AZERBAIJAN MEDICAL UNIVERSITY
DEPARTMENT OF MEDICAL MICROBIOLOGY and IMMUNOLOGY

Lecture 8.

Families of Herpesviridae, Picornaviridae, Rhabdoviridae and arboviruses group (families of Togaviridae, Flaviviridae, Bunyaviridae, Filoviridae, Reoviridae and Arenaviridae)

FACULTY: ***General Medicine***
SUBJECT: ***Medical microbiology - 2***

Discussed questions:

Lecture plan:

1. Family Herpesviridae. Classification. Virion structure, cultivation. Resistance, antigens. Persistence. Simple herpes viruses, types, role in human pathology, microbiological diagnosis. Chickenpox virus. Pathogenetic features of the disease, microb diagnosis. Cytomegalovirus and Epstein-Barr virus. Morpho-biological characteristics, diseases caused by it. Microb diagnostics. Other human herpesviruses (HIV-6, IHV-7, IHV-8).
2. Family Picornaviridae. General characteristics, classification.

- Enteroviruses. Poliomyelitis virus, cultivation. Serotypes. Pathogenicity for humans. Coxsackie and ECHO viruses, human diseases. Microbiological diagnostics. Specific prevention and treatment.

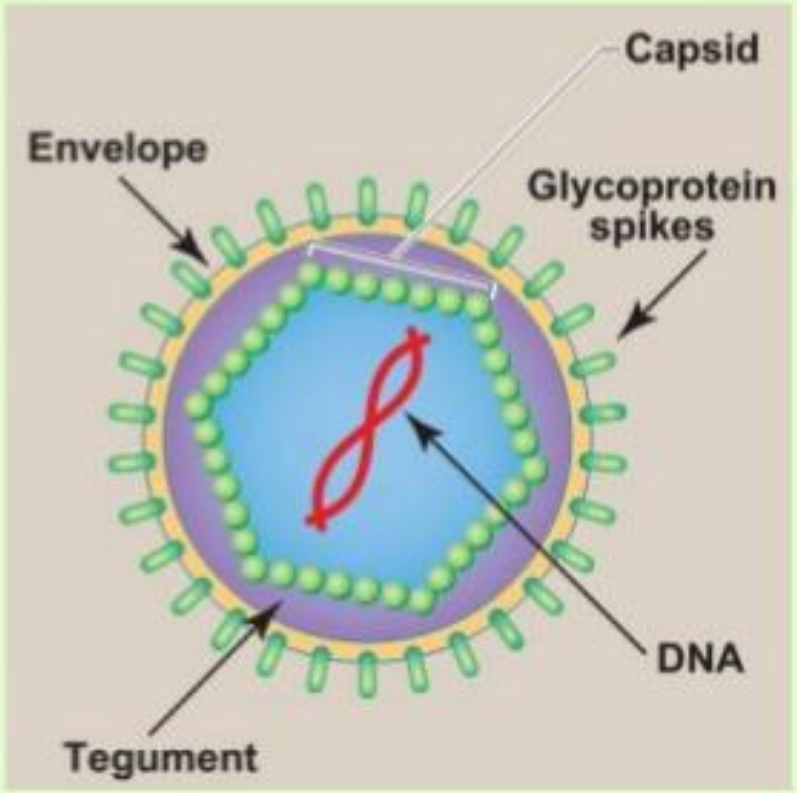
3. Rhabdoviridae family. Rabies virus. Virion structure, cultivation. Pathogenesis of the disease. Microbiological diagnosis of rabies, specific prevention.
4. Rubivirus genus. Rubella virus. Complications, microb diagnosis, specific prevention and treatment for pregnant women.
5. Group of arboviruses. General features.

- Family Togaviridae. General features. Classification. The role of the alphavirus genus in human pathology. Sindbis and Semlika forest viruses, diseases caused by them, microbiological diagnosis.
- Family Flaviviridae. Yellow fever, Dengue fever, tick-borne encephalitis, hemorrhagic fever viruses, characteristics, cultivation. Immunity, microb diagnosis.
- Bunyaviridae family, characteristics. Its role in human pathology (Crimea-Congo hemorrhagic fever, Hantavirus pneumonia syndrome (HPS), hemorrhagic fever with renal syndrome (HRFS)).
- Filoviridae family, characteristics. Role in human pathology (Marburg and Ebola).
- Family Reoviridae, characteristics. Role in human pathology (Rotaviruses).
- Family Arenaviridae, characteristics. Role in human pathology (Lass fever).

Herpes viruses

Introduction

- It's a kind of enveloped DNA virus.
- **Icosahedral** core surrounded by a lipoprotein **envelope.**
- linear double-stranded DNA.
- Large (120–200 nm in diameter), second in size only to poxviruses.
- Capsid surrounds DNA core and over the capsid is tegument (a protein-filled region).
- Nuclear membrane derived lipid bilayer containing viral glycoproteins

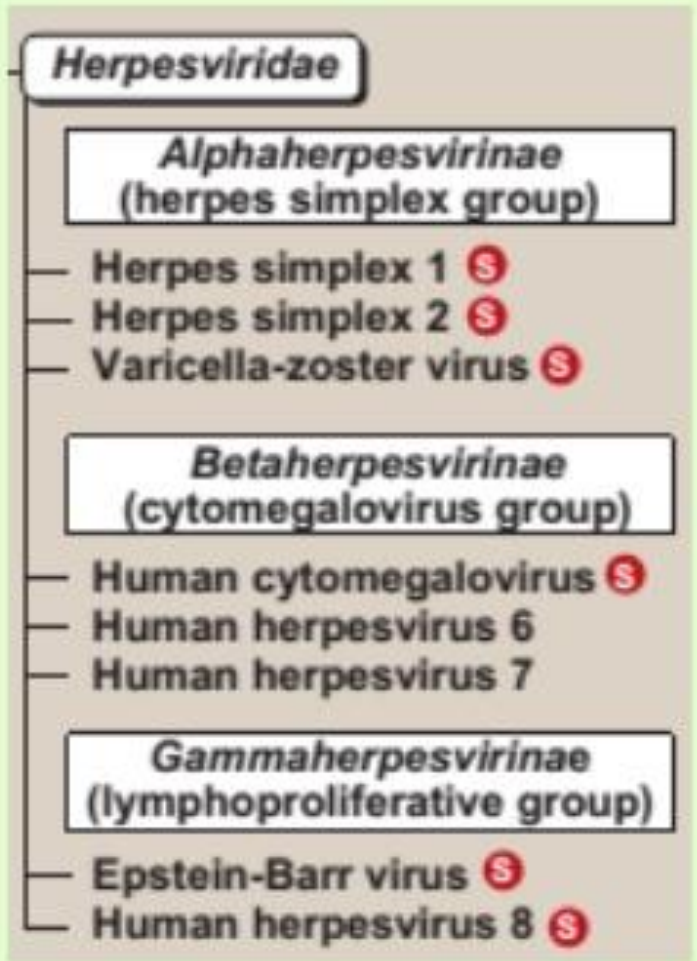


Classification

- Eight human herpesvirus species are known.
  - **Herpes Simplex Virus type 1 (HSV-1)**
  - **Herpes Simplex Virus type 2 (HSV-2)**
  - **Varicella-Zoster Virus (VZV)**
  - **Cytomegalovirus (CMV)**
  - **Epstein-Barr Virus (EBV)**
  - **Human Herpes Virus type 6 (HHV-6)**
  - **Human Herpes Virus type 7 (HHV-7)**
  - **Human Herpes Virus type 8 (HHV-8)**

Classification

- Its also classified on the basis of on biologic characteristics:
  - **Alphaherpesvirinae (herpes simplex virus group)**
  - **Betaherpesvirinae (cytomegalovirus group)**
  - **Gammaherpesvirinae (lymphoproliferative group)**



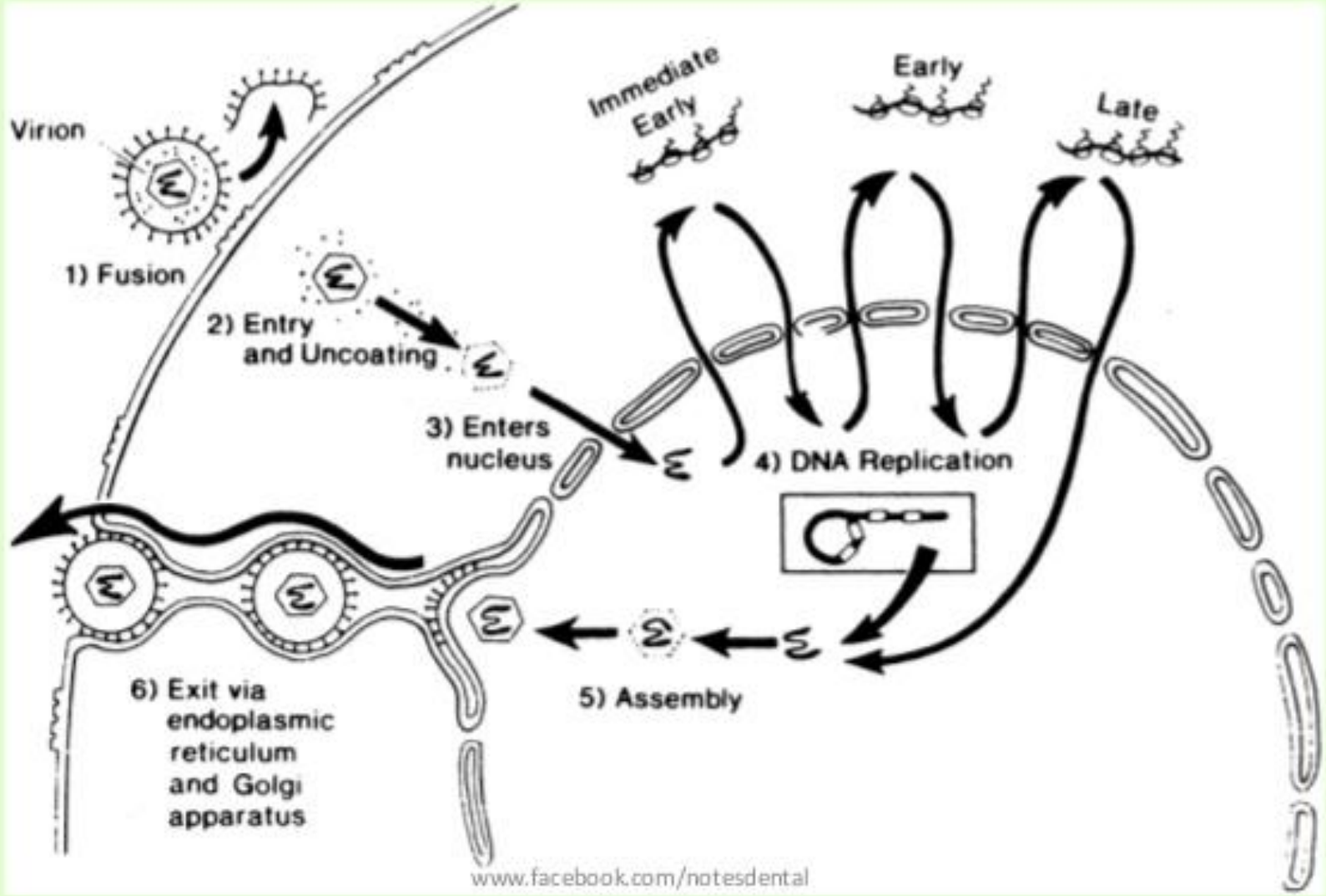
Herpes Simplex Viruses

- Herpes simplex virus **type 1 (HSV-1)** and **type 2 (HSV-2)** are distinguished by two main criteria
  - Antigenicity
  - location of lesions.
- HSV-1: **above the waist,** primarily in adults
  - Acute gingivostomatitis,
  - Recurrent herpes labialis (cold sores),
  - Keratoconjunctivitis (keratitis),
  - Encephalitis
- HSV-2: **below the waist**
  - herpes genitalis(genital herpes),
  - Neonatal encephalitis and other forms of neonatal herpes
  - Aseptic meningitis
- Humans are the natural hosts of both.

HSV - Replication

- DNA released in the cytoplasm
- DNA migrates to the nucleus
- mRNA (transcription) synthesis takes place in the nucleus by using host RNA polymerase
- mRNA transported to the cytoplasm
- New viral proteins made and migrate to nucleus
- Genomic DNA (replication) synthesis takes place in the nucleus by using viral DNA polymerase

HSV - Replication

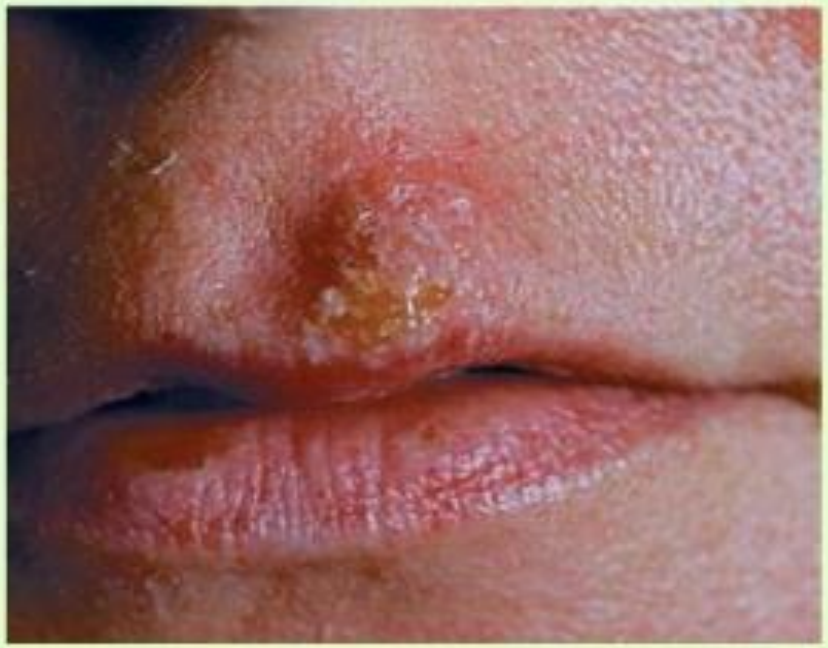


Transmission

- HSV 1: transmitted primarily in **saliva.**
- **HSV 2:** transmitted by **sexual contact**
- **Oral–genital sexual** activity: HSV-1 infections of the genitals and HSV-2 lesions in the oral cavity.
  - 10–20% of cases
- HSV-2 infections has markedly increase comparatively.

Clinical Findings: HSV-1

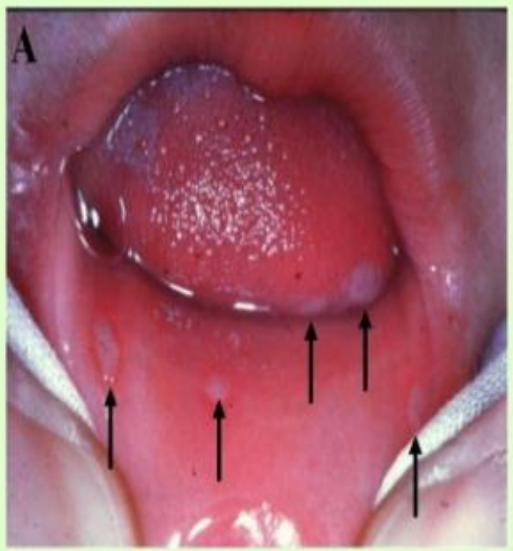
- causes several forms of primary and recurrent disease.
- **Gingivostomatitis**
  - Occurs primarily in children andis characterized by fever, irritability, and vesicular lesions in the mouth.
  - The primary disease is more severe and lasts longer than recurrences.
  - The lesions heal spontaneously in 2 to 3 weeks.
  - Many children have asymptomatic primary infections
- **Herpes labialis**
  - fever blisters or cold sores is the milder, recurrent form
  - characterized by crops of vesicles, usually at the mucocutaneous junction of the lips or nose
  - Recurrences frequently reappear at the same site.

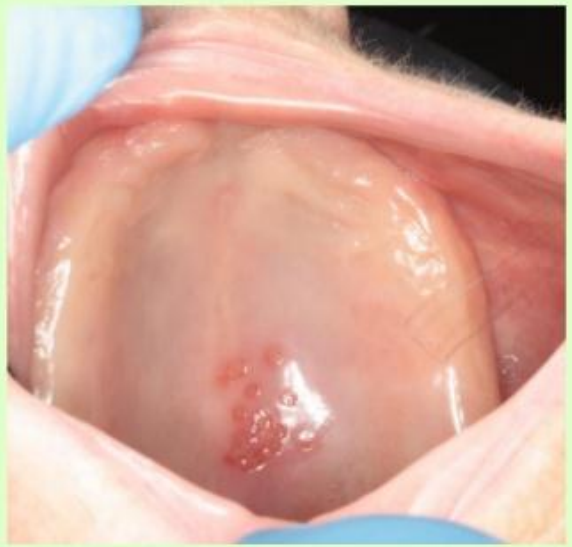


www.facebook.com/notesdental

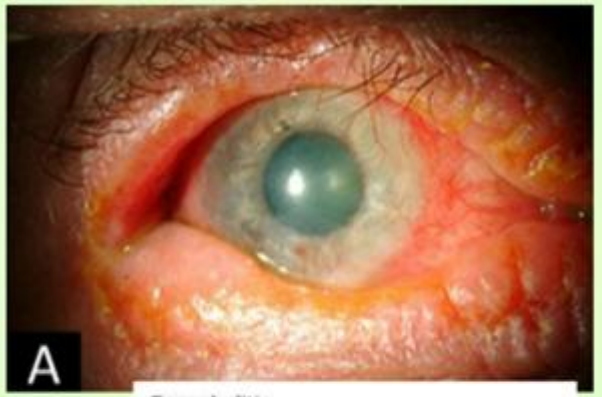
Clinical Findings: HSV-1

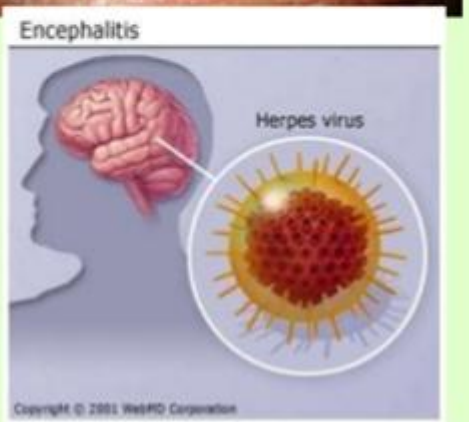
Gingivostomatitis





- **Keratoconjunctivitis**
  - characterized by corneal ulcers and lesions of the conjunctival epithelium.
  - Recurrences can lead to scarring and blindness
- **Encephalitis**
  - necrotic lesion in one temporal lobe.
  - Fever, headache, vomiting, seizures, and altered mental status



