# Measles, mumps and rubella

Measles, mumps and rubella are three of the most highly and commonly acquired infectious diseases in children; however, they can affect people of all ages. These viruses occur throughout the world and are highly communicable airborne pathogens which can spread by close contact with an infected person. Although still a problem in many developing countries, thanks to immunization programs around the world these viruses are much less common now. Efficient and early vaccination against measles, mumps, and rubella are highly successful at preventing the diseases and most children who receive their shots are being not only protected during childhood, but generally have a life long immunity.

The measles virus (MV), a member of the Morbillivirus genus in the Paramyxovirus family, is a 100-300 nm enveloped virus that contains a single-strand, negative-sense RNA genome in a helical nucleocapsid which encodes for six structural proteins and two others which are involved in viral entry. The F (fusion) and the H (hemagglutinin) proteins are important in pathogenesis since together they facilitate receptor biding, fusion of the viral membrane, and cellular entry of into the epithelial cells in the upper respiratory tract of the host [*,*]. Measles is highly infectious and once infected an individual can experience clinical features such as fever, maculopapular rash, cough, coryza (runny nose), conjunctivitis, and the pathognomonic Koplik spots ( punctuate blue-white spots which appear in the buccal and lower labial mucosa) which generally occur 1-2 days before the rash[ ]. In some cases complications such as diarrhea, otitis media, pneumonia, encephalitis, blindness, and secondary infections by common bacteria and viruses may arise. In some extreme cases subacute sclerosing

panencephalitis (SSPE), a rare degenerative disease of the brain which generally emerges six to eight years after a primary measles virus infection, may also onset.

Measles is typically an infection of childhood and protective immunity is life-long, such that a second case of measles in a child or adult would be highly unusual. Before the widespread vaccination efforts against measles in the 1960s the virus had a case-fatality ratio of about 5% in children, which was higher for children and infants in developing countries, where even today a fatality rate of up to 20% can occur. A highly effective live- attenuated vaccine for measles has contributed to the low incidence levels compare to the pre-vaccine era and even some regions of the world have documented its complete eradication. Measles is commonly diagnosed based on its distinctive symptoms, hence why laboratory diagnosis is rarely use. However, given the success of the vaccination campaigns, physicians in low measles prevalence areas may become less familiar with the disease and accurate diagnoses may become challenging in the future.

Mumps Virus, like measles, also belongs to the family Paramyxoviridae, but its genus is Rubulavirus. Akin to measles, mumps is a 150-200 nm enveloped spherical virus with surface spikes projecting from the envelope. Inside the envelope, a large helically arranged nucleocapsid encloses negatively stranded RNA whose genome contains about 16, 000 nucleotides. Clinical Symptoms of mumps include mild fever, anorexia, malaise, headaches and acute onset of unilateral or bilateral parotitis. Parotitis tends to take place within the first couple of days of the infection and may first be expressed through earache and tenderness of the swollen parotid or salivary gland.

Mumps is highly contagious, and 90% of those that are susceptible and are exposed to the infection will themselves become infected. However, 30-40% of those with the infection are actually asymptomatic (Rubin and Farber, 1994). Complications can include meningoencephalitis, orchitis in males or oophoritis in females, as well as pancreatitis. The live-attenuated mumps vaccine is often given along with measles and rubella in the MMR vaccine. The diagnosis of mumps is usually done based on the expression of the clinical features, in particular the presence of parotitis. There are unique challenges for the laboratory diagnosis of mumps in previously immunized individuals whose immunity may have diminished either in the absence of a second booster dose of vaccine or in areas where mumps disease, and thus exposure, is minimal. However, It has been concluded that the most rapid and sensitive diagnosis of mumps can be acquire by ELISA (Enzyme- linked Immunisorbent Assay) method.

Rubella virus, commonly known as ‘ German measles,’ belongs to the family Togavirida, genus Rubivirus. Rubella virions, although enveloped like measles and mumps, are much smaller, approximately 60-70 nm in diameter and contain approximately 10, 000 nucleotides in a single-stranded, non-segmented, positive-sense RNA genome inside a semi-spherical nucleocapsid. Rubella is usually a mild disease and is characterized by a low fever and a generalized maculopapular rash. Other symptoms may include lympadenopathy, conjunctivitis, and sore throat. Symptoms of acquired rubella are often mild and in up to 50% of cases asymptomatic. Complications are not common in rubella patients, but generally occur more often in adults than in children. Arthralgia and arthritis are common

complications among 70% of infected adult women. Other complications such as encephalitis and hemorrhagic manifestations can also be experience, but these are generally rare. Although a relatively mild disease rubella can be quiet serious if acquire by pregnant women.

