Measles, Mumps & Rubella

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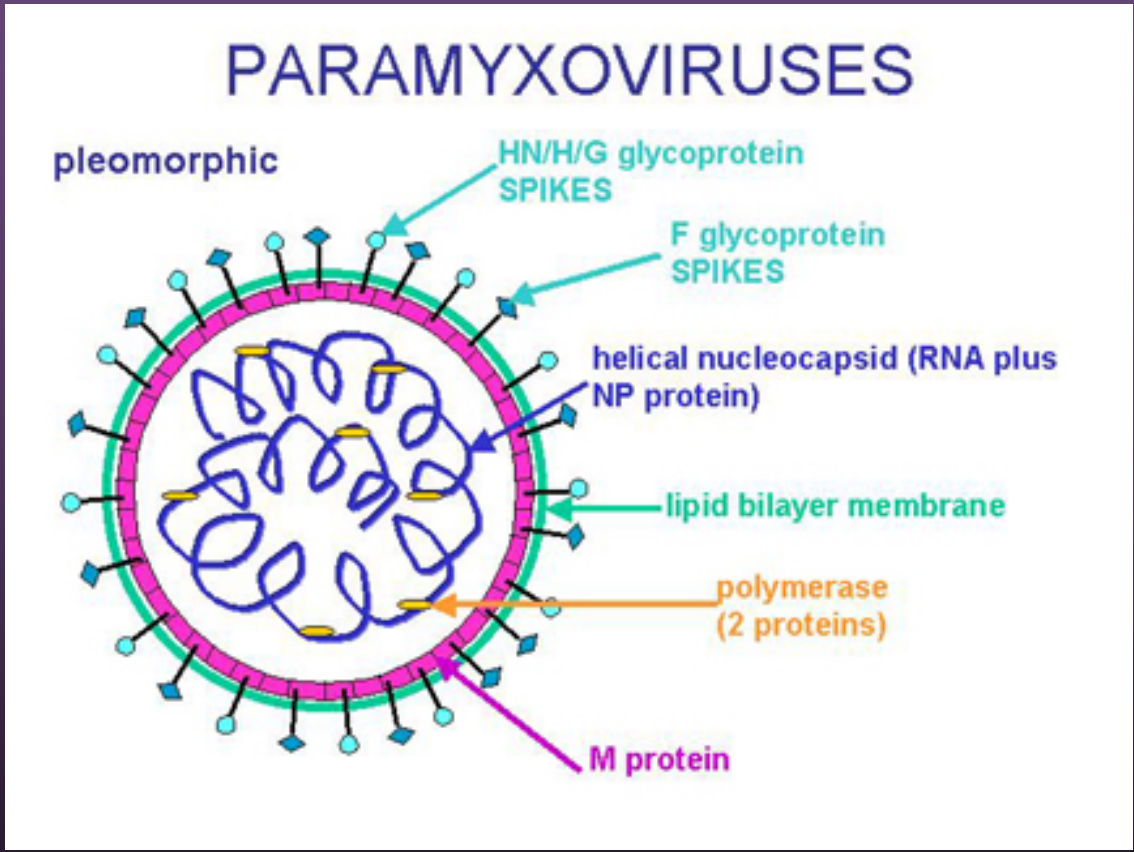
Introduction

- ✓ Infections with measles, mumps and rubella viruses are confined to man and occur worldwide.
- ✓ They are all spread primarily via the aerosol route. Each of these viruses exists as a single serotype.
- ✓ MMR (mumps, measles, rubella) vaccine contains live, attenuated forms of all three of these viruses.
- ✓ Measles and mumps viruses belong to the Paramyxovirus Family and are enveloped, non-segmented, negative-sense RNA viruses with helical symmetry. (Rubella virus is a member of the Togavirus Family and is an enveloped, non-segmented, positive-sense RNA virus with icosahedral symmetry).

