MEDICAL UNIVERSITY – PLEVEN
FACULTY OF MEDICINE

DEPARTMENT OF INFECTIOUS DISEASE, EPIDEMIOLOGY, PARASITOLOGY AND TROPICAL MEDICINE

Lecture №5

EPIDEMIOLOGY AND PREVENTION OF MEASLES, MUMPS AND RUBELLA.

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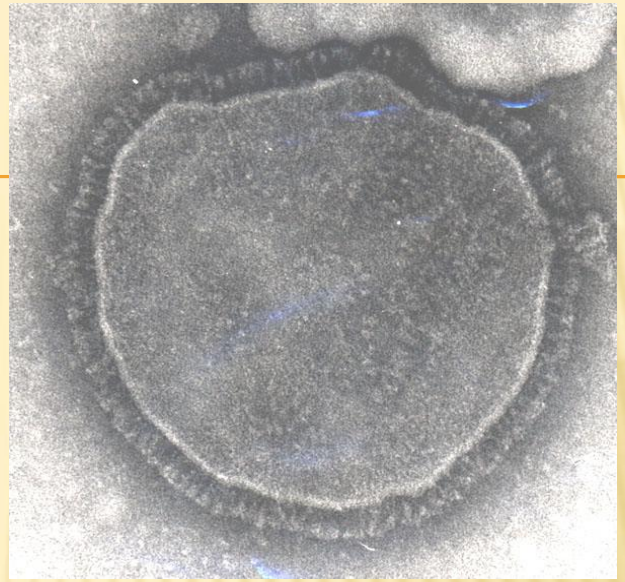
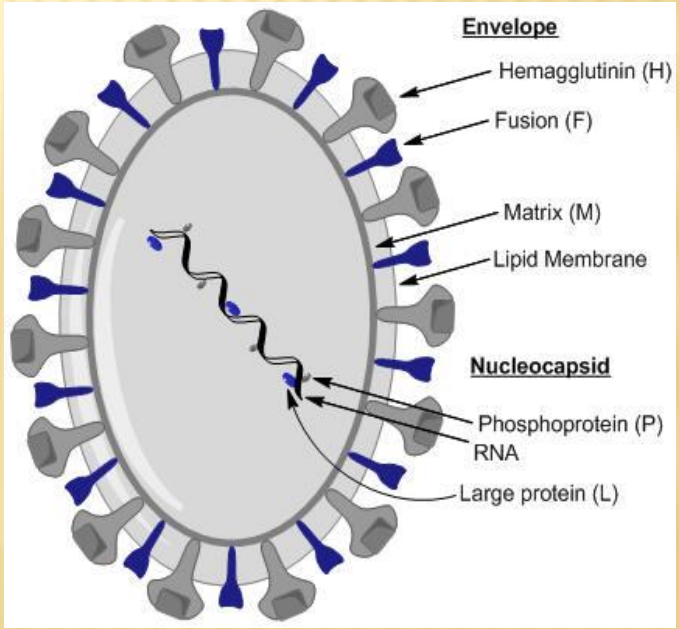
MEASLES /MORBILLI/

- Highly contagious viral illness
- First described in 7th century
- Near universal infection of childhood in prevaccination era
- Common and often fatal in developing areas

AGENT



- Measles virus
- Paramyxovirus (RNA)
- Hemagglutinin important surface antigen
- One antigenic type
- Rapidly inactivated by heat and light



COMPLICATIONS

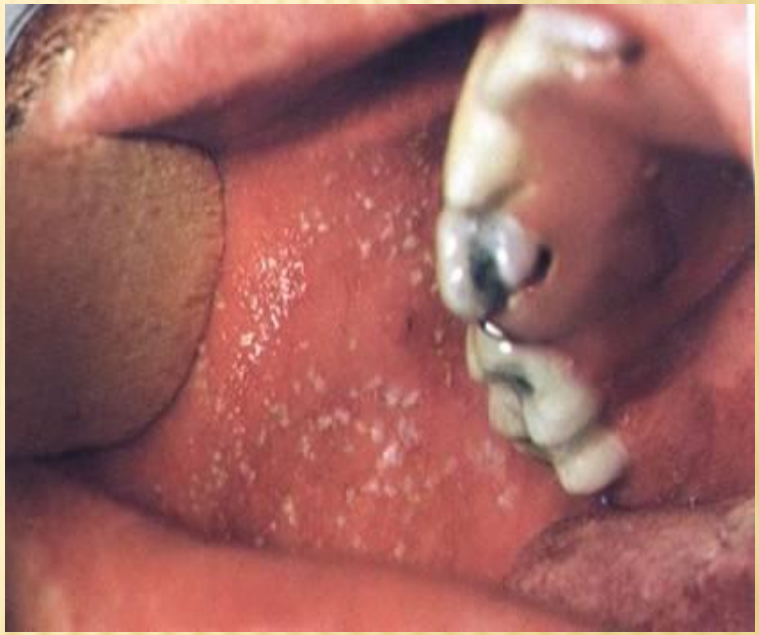
Condition	Percent reported
Diarrhea	8
Otitis media	7
Pneumonia	8
Encephalitis	7
Hospitalization	6
Death	0.1
	18
	0.2
	6
	0.1
	18
	0.2

PATHOGENESIS

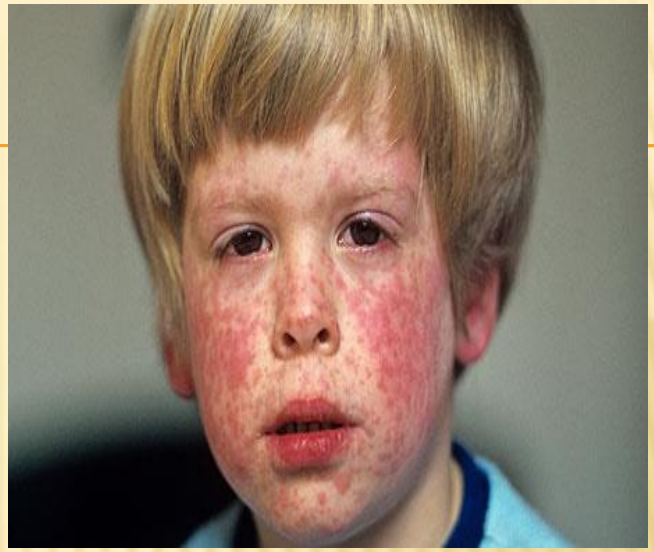
- Respiratory transmission of virus
- Replication in nasopharynx and regional lymph nodes
- Primary viremia 2-3 days after exposure
- Secondary viremia 5-7 days after exposure with spread to tissues

