

MUMPS

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Mumps is caused by a paramyxovirus. Other causes of bilateral parotitis include cytomegalovirus and enterovirus; other causes of unilateral parotitis include tumor, parotid duct obstruction and bacteria.

Virology

Mumps virus is a member of the *Paramyxovirus* family; it is a relatively simple enveloped, negative-sensed RNA virus which contains only seven genes. It has a single molecule of 16-18 kbp in a helical nucleocapsid in association with a nucleoprotein (NP) M protein which underlies the structure of the viral envelope. The HN (haemagglutination and neuraminidase protein), and the F (fusion) protein form the spikes present on the lipid bilayer envelope. There is only one serotype of the virus. Significant antigenic cross-reaction occurs with other members of the *Paramyxovirus* genus.

Epidemiology

The virus is spread by direct contact via droplets.

Humans are the only known natural hosts.

Mumps is a disease of childhood; the highest incidence occurs in children between five to nine years of age. The disease is less contagious than other childhood diseases such as measles and varicella.

According to a recent epidemiological survey in America, 10% of the population had mumps during each of the first five years of life, 74% had it by age 10, and 95% by 20 years of age. Mumps is endemic in most urban areas. In temperate zones, a seasonal variation is evident, the highest incidence being around January to May. No such seasonal variation exists in tropical countries. Subclinical infections are common in very young infants (two to three years of age), and the proportion increases with age in adulthood. Up to 90% of infections at the age of 10 to 14 years of age were associated with symptoms while almost all infections are subclinical beyond 60 years of age.

Infection can occur throughout childhood. During adulthood, infection is likely to produce more severe disease, including orchitis in men. Death due to mumps is rare; more than half the fatalities occur in persons older than 19 years of age.

Mumps infection during the first trimester of pregnancy can increase the rate of spontaneous abortion. Although mumps virus can cross the placenta, no evidence exists that mumps infection in pregnancy causes congenital malformations.

The number of reported mumps cases in the United States has decreased (since licensure of the mumps vaccine in 1967), from 152,209 cases in 1968 to 1,223 for 2014. Louisiana has reported two cases for 2014.

Most cases occur among persons five years to 19 years of age. In immunized children, most cases of parotitis are not due to mumps. Outbreaks can occur in highly immunized populations.

The period of maximum communicability is from one to two days before the onset of parotid swelling to five days after the onset of parotid swelling. Virus has been isolated from saliva up to seven days before through nine days after onset of swelling. Fever may persist for three to four days; parotitis, when it occurs, usually lasts seven to ten days. Mumps patients should be isolated for nine days following the onset of parotitis, or less if the parotitis has resolved. Persons with mumps are usually considered infectious from two days before, until nine days after onset of parotitis.

The incubation period is usually from 16 to 18 days, but cases may occur from 12 to 25 days after exposure.

Pathogenesis

Mumps is transmitted by droplet spread or by direct contact. The primary site of viral replication is the epithelium of the upper respiratory system, or the GI tract, or eye. The virus quickly spreads to the local lymphoid tissue and a primary viraemia ensues, whereby the virus spreads to distant sites in the body. The parotid gland is usually involved, but so may the CNS, testis or epididymis, pancreas and ovary. A few days after the onset of illness, virus can again be isolated from the blood, indicating that virus multiplication in target organs leads to a secondary viraemia. Parotitis is the most frequent presentation, occurring in 95% of those with clinical symptoms. Occasionally, meningitis may precede parotitis by a week. Virus is excreted in the urine in infectious form during the two weeks following the onset of clinical illness. It is not known whether virus actually multiplies in renal tissues or whether the virus is of haematogenous origin. Life-long immunity is the rule after natural infection, but reinfections can occur; 1% - 2% of all cases are thought to be reinfections.

Clinical Description

Parotid swelling develops in 95% of those with clinical illness. The rate of subclinical infection varies with age, but is on average 30%. In a small proportion of patients, the symptoms may resemble mild URTI. Typically, a prodromal illness consisting of headache, malaise, myalgia and low grade fever occurs one to two days before the onset of parotid enlargement. Patients with classic mumps develop enlargement of one parotid gland, followed one to five days later by enlargement of the contralateral gland. The patient complains of pain and tenderness in the area of the gland. The submandibular and sublingual glands may occasionally be involved. The parotid swelling starts to subside after four to seven days. Virus shedding into the saliva begins a couple of days before the onset of parotitis and ends seven to eight days later.