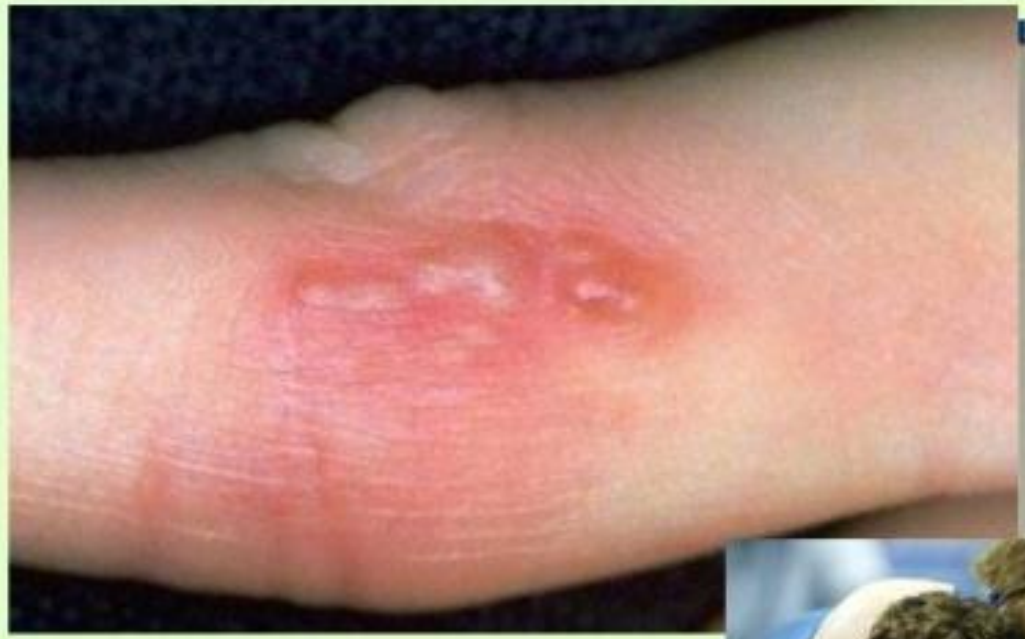


www.facebook.com/notesdental

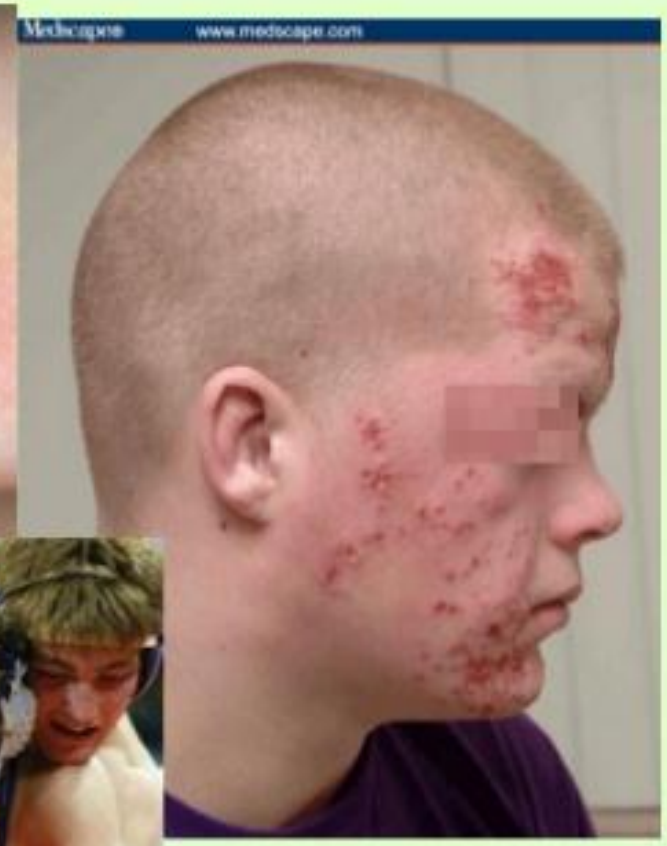
Clinical Findings: HSV-1

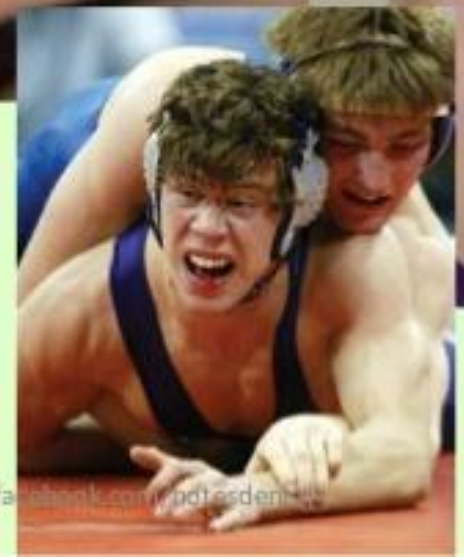
- **Herpetic whitlow**
  - pustular lesion of the skin of the finger or hand.
  - It can occur in medical personnel as a result of contact with patient's lesions.
- **Herpes gladiatorum**
  - wrestlers and others who have close body contact.
  - vesicular lesions on the head, neck, and trunk.
- **Disseminated infections,**
  - such as esophagitis and pneumonia,
  - occur in immunocompromised patients with depressed T-cell function.

Clinical Findings: HSV-1



Herpetic whitlow

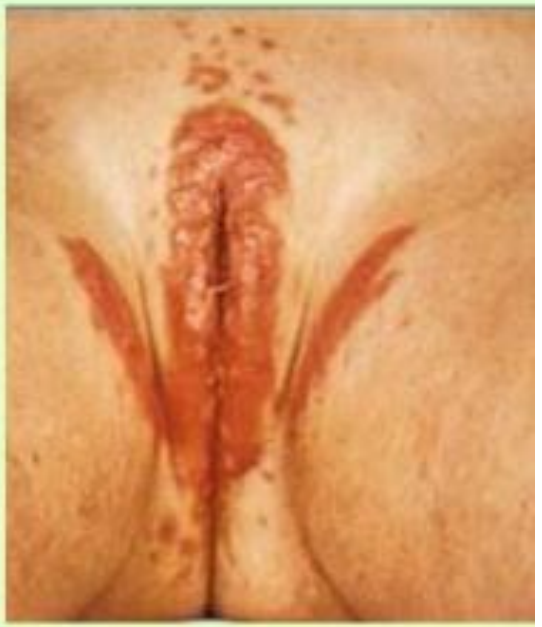


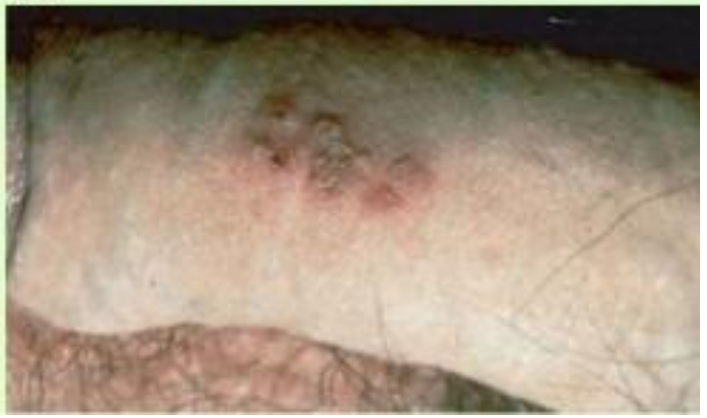


Herpes gladiatorum

Clinical Findings: HSV-2

- **Genital herpes**
  - painful vesicular lesions of the male and female genitals and anal area
  - The lesions are more severe and protracted in primary disease than in recurrences.
  - Primary infections are associated with fever and inguinal adenopathy.
  - Asymptomatic infections - source of infection of other individuals
    - Men: prostate or urethra
    - Women: cervix

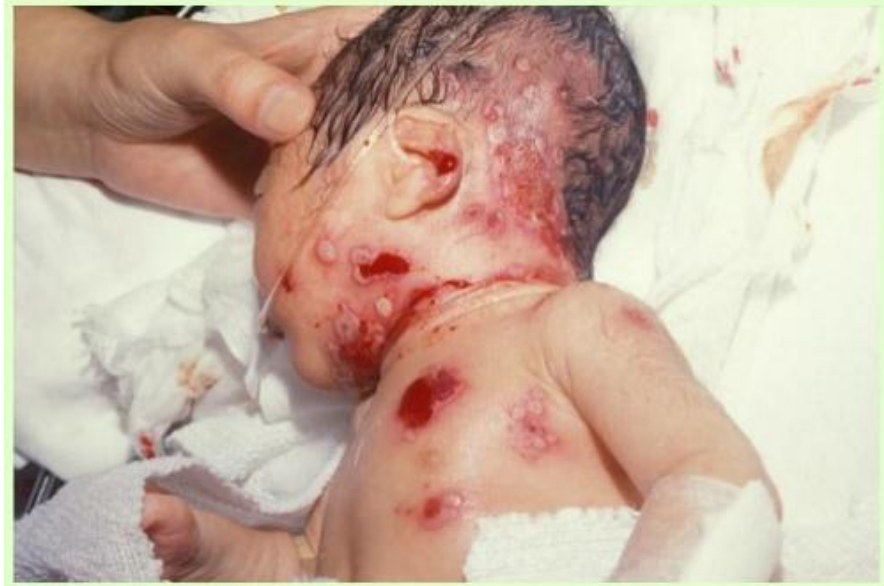




www.facebook.com/notesdental

Clinical Findings: HSV-2

- **Neonatal herpes**
  - originates chiefly from contact with vesicular lesions within the birth canal.
  - varies from severe disease (e.g., disseminated lesions or encephalitis) to milder local lesions (skin, eye, mouth) to asymptomatic infection.
  - prevented by performing cesarean section on women with either active lesions or positive viral cultures.
  - neither HSV-1 nor HSV-2 causes congenital abnormalities to any significant degree.



Laboratory Diagnosis

- Isolation of the virus from the lesion by growth in cell culture
  - typical cytopathic effect occurs in 1 to 3 days,
  - identified by **fluorescent antibody staining** of the infected cells or ELISAs
- **Tzanck smear**: rapid diagnosis
  - Giemsa stain: Multinucleated Giant Cell presence in vesicles
- Serologic tests such as the neutralization test

Treatment

- **Acyclovir :** treatment of choice
  - **shortens the duration** of the lesions
  - **reduces the extent of shedding** of the virus
- **Penciclovir** (a derivative of acyclovir) or **docosanol:** recurrences of orolabial HSV-1
- **Valacyclovir and famciclovir**: genital herpes and in the suppression of recurrences.

Prevention

- avoiding contact with the vesicular lesion or ulcer.
- Cesarean section is recommended for women who are at term and who have genital lesions or positive viral cultures.

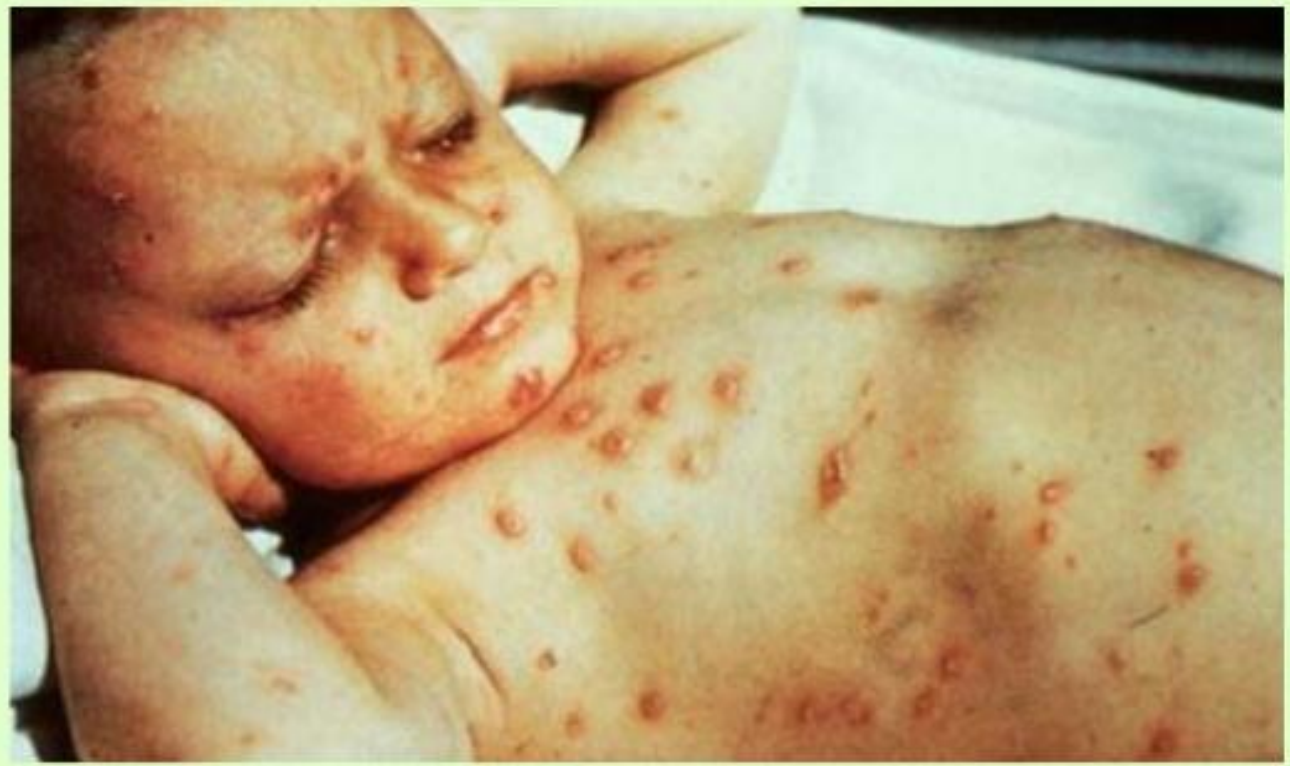
Varicella-Zoster Virus (VZV)

- Clinical chicken pox (primary infection)
- 90% of cases before age 10, peak incidence 2-8 years
- Virus entry through inhalation
- Replicates in respiratory tract and invades lymph nodes.
- Viremia: spreads virus to target organs
- Incubation period 14-18 days

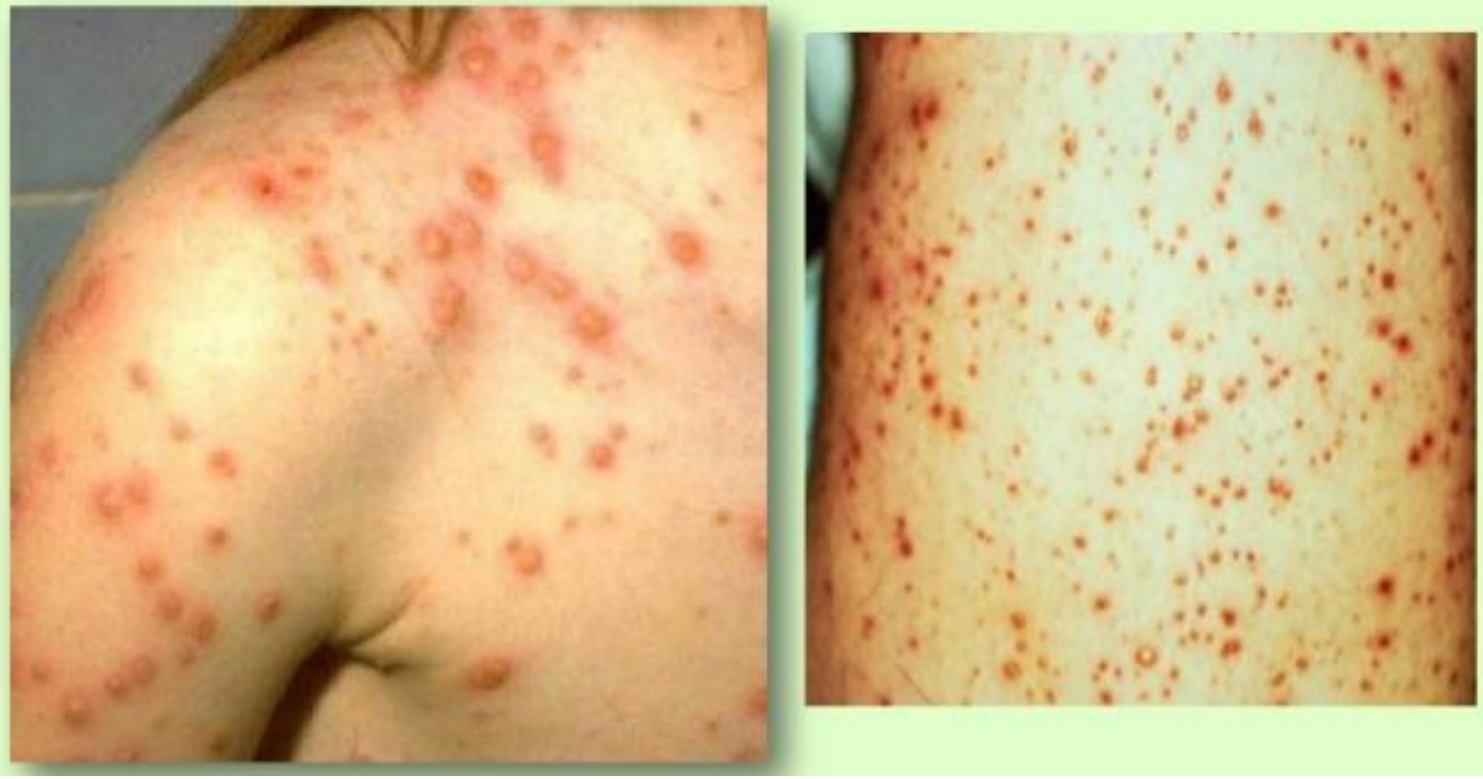
VZV - Chicken Pox

- Rash appears first on head, neck, trunk
- Vesicles contain clear fluid (itch)
- New vesicles appear during first week
- Mild fever, malaise, headache
- Recovery in 2 weeks
- Adult infections more severe (pneumonia)
- Neonatal infection (encephalitis) Immunosuppressed (severe progressive infection)

VZV - Chicken Pox



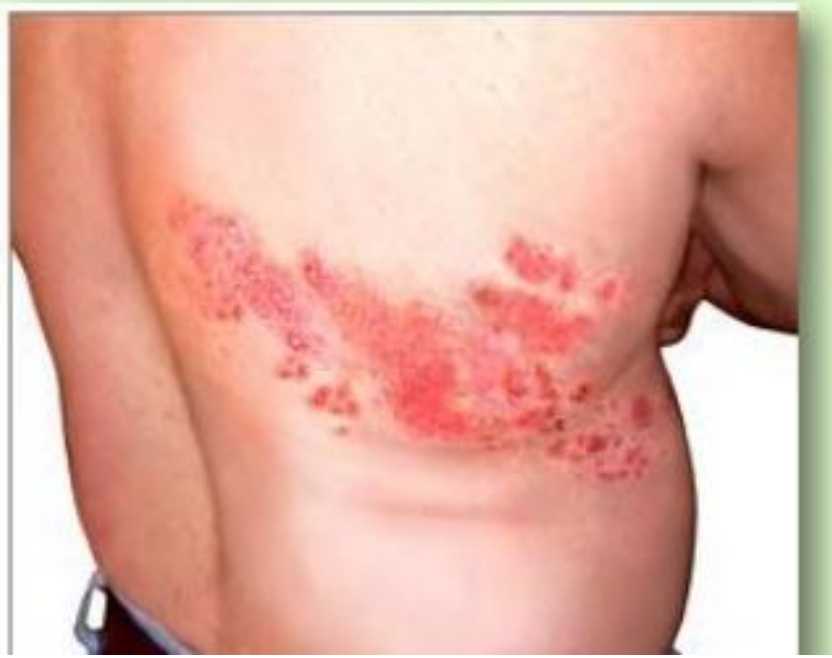
VZV - Chicken Pox

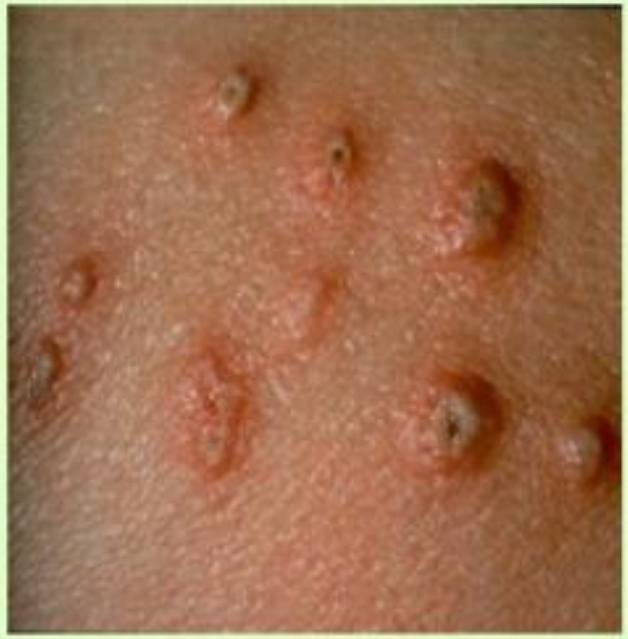


VZV - Shingles

- Shingles: reactivation of varicella-zoster
- DNA remains latent in ganglia
- Occurrence increases with age (50% over 50 yrs)
- Onset of pain occurs before appearance of vesicles
- Usually unilateral
- Immunosuppressed patients especially vulnerable