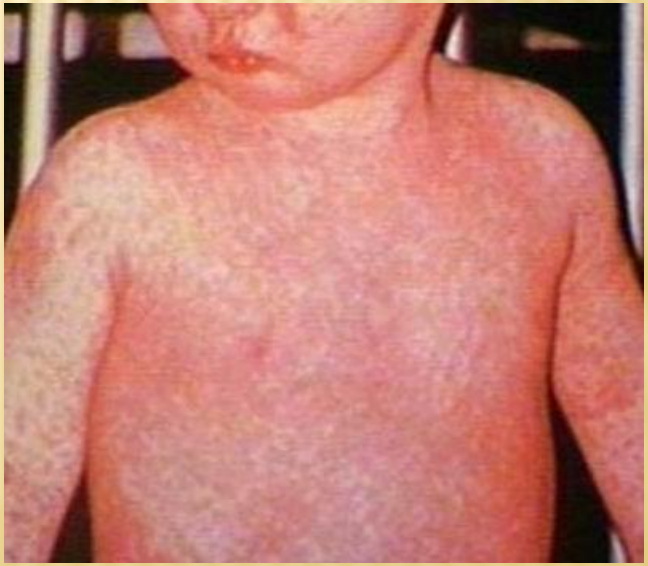
CLINICAL FEATURES

- Incubation period 10-12 days
- Prodrome
  - Stepwise increase in fever to 103°F or higher
  - Cough, coryza, conjunctivitis
  - Koplik spots (rash on mucous membranes)

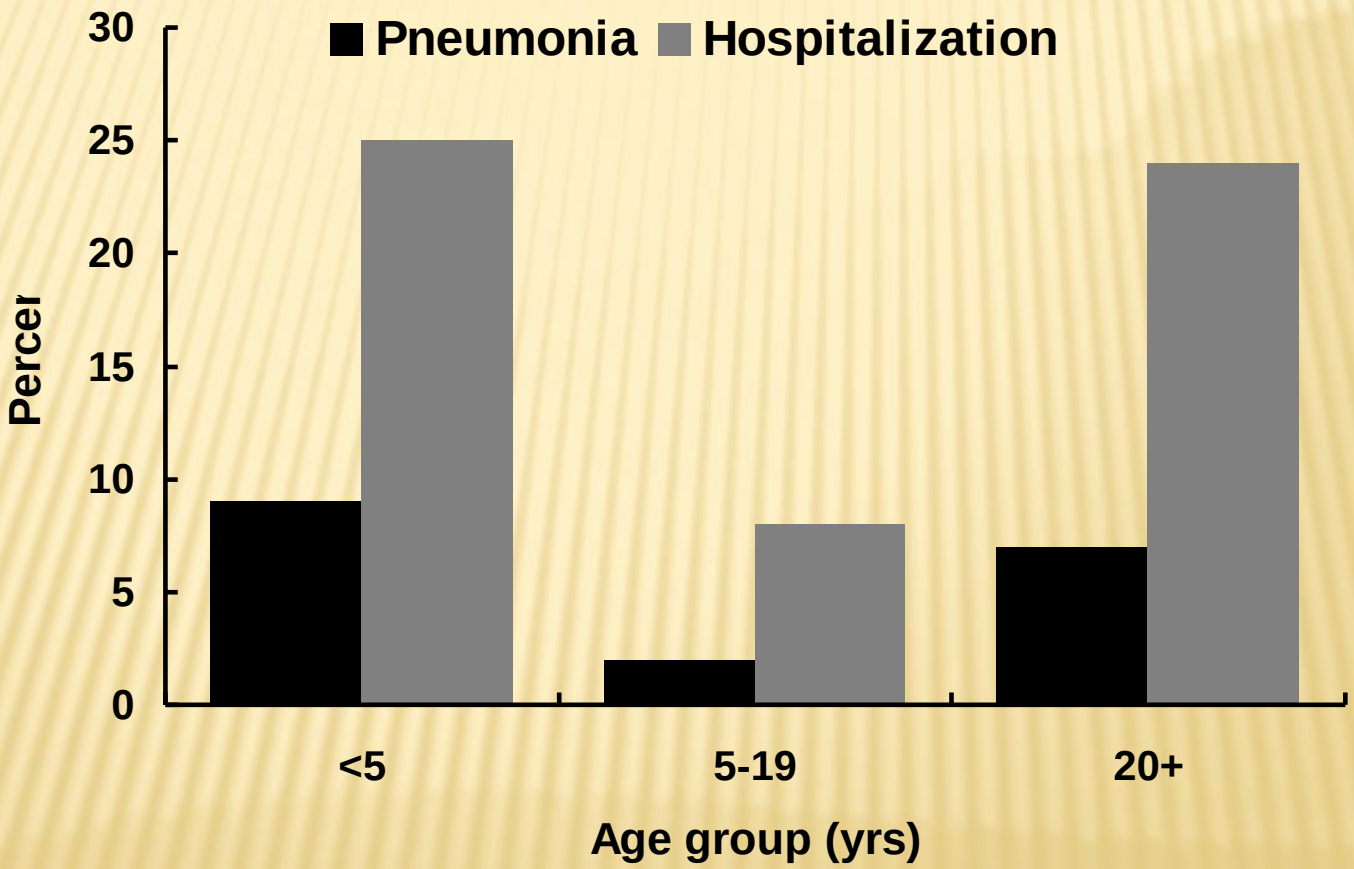


- Rash
  - 2-4 days after prodrome, 14 days after exposure
  - Maculopapular, becomes confluent
  - Begins on face and head
  - Persists 5-6 days
  - Fades in order of appearance