Complications

- **Meningitis:** Aseptic meningitis occurs in 10% of patients with mumps but as many as 50% show abnormalities in the CSF. Mumps is the most frequent causative agent of aseptic meningitis, in many countries being responsible for 10% -15% of all cases. Symptoms are indistinguishable from other types of aseptic meningitis and can start one week before parotid swelling before parotid swelling to three weeks after it. The CSF reveals a lymphocytosis of usually below 500 lymphocytes/mm³, and normal or elevated protein. Virus can be isolated from the CSF during the first two to three days after onset. Later, specific antibodies can be demonstrated in the CSF. Symptoms of meningitis subside three to ten days after onset and recovery is usually complete. A study suggests that the majority of cases of meningitis occur without apparent parotiditis.

- **Encephalitis:** Encephalitis occurs rarely as a complication of mumps, where lesions are found in the brain and spinal cord. The incidence of encephalitis is approximately one in 6000 cases of mumps. Probably both direct viral invasion and allergic inflammatory reactions lie behind the nervous tissue damage. Clinical features suggesting encephalitis are convulsions, focal neurological signs, movement disorder and changes in sensory perception. Sometimes polio-like paralysis ensues; fatalities have been reported.
- **Hearing Loss:** Before vaccinations, mumps used to be one of the leading causes of hearing loss in children and young adults. In most cases, the hearing loss is transient but permanent dysfunction may occur. Hearing problems did not correlate with meningitis and appears to be due to direct damage to the cochlea. The incidence of hearing loss is estimated to be in the region of one per 15,000 cases.
- **Orchitis and oophoritis:** Orchitis and oophoritis are more likely to occur after puberty where the incidence is 20% - 30%. In 20% - 40% of cases, there is bilateral involvement. Men are much more likely to be affected than women.
- **Pancreatitis:** The exact incidence of pancreatitis is hard to determine, but is thought to be as high as 5%.
- **Arthralgia:** Arthralgia affecting a large joint may develop two weeks after parotitis. This is more frequent in young male adults.
- **Myocarditis:** This can usually only be found on ECG examination in 10% -15% of patients. Rarely, congestive heart failure and deaths have been reported.
- **Transient Renal Dysfunction:** This is a frequent complication of clinical mumps. Cases of symptomatic nephritis following mumps are unusual.
- **Insulin Dependent Diabetes:** There is some epidemiological evidence to suggest that mumps may be a triggering mechanism for Insulin Dependent Diabetes Mellitus (IDDM). It is thought that immunological mechanisms may be involved; certain HLA-D haplotypes are particularly susceptible.
- **Abortion:** If a pregnant woman contracts mumps during her pregnancy, there is increased risk for abortion. This is thought to be due to hormonal imbalances caused by virus infection.
- **Thyroiditis:** There is evidence for a role of mumps virus in the causation of subacute thyroiditis. However, the evidence is not strong.

Case Definition

Clinical Case Definition

An illness with acute onset of unilateral or bilateral tender, self-limited swelling of the parotid or other salivary gland, lasting greater than or equal to two days, and without other apparent cause.

Laboratory Criteria for Diagnosis

- Detection of mumps nucleic acid by standard or real time RT-PCR assays, or
- Isolation of mumps virus from clinical specimen, or
- Positive serologic test for mumps immunoglobulin M (IgM) antibody, or
- Significant rise between acute- and convalescent-phase titers in serum mumps immunoglobulin G (IgG) antibody level by any standard serologic assay

Case Classification

Suspected: A case with clinically compatible illness or meets the clinical case definition without laboratory testing, or a case with laboratory tests suggestive of mumps without clinical information.

Probable: A case that meets the clinical case definition without laboratory confirmation and is epidemiologically linked to a clinically compatible case.

Confirmed: a case that meets the clinical case definition and is laboratory confirmed or epidemiologically linked to a confirmed case.