VZV - Shingles





VZV - Diagnosis and Treatment

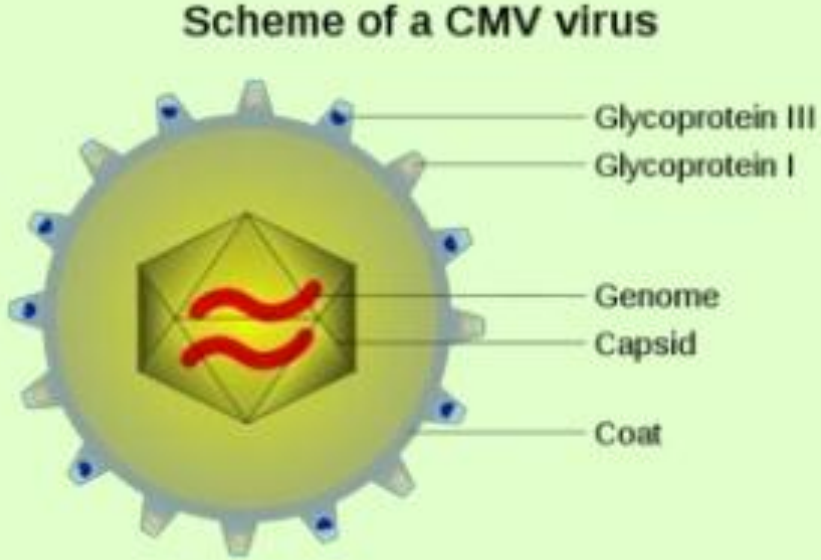
- **Diagnosis**
  - Clinical picture (almost always)
  - Immunofluorescent antibody staining biopsy
- **Treatment**
  - Supportive
  - acyclovir for extreme case

Chicken Pox - Prevention

- **Prevention**
  - immune globulin for patients at risk
  - *Vaccine:* live vaccine (VARIVAX, Merck & Co.)
  - *Recommended dose*
    - For susceptible children aged 12 months to 12 years is one 0.5 ml dose subcutaneously
    - For susceptible adolescents aged 13 years and adults is two 0.5 ml doses 4 to 8 weeks apart

Cytomegalovirus (CMV)

- ds DNA virus
- largest genome of the herpes virus group
- similar to HSV but highly regulated by cis-acting elements and regulatory proteins-slow replication and slow disease effects
- Nuclear and cytoplasmic inclusion bodies, induction of giant cells



CMV - Clinical Features

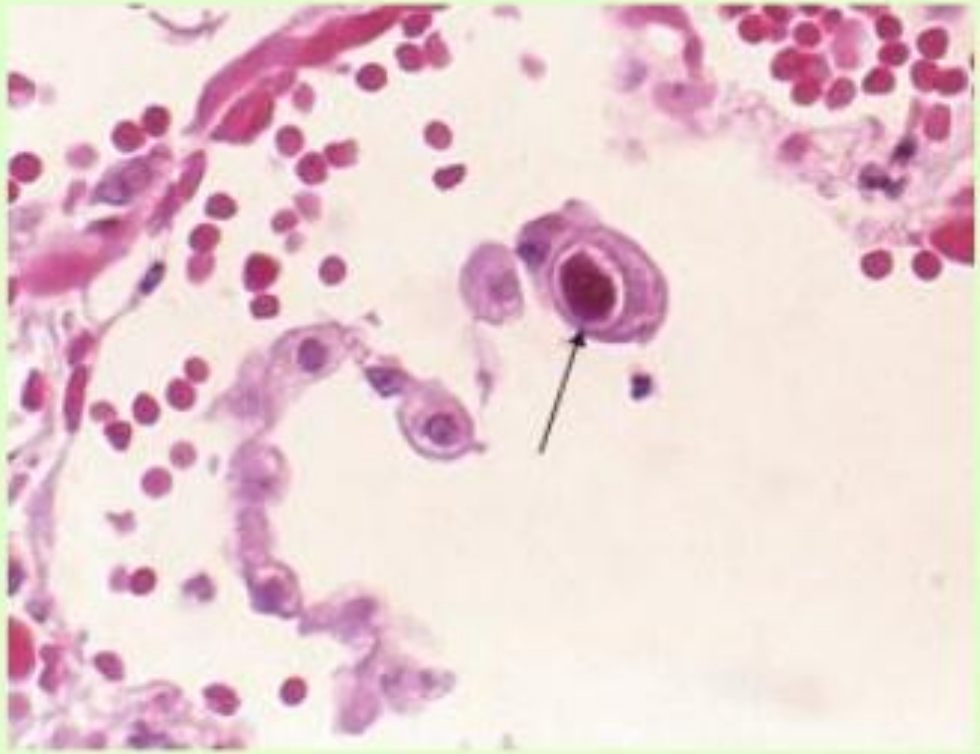
- **Transmission:** close contact, sexually transmitted, virus can be recovered from all body fluids much as saliva, urine, semen, & cervical secretions
- **Clinical features**
  - high infection rates in early childhood and early adulthood
  - usually asymptomatic
  - Systemic CMV infection; pneumonia and hepatitis in immunosuppressed patients (transplant patients)
  - In AIDS patient; diarrhea, retinitis

CMV - Clinical Features

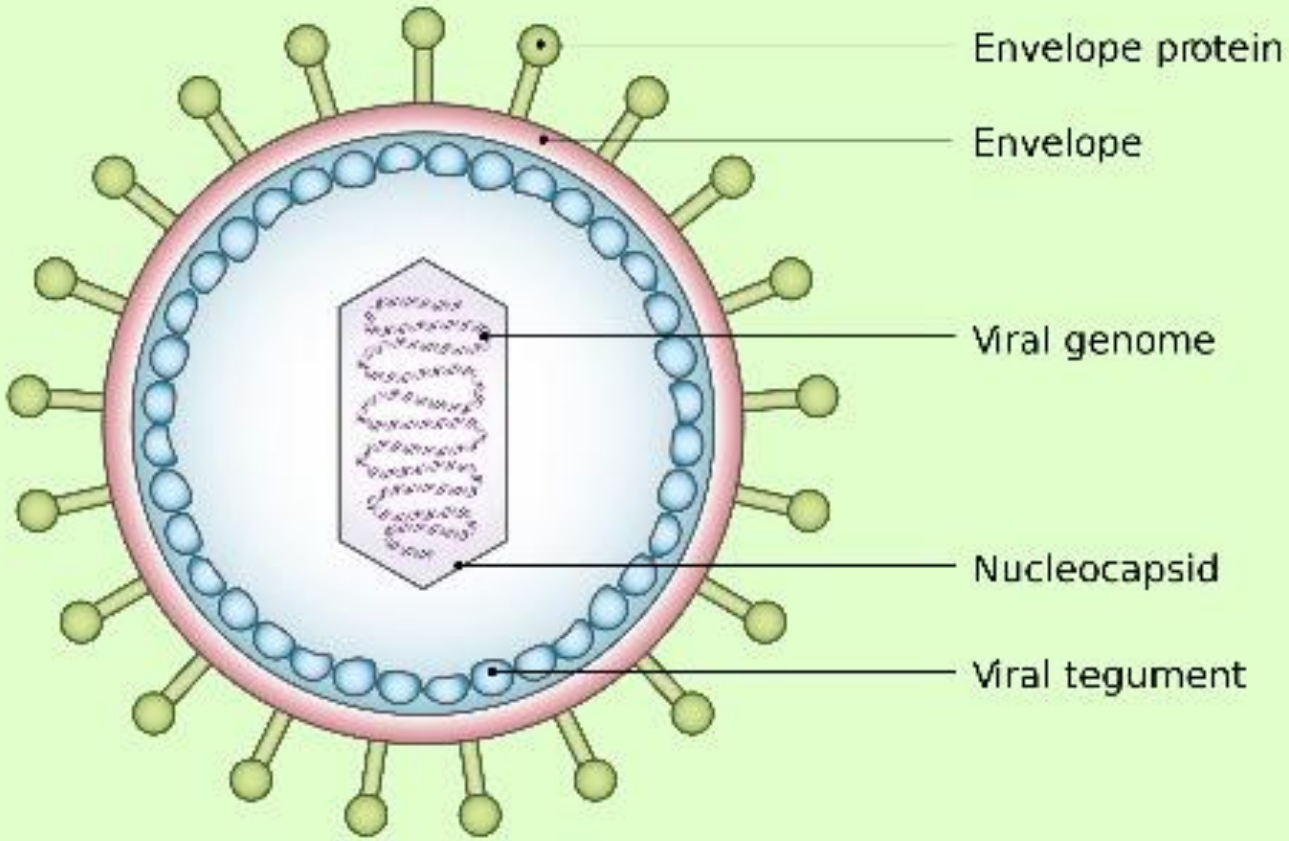
- **Congenital CMV**
  - most infants appear normal at birth
  - may develop hearing loss or some mental retardation often later.
  - Infants with symptomatic illness at birth demonstrate hepatosplenomegaly, jaundice, anemia, low weight, microcephaly, rash, thrombocytopenia
  - Neonatal – asymptomatic
  - Immunosuppressed: CMV pneumonia, disseminated CMV
  - CMV retinitis

CMV - Diagnosis and Treatment

- **Diagnosis**
  - isolation of virus, electron microscopy, serology,
  - DNA amplification by PCR
- **Treatment**
  - hyperimmune globulin, ganciclovir



Epstein-Barr Virus (EBV)

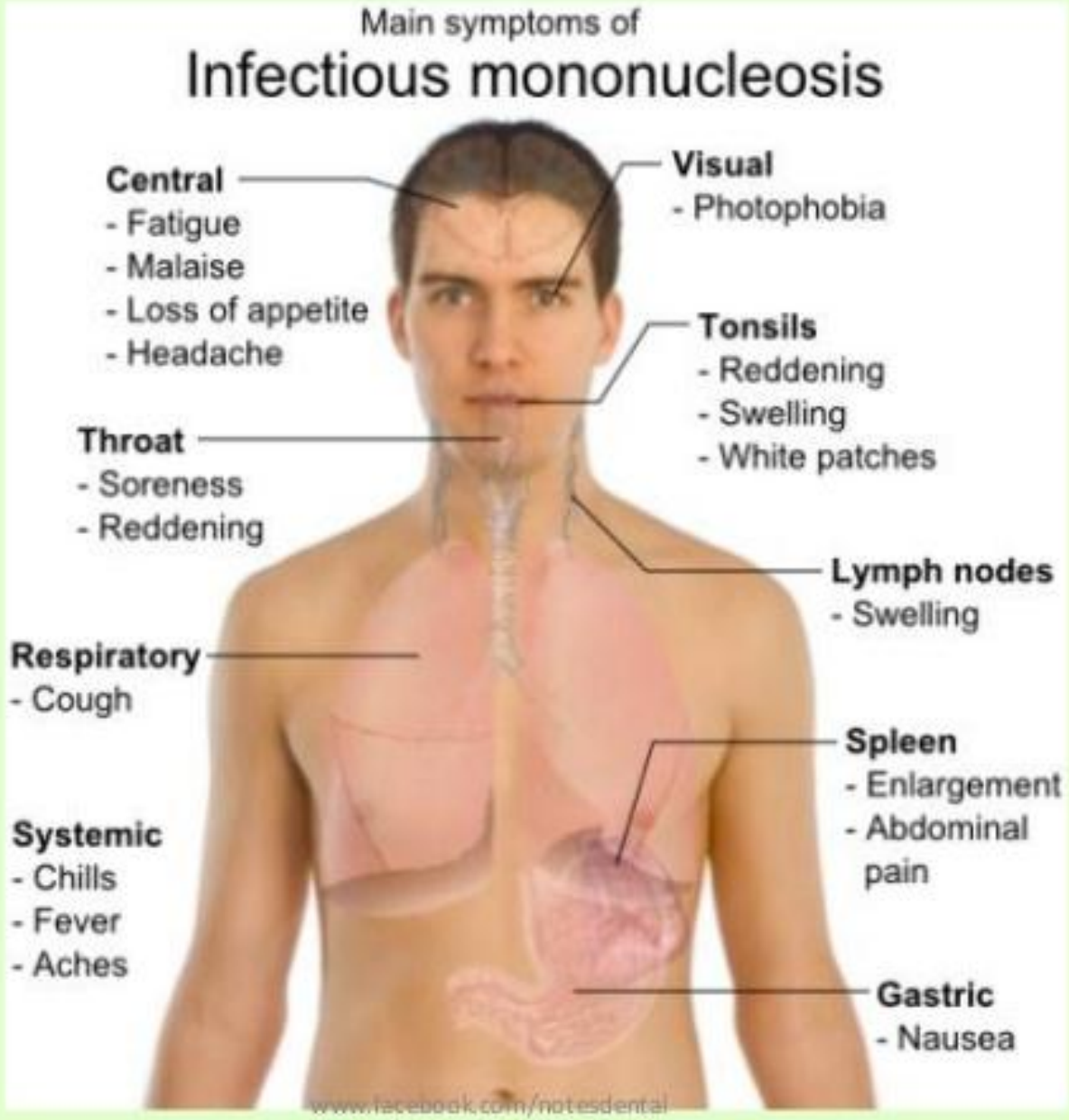


Epstein-Barr Virus (EBV)

- **Structure:** DNA virus, enveloped
- Etiologic agent of infectious mononucleosis and African Burkitt's Lymphomas.
- Recent study has linked with Hodgkins lymphoma
- Cultured in only lymphoblastoid cell lines derived from B lymphocytes of humans and higher primates
- Viral genome can be cultivated continuously and are transformed or immortalized.

Epstein-Barr Virus (EBV)

- EBV nuclear antigens (EBNAs) appear in the nucleus prior to virus directed protein synthesis.
- Viral capsid antigen (VCA) is detected in virus producing cell lines
- EBV can be cultured from saliva and thus infection is acquired by contact.
- **Transmission**
  - contact with infected secretions,
  - low contagiousness,
  - virus can be cultured from throat washings


Main symptoms of
Infectious mononucleosis
Central
- Fatigue
- Malaise
- Loss of appetite
- Headache
Visual
- Photophobia
Tonsils
- Reddening
- Swelling
- White patches
Throat
- Soreness
- Reddening
Lymph nodes
- Swelling
Respiratory
- Cough
Spleen
- Enlargement
- Abdominal pain
Systemic
- Chills
- Fever
- Aches
Gastric
- Nausea
www.facebook.com/notesdental

EBV: Clinical Features

- Infectious mononucleosis, usually asymptomatic
- If symptoms persist (young adults)
  - low fever
  - headache,
  - sore throat,
  - fatigue,
  - night chills (sweats),
  - enlarged lymph nodes and spleen,
  - elevated lymphocytes and monocytes and atypical lymphocytes
- **Complications**
  - laryngeal obstruction, meningitis,
  - encephalitis, hemolytic anemia,
  - thrombocytopenia or splenic rupture may occur in 1 to 5% of the patients

BURKITT'S LYMPHOMA

www.facebook.com/notesdental

Hairy leukoplakia : Strong Association with EBV

EBV - Diagnosis

- Clinical picture
- Complete Blood Cell Count – Atypical lymphocytes
- **Serology**
  - Expensive
  - Demonstrate antibody to viral capsid antigen (VCA) which rises quickly and persists for life.
  - Antibodies to EBNAs rise later and decrease in about 1 month

EBV - Diagnosis

- **Serology**
  - A high titer of VCA and no titer of EBNA suggest recent infection
  - Antibodies to early antigen (EA) may be useful in correlating with nasopharyngeal CA and African Burkitt's lymphomas
- **Culture**
  - Usually positive in acute illness,
  - but asymptomatic viral shedding is so common, that culture is seldom helpful.

EBV - Epidemiology and Treatment

- **Epidemiology**
  - Burkitt's lymphoma- Central & East Africa
  - Tumor in jaw area: Nasopharyngeal carcinoma: China & Southeast Asia
- **Treatment and Prevention**
  - Supportive
  - Acyclovir can suppress the replication process
  - No vaccine available

Human Herpes Virus - 6

- HHV-6 detected in patients with lymphoproliferative diseases.
- Genetically distinct but morphologically similar to other herpes virus.
- Replicates in lymphoid tissue preferentially in T lymphocytes.
- Cytopathic for T lymphocytes in cell culture.
- Establishes a latent infection and may be activated by mitogenic stimulation.

HHV-6 - Clinical Features

- Serologic studies indicate that almost all children are infected by age 5.
- Most communicable of all herpes virus.
- Spread by close personal contact or by respiratory route.
- **Disease**: Roseola infantum (rash like disease)
- Reacativated in transplant patients
- **Treatment**: Acyclovir is 15 to 30% absorbed by oral route

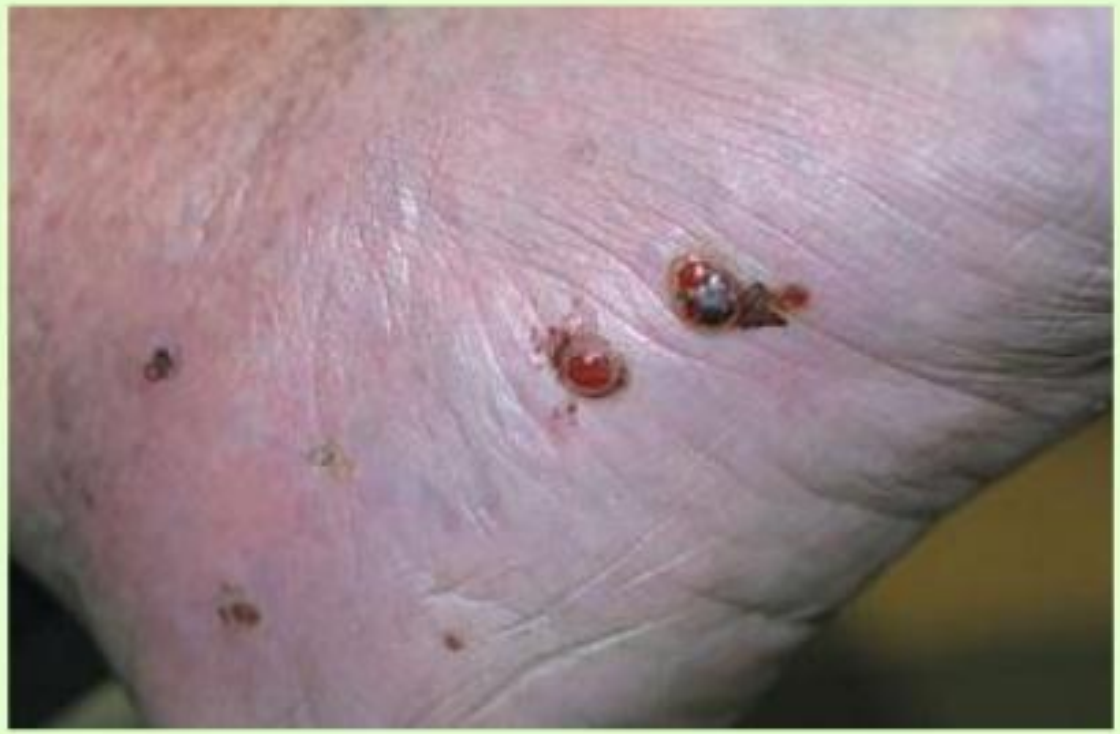
Human Herpes Virus -7

- HHV-7 discovered in 1990
- Isolated from activated CD4+ T lymphocytes.
- HHV-7 is distinct from all other known human herpesviruses but closely related to HHV-6.
- Infects most children by age 2 and 97% of adults are seropositive
- Culture restricted to specialized virology lab.
- Diagnosis of acute infection by seroconversion.