Paramyxovirus Family



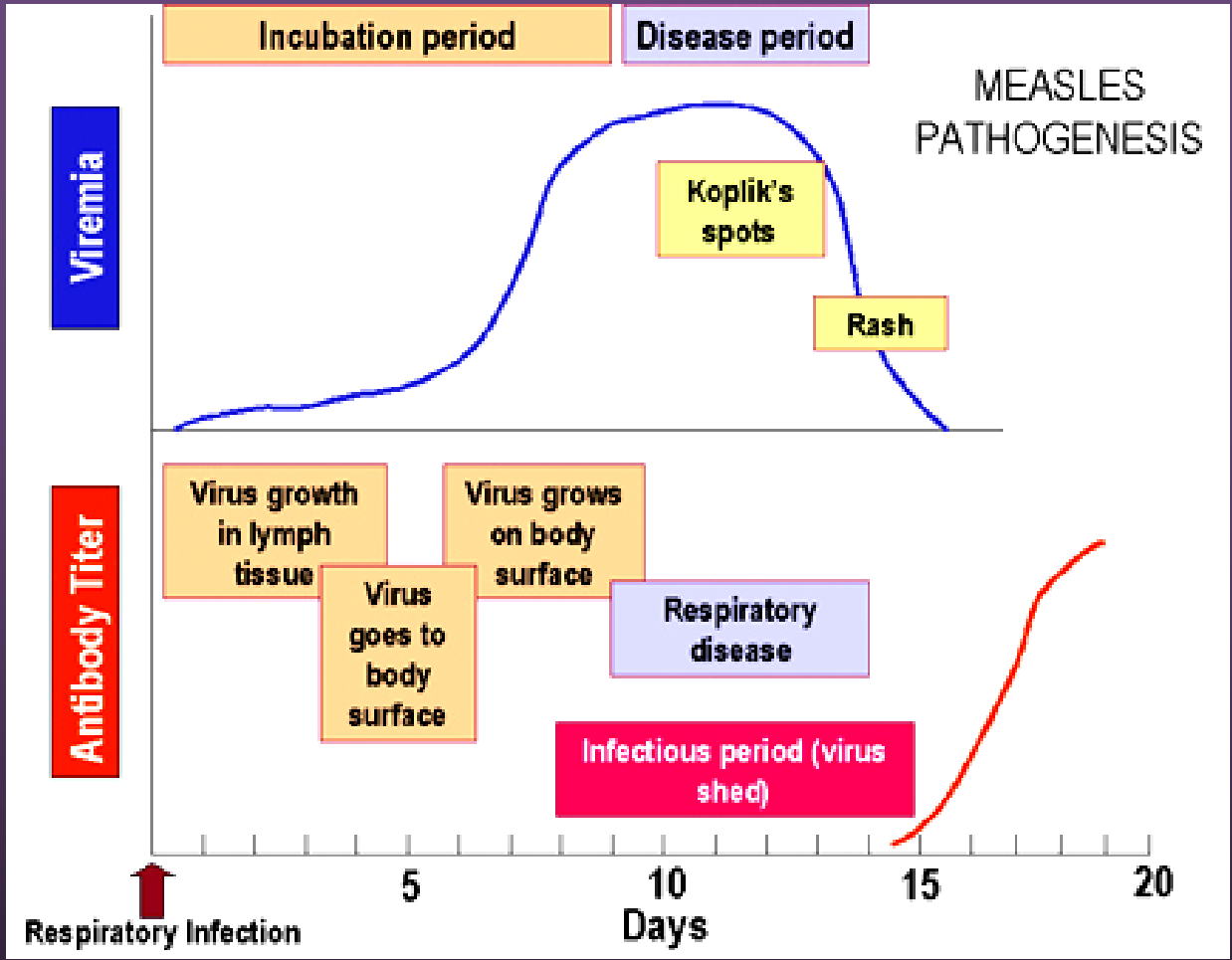
Paramyxovirus structure

Paramyxovirus Family

GENUS	MEMBERS	GLYCOPROTEINS
Paramyxovirus	mumps human Parainfluenza viruses (HPIV 1-4)	HN, F
Morbillivirus	measles	H, F
Pneumovirus	respiratory syncytial virus	G, F

Measles Pathogenesis And Disease

- ✓ Infection is via an aerosol route and the virus is very contagious.
- ✓ The virus replicates initially in the upper/lower respiratory tract.
- ✓ This is followed by replication in lymphoid tissues leading to viraemia and growth in a variety of epithelial sites.
- ✓ The disease develops 1-2 weeks after infection.



The virus invades the body via blood vessels and reaches surface epithelium first in the respiratory tract where there are only 1-2 layers of epithelial cells then in mucosae (Koplik's spots) and finally in the skin (rash).

Uncomplicated disease

- ✓ **Fever**
- ✓ **Respiratory tract symptoms: running nose (coryza), cough**
- ✓ **Conjunctivitis**
- ✓ ***Koplik's spots on mucosal membranes*** **- small (1-3mm), irregular, bright red spots, with bluish-white speck at center - may get enormous number, red areas may become confluent.**
- ✓ **Maculopapular rash (extends from face to extremities).**
- ✓ **Recovery is usually rapid, cell mediated response important (patients with agamma-globulinemia recover normally).**
- ✓ **Tends to be more severe in adults than children.**

Complications of Measles

- ✓ **If patient has an impaired cell-mediated immune response, there is continued growth in lungs leading to giant cell pneumonia (such patients may not have a rash). This is rare, but often fatal.**
- ✓ **Since virus grows in epithelia of the nasopharynx, middle ear, lung, all of these sites may then be susceptible to secondary bacterial infection. Otitis media and bacterial pneumonia are quite common.**
- ✓ **Outcome is affected by the nourishment of the patient and access to medical care. Measles is still a major killer in underdeveloped countries and several studies in areas with severe vitamin A deficiency problems have found that vitamin A treatment of children with measles has resulted in reduction in morbidity and mortality. Pneumonia accounts for 60% of deaths from measles.**

Complications of Measles – Cont.