MEASLES COMPLICATIONS BY AGE GROUP

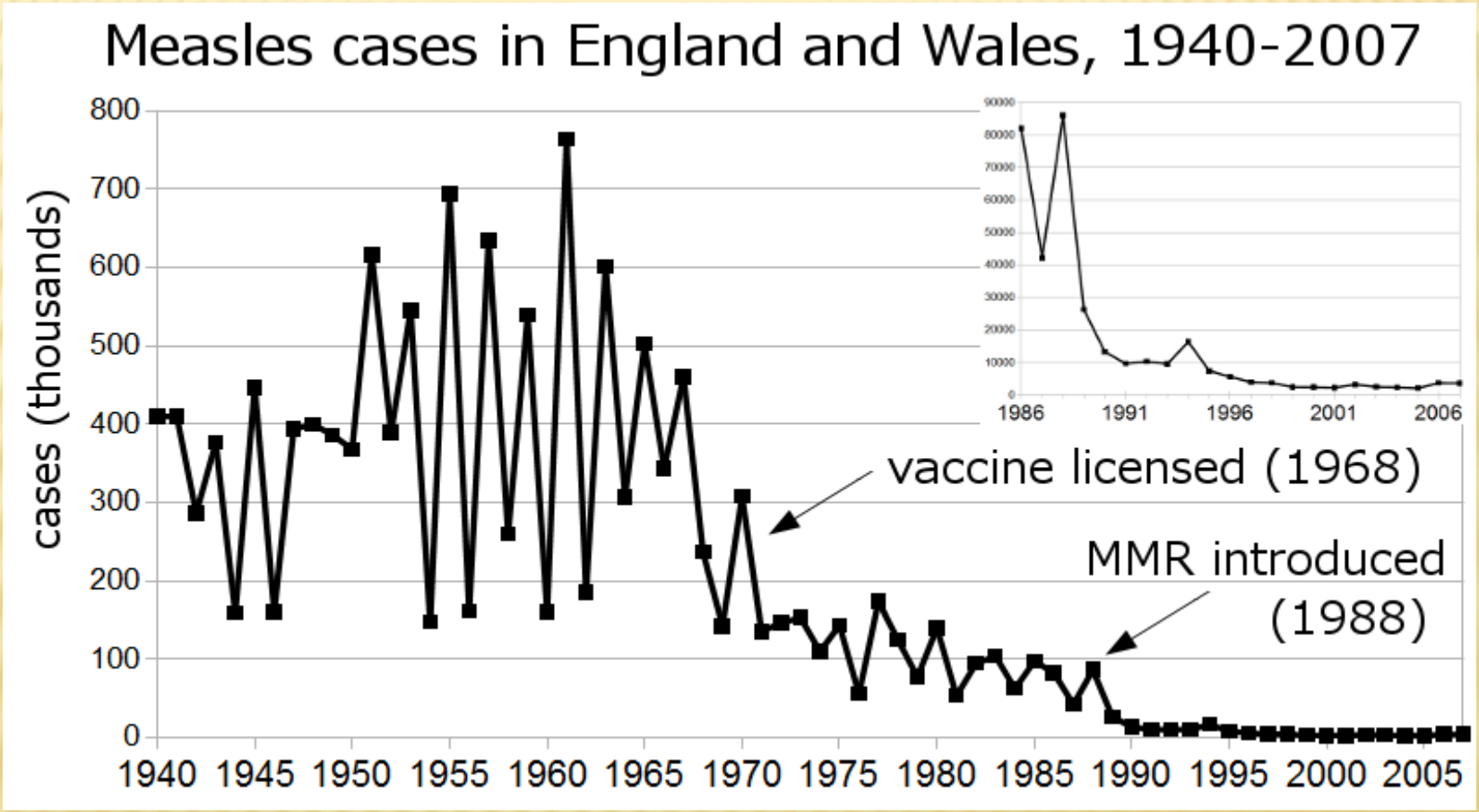


LABORATORY DIAGNOSIS

- Isolation of measles virus from a clinical specimen (e.g., nasopharynx, urine)
- Significant rise in measles IgG by any standard serologic assay (e.g., EIA, HA)
- Positive serologic test for measles IgM antibody

EPIDEMIOLOGY

- Reservoir — Human
- Transmission — Respiratory
  Airborne
- Temporal pattern — Peak in late winter–spring
- Communicability — 4 days before to 4 days after rash onset


Measles cases in England and Wales, 1940-2007
cases (thousands)
800
700
600
500
400
300
200
100
0
1940 1945 1950 1955 1960 1965 1970 1975 1980 1985 1990 1995 2000 2005
vaccine licensed (1968)
MMR introduced (1988)
1986 1991 1996 2001 2006

MEASLES VACCINE

- Live attenuated vaccine.
- The vaccine is available combined with mumps and rubella vaccines as MMR, or combined with mumps, rubella, and varicella vaccine as MMRV (ProQuad).
- Measles vaccine is prepared in chick embryo fibroblast tissue culture.
- MMR and MMRV are supplied as a lyophylized (freeze-dried) powder and are reconstituted with sterile, preservative-free water.
- The vaccines contain a small amount of human albumin, neomycin, sorbitol, and gelatin.

- **Vaccination Schedule and Use**
- Two doses of measles vaccine, as combination MMR, separated by at least 4 weeks, are routinely recommended for all children.
- The first dose of MMR should be given on or after the first birthday.
- The second dose of MMR vaccine should routinely be given at age 4–6 years, before a child enters kindergarten or first grade. The recommended visit at age 11 or 12 years can serve as a catch-up opportunity to verify vaccination status and administer MMR vaccine to those children who have not yet received two doses of MMR.

POSTEXPOSURE PROPHYLAXIS

- Live measles vaccine provides permanent protection and may prevent disease if given within 72 hours of exposure. Immune globulin (IG) may prevent or modify disease and provide temporary protection if given within 6 days of exposure.
- The dose is 0.25 mL/kg body weight, with a maximum of 15 mL intramuscularly.
- The recommended dose of IG for immunocompromised persons is 0.5mL/kg of body weight (maximum 15 mL) intramuscularly.

- IG may be especially indicated for susceptible household contacts of measles patients, particularly contacts younger than 1 year of age (for whom the risk of complications is highest).
- If the child is 12 months of age or older, live measles vaccine should be given about 5 months later when the passive measles antibodies have waned.
- IG should not be used to control measles outbreaks.