Human Herpes Virus - 8

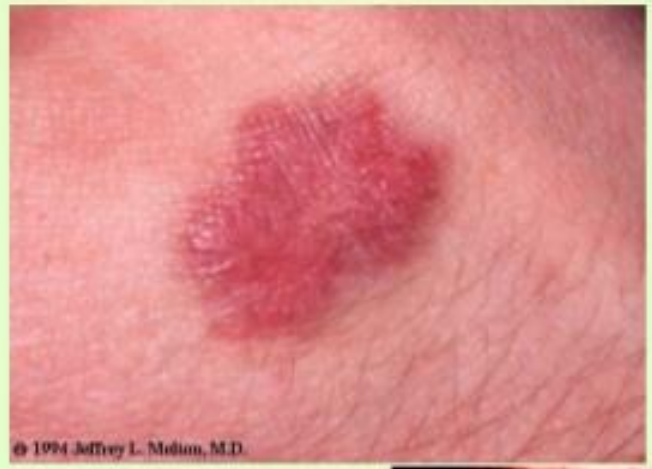
- HHV-8, Kaposi's sarcoma-associated herpesvirus, KSHV
- Discovered as herpesvirus sequences in AIDS related Kaposi’s sarcoma (KS) patients
- HHV-8 DNA sequences found in 95% of KS tissues, both AIDS and non-AIDS related cases
- KSHV DNA has also been detected in cells from lymphoproliferative diseases

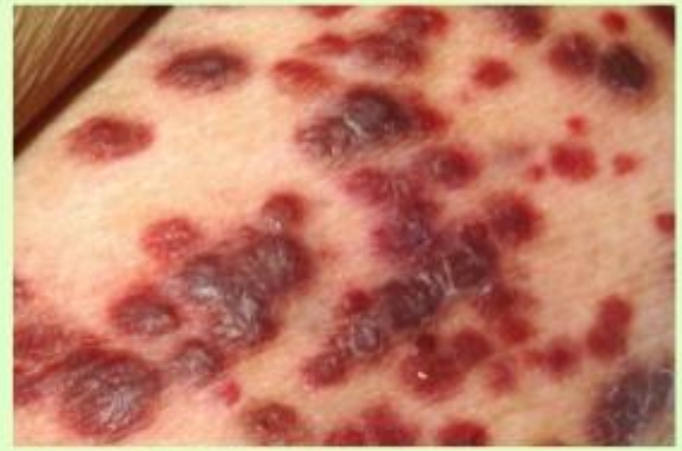
Kaposi's sarcoma

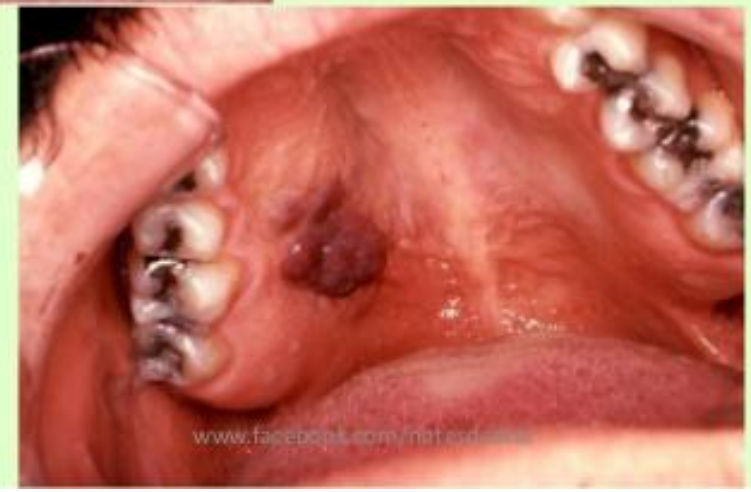


two raised reddish purple lesions on the foot caused by human herpesvirus-8

Kaposi's sarcoma

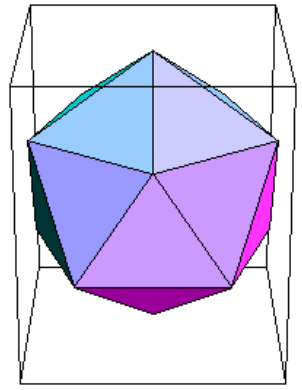


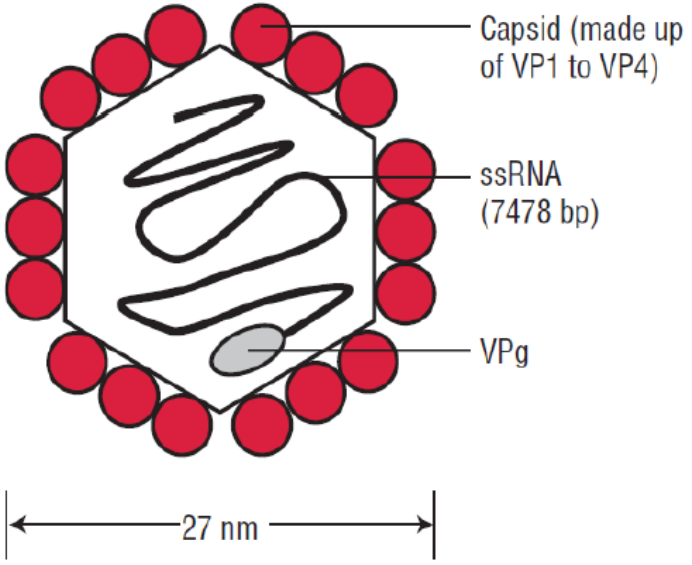




Picornaviridae family

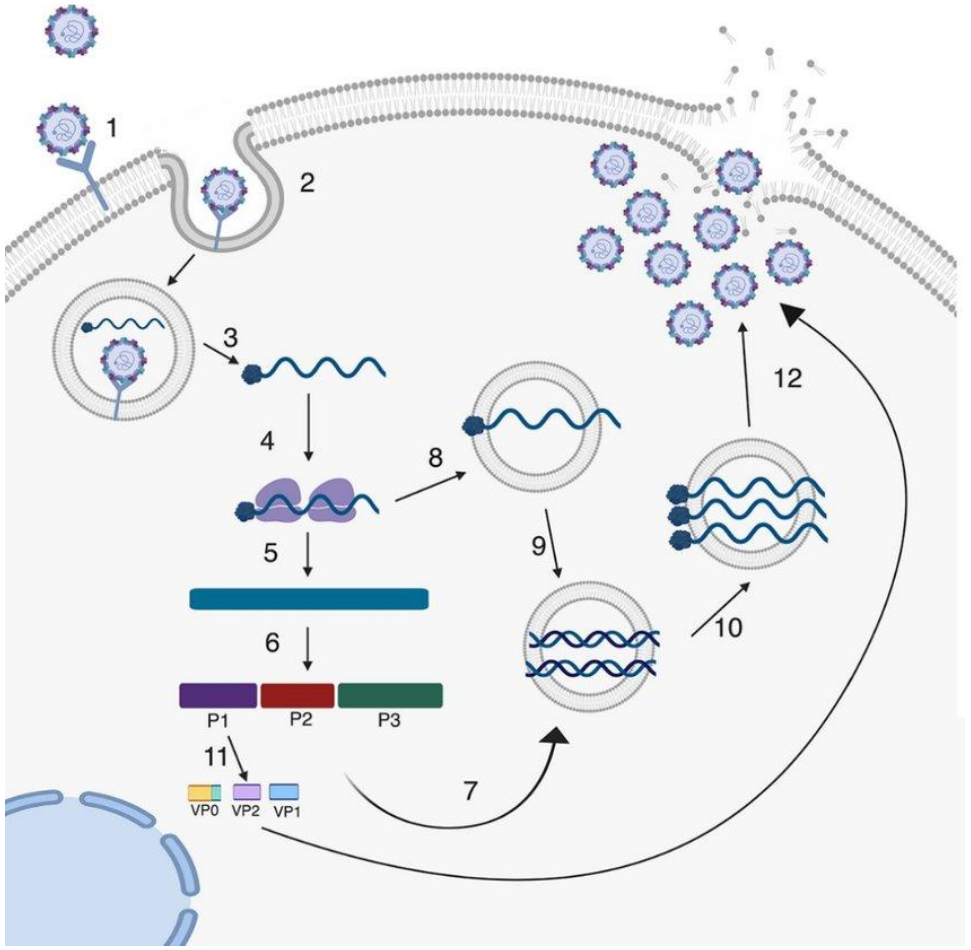
- Members of the Picornaviridae family are non-enveloped viruses with single-stranded RNA. The name of the section is related to the very small size of these viruses (pico-small, rna-RNA).
- They are viruses with a simple structure (without a membrane), 28-30 nm in size.
- The capsid has 12 pentomers with icosahedral symmetry. On the surface of each pentomer there are special grooves ("canyons") that ensure the connection of the virus with the host cell, as well as with the Fab-fragments of antibodies.
- The genome of viruses consists of positive RNA of infectious nature and VPg-protein combined with it.





Reproduction of picornaviruses

- Reproduction occurs in the cytoplasm of host cells.
- The virus enters the host cell by endocytosis.
- Genome RNA plays the role of information-RNA and participates in the synthesis of viral proteins, including RNA-dependent RNA-polymerase.
- This enzyme synthesizes negative-RNA over positive-RNA, and again positive-RNA (genomic RNA) over it.
- The genome-RNA is surrounded by a capsid made of structural proteins and forms the mature virion.
- As a result of cell lysis, virions are released.



Classification of picornaviruses:

- The Picornaviridae family consists of 9 genera: *Enterovirus* (enteroviruses), *Hepatovirus* (hepatitis A virus), *Rhinovirus* (rhinoviruses), *Aphtovirus* (skin virus), *Parechovirus* (parechoviruses), *Cardiovirus*, etc. consists of. The first 5 genera are more important in human pathology.

ENTEROVIRUSES

- Enteroviruses are a genus of the picornavirus family which replicate mainly in the gut.
- Single stranded naked RNA virus with icosahedral symmetry.
- Unlike rhinoviruses, they are stable in acid pH.
- Capsid has 60 copies each of 4 proteins, VP1, VP2, VP3 and VP4 arranged with icosahedral symmetry around a positive sense genome.

ENTEROVIRUSES

- At least 71 serotypes are known: divided into 5 groups
  - Polioviruses
  - Coxsackie A viruses
  - Coxsackie B viruses
  - Echoviruses
  - Enteroviruses (more recently, new enteroviruses subtype have been allocated sequential numbers (68-71))

CATAGORIES OF ENTEROVIRUSES

VIRUS	SEROTYPES	CLINICAL DISEASES
Polioviruses	3 types	Asymptomatic infection, viral meningitis, paralytic disease, poliomyelitis
Coxsackie A viruses	23 types (A1-A22, A24)	Viral meningitis plus, rash, ARD, myocarditis, orchitis
Coxsackie B viruses	6 types (B1-B6)	Viral meningitis, but no orchitis
Echoviruses	32 types	Viral meningitis, with orchitis
Other Enteroviruses	4 types(68-71)	Viral meningitis

PROPERTIES OF ENTEROVIRUSES

PROPERTY	ENTEROVIRUSES
Size (nm)	22 – 30
Capsid Form	Icosahedral
Polypeptide	VP1, VP2, VP3, VP4
RNA Type	SS – PS
RNA Molecular Weight	2000,000 – 2600,000
Acid	Stable
Optimal Temp.for growth (^{0} C)	37^0 C
Density in Cesium chloride (g / m)	1 . 34

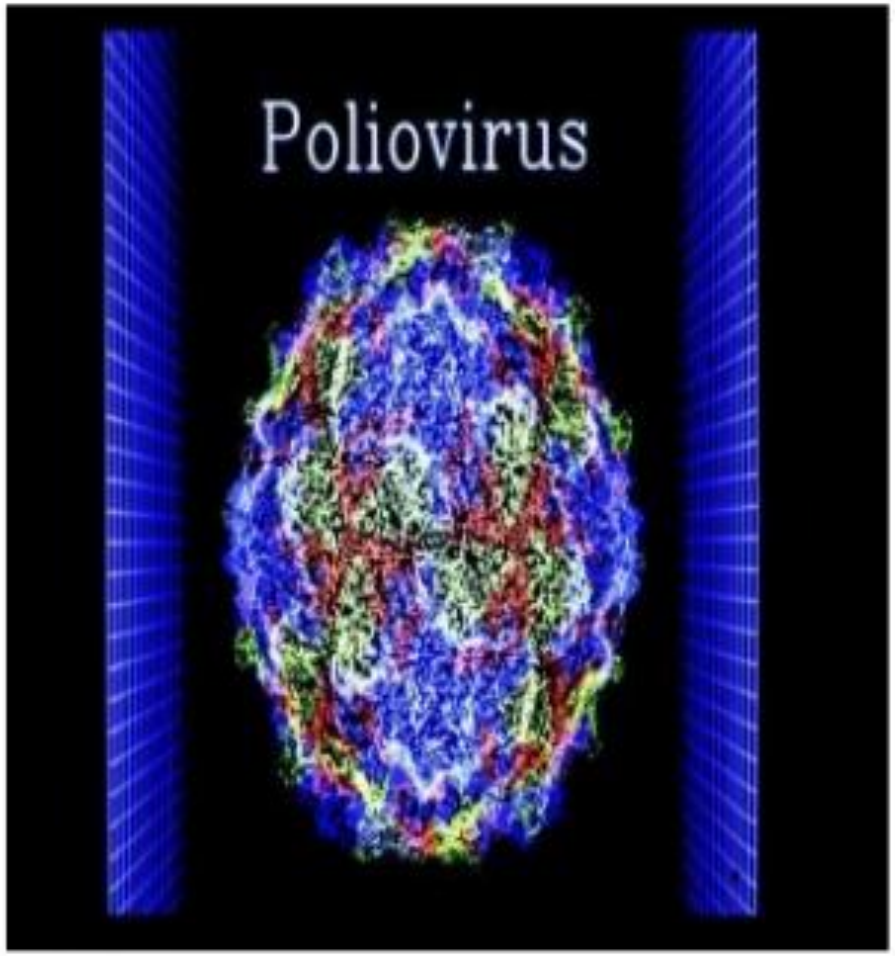
TRANSMISSION OF ENTEROVIRUSES

- Fecal – oral route: poor hygiene, dirty diapers(especially in day-care settings)
- Ingestion via contaminated food and water
- Contact with infected hands
- Inhalation of infectious aerosols

POLIO – AN ENTEROVIRUS

- Poliovirus, the causative agent of poliomyelitis, is a human enterovirus and member of the family of Picornaviridae. Poliovirus is composed of a RNA genome and a protein capsid. The genome is single-stranded positive-sense RNA genome that is about 7500 nucleotides long. The viral particle is about 300 Angstrom in diameter with icosahedral symmetry.

CLASSIFICATION OF POLIOVIRUS



- Size is 27 nm
- Contains 4 viral protein VP1 to VP 4
- VP1 Carries the major antigenic site, and combines with type specific neutralizing antibodies

PROPERTIES OF POLIOVIRUS

- Typical Entero virus.
- Inactivated at 55^0 c for 30 mt.
- Chlorine at 0.1 ppm
- Ether is not effective.
- Animal susceptibility.

  Monkey brain

  Requires Primate specific membranes.

  Contains 3 Antigenic types 1,2,3

Can be differentiated by ELISA and CF methods.

POLIOMYELITIS

- Poliomyelitis (polio) is a highly infectious viral disease, which mainly affects young children. The virus is transmitted through contaminated food and water, and multiplies in the intestine, from where it can invade the nervous system.

DWD

POLIOMYELITIS

- Polio = gray matter, Myelitis = Inflammation of the spinal cord.
- Involves CNS, produces serious Illness.
- Causes Destruction of Motor Neurons in Spinal cord.
- Produces FLACID PARALYSIS.
- India has still has many cases of Poliomyelitis.

EPIDEMIOLOGY

- Endemic
- Epidemic
- Hygiene plays in spread of diseases.
- Children < 5 in Developing countries.

POLIO INFECTION

- Incubation 3 – 21 days
- On average 14 days
- Predisposing factors.

  Severe muscular activity can lead to paralysis, as it increases the blood flow

  May produce paralysis in the limb or bulbar region

  Injecting vaccines with adjuvant can predispose to paralysis

  Patients who underwent tonsillectomy have higher incidence as Ig G secretion is reduced

  Rarely oral Polio vaccine produces poliomyelitis.

PATHOLOGY & PATHOGENESIS

- Destroy the Anterior horn cells of the Spinal Cord
- Do not Multiply in Muscles only muscles manifest with weakness and flaccid paralysis result is secondary.
- Occasionally produce
  - Myocarditis,
  - Lymphatic hyperplasia.

PATHOLOGY & PATHOGENESIS

- Enter through Mouth,
- Multiplies in Oropharynx tonsils and Intestines,
- Excreted in Stool.
- Enters the CNS from Blood.
- Spread along the Axons of peripheral nerves to CNS.
- Progress along the fibers of the lower motor neurons spinal cord or brain.

VIRUS INFECTION PROCESS

- The polio virus infects human cells by binding to an immunoglobulin-like receptor called CD155 (poliovirus receptor).
- The exact mechanism that poliovirus uses for entering the cell is unknown. However, the interaction of poliovirus and CD155 causes a change in the shape of the viral particle that is needed to enter the cell
- There are two thesis' for the way the viral nucleic acid to enters the cell. The first thesis is that the RNA of poliovirus is injected into the host cell through a pore in the membrane of the host cell. The second, and the one that is most likely and has the most support through research, is that the poliovirus is taken in by the host cell through endocytosis.
- Poliovirus has ssRNA. Also known as single-strand RNA.

CLINICAL MANIFESTATIONS

- In apparent, Only 1% manifest with clinical features.
- Can lead to permanent paralysis.
- Incubation 7-14 days, (3-35)
- May be abortive Poliomyelitis,

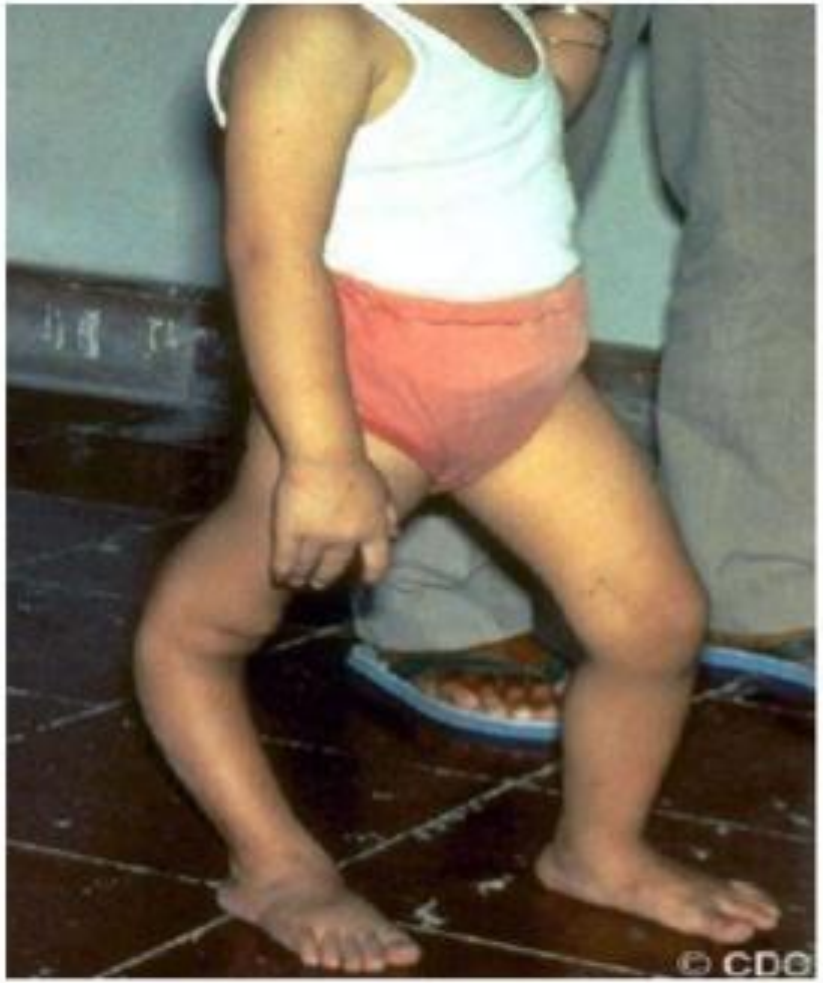
Only Fever, Malaise, Drowsiness,

Non paralytic Poliomyelitis,

Aseptic Meningitis.