- **1 in 1000 cases may get encephalitis a few days after the rash disappears. Most patients (90%) survive encephalitis but there may be complications - deafness,mental disorders.**

Subacute Sclerosing Panencephalitis (SSPE)

- ✓ **Very rarely (7 in 1,000,000 cases) the patient may get SSPE.**
- ✓ **This develops 1-10 years after initial infection. It is a progressive, fatal disease.**
- ✓ **Risk factors include acquiring primary measles at an early age.**
- ✓ **The incidence of SSPE has decreased since vaccination. SSPE is associated with defective forms of the virus in the brain and so it is difficult to isolate infectious virus from such patients.**
- ✓ **Certain viral proteins are often not expressed, the M protein being frequently absent.**

CLINCAL ASPECTS OF MEASLES

- **Site of replication of virus** — **Lung**
- **Symptoms in a well nourished child with good medical care** — **Temporary respiratory illness**
- **Symptoms in a malnourished child with poor medical care** — **Pneumonia (life threatening)**

CLINCAL ASPECTS OF MEASLES

- **Site of replication of virus**
- **Symptoms in a well nourished child with good medical care**
- **Symptoms in a malnourished child with poor medical care**

Ear

Otitis media is quite common

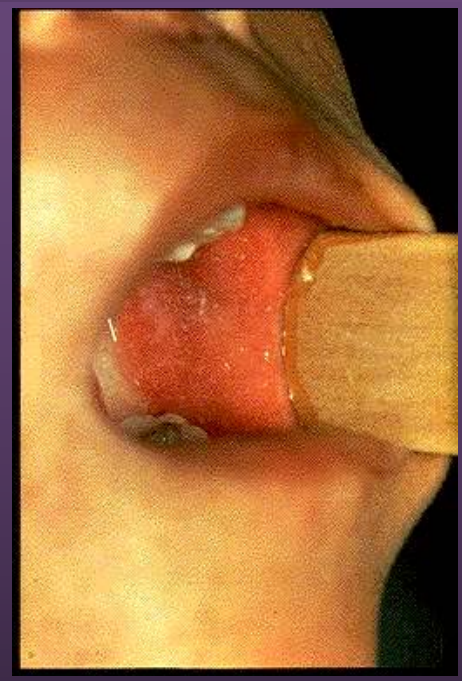
Otitis media is experienced more often and is more severe.

CLINCAL ASPECTS OF MEASLES

- **Site of replication of virus**
- **Symptoms in a well nourished child with good medical care**
- **Symptoms in a malnourished child with poor medical care**

Oral mucosa

Koplik's spots



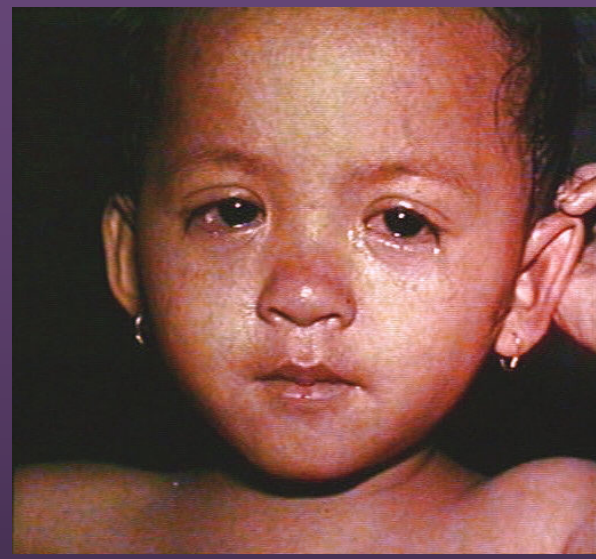
Severe ulcerating lesions

CLINCAL ASPECTS OF MEASLES

- **Site of replication of virus**
- **Symptoms in a well nourished child with good medical care**
- **Symptoms in a malnourished child with poor medical care**

Conjunctiva

Conjunctivitis Eyes of child with measles



Severe corneal lesions. There may be secondary bacterial infections of the eyes and blindness may occur.