MUMPS /PAROTITIS EPIDEMICA/

DEFINITION

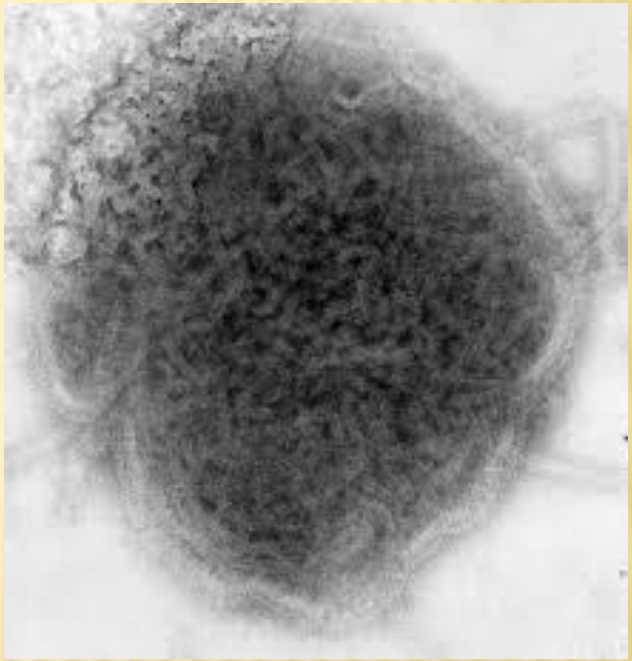
- Mumps is an acute viral illness.
- Parotitis and orchitis were described by Hippocrates in the 5th century BCE.
- In 1934, Johnson and Goodpasture showed that mumps could be transmitted from infected patients to rhesus monkeys and demonstrated that mumps was caused by a filterable agent present in saliva.
- This agent was later shown to be a virus.

PROBLEM STATEMENT

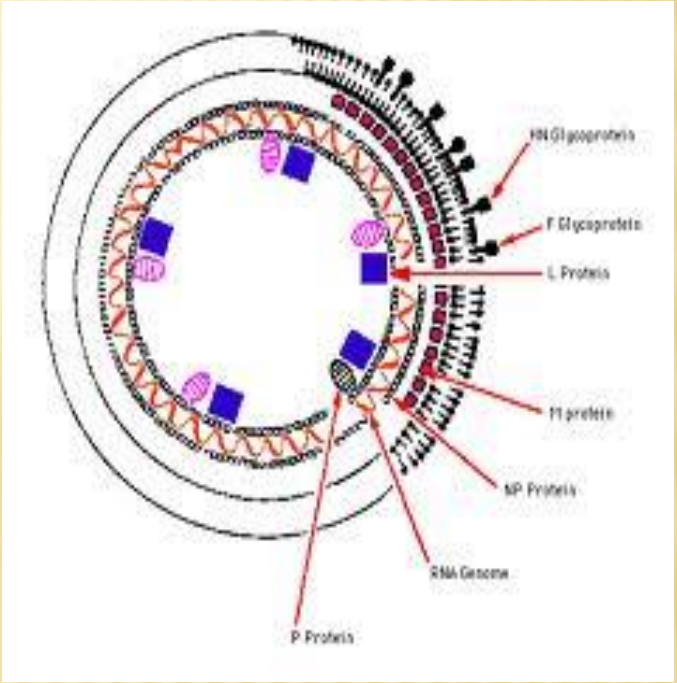
- Mumps was a frequent cause of outbreaks among military personnel in the prevaccine era, and was one of the most common causes of aseptic meningitis and sensorineural deafness in childhood.
- During World War I, only influenza and gonorrhea were more common causes of hospitalization among soldiers.
- A multistate mumps outbreak in 2006 resulted in more than 6,000 reported cases in USA.

AGENT

- Mumps Virus
- Family Paramyxoviridae
- The virus can be isolated or propagated in cultures of various human and monkey tissues and in embryonated eggs.
- It has been recovered from the saliva, cerebrospinal fluid, urine, blood, milk, and infected tissues of patients with mumps.



- spherical or pleiomorphic (variable) shape
- paramyxovirus particles can have sizes ranging from 120–450 nm in diameter
- These particles consist of what is known as a ribonucleoprotein (RNP) complex:

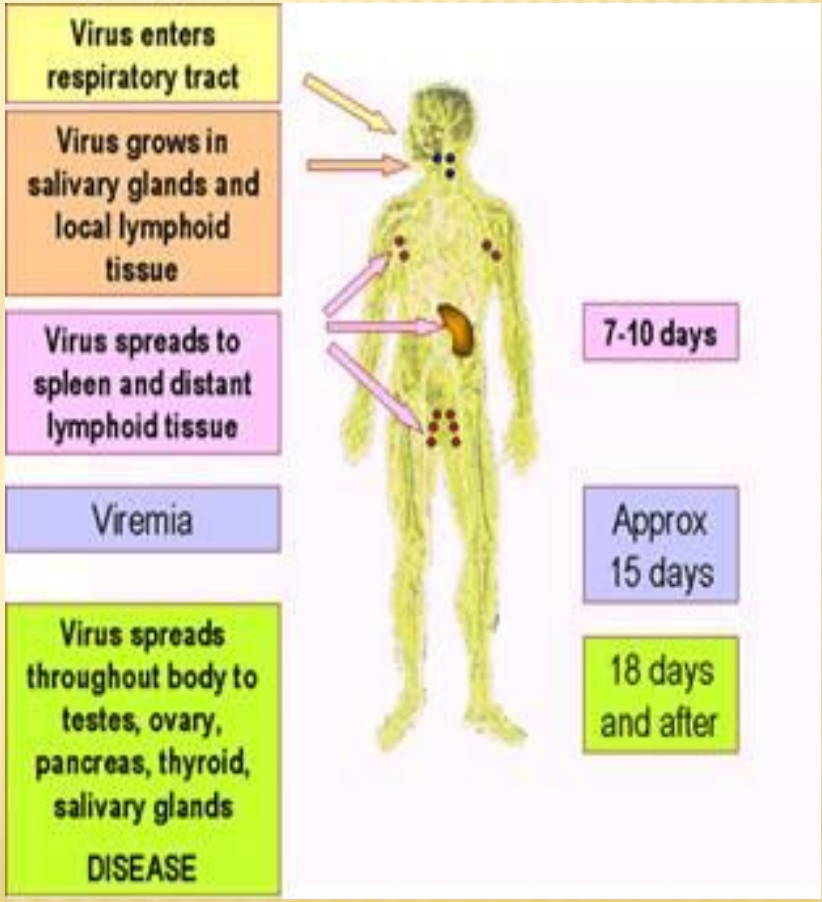


- a single-stranded, linear RNA genome coated by nucleocapsid proteins (NP) in association with an RNA polymerase complex of both large (L) and phosphoprotein (P) subunits.
- It has been estimated that over 2,000 such NP molecules coat the genome along with about 250 P and 25 L molecules.