Laboratory Tests

All suspected cases of mumps should be laboratory tested. An infection can be confirmed by the detection of virus by reverse transcriptase polymerase chain reaction (RT-PCR), the presence of serum mumps IgM, a significant rise in IgG antibody titer in acute- and convalescent-phase serum specimens or a positive mumps virus culture. In highly vaccinated populations, serologic tests are more likely to produce false positives, and therefore are not very reliable. **The current preferred method of laboratory confirmation is detection of the virus by RT-PCR.**

Viral Detection (RT-PCR & Culture)

Mumps virus can be isolated from throat swabs, urine, and cerebrospinal fluid (CSF). Parotid duct swabs yield the best viral sample. They should be obtained as soon as mumps virus is suspected—ideally within three days of, but up to ten days after, parotiditis onset. To obtain sample, massage the salivary gland area 30 seconds prior to swabbing the buccal/parotid duct to ensure that the specimen contains secretions from the glands. Urine samples are not typically used because they are less likely to contain enough viral copies or infected cells for culture or detection. Specimens should be placed in a cold storage container and transported to the laboratory as soon as possible.

Detection by RT-PCR is the most effective diagnostic test and the preferred method for case confirmation. It is, however, sensitive to the timing of collection and quality of the sample. Especially for vaccinated patients, samples should be collected within the first three days after the onset of symptoms to ensure viral yield is high enough. False positives are possible, and the most common cause is contamination of the sample.

Molecular typing provides important epidemiologic information. Genotyping the virus can make it easier to identify the source. It allows the building of a sequence database to keep track of transmission pathways of different strains in the United States. Typing methods can also be used to distinguish wild-type mumps virus from vaccine virus.

Serologic Testing

IgM antibodies are detectable within the first five days of illness, reach a maximum level about a week after onset of symptoms, and remain elevated for several weeks or months. Serum should be obtained at the initial visit. Tests for IgM antibodies are inexpensive and widely available. The enzyme immunoassay (EIA) is widely available commercially and is more sensitive than complement fixation, hemagglutination inhibition (HI), or radial hemolysis. Immunofluorescence assays (IFA) are inexpensive, but they require skill and experience to read, causing many false-positives.

Tests for IgM antibody are unreliable, especially in previously vaccinated individuals because the timing of the IgM response can vary greatly and may even be absent. False-positives and false-negatives are extremely common. For this reason, while IgM may be used as supportive evidence, it should not be the sole method of confirmation.

Immunity to mumps may be documented by the presence of serum IgG mumps-specific antibodies by EIA, IFA, or neutralization. IgG antibodies may be detectable when the patient is first seen; for this reason, a four-fold rise in IgG must be demonstrated for diagnosis. This test is the least practical method of confirmation. It takes a much longer time than other methods, and it is unreliable in vaccinated persons, as the IgG may already be elevated in the initial sample.

The availability of mumps diagnostic tests varies. The state health department can provide guidance regarding the location of diagnostic labs and the type of diagnostic tests available to confirm mumps diagnosis.

Amylase Level in Blood

Amylase is a digestive enzyme made primarily by the pancreas and salivary glands. Hyperamylasemia may be described as an excess of the enzyme - amylase in the blood.

Blood amylase and lipase levels are most frequently drawn to diagnose pancreatitis. Some physicians are still using it for mumps diagnosis although serum amylase is not very specific for mumps infection of the salivary glands. The normal level for amylase is 0 to 137 U/L.

There are many causes of hyperamylasemia. Some may include:

- Pancreatitis: This can cause amylase and lipase levels to be increased up to three times the normal limit. Both values should be increased, in order to carry the diagnosis of pancreatitis.
- Tumors: Amylase enzyme levels may be increased in pancreas, salivary, prostate, lung / ovarian tumors.
 - Gall bladder infection
 - Kidney failure
 - Recent Endoscopic Retrograde Cholangio-Pancreatography (ERCP) procedure.

Surveillance

Mumps is a condition reportable within one business day.

Investigation

Information to collect: The following data are epidemiologically important and should be collected in the course of case investigation:

- Demographic information
- Vaccination status including
 - Number of doses of mumps vaccine
 - Date(s) of mumps vaccination
 - If not vaccinated, describe reason
- Risk factors for disease including
 - Transmission setting (i.e., infection acquired in day care, school)
 - Relationship to outbreak (i.e., is case part of an outbreak or is it a sporadic case)
- Source of exposure and travel history [i.e., import status (indigenous, international import, or out-of-state import, state name, country name)]
 - Contact with a probable or confirmed case
 - Contact with immigrants or travelers
- Clinical presentation including
 - Date of onset of symptoms, especially parotitis

- Duration of parotitis
- Complications (e.g., meningitis, deafness, encephalitis, orchitis)
- Laboratory information including
 - Viral isolation
 - Serologic test results with IgM or IgG (indicating a significant rise between acute and convalescent samples).