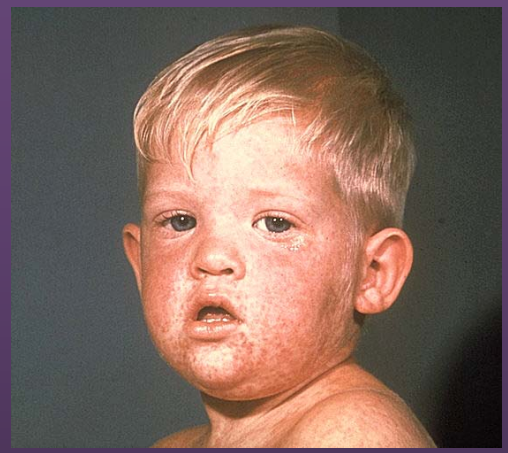
CLINCAL ASPECTS OF MEASLES

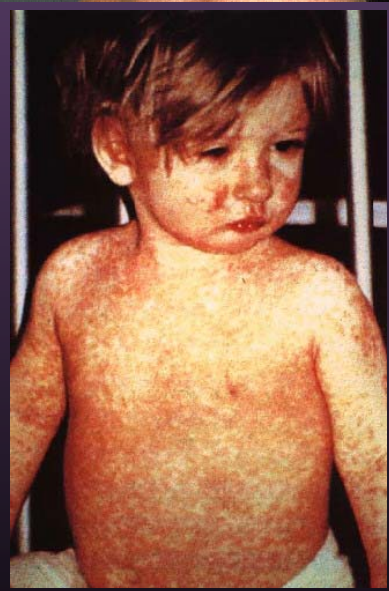
- **Site of replication of virus**
- **Symptoms in a well nourished child with good medical care**
- **Symptoms in a malnourished child with poor medical care**

Skin

- Maculopapular rash Face of boy with measles.
3rd day of rash.
- This child shows a classic day-4 rash with measles.

Possibility of hemorrhagic rashes (black measles)





CLINCAL ASPECTS OF MEASLES

•Site of replication of virus	Intestinal tract
•Symptoms in a well nourished child with good medical care	No lesion
•Symptoms in a malnourished child with poor medical care	Diarrhea which increases malnutrition, halts growth and impairs recovery

CLINCAL ASPECTS OF MEASLES

•Site of replication of virus	Urinary tract
•Symptoms in a well nourished child with good medical care	Virus in urine
•Symptoms in a malnourished child with poor medical care	No further effect

Epidemiology

- ✓ Almost all infected individuals show signs of disease.
- ✓ There is only one serotype of measles and a single natural infection gives life-long protection.
- ✓ The main route of infection is via inhalation.
- ✓ Measles virus is highly contagious. Note the period of maximum contagiousness is the 2-3 day period before onset of rash.

Diagnosis

- ✓ Clinical picture is the first part of diagnosis (that is: exposure plus upper respiratory tract symptoms, Koplik's spots and rash (which is usually quite characteristic for physicians familiar with measles).
- ✓ This diagnosis is confirmed by serodiagnosis or isolation.
- ✓ Serodiagnosis is simpler but two samples are needed, one 10-21days post rash, and so takes longer.
- ✓ It is recommended that all suspect cases should be confirmed by laboratory testing.

Prevention

- ✓ There is an attenuated virus vaccine.
  - 1st dose of the vaccine at 12-15 months.
  - 2nd dose is administered at 4-6 yrs of age

  The vaccine gives long term immunity and does not spread from the vaccinee.
- ✓ Immune serum globulin can be used for at risk patients during an outbreak; that is those less than 1 year old or with impaired cellular immunity.

Treatment

No antiviral therapy available for primary disease.
Treat complications appropriately.

MUMPS

- ✓ Mumps is very contagious and is probably usually acquired from respiratory secretions and saliva via aerosols or fomites.
- ✓ The virus is secreted in urine and so urine is a possible source of infection.

Pathogenesis of Mumps

Virus enters respiratory tract

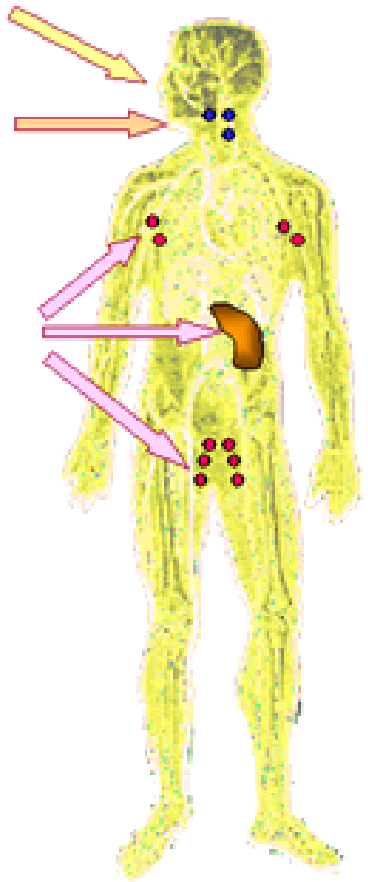
Virus grows in salivary glands and local lymphoid tissue

Virus spreads to spleen and distant lymphoid tissue

Viremia

Virus spreads throughout body to testes, ovary, pancreas, thyroid, salivary glands