- This RNP structure interacts with the viral envelope via matrix (M) proteins that are evenly distributed around the virion.
- The envelope, a lipid bilayer derived from the host-cell plasma membrane, harbours multiple copies of a number of glycoproteins required for virus entry and exit:
- hemagglutinin-neuraminidase (HN),
- fusion (F),
- and the small hydrophobic (SH) protein.

PATHOGENESIS

- The virus is acquired by respiratory droplets.
- It replicates in the nasopharynx and regional lymph nodes.
- After 12 to 25 days a viremia occurs, which lasts from 3 to 5 days.

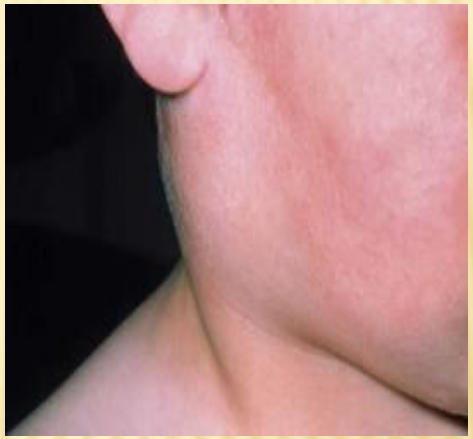


PATHOGENESIS

- During the viremia, the virus spreads to multiple tissues, including the meninges, and glands such as the salivary, pancreas, testes, and ovaries.
- Inflammation in infected tissues leads to characteristic symptoms of parotitis and aseptic meningitis.

CLINICAL FEATURES

- The incubation period of mumps is 14 to 18 days (range, 14 to 25 days).
- The prodromal symptoms are nonspecific, and include myalgia, anorexia, malaise, headache, and low-grade fever.
- **Parotitis** is the most common manifestation and occurs in 30% to 40% of infected persons.
- As many as 20% of mumps infections are asymptomatic.



COMPLICATIONS

- **Central nervous system (CNS)** involvement in the form of **aseptic meningitis** (inflammatory cells in cerebrospinal fluid) is common, occurring asymptomatically **in 50% to 60% of patients.**
- **Symptomatic meningitis** (headache, stiff neck) occurs in up to **15%** of patients and resolves without sequelae in 3 to 10 days.
- **Adults are at higher risk** for this complication than are children, and **boys are more commonly affected** than girls (3:1 ratio).
- Parotitis may be absent in as many as 50% of such patients.
- Encephalitis is rare (less than 2 per 100,000 mumps cases).

- **Orchitis (testicular inflammation)** is the most common complication in post pubertal males.
- It occurs in as many as **50% of post pubertal males**, usually after parotitis.
- It is bilateral in approximately 30% of affected males.
- Approximately **50% of patients** with orchitis have some degree of testicular atrophy, but sterility is rare.

- **Oophoritis (ovarian inflammation)** occurs in 5% of post pubertal females.
- It may mimic appendicitis.
- There is no relationship to impaired fertility.
- **Pancreatitis** is infrequent, but occasionally occurs without parotitis; the hyperglycemia is transient and is reversible.
- Although single instances of diabetes mellitus have been reported, a causal relationship with mumps virus infection has yet to be conclusively demonstrated.

- **Deafness** caused by mumps virus occurs in approximately 1 per 20,000 reported cases. Hearing loss is unilateral in approximately 80% of cases and may be associated with vestibular reactions.
- Electrocardiogram changes compatible with **myocarditis** are seen in 3%–15% of patients with mumps, but symptomatic involvement is rare.
- Other less common complications of mumps include **arthralgia, arthritis, and nephritis.** An average of one death from mumps per year was reported during 1980–1999.

- Mumps is a disease with a favorable outcome.
- An average of one death from mumps per year was reported during 1980–1999 in USA.
- In Bulgaria past 60 years – 8 cases.

LABORATORY DIAGNOSIS

- The diagnosis of mumps is usually suspected based on clinical manifestations, in particular the presence of parotitis.
- Mumps virus can be isolated from clinical specimens.
- Mumps virus can also be detected by polymerase chain reaction (PCR).
- Serology is the simplest method for confirming mumps virus infection and enzyme immunoassay (EIA), is the most commonly used test.
- IgM antibodies usually become detectable during the first few days of illness and reach a peak about a week after onset.
- IgG indicated seroconversion.

EPIDEMIOLOGY

- **Occurrence**
- Mumps occurs worldwide.
- **Reservoir**
- Mumps is a human disease. Although persons with asymptomatic or nonclassical infection can transmit the virus, no carrier state is known to exist.
- **Transmission**
- Mumps is spread through airborne transmission or by direct contact with infected droplet nuclei or saliva.

- **Temporal Pattern**
- Mumps incidence peaks predominantly in late winter and
- spring, but the **disease has been reported throughout the year.**
- **Communicability**
- Contagiousness is similar to that of influenza and rubella, but is less than that for measles or varicella.
- The infectious period is considered to be from 3 days before to the 4th day of active disease; virus has been isolated from saliva 7 days before to 9 days after onset of parotitis.

PROPHYLAXIS

- Mumps virus was isolated in 1945, and an inactivated vaccine was developed in 1948. This vaccine produced only short-lasting immunity, and its use was discontinued in the mid-1970s.
- The currently used Jeryl Lynn strain of live attenuated mumps virus vaccine was licensed in December 1967.
- Mumps vaccine is available combined with measles and rubella vaccines (as **MMR**), or combined with measles, rubella, and varicella vaccine as **MMRV** (ProQuad).