PARALYTIC POLIOMYELITIS

- Manifest as Flaccid Paralysis.
  (Caused due to damage to Lower Motor Neurons.)
- Partial recovery within 6 months.
- Patient may continue with life time disability
- Can involve Spinal cord, and Bulbo spinal region
- Bulb spinal involvement can paralyze respiratory muscle and lead to Respiratory failure



ASEPTIC MENINGITIS

- Present with Non paralytic form with stiffness and pain in the back and neck region
- Lasts for 2 -10 days
- Recovery rapid and complete
- On rare occasions advance to paralysis

LABORATORY DIAGNOSIS

- Viral isolation from
  - Throat swabs,
  - Rectal swabs.
  - Stool specimens,
- Transported in frozen containers.
- Produce cytopathic effect on
  - Human and Monkey cells
- Produce cytopathic effects.

VIRAL ISOLATION

- From feces - present in 80% of cases in 1st week
- In 50 % till 3rd week
- In 25 % till several weeks
- Collect the fecal sample at the earliest.
- Primary monkey kidney is the ideal cell line for isolation of virus
- Viral isolation must be interpreted with caution and clinical presentation

LABORATORY DIAGNOSIS (SEROLOGY)

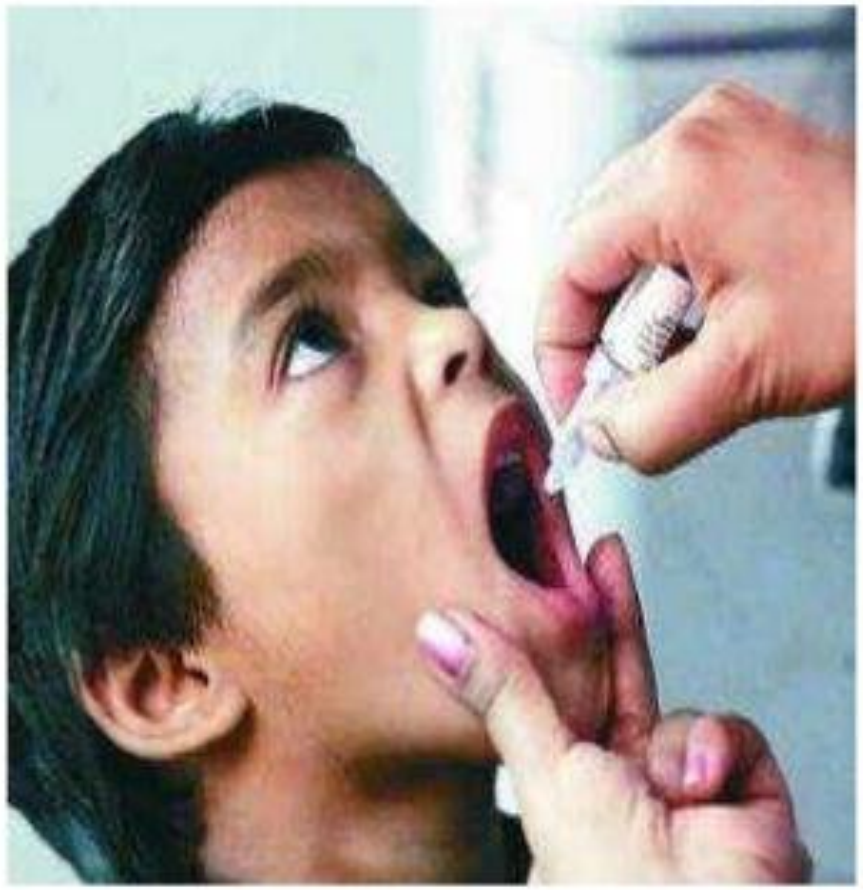
- Estimation of Antibodies IgM
- A paired sample is essential.
- ELISA
- CFT
- Neutralisation.

PREVENTION & CONTROL

- Sabin's Live attenuated vaccine
- Grown in Monkey kidney cells, Human Diploid cells. Preserved at 4^0 C
- Multiple doses are given
- Given as oral Drops
- At present only vaccine given in our National Programme of Immunization
- Boosts Immunity with Production IgG ,IgM
- And also IgA Participate as participant in Prevention.

ORAL POLIO VACCINE (SABIN'S)

- Highly effective in producing immunity to poliovirus
- 50% immune after 1 dose
- >95% immune after 3 doses
- Immunity probably lifelong



ADVANTAGES OF LIVE VACCINE

- Induces long lasting immunity.
- Induces local immunity in the form of IgA production (gut immunity).
- Administered orally, without the need of sterile syringes.

DISADVANTAGES OF LIVE VACCINE

- The only disadvantage of this vaccine is the vaccine strain particular type 3 strain can reverts to virulerence and cause paralysis in those who just been vaccinated.

- It is estimated that vaccine induced poliomyelitis is seen in rate of 1 in 3000,000 vaccinations.

INJECTABLE KILLED SALK VACCINE

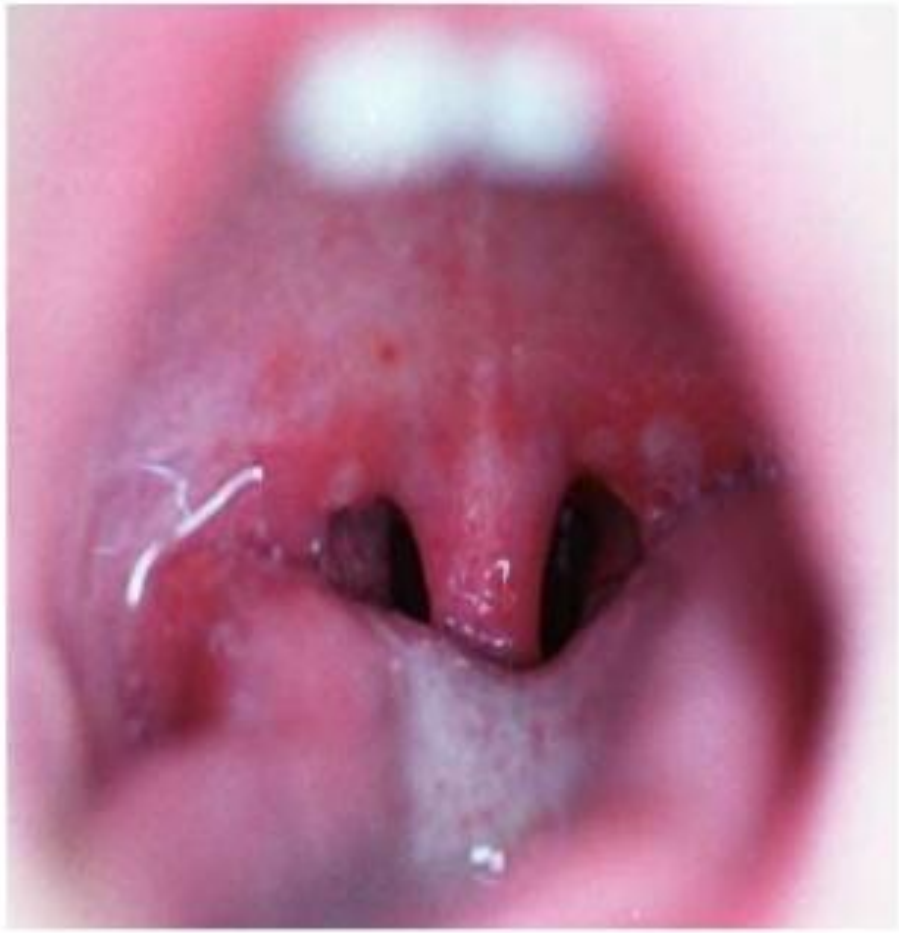
- Salk Vaccine - A Killed Vaccine. (INACTIVATED)
- Four Injections are administered in a period of two years,
- Administration of periodic booster recommended.
- Most of the Western Nations do use it.

DISEASES ASSOCIATED WITH COXASKIE A VIRUS

- Febrile illness with maculopapular rash.
- Upper respiratory tract infection.
- Paralytic disease.
- Meningitis & encephalitis.
- Peri and myocarditis.
- Herpangina.
- Hand, foot & mouth disease.
- Acute hemorrhagic conjunctivitis.

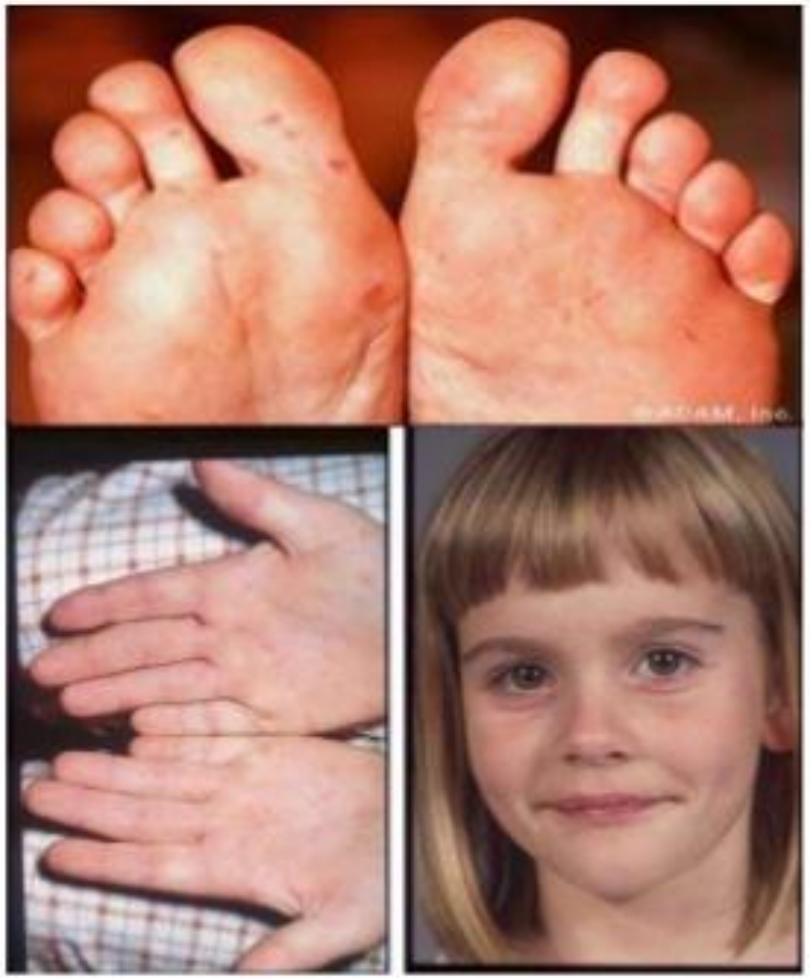
DISEASES ASSOCIATED WITH COXASKIE A VIRUS

- Caused by group A Coxsackieviruses.
- Characterized by fever, sore throat, pain on swallowing .
- Small vesicles appear on the pharynx, Palate, uvula and tonsils .
- Recovery is usual .



HAND FOOT & MOUTH DISEASE

- Caused by group A coxsackie viruses .
- Small papules &vesicles develop on the buccal mucosa, hands and feet .
- Recovery is usual .



DISEASES ASSOCIATED WITH COXASKIE B VIRUS

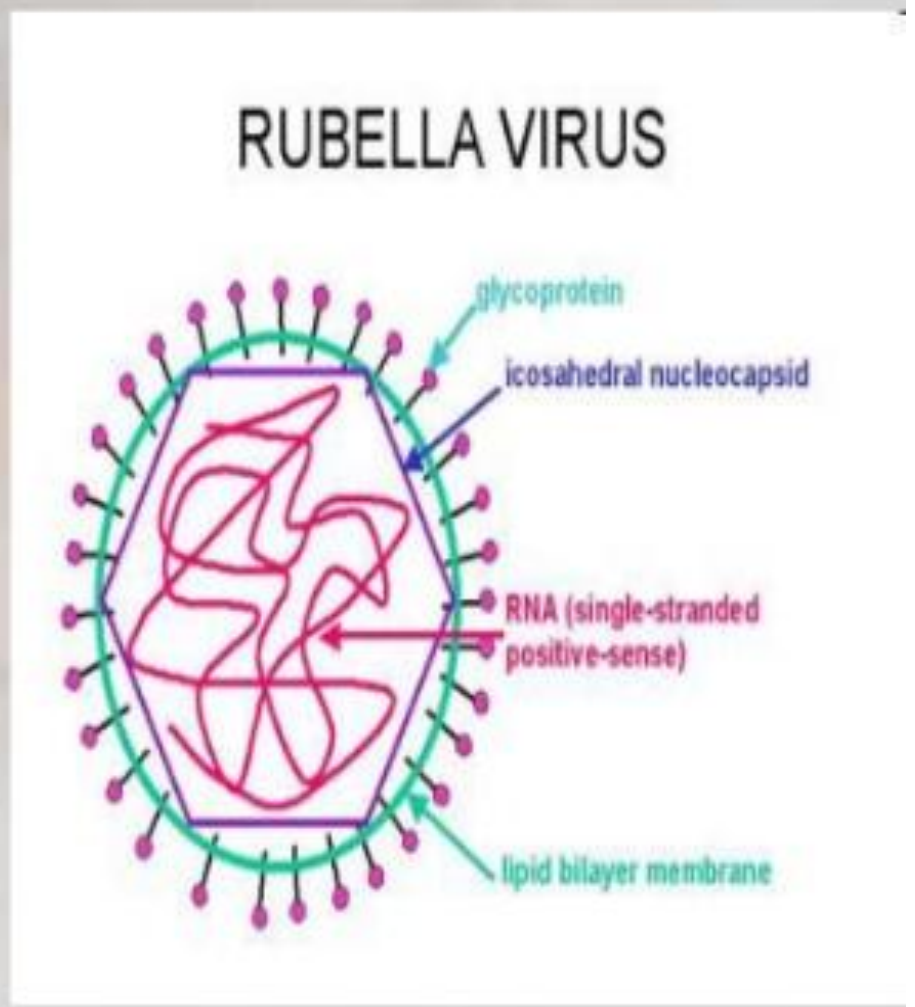
- Febrile illness with maculopapular rash.
- Upper respiratory tract infection.
- Paralytic disease.
- Meningitis & encephalitis.
- Peri & myocarditis.
- Pleurodynia.
- Juvenile diabetes/ pancreatitis .

DISEASES ASSOCIATED WITH ECHO VIRUS

- Febrile illness with maculopapular rash.
- Upper respiratory tract infection.
- Paralytic disease.
- Meningitis & encephalitis.
- Peri & myocarditis.

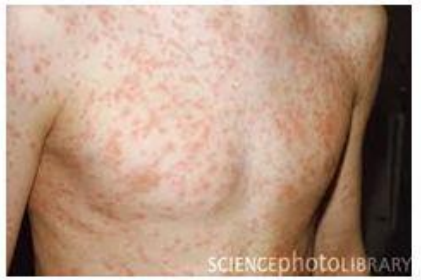
RUBELLA VIRUS

- Rubella virus is single stranded RNA virus
- Diameter 50 – 70 nm
- Enveloped Spherical
- Virus multiply in the cytoplasm of infected cell