## Pathogenesis

Measles, mumps, and rubella are highly contagious viral illnesses that can be transmitted by aerosol generated when an infected person expels saliva through coughing or sneezing, or by direct contact with respiratory secretions. Following infection of a vulnerable host, all three pathogens begin replication in the respiratory tract where they initially target the respiratory ephatelium of the nasopharynx and continue onto the regional lymph nodes. This localized replication phase is followed by a viremia in which the viruses spread onto multiple other organs. In the case of measles, a primary viremia where the virus moves onto other lymphoid tissue takes place 2-3 days after infection. Around days 5-7, the virus spreads to multiple other organs such as the kidney, liver, and skin through a secondary viremia. In mumps, after 12 to 25 days of exposure a viremia arises which lasts from 3 to 5 days. This viremia allows the virus to spread to multiple tissues which include the meninges, and glands such as the salivary, pancreas, testes, and ovaries. Inflammation of the infected tissues causes the hallmark symptoms of the disease, parotitis and aseptic meningitis. Akin to the mumps and measles, rubella after 5-7 days of replication in the nasopharynx area follows a viremia which spreads to the lymphatic system and establishes a systematic infection.

Clinical signs and symptoms for measles, mumps, and rubella occur after an incubation period of about 10-12, 14-18, and 12-23 days respectively. For measles, a prodromal period of 2-4 days marks the beginning of the clinical stage of the infection. Here, thin epithelial cells of the respiratory tract and the conjunctive began to be broken down by the virus leading to an inflammatory reaction, also a characteristic symptom of the disease. Thicker mucosal surfaces of the buccal cavity are then affected given rise to the Koplik's spots. The appearance of the spots marks the start to a delayed-type hypersensitive reaction (DTH) which gives rise to the rash. The primary antiviral immune responses to MV coincides with the appearance of the rash, and is here when the presence of IgM antibodies and of CD4+ and CD8+ T cells in areas of MV-infected epithelial cells takes place. Following this, neutralizing IgG antibodies are also introduced and in conjunction all four immune responses are completely effective in controlling viral replication and concluding the infectious process. Viral antigen is absent from skin lesions and the virus is not shed from this surface, however shedding of the virus occurs from the nasopharynx from the beginning of the prodrome until 3-4 days after the rash emerges. As mentioned, measles is a typical self-limiting infection, and can be resolved by an efficient immune response; however patients with T-cells deficiencies, unable to develop a rash, commonly experience complications such as SSPE. Several months following an acute MV infection, a prolonged state of immunosuppression, which frequently predisposes patients to many secondary bacterial, viral, and parasitic infections, ensues.

Mumps virus (MuV), similar to measles, causes non-specific prodromal symptoms such as mild fever and malaise during its incubation period. Upon viral entry, replication primarily takes place in the nasal mucosa and the epithelial layer of the upper respiratory track, which progressively moves on to penetrating the draining lymph nodes. From here, the viremia spreads the virus onto the parotid glands, kidney, pancreas, and central nervous system (CNS). Infection in the salivary glands produces parotitis-inflammation of the parotid glands-the most common clinical manifestation of mumps. Inflammation and swelling of the glands, visible during the first two days of infection in 30-40% of patients, is due to tissue damage and a subsequent immune response prompted by viral replication. Additionally, propagation into the kidneys can extend the infection and cause viruria. Potentially infectious virus is excreted in the urine for a period of two weeks following onset of the disease. Nonetheless 1/3 of infections are subclinical, this being more common among adults than children. About eleven days after exposure, humoral immune response is established and the presence of neutralizing antibodies such as IgG (immunoglobulin G), IgM and IgA emerges. These antibodies help terminate the viremia and in the case of IgA it stops secretion of infectious mumps virus in the saliva. Virus shedding into the saliva begins a couple of days before the onset of clinical parotitis and ends about 8 days later. Parotid swelling culminated after 4-7 days.

Although the most common expression of mumps leads to parotitis, it is important to note that the clinical course of mumps is extremely variable. Diseases such as meningitis and orchitis, commonly regarded as complications, could instead be seen as systemic manifestations of mumps.

Meningitis is a common course of mumps and is characterized by inflammatory cells in the cerebrospinal fluid of the patient. This development is common in 15% of the patients and normally resolves within 3-10 days without secondary consequence. Orchitis-testicular inflammation-is the most common complication among post-pubertal male patients occurring in as many as 50% of cases. Ochitis usually follows parotitis, with an abrupt onset of testicular swelling, tenderness, nausea, and fever; pain and swelling generally only last 1 week, although tenderness may last longer.

