

Virology

Lec (8)

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Teaching Objectives:

1. To list general characteristic of Mumps and Measles.
2. To recognize the mechanism of replication and pathogenesis for both of them.
3. To describe methods of diagnosis, treatment and prevention.

Mumps: is acute contagious disease characterized by non suppurative enlargement of one or both salivary gland. Mumps virus mostly causes a mild childhood disease but in adults complications.

Word derive from British "to mump" to grimace or grin, from appearance due to parotid gland swelling.

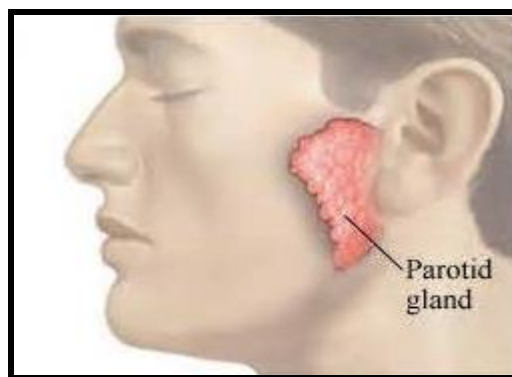


Figure (1): Parotid gland

Important properties of mumps

- The genome RNA and nucleocapsid are those of a typical paramyxovirus
- The internal nucleocapsid protein is the S (soluble) antigen detected in the complement fixation test used for diagnosis.
- The virion has two types of envelope spikes. One with both hemagglutinin and neuraminidase activities and the other with cell - fusing and hemolytic activities.
- Human are the natural host .The virus has a single serotype; neutralizing antibody is directed against the hemagglutinin.

Spread

Usually acquired from respiratory secretions and saliva via aerosols or fomites. Secreted in urine - so urine possible source of infectious virus. Occurs worldwide with peak incidence in winter, 30% of children have a subclinical (in apparent) infection, which confers immunity

Summary of replicative cycle

The replication of this virus is similar to that of respiratory syncytial virus.

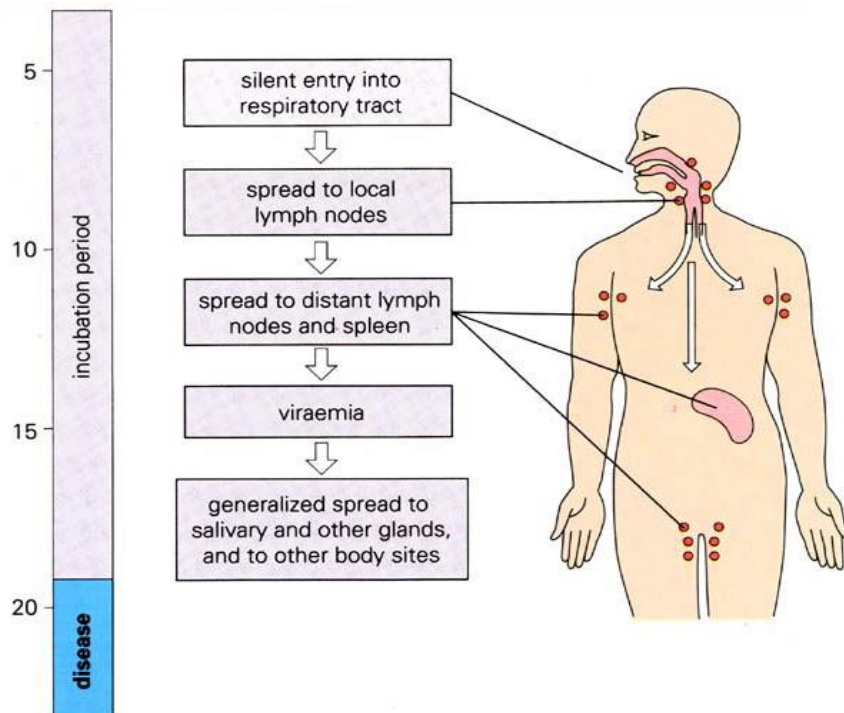


Figure (2): Pathology of Mumps

Pathogenesis and clinical features

Pathogenesis: Infection starts in the upper respiratory tract then, Spread to the blood then produce viraemia, Infect parotid glands, testes, ovaries, pancreas and in some cases cause meningitis. Lifelong immunity occurs in persons who have had. There is a popular misconception that unilateral mumps can be followed by mumps on the other side. Maternal Ab passes the placenta and provides protection during the 1st 6 months of life.