Classification

- Family : Togaviridae
- Genus : Rubivirus
- Species : Rubella virus

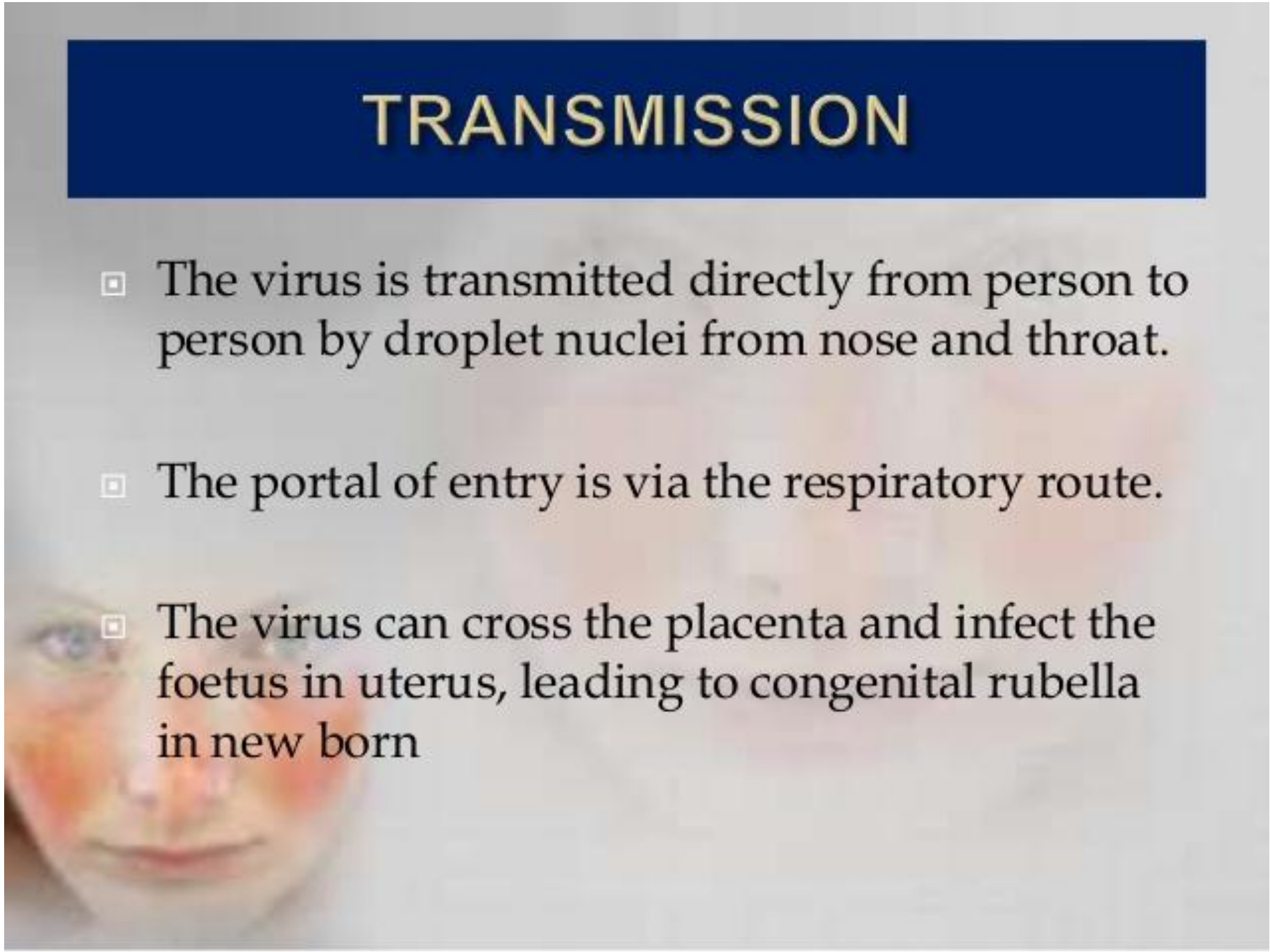


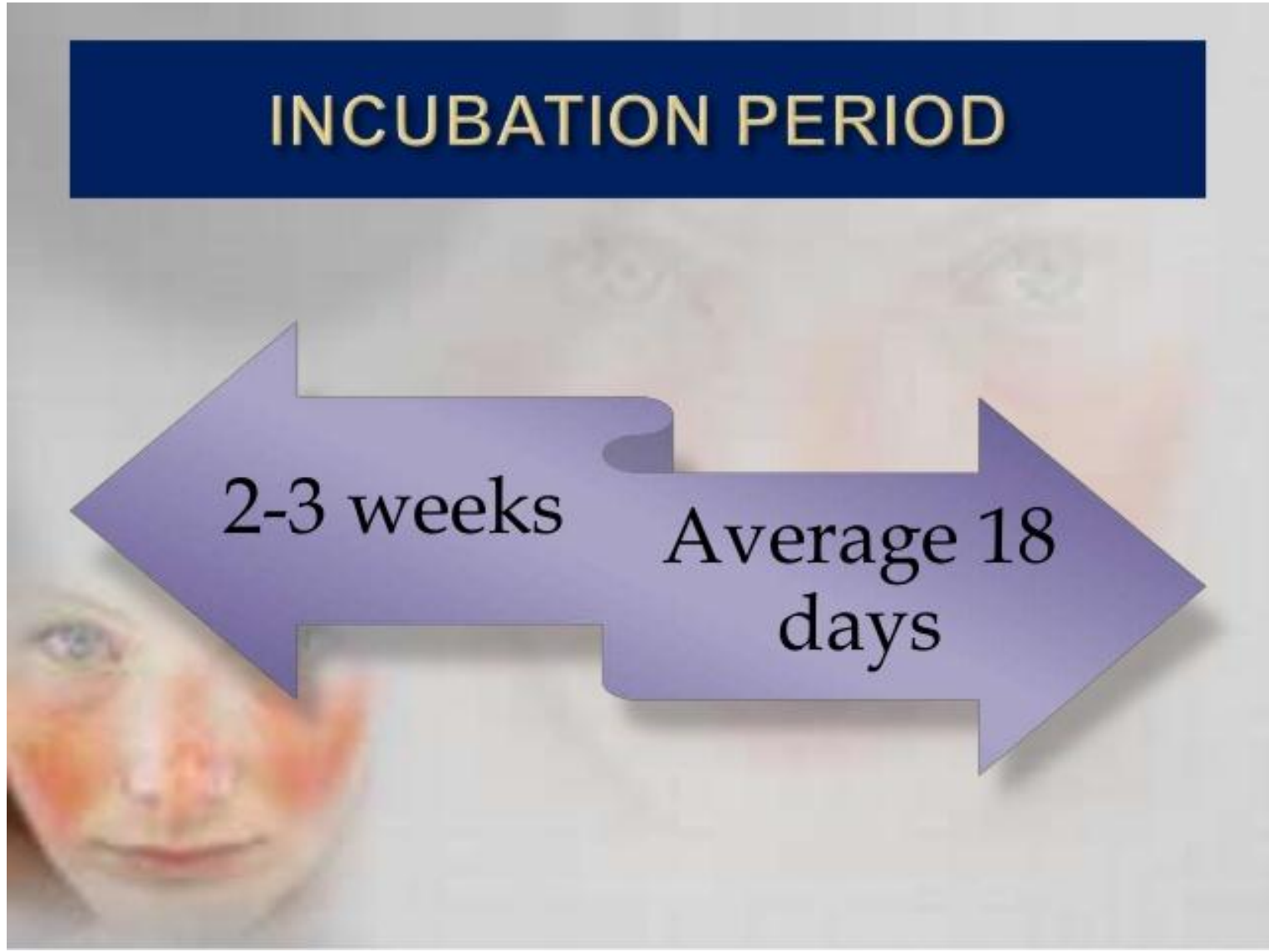
INTRODUCTION

- **Rubella,** commonly known as **German measles**, is a disease caused by Rubella virus. The name is derived from the Latin, meaning ***little red.***
- Rubella is also known as German measles because the disease was first described by German physicians, Friedrich Hoffmann, in the mid-eighteenth century.

TRANSMISSION

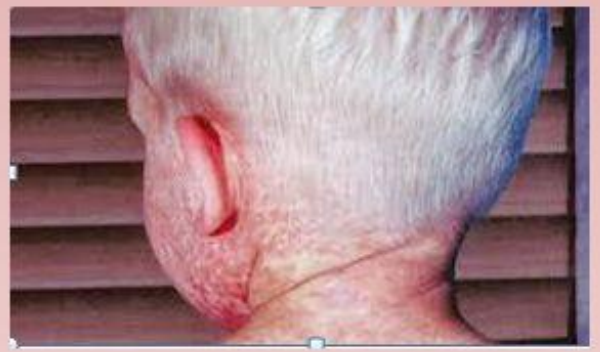
- The virus is transmitted directly from person to person by droplet nuclei from nose and throat.
- The portal of entry is via the respiratory route.
- The virus can cross the placenta and infect the foetus in uterus, leading to congenital rubella in new born



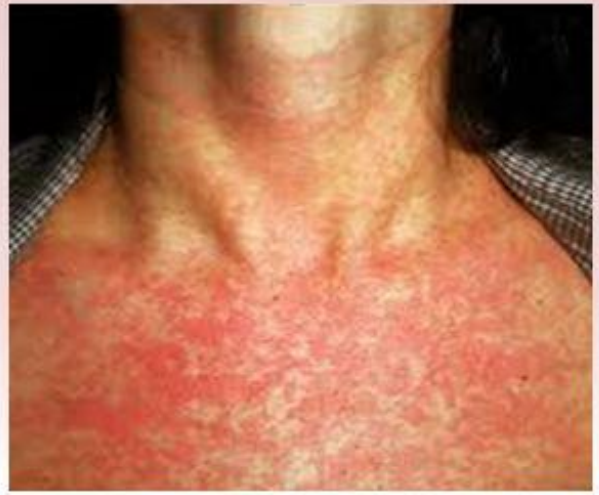

INCUBATION PERIOD
2-3 weeks
Average 18 days

Main Symptoms of Rubella

- the primary symptom of rubella virus infection is a **red-pink rash**



- the rash usually starts
  - ✓ behind the ears, then around the head and neck
  - ✓ it may then spread to the chest and tummy, legs and arms



- secondary symptoms are **swollen lymph nodes**

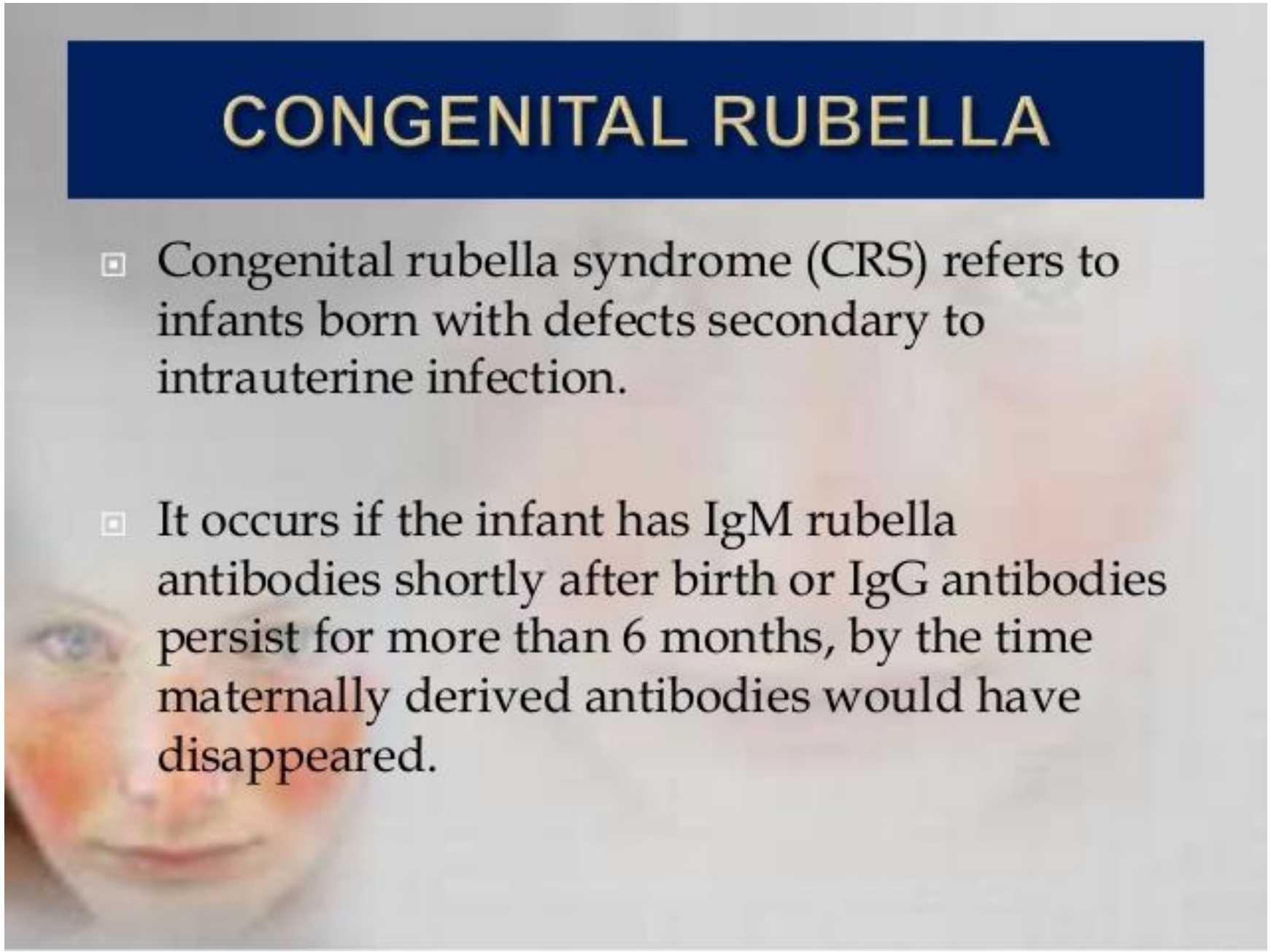
RUBELLA DURING PREGNANCY

- "Rubella infection in pregnant women during the first three months of pregnancy may result in the baby being born with birth defects or congenital rubella syndrome.

CONGENITAL RUBELLA

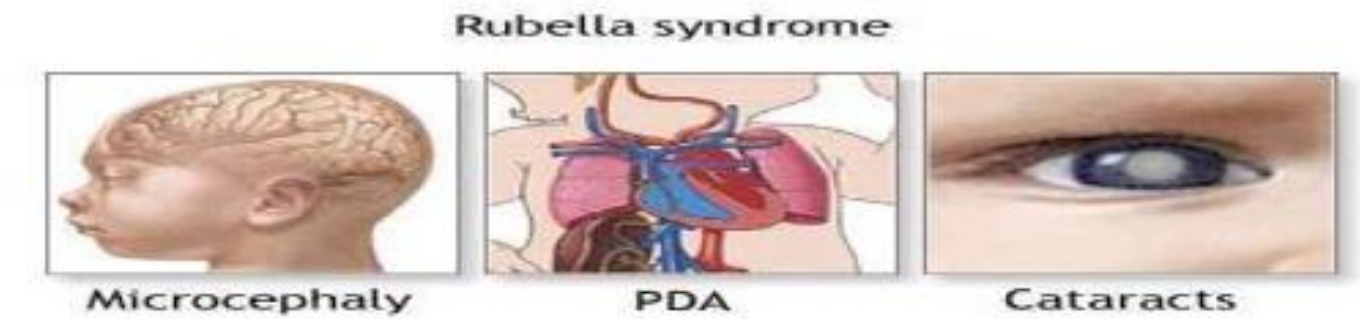
- Congenital rubella syndrome (CRS) refers to infants born with defects secondary to intrauterine infection.

- It occurs if the infant has IgM rubella antibodies shortly after birth or IgG antibodies persist for more than 6 months, by the time maternally derived antibodies would have disappeared.



Classical Triad of congenital Rubella

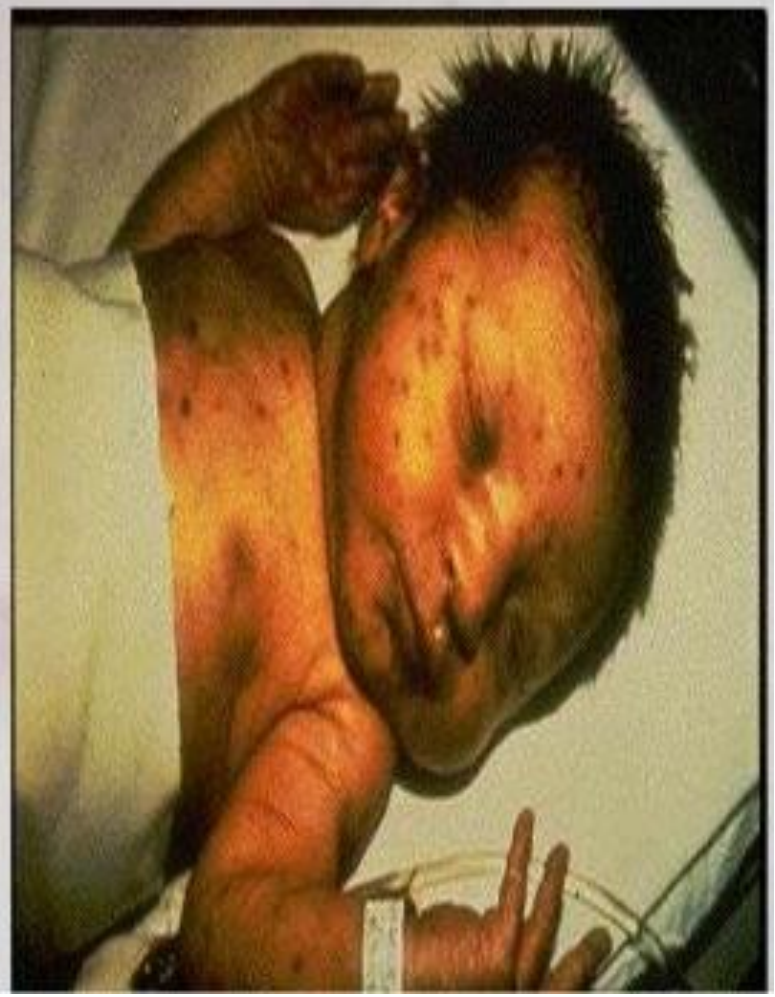
- Cataract
- Cardiac abnormalities
- Deafness



POSTNATAL RUBELLA

Occurs in Neonates and Childhood

- Lasts for 13 – 15 days
- Leads to development of antibodies
- The appearance of antibodies coincides the appearance of suggestive immulogic basis for the rash
- In 20 – 50 % cases of primary infections are subclinical

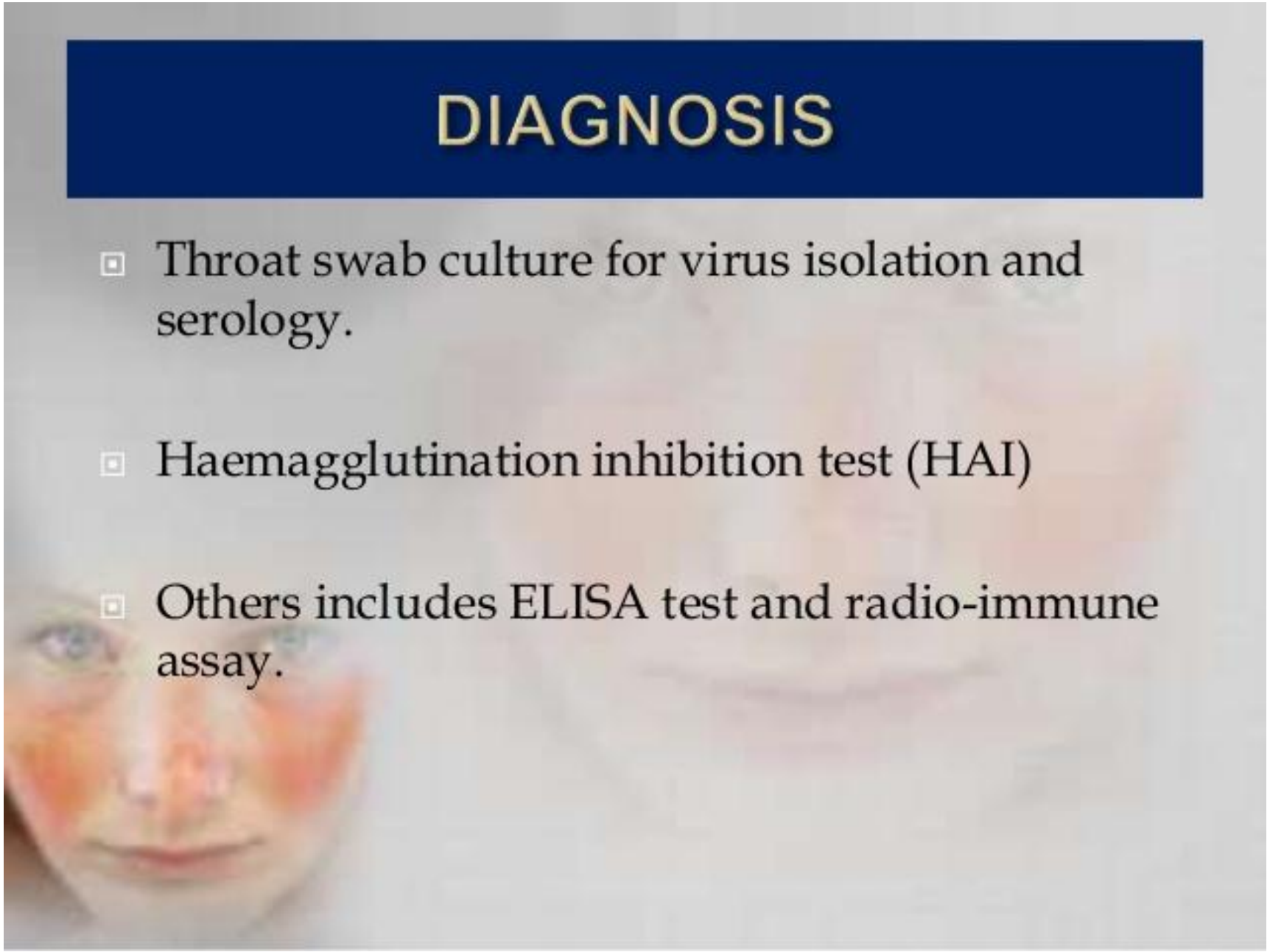


Continue.....

- Other defects includes
  - Glaucoma
  - Retinopathy
  - Microcephalus
  - Cerebral palsy
  - Intrauterine growth retardation
  - Hepato-splenomegaly
  - Mental and motor retardation

DIAGNOSIS

- Throat swab culture for virus isolation and serology.
- Haemagglutination inhibition test (HAI)
- Others includes ELISA test and radio-immune assay.