DISEASE



7-10 days

Approx 15 days

18 days and after

MUMPS INFECTION

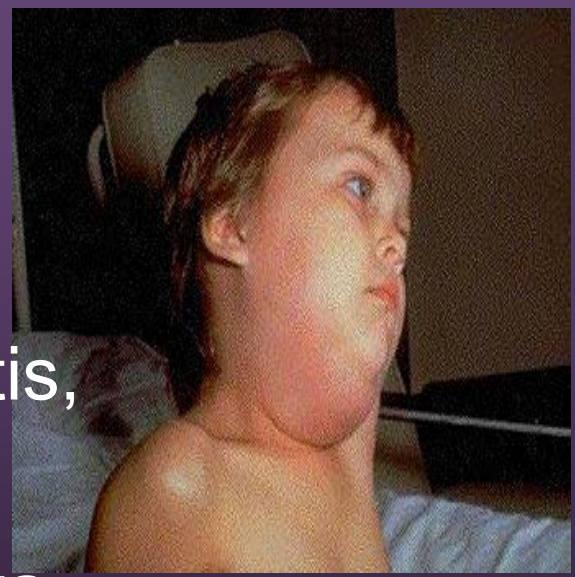
- ✓Virus infects upper/lower respiratory tract leading to local replication.
- ✓The virus spreads to lymphoid tissue which, in turn, leads to viraemia.
- ✓The virus thus spreads to a variety of sites, including salivary, other glands and other body sites.
- ✓The average time to full manifestation of disease is 2-3 wks but there may be fever, anorexia, malaise.

CLINCAL ASPECTS OF MUMPS

- **Site of replication of virus**

Salivary glands

- **Symptoms**



- Inflammation, parotitis, in a child with mumps
- Virus is shed in saliva from 3 days before to 6 days after symptoms

CLINCAL ASPECTS OF MUMPS

- **Site of replication of virus**
- **Symptoms**
- **Notes**

Meninges Brain

Meningitis Encephalitis
Up to 7 days after parotitis

Meningitis is found in about 10% of cases. Encephalitis is less common. Usually there is complete recovery; nerve deafness is a rare complication

CLINCAL ASPECTS OF MUMPS

•Site of replication of virus	Kidney
•Symptoms	Virus in urine
•Notes	No clinical consequences

CLINCAL ASPECTS OF MUMPS

•Site of replication of virus	Testis, ovary
•Symptoms	Epididymo-Orchitis more damaging in male
•Notes	Common in adults (20% in adult males).

CLINCAL ASPECTS OF MUMPS

•Site of replication of virus	Pancreas
•Symptoms	Pancreatitis
•Notes	Rare complication (There is possible role in juvenile diabetes)

CLINCAL ASPECTS OF MUMPS

- **Site of replication of virus** — Mammary gland
- **Symptoms** — Virus detectable in milk; mastitis in 10% Post pubertal females

CLINCAL ASPECTS OF MUMPS

•Site of replication of virus	Thyroid
•Symptoms	Thyroiditis
•Notes	Rare

CLINCAL ASPECTS OF MUMPS

•Site of replication of virus	Myocardium
•Symptoms	Myocarditis
•Notes	Rare

CLINCAL ASPECTS OF MUMPS

•Site of replication of virus	Joints
•Symptoms	Arthritis
•Notes	Rare

Symptoms of Mumps

- ✓ **Fever**
- ✓ **Pain from parotitis swelling persists 7-10 days**
- ✓ **Meningitis more common in males, usually mild**
- ✓ **Hearing loss, rare.**
- ✓ **Orchitis - especially severe in adolescent and adult males, usually unilateral, some degree of testicular atrophy, rarely causes infertility.**
- ✓ **Pancreatitis - occurs, but very little evidence from controlled studies that mumps plays any role in diabetes mellitus.**
- ✓ **More severe in adults.**

Epidemiology

- ✓ Man is the only known natural host. Many (~30%) infections are sub-clinical.
- ✓ Single serotype.
- ✓ Mumps is contagious from ~7 days before infection becomes clinically apparent at ~9 days afterwards.

Diagnosis

- ✓ Approximately 30% of infections are sub-clinical.
- ✓ Parotitis is suggestive (30-40% infections).
- ✓ The disease is confirmed by isolating the virus or by serology (HI, CFT, ELISA).
- ✓ IgM Ab can be detected when the rash is present, or by a 4 fold increase in the titer of mumps-specific Abs between paired sera.