Clinical findings: The incubation period may range from 2 weeks to 4 weeks but is typically about 14-18 days, at least one - third of all mumps infections are sub clinical, including the majority of infections in children less than 2 years of age. A prodromal stage of fever, malaise and anorexia is followed by tender swelling of the parotid gland.

Complicated infection

1- Testes and ovaries may be affected especially after puberty, 20-50 percent of men who are infected with mumps virus develop orchitis in post pubertal males, which if bilateral, can result is sterility, post pubertal male have a fibrous tunica albuginea, which resists expansion, thereby causing pressure necrosis of the spermatocytes. Unilateral due to the lack of elasticity of the tunica albuginea although quite painful, does not lead to sterility.

2- Central nervous system involvement is common 10-30% of case, mumps causes aseptic meningitis and is more common among males than females, meningoencephalitis usually occurs 5-7 days after inflammation of the salivary glands.

3-Pancreatitis- occurs in about 4% of cases, but very little evidence from controlled studies that mumps plays any role in diabetes mellitus. Disease tends to be more severe in adults.

4- Hearing loss - rare, usually unilateral, may improve with time. The affected individual may not have had overt mumps.



Figure (3): Swelling in the parotid gland.

Diagnosis

A- Approximately 30% of infections are sub clinical. Most infections are diagnosed clinically.

B- Laboratory diagnosis.

- Isolating the virus in cell culture from saliva, spinal fluid or urine.
- Serology (significant increase in IgG and IgM). Ab titer rises greater than 4-fold, in either hemagglutination inhibition test or CF test.

Treatment and prevention

Treatment: There is no antiviral therapy for mumps.

Prevention: Vaccination with live attenuated vaccine (MMR), is given as MMR vaccine (three live attenuated viruses: mumps, measles and rubella). It should not be given to immunocompromized person or pregnant women

Measles (rubeola) morbillivirus

Measles, also known as morbilli, English measles, or rubeola, Is an acute, highly infectious disease characterized by fever, respiratory symptoms and a maculopapular rash, complication are common and be quite serious.

Important properties of measles

- The genome is single - stranded RNA, negative-sense, linear non-segmented and nucleocapsid of measles virus are these of a typical paramyxovirus.
- The viron has to types of envelop spikes, (hemagglutinin) only which play important role in hemagglutinating activity and other with cell-fusing and hemolytic activities (F-protein).
- The virus has a single serotype. Antigenically stable particles are labile yet highly infection.
- Three receptor for H protein have been identify to date, complement regulatory molecules CD46,the signaling lymphocyte activation molecule (SLAM) and the cell adhesion molecule nectin-4.

Mode of infection

Measles is typically a childhood infection of humans, spread by the respiratory route (droplets from the nose and mouth to fairly close contacts or by contact with contaminated surface.

Pathogenesis

The virus gains access to the human body via the respiratory tract, where it multiplies locally, the infection then spreads to the regional lymphoid tissue, where further multiplication occurs primary viremia disseminates the virus, which then replicates in the reticuloendothelial system, finally, a secondary viremia seeds the epithelial surface of the body, including the skin, respiratory tract and conjunctiva, where focal replication occurs. Measles can replicate in certain lymphocytes which aids in dissemination throughout the body. Multinucleated giant cells with intranuclear inclusions are seen in lymphoid tissues throughout the body (lymph nodes, tonsils, and appendix) the described events occur during the incubation period.

Clinical Findings

Incubation period of 8-12 days, illness with a prodromal phase of 2-4 days followed by an eruptive phase of 5-8 days.