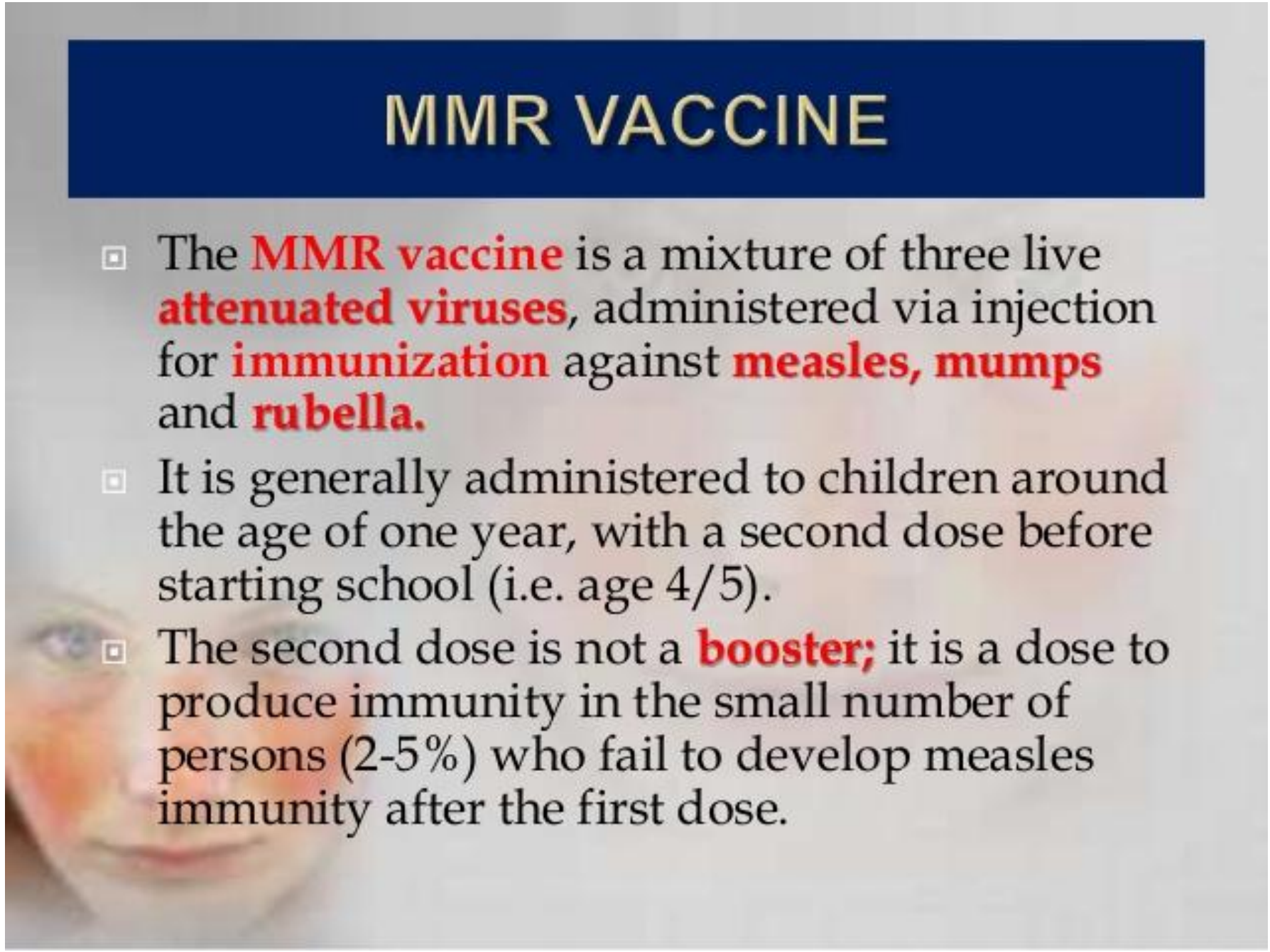


TREATMENT

- There is no specific treatment for Rubella; management is a matter of responding to symptoms to diminish discomfort.

MMR VACCINE

- The **MMR vaccine** is a mixture of three live **attenuated viruses**, administered via injection for **immunization** against **measles, mumps** and **rubella.**
- It is generally administered to children around the age of one year, with a second dose before starting school (i.e. age 4/5).
- The second dose is not a **booster;** it is a dose to produce immunity in the small number of persons (2-5%) who fail to develop measles immunity after the first dose.



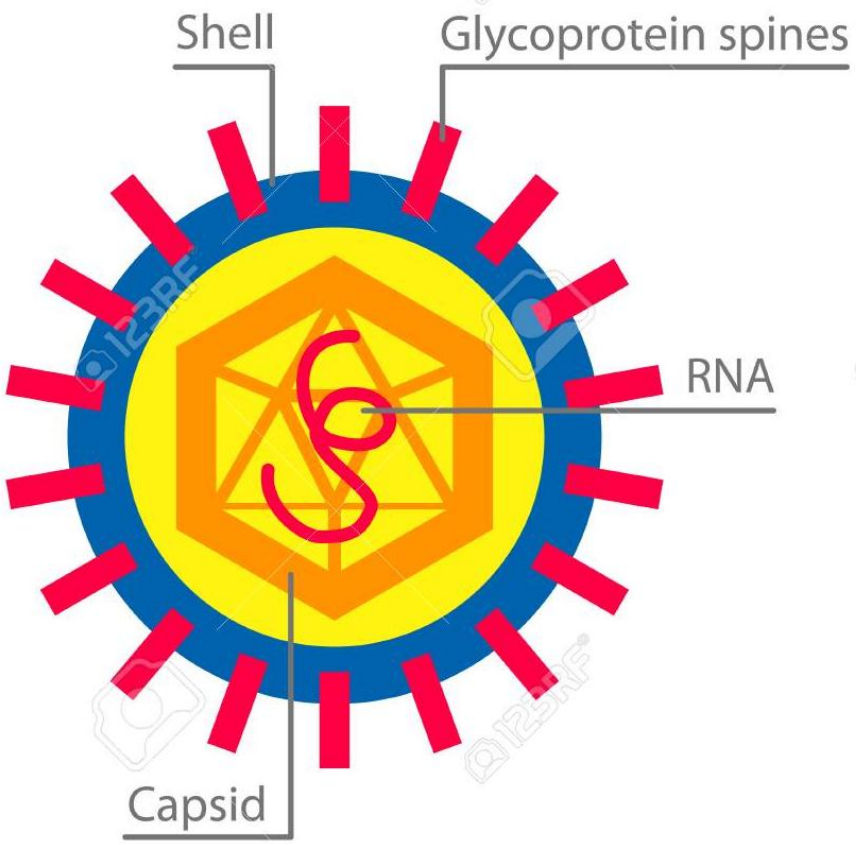
Arboviruses and Roboviruses

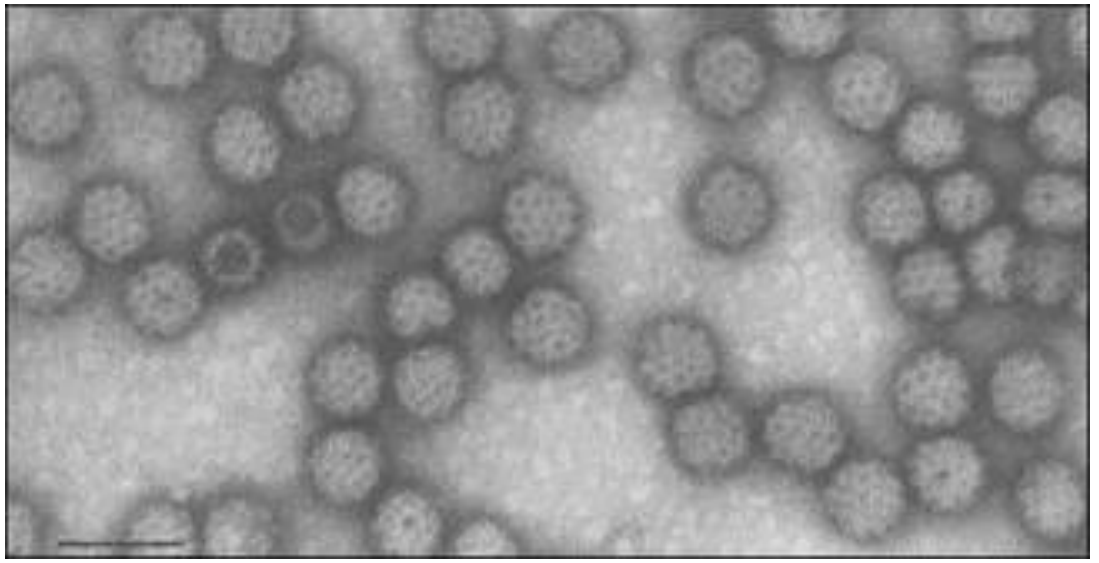
- **Arboviruses (arthropod born viruses)** are infected with blood-sucking arthropods (mainly mosquitoes and ticks).
- The main hosts for **roboviruses (rodent born viruses)** are rodents, the infection occurs in a non-transmissible way - through the biological excrement of rodents.

Arboviruses and Roboviruses

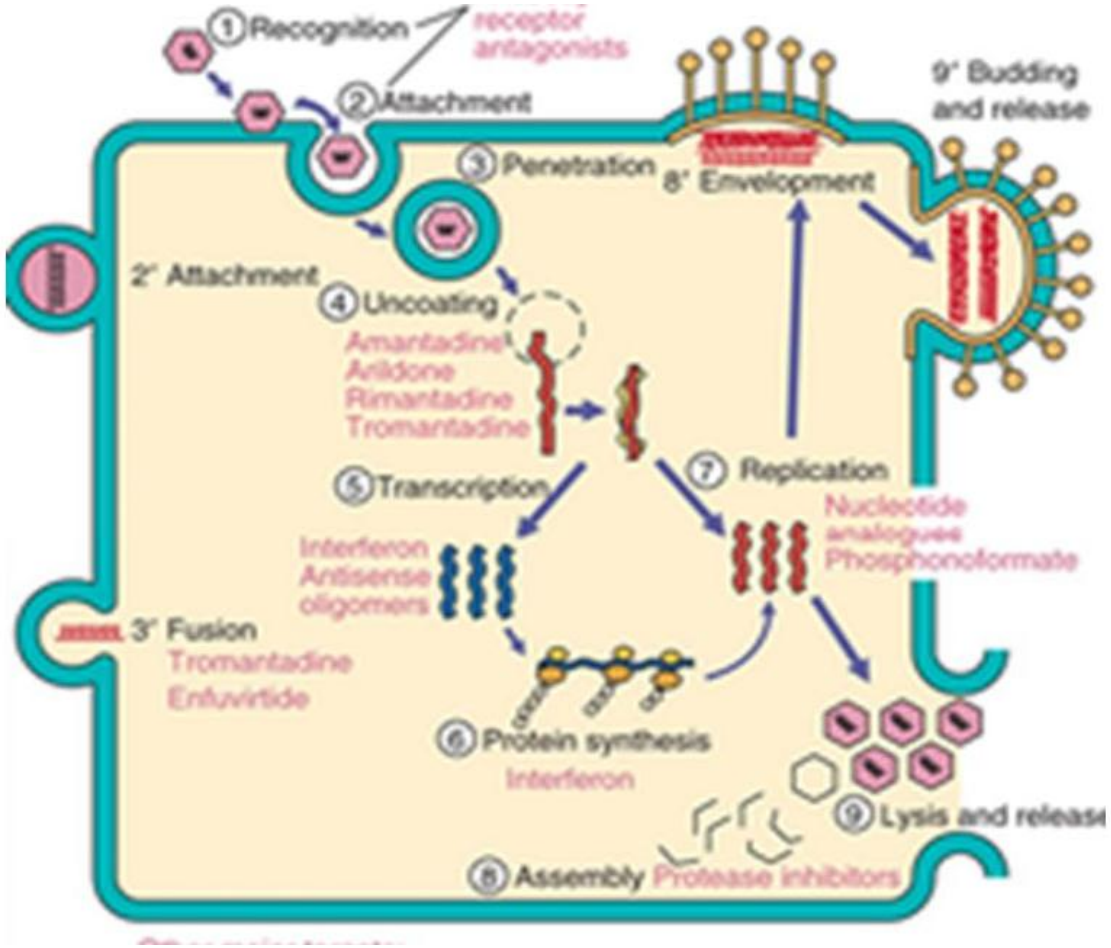
- **Arboviruses include:**
- **Toqaviridae,**
- **Flaviviridae,**
- **Arenaviridae,**
- **Bunyaviridae**
- **Roboviruses include:**
- ***Bunyaviridae* (genus *Hantavirus*),**
- ***Arenoviridae***
- ***Filoviridae***

Togaviridae





Reproduction of togaviruses

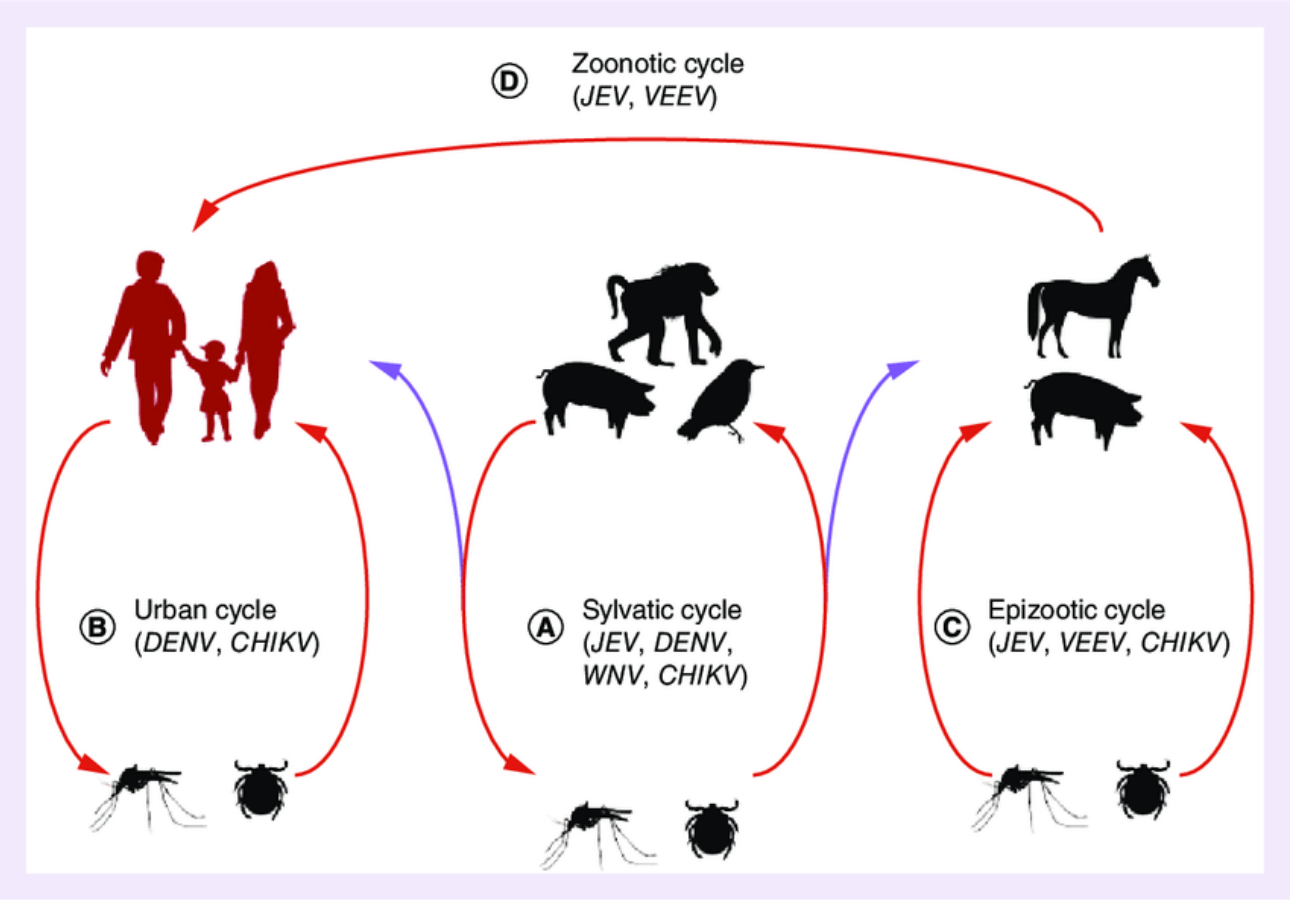


Classification of togaviruses

- Two genus of Togaviridae – **Alphavirus and Rubivirus** have clinical importance in human pathology
- ***Alfa viruses*** belong to arboviruses and caused disease that transmitted by arthropods
- ***Rubivirus*** not belong to arboviruses and transmitted by ear dropled mechanism

Sources of Infection and transmission ways

- Alphaviruses cause naturally occurring zoonotic diseases.
- In natural habitats, the reservoir of the virus are vertebrates - birds, rodents, primates and other animals.
- In natural habitats, people become infected through the bite of arthropods.
- The virus multiplies in the tissues and organs of arthropods, including the salivary glands.



Pathogenesis of Alfavirus infections

- Viruses that enter the body through the blood-sucking of arthropods first multiply in the local subcutaneous tissue and regional lymph nodes.
- The viruses then pass into the bloodstream and spread throughout the body, and depending on the nature of the causative agent, their subsequent proliferation occurs in monocytes and macrophages, vascular endothelium, lungs, liver, muscles, etc. possible.
- Neurotropic viruses enter the central nervous system and cause degenerative changes in brain cells, resulting in encephalitis.

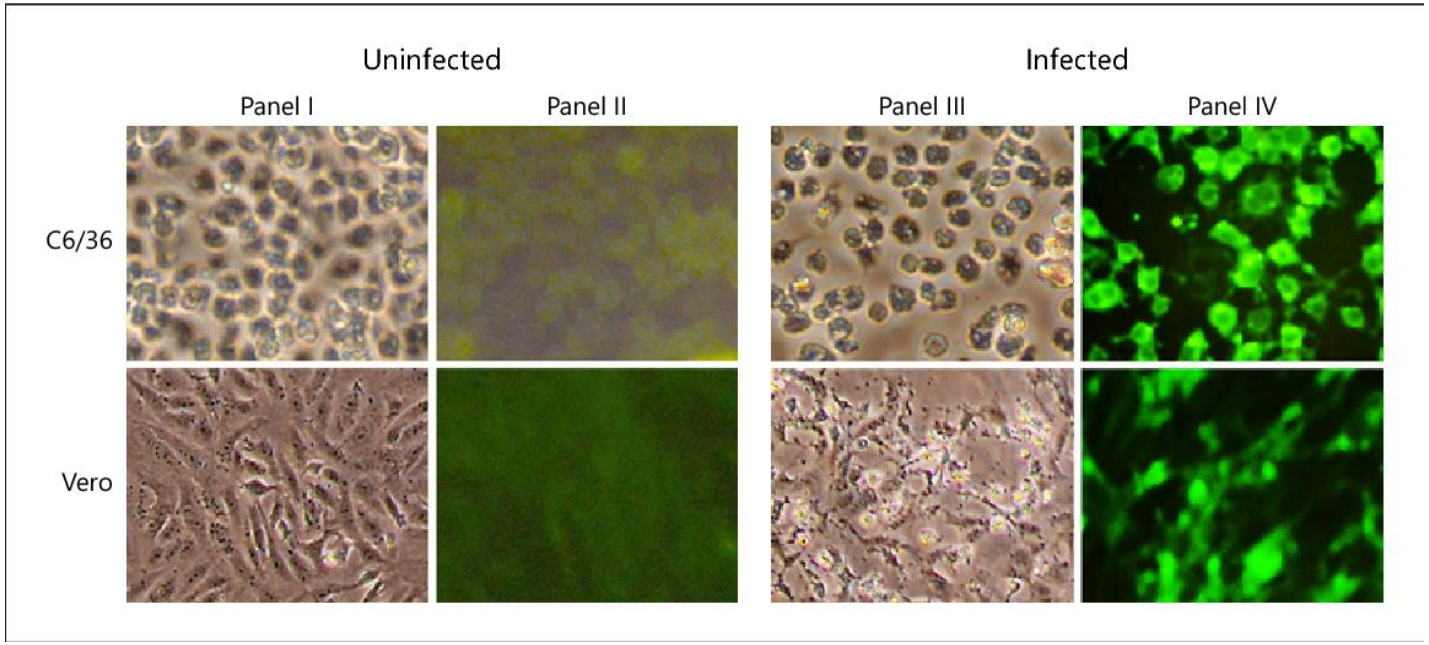
Clinical forms of alfavirus infections

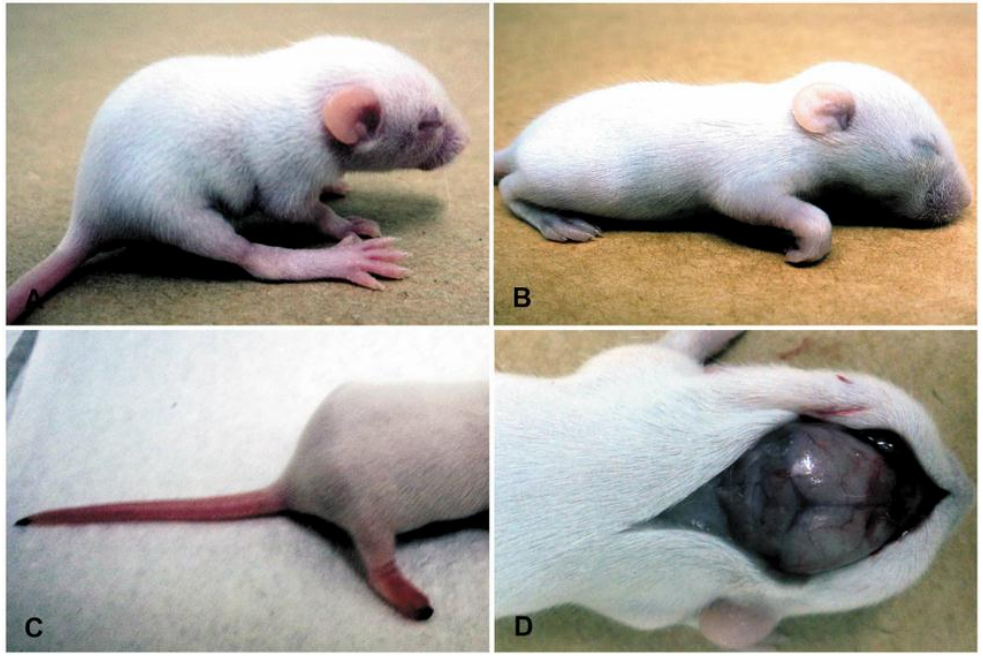
- ***Sindbis fever.*** The causative agent of the virus was obtained from mosquitoes in the village of Sindbis in Cairo (Egypt). The disease begins with fever, headache, arthralgia, skin rash and lasts 5-8 days. Although it has a benign end, it can become chronic and disability with the development of osteoarthritis.
- ***Semliki forest fever.*** The causative agent of the virus was obtained from mosquitoes in the Semliki forest of Uganda. The disease is sporadic in humans and is manifested by fever, in some cases encephalitis and aseptic meningitis.
- ***Chikungunya fever*** is common in tropical and subtropical climates and is characterized by double-wave fever, intoxication, myalgia, severe joint pain, lymphadenopathy, maculopapular rash, and sometimes meningeal and hemorrhagic symptoms.
- ***Equine encephalomyelitis.*** Diseases in humans are mainly found in many countries of the American continent (Brazil, Argentina, Mexico, USA, Canada, etc.), mainly accompanied by symptoms of encephalitis - darkening of consciousness, headache, fever, paralysis.

