measles pneumonitis. *Advances in Respiratory Medicine*, *87*(1), 63–67.