Prevention & Treatment

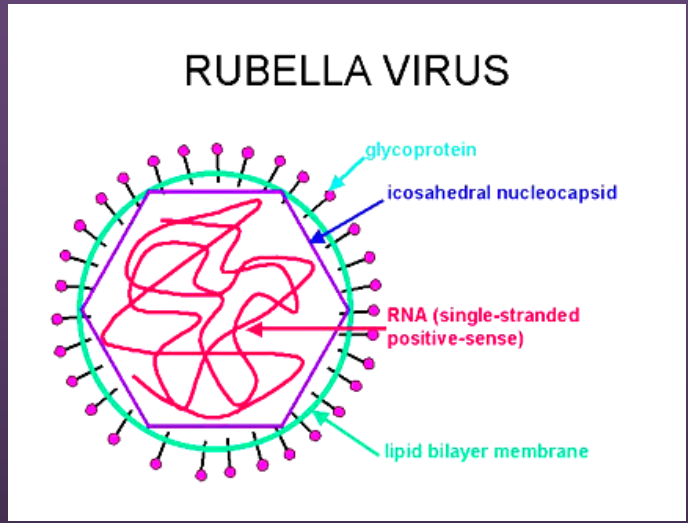
- ✓ Attenuated vaccine. The vaccine virus does not spread to contacts and gives long-term immunity.
- ✓ It is given as MMR vaccine (three live, attenuated viruses: **M**umps, **M**easles and **R**ubella).
- ✓ Vaccine is contraindicated in immunosuppressed patients and in pregnant women.
- ✓ There is no specific treatment for mumps.

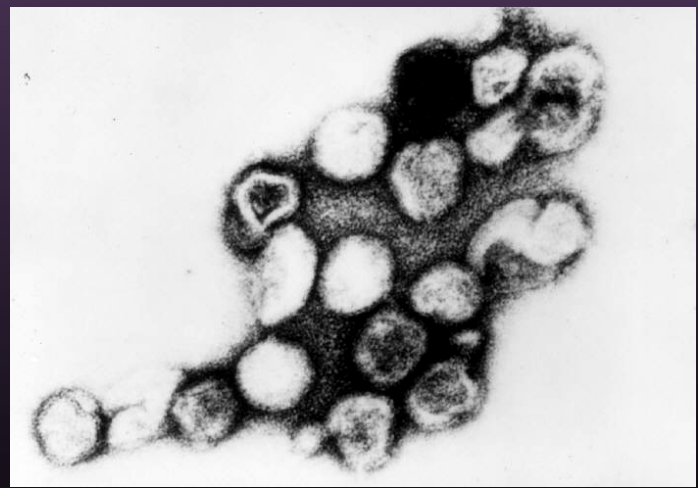
Rubella (German Measles) Virus

Rubella (means "little red" also known as German measles) is a mild disease in children and adults, but can cause devastating problems if it infects the fetus, especially if infection is in the first few weeks of pregnancy.