RUBELLA /RUBEOLA/

DEFINITION

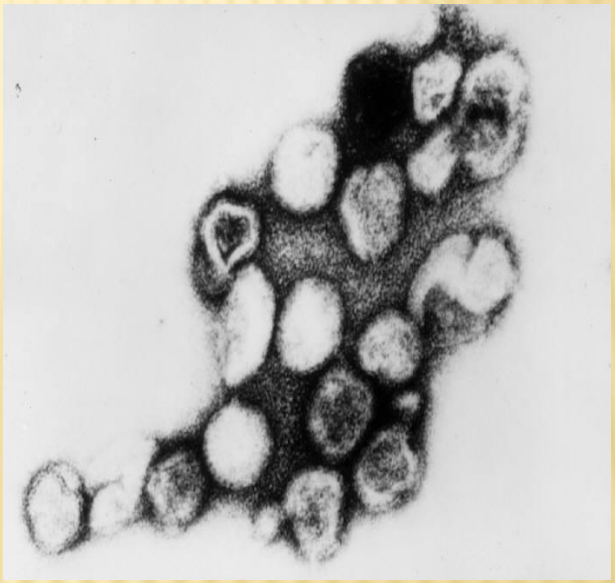
- Rubella is an acute viral illness.
- The disease is a common childhood infection.
- Rubella is transmitted via airborne droplet emission from the upper respiratory tract of active cases.
- Infection of the mother by Rubella virus during pregnancy can be serious; if the mother is infected within the first 20 weeks of pregnancy, the child may be born with congenital rubella syndrom (CRS).

- The name rubella is derived from Latin, meaning “little red.”
- Rubella was initially considered to be a variant of measles or scarlet fever and was called “third disease.”
- It was not until 1814 that it was first described as a separate disease in the German medical literature, hence the common name “German measles.”
- In 1914, Hess postulated a viral etiology based on his work with monkeys.
- Hiro and Tosaka in 1938 confirmed the viral etiology by passing the disease to children using filtered nasal washings from persons with acute cases.

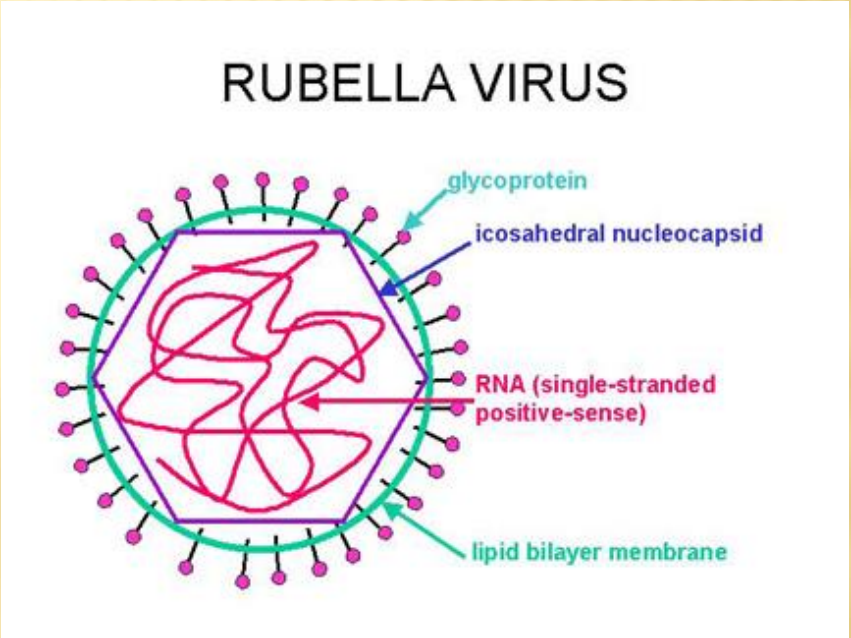
- Following a widespread epidemic of rubella infection in 1940, Norman Gregg, an Australian ophthalmologist, reported in 1941 the occurrence of congenital cataracts among 78 infants born following maternal rubella infection in early pregnancy.
- This was the first published recognition of congenital rubella syndrome (CRS).
- Rubella virus was first isolated in 1962 by Parkman and Weller.
- The first rubella vaccines were licensed in 1969.

AGENT

- Rubella Virus
- Genus Rubivirus
- Family Togaviridae
- RNA virus
- with a single antigenic type