Immunization

Live-virus vaccine is prepared in chick embryo cell cultures. Vaccine is administered by subcutaneous injection of 0.5 mL, either alone as a monovalent vaccine or, preferably, as the combined vaccine containing measles, mumps, and rubella vaccines (MMR). Antibody develops in more than 95% of all susceptible persons after a single dose. Serologic and epidemiologic evidence extending for more than 25 years indicates that vaccine-induced immunity is long-lasting.

Child Vaccine Recommendations.

Mumps vaccine should be given as MMR routinely to children at 12 to 15 months of age with a second dose of MMR at four to six years of age. Re-immunization for mumps can be important because mumps can occur in highly immunized populations, including persons with a history of mumps immunization. Administration of MMR is not harmful if given to a person already immune to one or more of the viruses (from previous infection or immunization).

Mumps immunization is of particular importance for children approaching puberty, adolescents, and adults who have not had mumps or mumps vaccine. At office visits of prepubertal children and adolescents, the status of immunity to mumps should be assessed. Persons should be considered susceptible unless they have documentation of at least one dose of vaccine on or after their first birthday, documentation of physician-diagnosed mumps, or serologic evidence of immunity, or were born before 1957.

Susceptible children, adolescents and adults born after 1956 should be offered mumps immunization (usually as MMR) before beginning travel since mumps is still endemic throughout most of the world. Because of concern about inadequate seroconversion related to persisting maternal antibodies, and because the risk of serious disease from mumps infection is relatively low, persons younger than 12 months of age need not be given mumps vaccine before travel.

The routine use of mumps vaccine is not advised for persons born before 1957 unless they are considered susceptible, as defined by seronegativity. However, immunization is not contraindicated in these persons if their serologic status is unknown.

Mumps vaccine can be given simultaneously with other vaccines.

Adverse Reactions. Adverse reactions attributed to mumps live-virus vaccine are rare. Temporally related reactions, including febrile seizures, nerve deafness, parotitis, meningitis, encephalitis, rash, pruritus, and purpura, may not be related causally. In the United States, the frequency of central nervous system complications after mumps immunization has been lower than the observed incidence in the unimmunized population. Orchitis and parotitis have been reported rarely. Allergic reactions also are rare. Other reactions that occur after immunization with MMR are attributable to the measles and rubella components of the vaccine.

Reimmunization with mumps vaccine (monovalent or MMR) is not associated with an increased incidence of reactions. Reactions might be expected only among persons not protected by the first dose.

Precautions and Contraindications

Febrile Illness. Children with minor illnesses with or without fever, such as upper respiratory tract infections, may be immunized. Fever per se is not a contraindication to immunization. However, if other manifestations suggest a more serious illness, the child should not be immunized until recovery.

Allergies. The widespread use of the mumps vaccine since 1967 has resulted in only rare isolated reports of allergic reactions. Allergic reactions to components of the vaccine (eg, neomycin) occasionally may occur. Severe allergic reactions, such as anaphylaxis, rarely are reported. Most children with egg hypersensitivity can be safely immunized with MMR. Skin testing before administration of MMR vaccine is not indicated (see Measles).

Recent Administration of Immune Globulin. Live mumps vaccine should be given at least two weeks before or at least three months after administration of immune globulin (IG) or blood transfusion because of the theoretical possibility that anti-body will neutralize vaccine virus and inhibit a successful immunization. Because high doses of IG (such as those given for the treatment of Kawasaki disease) can inhibit the response to measles vaccine for longer intervals, mumps vaccination, when administered as MMR, should be deferred for a longer period after administration of IG (see Measles).

Altered Immunity. Patients with immunodeficiency diseases and those receiving immunosuppressive therapy (e.g., patients with leukemia, lymphoma, or generalized malignant disease), including high doses of systemically administered corticosteroids, alkylating agents, antimetabolites, or radiation, or who are otherwise immunocompromised should not receive mumps vaccine. The exceptions are patients with human immunodeficiency virus (HIV) infection who are not severely immunocompromised; these patients should be immunized against mumps with MMR. The risk of mumps exposure for patients with altered immunity can be reduced by immunizing their close susceptible contacts. Immunized persons do not transmit mumps vaccine virus.