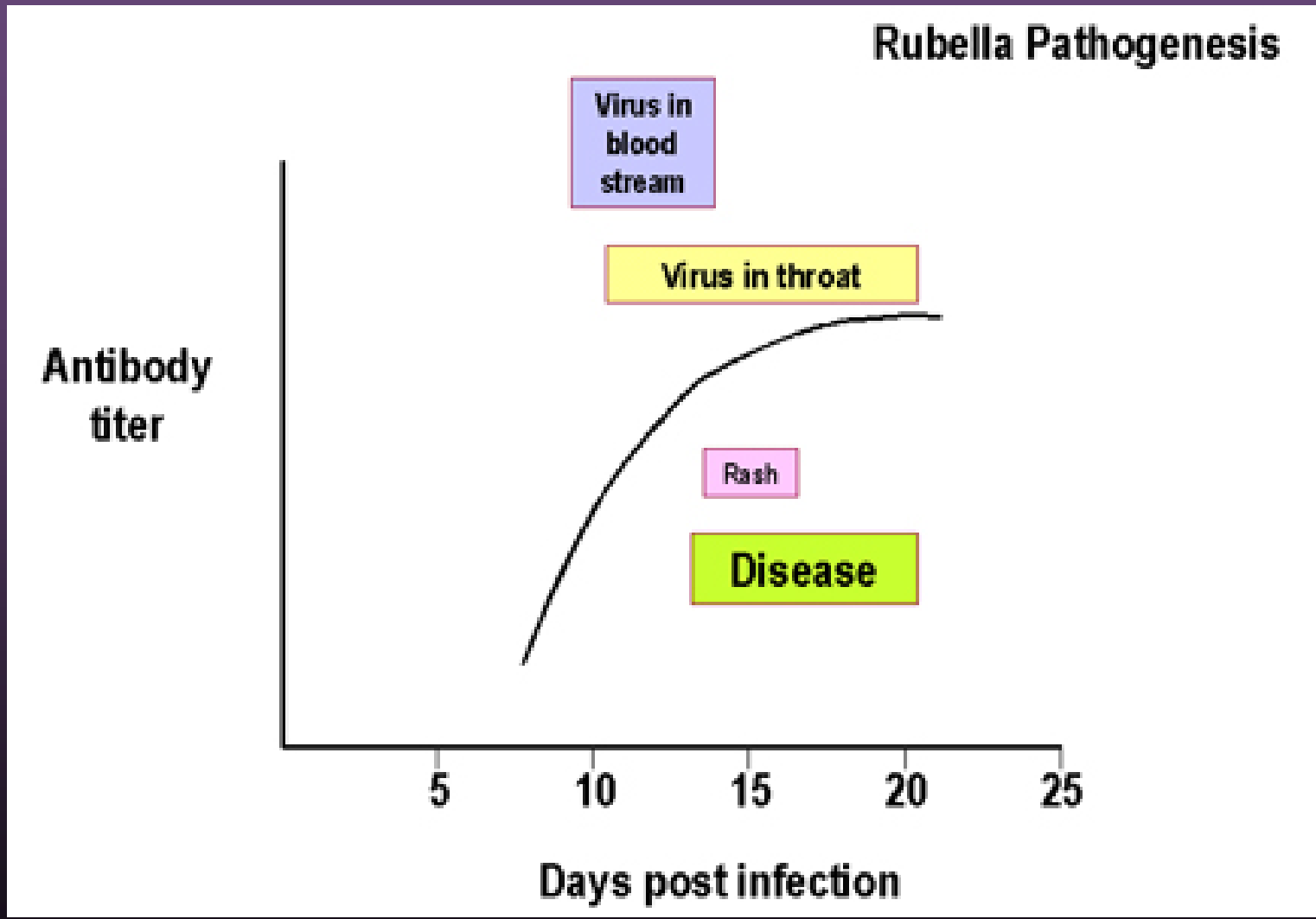
The Virus

- ✓ **Rubella virus is the only member of the Rubrivirus genus of the Togavirus family.**
- ✓ **Unlike most Togaviruses it is NOT arthropod borne, but is acquired via the respiratory route.**
- ✓ **It is an enveloped, non-segmented, positive sense, RNA virus and replicates in the cytoplasm.**
- ✓ **Its nucleocapsid has icosahedral symmetry.**
- ✓ **There is only one major antigenic type.**





Pathogenesis And Disease



CLINCAL ASPECTS OF RUBELLA

•Site of replication of virus	Respiratory tract
•Symptoms	Minor symptoms although virus is shed (Mild sore throat, cough)
•Notes	Patient is infectious 5 days before to 3 days after symptoms

CLINCAL ASPECTS OF RUBELLA

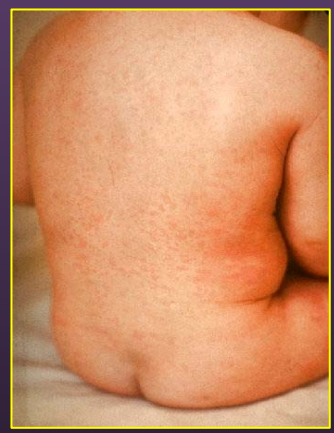
- **Site of replication of virus**

Skin

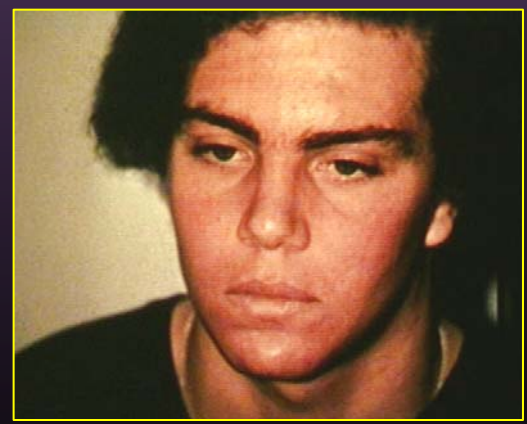
Infant with congenital rubella and "blueberry muffin" skin lesions.

- **Symptoms**

Rash



Rash of rubella on skin of child's back. Distribution is similar to that of measles but the lesions are less intensely red.



CLINCAL ASPECTS OF RUBELLA

•Site of replication of virus	Lymph nodes
•Symptoms	Lymphadenopathy
•Notes	Commoner in posterior triangle of neck or behind ear