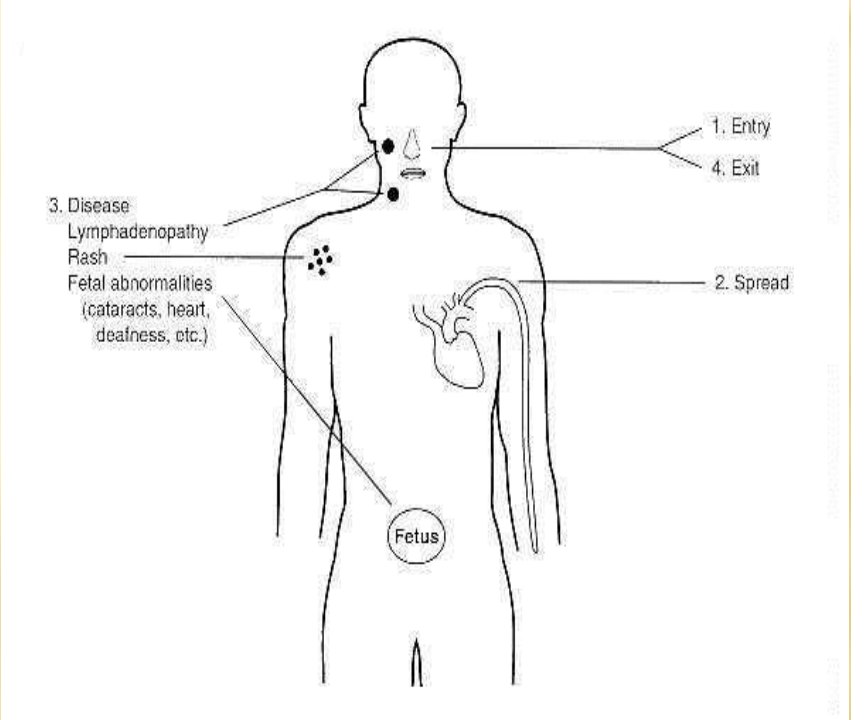


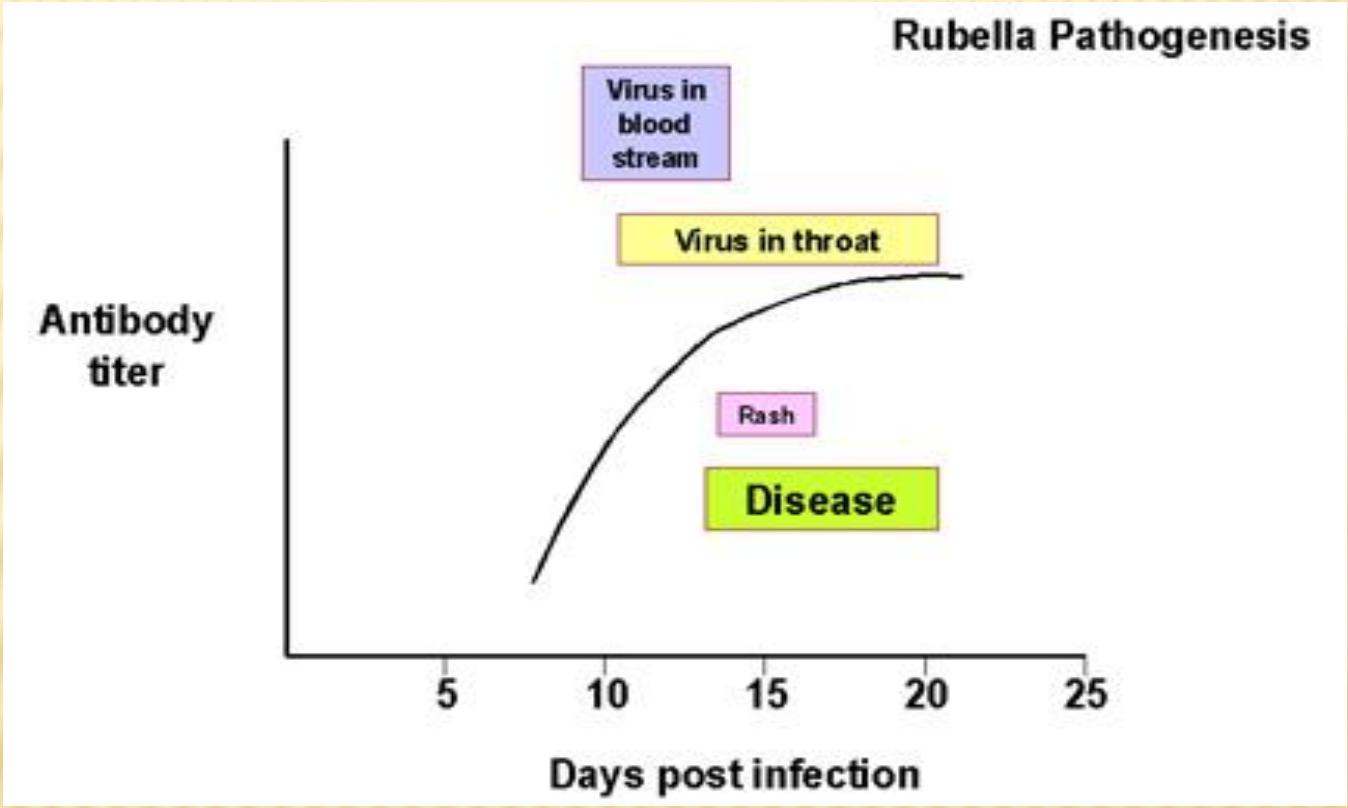
- Spherical form
- Diameter of 50 to 70 nm
- Lipid membrane (viral envelope)
- There are prominent "spikes" (projections) of 6 nm composed of the viral envelope proteins E1 and E2 embedded in the membrane
- Inside the lipid envelope is a capsid of 40 nm in diameter
- The E1 glycoprotein is considered immunodominant in the humoral response induced against the structural proteins and contains both neutralizing and hemagglutinating determinants.



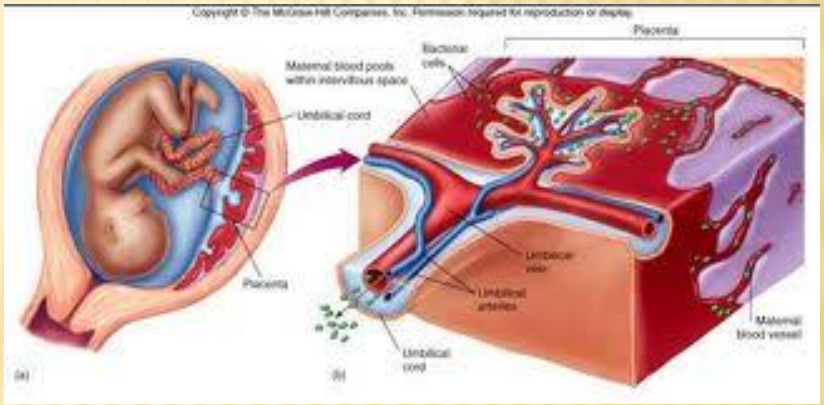
PATHOGENESIS

- Following **respiratory transmission of rubella virus**, **replication** of the virus is thought to occur in the **nasopharynx** and **regional lymph nodes**.
- A viremia occurs 5 to 7 days after exposure with spread of the virus throughout the body.



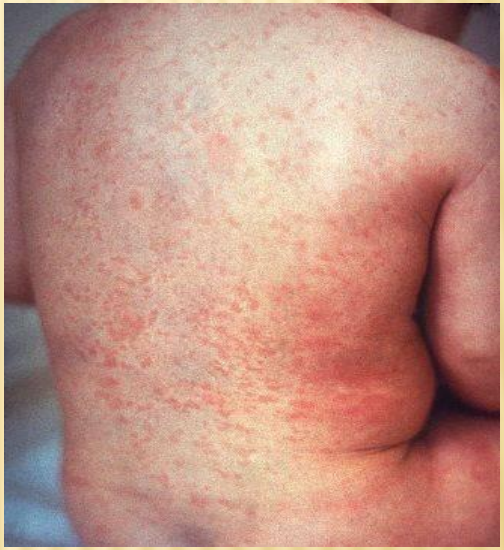

Rubella Pathogenesis
Virus in blood stream
Virus in throat
Antibody titer
Rash
Disease
5
10
15
20
25
Days post infection

- Transplacental infection of the fetus occurs during viremia.
- Fetal damage occurs through destruction of cells as well as mitotic arrest.