After cessation of immunosuppressive therapy, mumps vaccine usually should be withheld for an interval of at least three months (with the exception of corticosteroid recipients, see the next paragraph). This interval is based on the assumptions that immunologic responsiveness will have been restored in three months and the underlying disease for which immunosuppressive therapy was given is in remission or under control. However, because the interval can vary with the intensity and type of immunosuppressive therapy, radiation therapy, underlying disease, and other factors, a definitive recommendation for an interval after cessation of immuno-suppressive therapy when mumps vaccine can be administered safely and effectively often is not possible.

Corticosteroids. For patients who have received high doses of corticosteroids for 14 days or more and who are not otherwise immunocompromised, the recommended interval is at least one month.

Pregnancy. Susceptible postpubertal females should not be immunized if they are known to be pregnant. If not pregnant, they should be counseled about the potential hazard of fetal infection with vaccine virus before immunization. Live-virus mumps vaccine can infect the placenta, but the virus has not been isolated from fetal tissues of susceptible females who received vaccine and underwent elective abortions. In view of the theoretical risk, however, conception should be avoided for three months after mumps immunization with MMR vaccine. Women given monovalent mumps vaccine should not become pregnant for at least 30 days.

Acceptable Presumptive Evidence of Immunity: Documentation of adequate vaccination is now two doses of a live mumps virus vaccine instead of one dose for :

- School-aged children (i.e., grades K–12).
- Adults at high risk (i.e., persons who work in health-care facilities, international travelers, and students at post–high school educational institutions).

Mumps Outbreak Control

Care of Exposed Persons. Mumps vaccine has not been demonstrated to be effective in preventing infection after exposure. However, mumps vaccine can be given after exposure, as immunization will provide protection against subsequent exposures. Immunization during the incubation period has no increased risk. The routine use of mumps vaccine is not advised for persons born before 1956 since most persons are immune. Mumps Immune Globulin is of no value and is no longer manufactured or licensed in the United States.

School and Child Care. Children should be excluded for nine days from onset of parotid gland swelling.

Outbreak Control. When determining means to control outbreaks, exclusion of susceptible students from affected schools and schools judged by local public health authorities to be at risk for transmission should be considered. Such exclusion should be an effective means of terminating school outbreaks and rapidly increasing rates of immunization. Excluded students can be readmitted immediately after immunization. Pupils who continue to be exempted from mumps immunization because of medical, religious, or other reasons should be excluded until at least 26 days after the onset of parotitis in the last person with mumps in the affected school. Experience with outbreak control for other vaccine-preventable diseases indicates that this strategy has been highly effective.

Depending on the epidemiology of the outbreak (e.g., the age groups and/or institutions involved), a second dose of mumps vaccine should be considered for children aged one year to four years and adults who have received one dose.

Health Care Facilities:

Hospital precautions and isolation: Droplet precautions are recommended until nine days after onset of parotid swelling.

Routine Vaccination for Health-Care Workers

All persons who work in health-care facilities should be immune to mumps. Adequate mumps vaccination for health-care workers born during or after 1957 consists of two doses of a live mumps virus vaccine. Health-care workers with no history of mumps vaccination and no other evidence of immunity should receive two doses (at a minimum interval of 28 days between doses). Health-care workers who have received only one dose previously should receive a second dose. Because birth before 1957 is only presumptive evidence of immunity, health-care facilities should consider recommending one dose of a live mumps virus vaccine for unvaccinated workers born before 1957 who do not have a history of physician-diagnosed mumps or laboratory evidence of mumps immunity.

Outbreak control in health-care settings, an effective routine MMR vaccination program for health-care workers is the best approach to prevent nosocomial transmission. During an outbreak, health-care facilities should strongly consider recommending two doses of a live mumps virus vaccine to unvaccinated workers born before 1957 who do not have evidence of mumps immunity. These new recommendations for health-care workers are intended to offer increased protection during a recognized outbreak of mumps. However, reviewing health-care worker immune status for mumps and providing vaccine during an outbreak might be impractical or inefficient. Therefore, facilities might consider reviewing the immune status of health-care workers routinely and providing appropriate vaccinations, including a second dose of mumps vaccine, in conjunction with routine annual disease-prevention measures such as influenza vaccination or tuberculin testing.

Routine Vaccination for Health-Care Workers

- Persons born during or after 1957 without other evidence of immunity: two doses of a live mumps virus vaccine.*
- Persons born before 1957 without other evidence of immunity: consider recommending one dose of a live mumps virus vaccine.

For Outbreak Settings

- Health-care workers born before 1957 without other evidence of immunity: strongly consider recommending two doses of live mumps virus vaccine.

*Minimum interval between doses = 28 days.