The prodromal phase is characterized by fever, sneezing, coughing, running nose, redness of eyes, lymphopenia, and Koplik's spots (are small, bluish-white ulcerations on the buccal mucosa opposite the lower molars, these spots contain giant cells and viral antigens and appear about 2 days before the rash, the fever and cough persist until the maculopapular rash appears and then subside within 1-2 days. The prodromal phase ends when the rash appears, the rash which starts on the head and then spreads progressively to chest the trunk and down the limbs (the rash develops as result of interaction of immune T-cell with virus-infected cells in small blood vessels and lasts about 1 week, in patients with defective cell-mediated immunity, no rash develops). Measles in a pregnant woman leads to an increased risk of stillbirth rather than congenital abnormalities. Measles virus infection of the fetus is more severe than rubella virus infection, so the former typically causes fetal death, whereas the latter causes congenital abnormalities.

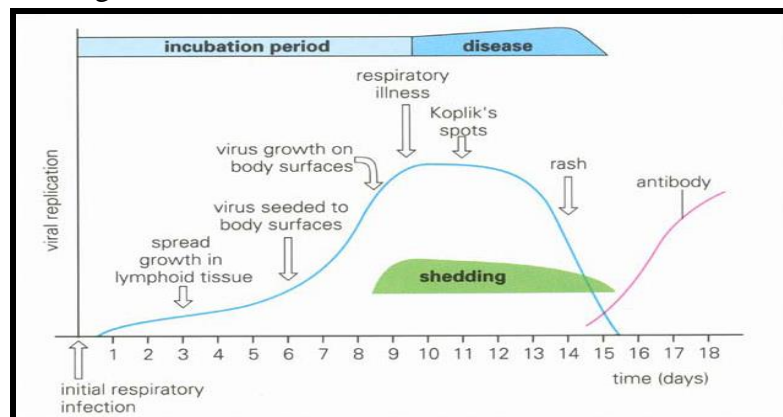


Figure (4): Pathogenesis of measles

Site of virus growth	Good medical care, good immune system	Malnourished child, poor medical care, poor immune system
Respiratory tract	Temporary respiratory illness	Pneumonia is the most common bronchitis, croup and giant cell pneumonia (is a serious complication since F protein can function at physiological pH can facilitate cell-cell fusion)
Ear	Otitis media quite common	Otitis media common and more severe may be susceptible to secondary bacterial infection
Oral mucosa	Koplike's spots	Sever ulcerating lesions
Eye	Conjunctivitis	Childhood blindness, severe corneal lesions, conjunctivitis is associated with photophobia. secondary bacterial infection
Skin	Maculopapular rash	Maculopapular rash absent but haemorrhagic rashes may occur(black-measles)
Gastrointestinal tract	No lesions	diarrhea is a common complication of measles, hepatitis and enteritis.
Cardiovascular	Normal	ECG) abnormalities, including prolongation of the P-R interval, ST-segment and T wave changes
Urinary tract	Virus detected in urine	No known complications
CNS	No infection	1-Acute encephalitis 2-Slowly progressive neurological disease (measles Inclusion Body Encephalitis, MIBE 3-Subacute sclerosing panencephalitis (SSPE) most commonly occurs in individuals under 20 years of age).

Diagnosis

1- **Clinical diagnosis:** The classical clinical features of measles fever, erythematous maculopapular rash and Koplik's spots.

2- **Laboratory diagnosis:**

A-Specimen collection includes (Peripheral blood mononuclear cell, respiratory secretion, conjunctival swabs and urine.

B- Cell culture

- Primary monkey kidney cells or human cord blood leukocytes.
- Cytopathic effect, multinucleated giant cells containing intranuclear or intracytoplasmic inclusion bodies; it takes 7-10 days to develop.
- Immunofluorescence or hemadsorption can be used.

C-Serological test

- IgM antibody appears at the time of the rash in most individuals and IgG appear after 2 weeks late. Usually used Enzyme Immune Assay (EIA) allows for differential detection of IgM and IgG.

- Hemagglutinin inhibition (HI) test detects antibody primarily to the H protein.
- Neutralization test (NT).
- Complement fixation test (CFT) has been used to determine measles immunity in the past.

Treatment and Prevention

- Give the patient antiviral drug it is (Ribavirin) usually inhibit replication of virus and high doses of vitamin A during acute measles (because prevent blindness)
- Measles vaccine, live attenuated vaccine MMR vaccine (measles-mumps- rubella) give in three dose the first at 13-15 months the second before entering school the third at 18 years before entering college.
- Passive protection → Human immunoglobulin for neonatal, children, pregnant women, and immunosuppressed patient.