CLINICAL FEATURES

- The incubation period of rubella is 14 days, with a range of 12 to 23 days.
- Symptoms are often mild, and up to 50% of infections may be subclinical or inapparent.
- In children, rash is usually the first manifestation and a prodrome is rare.



- In older children and adults, there is often a 1 to 5 day prodrome with low-grade fever, malaise, lymphadenopathy, and upper respiratory symptoms preceding the rash.
- The rash of rubella is maculopapular and occurs 14 to 17 days after exposure.
- The rash usually occurs initially on the face and then progresses from head to foot.
- It lasts about 3 days and is occasionally pruritic.

- The rash is fainter than measles rash and does not coalesce.
- The rash is often more prominent after a hot shower or bath.
- Lymphadenopathy may begin a week before the rash and last several weeks.
- Postauricular, posterior cervical, and suboccipital nodes are commonly involved.

- Arthralgia and arthritis occur so frequently in adults that they are considered by many to be an integral part of the illness rather than a complication.
- Other symptoms of rubella include conjunctivitis, testalgia, or orchitis.
- Forschheimer spots may be noted on the soft palate but are not diagnostic for rubella.

COMPLICATIONS

- Complications of rubella are not common, but they generally occur more often in adults than in children.
- Arthralgia or arthritis may occur in up to 70% of adult women who contract rubella, but it is rare in children and adult males.
- Fingers, wrists, and knees are often affected.
- Joint symptoms tend to occur about the same time or shortly after appearance of the rash and may last for up to 1 month; chronic arthritis is rare.
- Encephalitis occurs in one in 6,000 cases, more frequently in adults (especially in females) than in children.
- Mortality estimates vary from 0 to 50%.

- Hemorrhagic manifestations occur in approximately one per 3,000 cases, occurring more often in children than in adults.
- These manifestations may be secondary to low platelets and vascular damage, with thrombocytopenic purpura being the most common manifestation.
- Gastrointestinal, cerebral, or intrarenal hemorrhage may occur. Effects may last from days to months, and most patients recover.
- Additional complications include orchitis, neuritis, and a rare late syndrome of progressive panencephalitis.

CONGENITAL RUBELLA SYNDROME

- Infection with rubella virus is most severe in early gestation. The virus may affect all organs and cause a variety of congenital defects.
- Infection may lead to fetal death, spontaneous abortion, or premature delivery.
- The severity of the effects of rubella virus on the fetus depends largely on the time of gestation at which infection occurs.

- As many as 85% of infants infected in the first trimester of pregnancy will be found to be affected if followed after birth.
- While fetal infection may occur throughout pregnancy, defects are rare when infection occurs after the 20th week of gestation.
- The overall risk of defects during the third trimester is probably no greater than that associated with uncomplicated pregnancies.

- Congenital infection with rubella virus can affect virtually all organ systems.
- Deafness is the most common and often the sole manifestation of congenital rubella infection, especially after the fourth month of gestation.
- Eye defects, including cataracts, glaucoma, retinopathy, and microphthalmia may occur.

- Cardiac defects such as patent ductus arteriosus, ventricular septal defect, pulmonic stenosis, and coarctation of the aorta are possible.
- Neurologic abnormalities, including microcephaly and mental retardation, and other abnormalities, including bone lesions, splenomegaly, hepatitis, and thrombocytopenia with purpura may occur.

LABORATORY DIAGNOSIS

- The only reliable evidence of acute rubella infection is a positive viral culture for rubella or detection of rubella virus by polymerase chain reaction, the presence of rubella-specific IgM antibody, or demonstration of a significant rise in IgG antibody from paired acute- and convalescent-phase sera with Enzyme-linked immunosorbent assay (ELISA) .

- Rubella virus can be isolated from **nasal, blood, throat, urine and cerebrospinal fluid specimens** from rubella and CRS patients.
- Virus may be isolated **from the pharynx 1 week before and until 2 weeks after rash onset.**

EPIDEMIOLOGY

- **Occurrence**
- Rubella occurs worldwide.
- **Reservoir**
- Rubella is a human disease. There is no known animal reservoir.
- Although infants with CRS may shed rubella virus for an extended period, a true carrier state has not been described.

- **Transmission**

- Rubella is spread from person to person via **airborne transmission or droplets** shed from the respiratory secretions of infected persons.
- There is no evidence of insect transmission.
- Rubella **may be transmitted by persons with subclinical or asymptomatic cases (up to 50% of all rubella virus infections**).

- **Temporal Pattern**
- In temperate areas, incidence is usually highest in late winter and early spring.
- **Communicability**
- Rubella is only moderately contagious. The disease is most contagious when the rash first appears, but virus may be shed from 7 days before to 5–7 days or more after rash onset.
- Infants with CRS shed large quantities of virus from body secretions for up to 1 year and can therefore transmit rubella to persons caring for them who are susceptible to the disease.

RUBELLA VACCINE

- Rubella vaccine is available combined with measles and mumps vaccines as MMR, or combined with mumps, measles, and varicella vaccine as MMRV (ProQuad).

RUBELLA IMMUNITY

- Persons generally can be considered immune to rubella if they have documentation of vaccination with at least one dose of MMR (or MMRV) or other live rubella-containing vaccine administered on or after their first birthday, have serologic evidence of rubella immunity, or were born before 1957.
- Persons who have an “equivocal” serologic test result should be considered rubella-susceptible.
- Although only one dose of rubella-containing vaccine is required as acceptable evidence of immunity to rubella, children should receive two doses of MMR vaccine according to the routine childhood vaccination schedule.

STRATEGIES TO DECREASE RUBELLA AND CRS

- Vaccination of Susceptible Postpubertal Females
- Elimination of indigenous rubella and CRS can be maintained by continuing efforts to vaccinate susceptible hosts.