CLINCAL ASPECTS OF RUBELLA

- Site of replication of virus

Joints

- Symptoms

Arthritis

CLINCAL ASPECTS OF RUBELLA

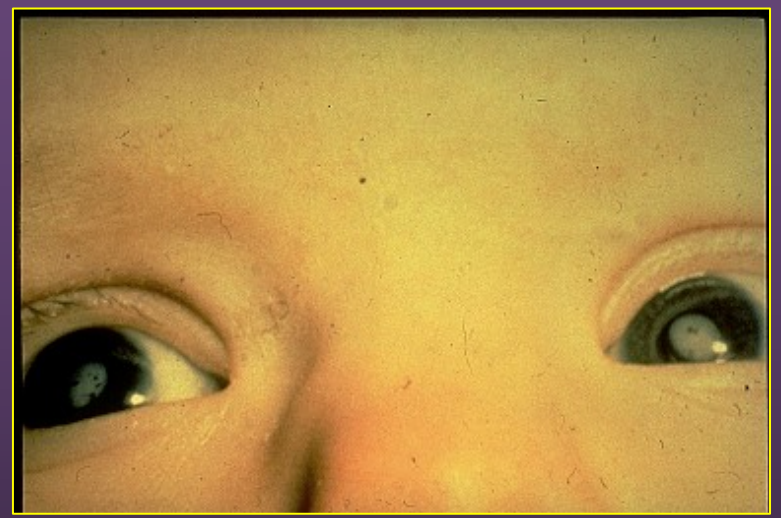
- **Site of replication of virus**
- **Symptoms**
- **Notes**

Placenta/fetus

Placentitis

Fetal damage

Congenital rubella



Baby born with rubella: Thickening of the lens of the eye that causes blindness (cataracts)

Children And Adults

- ✓ **Man is the only host. Virus is spread via an aerosol route and occurs throughout the world.**
- ✓ **Initial site of infection is the upper respiratory tract.**
- ✓ **The virus replicates locally (epithelium, lymph nodes) leading to viraemia and spread to other tissues. As a result the disease symptoms develop.**
- ✓ **Rash (if it occurs) starts approximately 2 weeks after initial infection.**
- ✓ **There is probably an immunological basis for rash (since it occurs as antibody titers rise).**
- ✓ **The patient is infectious from about 1 week before onset of rash to about 1 week after.**
- ✓ **Disease results in low grade fever, rash, sore throat, lymphadenopathy.**

Children And Adults – Cont.

- ✓ **Maculopapular rash begins on the face and lasts from 12hr to 5days.**
- ✓ **Some individuals (especially adults and especially women) get arthralgia and sometimes arthritis which usually clears up in a few weeks.**
- ✓ **Recovery: T-cell immunity plays an important role in recovery. IgM may persist for up to a year. There are also IgG, IgA responses.**
- ✓ **Complications are extremely rarely (1 in 6000 cases) - rubella encephalopathy (headache, vomiting, stiff neck, lethargy, convulsions) may occur about 6 days after rash. It usually lasts only a few days and most patients recover (no sequelae), If death occurs, it is within few days of onset of symptoms.**

FETUS

- ✓ **The risk to a fetus is highest in the first few weeks of pregnancy and then declines in terms of both frequency and severity, although there is still some risk in second trimester. Virus infects the placenta and then spreads to the fetus.**
- ✓ **If non-immune mothers are infected in the first trimester, up to 80% of neonates may have sequelae:**

- Hearing loss

- Congenital heart defects

- Neurological problems (psychomotor retardation, mental retardation)

- Ophthalmic problems (cataract, glaucoma)

- Intrauterine growth retardation

- Thrombocytopenia purpura

- Hepatomegaly **- Splenomegaly**

Other Complications

- ✓ Virus from congenital infections persists after birth; Those with congenital infections can infect others after birth for a year or more. Virus occurs in Naso-pharyngeal secretions, urine and feces.
- ✓ Later on, patients with congenital rubella syndrome may develop additional complications including diabetes mellitus (up to 20%), thyroid dysfunction, growth hormone deficiency, ocular complications.
- ✓ Progressive rubella panencephalitis; This is an extremely rare slow virus disease. It usually develops in the teens with death within 8 years. Most often it is associated with congenital rubella and may be associated with childhood rubella.

Epidemiology

- ✓ Man is the only host.
- ✓ Rubella occurs world wide.
- ✓ Periodic epidemics occur in an unvaccinated population.
- ✓ Natural infection protects for life (there is a single serotype).

Diagnosis Of Rubella

- ✓ **Many (possibly 50%) infections are apparently sub-clinical and many infections go unrecognized, even if symptoms develop (rash is not always present).**
- ✓ **Infections with many other agents give similar symptoms to rubella (e.g. infection with human parvovirus, certain arboviruses, many of the enterovirus group of Picornaviruses, some adenoviruses, EBV, scarlet fever, toxic drug reactions).**
- ✓ **Isolation of virus appears to be difficult**
- ✓ **Serological tests are needed to confirm infection of individual.**

  - anti-rubella-specific IgM

  - 4 fold increase in specific IgG Ab titer

  - Abs to rubella are assayed early in pregnancy to determine the immune status of the women

Prevention And Treatment

- ✓ MMR vaccine
- ✓ It is important that women are vaccinated prior to their first pregnancy.
- ✓ If the patient is pregnant and sero-negative, the pregnancy should be monitored carefully and the patient vaccinated postpartum.
- ✓ There is no specific treatment. Supportive care should be used