The rubella virus (RV), like mumps and measles, replicates around the epithelium of the buccal mucosa and the nasopharyngeal lymphoid tissue. Contrary to Mv and MuV, after its incubation period and the subsequent viremia, rubella symptoms abruptly appear in children with the emergence of a rash. Prodromal symptoms are only mildly observed in adults 1-5 days before the appearance of the rash. This rash may last up to three days, starting as distinct pink maculopapules on the face, moving onto the truck and following to the extremities. Patients are most infectious immediately prior to the rash and throughout its duration. Viremia ends with the onset of rubella-specific and IgM antibodies shortly after the rash phase, which is about 2-3 week after initial exposure. Chronic enlargement of lymph nodes-Lymphadenopathy-may also take place up to a week before the emergence of the rash and last up to 10-14 days after it. Cervical and occipital lymph are frequently affected. Rubella is usually mild in childhood and early adulthood, with up to 50% of cases being asymptomatic, however rubella presents a bigger threat when acquired during pregnancy, especially if infection is in the first few weeks of pregnancy.

Congenital acquire rubella virus infections in pregnant women during the first trimester of pregnancy can result in severe congenital abnormalities in the children (Congenital rubella syndrome, CRS) including deafness, cataracts, glaucoma, cardiovascular abnormalities, and mental retardation. Other outcomes of congenital rubella can lead to premature delivery and even fetal death. In 85% of cases of pregnant women who were infected during their first trimester, the babies were prematurely harmed. It is suggested that the rubella virus enter the fetus through the mother’s blood stream. Since the developing fetus is especially vulnerable to illness because its immune system is not yet strong enough to permanently fight off infection, the virus remains in the body, and can leads to CRS.

Concisely, while all three infections have a similar infection patterns, only measles and rubella virus are viral infections which affect the respiratory tract, whereas mumps is a viral infection of the salivary glands that causes swelling. Also all three diseases are relatively mild and in many cases asymptomatic. Nonetheless rubella, although a milder infection of the respiratory tract than measles when developed by a pregnant woman, it may lead to birth defects in the infant which the other two don’t generally cause.

## Therapeutic strategies

Currently there is no cure or treatment for measles, mumps, and rubella, efforts are generally focused on relieving symptoms until the body’s immune system manages to fight off the infection. However preventive measures such as attenuated live vaccines have been developed for all three pathogens and are currently being administered to children and adults around the world in a trivalent form known as the Measles-mumps-rubella

vaccine or MMR. Measles, mumps, and rubella vaccine is used to protect children, as well as adults from acquiring the disease. The administration of the vaccine provides with lifelong immunity to all three diseases and has a 95% efficacy. It is highly recommended that children should get 2 doses of MMR vaccine, the first being administered between 12-15 months of age and the second at ages 4-6, commonly right before the child begins kindergarten or first grade. The vaccine is also recommended for adults who have not been previously immunized against any of the three viruses or are at a higher risk of exposure such as health care providers, international traveler, and university students. It is important to note that there are also contraindications to the vaccine and some people should no use it. Those who have preciously experience severe allergic reactions to one or more of the vaccine components or to a prior dose of MMR should not be vaccinated. Pregnant women should not be administered MMR or any of its components. Additionally, women attempting to become pregnant should avoid pregnancy for at least 30 days after vaccination with measles or mumps vaccines and for 3 months after administration of MMR or other rubella-containing vaccine because the risk to the fetus from the administration of these live virus vaccines cannot be excluded.

Following the publication of a paper by British researcher Andrew Wakerfield in the medical journal The Lancet in 1998, huge controversy surrounded the idea of whether or not the MMR vaccine might cause autism. In his paper Wakerfield reported that MMR vaccine caused intestinal inflammation that led to translocation of nonpermeable peptides to the bloodstream and, subsequently, to the brain, where they affected development. In his report,

the cases of eight children who developed autism and intestinal problems after receiving the MMR vaccine were discussed. However, to determined if these suspicions were correct, researchers preformed a series of studies in which they compared hundreds of children who had received the MMR vaccine with hundreds who had never received the vaccine. They found that the risk of autism was the same in both groups, thus agreeing that the MMR vaccine does not cause autism. Some parents wary of the safety of the MMR vaccine stopped getting their children immunized although no data supporting an association between MMR vaccine and autism existed and a plausible biological mechanism is lacking which has cause immunization rates to dropped, particularly in the United Kingdom and the United States, given way to the outbreaks of measles and mumps led to hospitalizations and deaths that could have been prevented.

Rubin and Farber, 1994. Pathology. J. B. Lippincott Company. 227 East Washington Square, Philadelphia, Pennsylvania.