Microbiological diagnosis of alfavirus infections

- Viruses can be found in the blood in the early stages of the disease, and later in the cerebrospinal fluid. For this purpose, infantile white mice are infected intracerebral.
- Viruses can also be obtained by infecting appropriate cell cultures with pathological materials. Alphaviruses are identified in mice and cell cultures by NR, IFR, and ELISA.
- PCR is used in the diagnosis of some diseases.
- In the serum of patients it is possible to identify antibodies to the virus neutralizing and antihemagglutinin, which appear a few days after the disease and persist for many years. The simplest way to determine these antibodies is the inhibition of hem agglutination test. Determination of virus-specific IgM in serobrospinal fluid is considered a more sensitive test.
- The diagnosis is confirmed by the fact that the titer of antibodies in the blood serum taken at the beginning of the disease and 2-3 weeks later increased by 4 times or more.

Microbiological diagnosis of alfavirus infections





Flaviviridae

- >68 viruses
- small
- spherical
- enveloped
- SS RNA
- cross-related

Flaviviruses

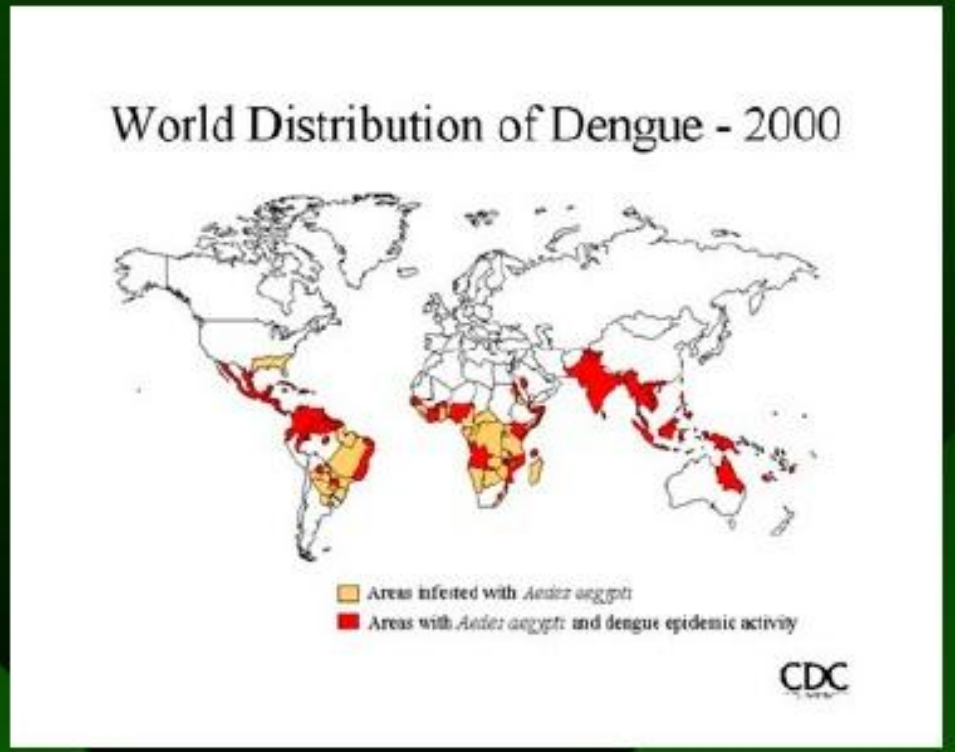
- Yellow Fever virus
- Dengue viruses
- St. Louis encephalitis virus
- Japanese encephalitis virus
- West Nile virus
- Murray Valley encephalitis virus, tick-borne encephalitis viruses and others

Yellow Fever

- vector: Aedes aegypti
- Latin America, Caribbean, Africa
- inapparent to severe infection (jaundice, hemorrhage, albuminuria)
- hepatic necrosis, Councilman and Torres bodies
- Dx: cell culture, serology, PCR, immunohistochemistry
- supportive treatment
- live attenuated 17D vaccine

Dengue Virus

- Causes dengue and dengue hemorrhagic fever
- Transmitted by mosquitoes
- Has 4 serotypes (DEN-1, 2, 3, 4)



Aedes aegypti

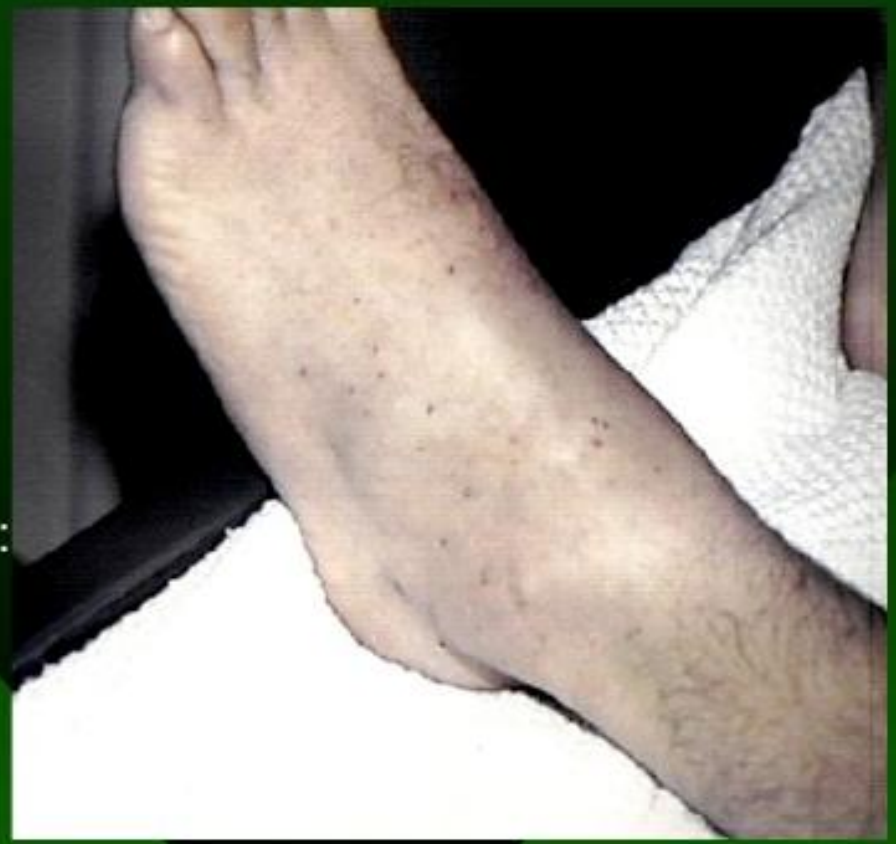
- Dengue transmitted by infected female mosquito
- Primarily a daytime feeder
- Lives around human habitation
- Lays eggs and produces larvae preferentially in artificial containers with clean stagnant water

Clinical Characteristics of Dengue Fever

- Fever
- Headache
- Muscle and joint pain
- Nausea/vomiting
- Rash
- Hemorrhagic manifestations

Hemorrhagic Manifestations of Dengue

- Skin hemorrhages: petechiae, purpura, ecchymoses
- Gum bleeding
- Nose bleeding
- Gastro-intestinal bleeding: hematemesis, melena, hematochezia
- Hematuria
- Increased menstrual flow



Laboratory Methods for Dengue Diagnosis

- Virus isolation to determine serotype of the infecting virus
- IgM ELISA test for serologic diagnosis

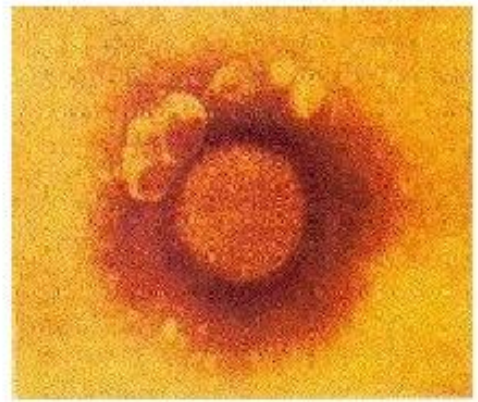
Japanese encephalitis virus

- single serotype, 5 genotypes based on E protein
- Asia, including SEA
- cycle: birds - Culex mosquitoes - swine
- humans, horses

Japanese encephalitis

- 99% subclinical
- lethargy, behavioral changes, motor abnormalities
- Dx: CSF analysis, EEG, IgM ELISA, NT, HI, CF, PCR
- Rx: supportive
- Prevention: inactivated vaccine (3 yr protection)

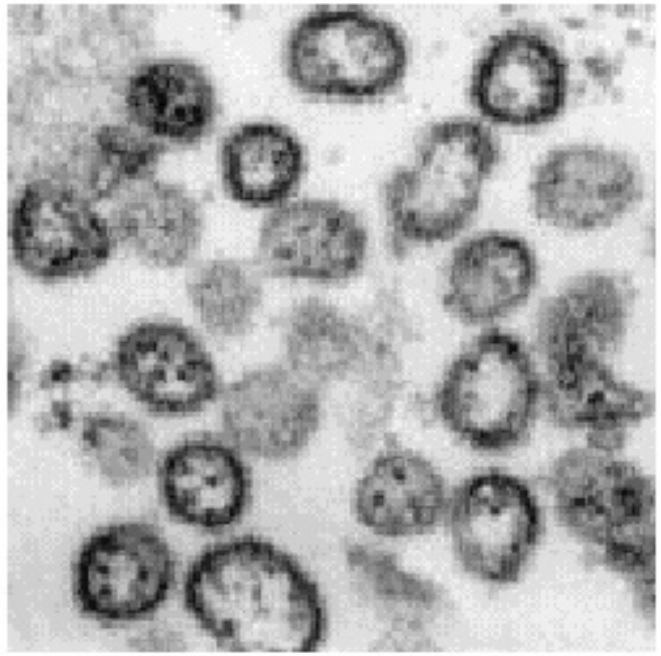
Arenaviruses



Introduction

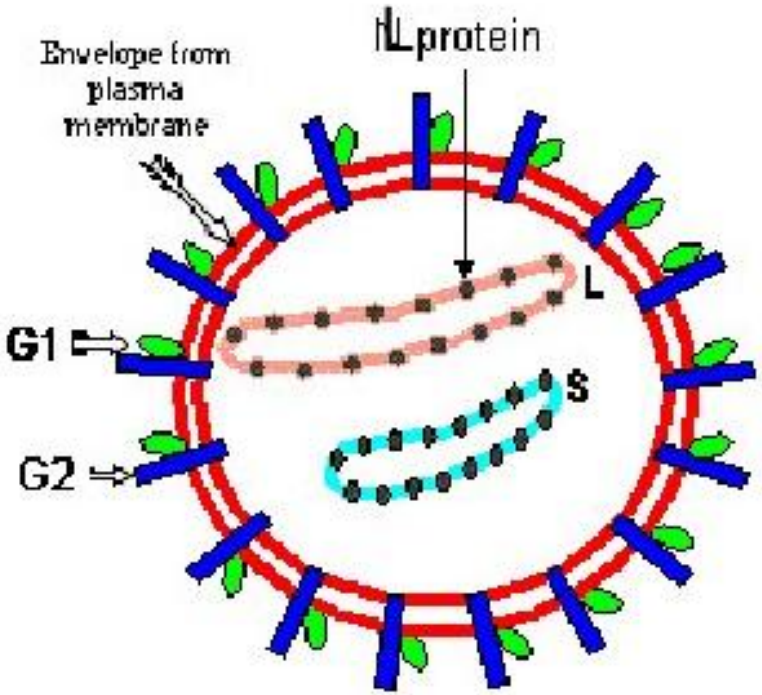
- Family = Arenaviridae
- Genus = Arenavirus
- Currently 22 recognized species
- 2 groups

- Old World
- New World



- Rodent – borne pathogens
- Important cause of VHF
- Host cell ribosomes are present in the viral particles are responsible for a "sandy" appearance on EM
- Hence the name Arenavirus (Latin: arena=sand)

Virology



Arenavirus particle

- ssRNA virus “ambisense”
- Genome consists of 2 RNA segments (L) = Large
  (S) = Small
- (L) encodes RNA-polymerase & Zn-binding protein
- (S) encodes NP and GPC
- Virions are spherical to pleomorphic
- Enveloped
- Average diameter = 120nm
- Envelope covered with 8-10nm long projections

Classification

2 groups

New World

Tacaribe Serocomplex

17 species

3 clades (A,B,C)

Family: *Muridae*

Subfamily: *Sigmodontinae*

American rodents *

Old World

Lassa-LCM Serocomplex

5 Species

Family: *Muridae*

Subfamily: *Murinae*

Eurasian rodents

Reservoirs

Rodent - mastomys sp

- Usually one species, less often 2 closely related species
- Chronic mild infection
- Life long shedding of virus
- Except Tacaribe virus *

*Fruit-eating bat – Artibeus sp

Transmission

- Rodent – Rodent

-Vertical

- Horizontal (aerosolized urine, faeces, saliva, bites)

- Rodent – Human

-Aerosolized secreta

- inoculation via cuts, bites

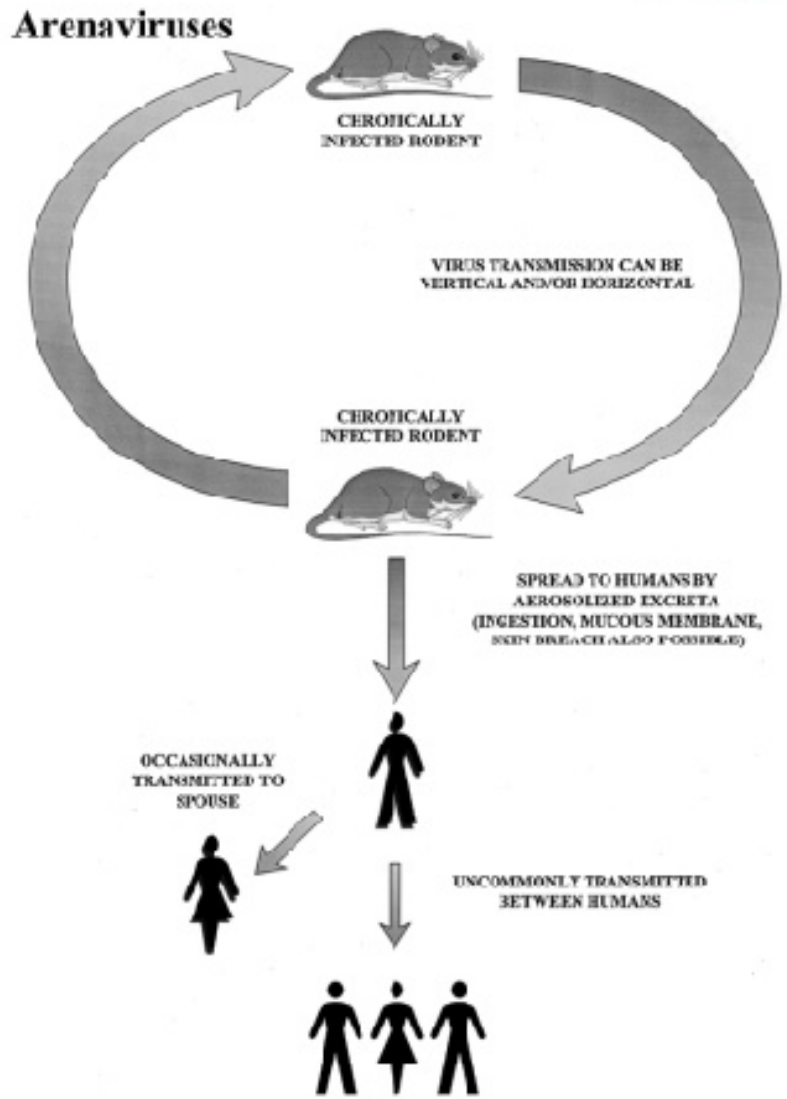
- contaminated fomites, food

-Rodent consumption

- Human – Human

- contaminated secretions, sexual

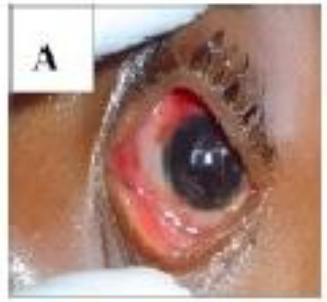
-Inoculation

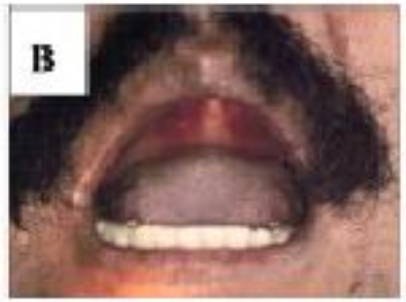


Clinical presentation

Table 2 Clinical stages of Lassa fever (adapted from McCarthy 2002[11])

Stage	Symptoms
1 (days 1-3)	General weakness and malaise. High fever, >39°C, constant with peaks of 40-41°C
2 (days 4-7)	Sore throat (with white exudative patches) very common; headache; back, chest, side, or abdominal pain; conjunctivitis; nausea and vomiting; diarrhoea; productive cough; proteinuria; low blood pressure (systolic <100 mm Hg); anaemia
3 (after 7 days)	Facial oedema; convulsions; mucosal bleeding (mouth, nose, eyes); internal bleeding; confusion or disorientation
4 (after 14 days)	Coma and death





Laboratory Diagnosis

Test	Specimen	Comments
Culture	Blood, CSF, Tissue	Cell Culture: Vero, Vero B6, BHK Animal: suckling mice, hamsters, guinea pigs
EM	Blood, urine, tissue	
Antigen detection	Blood	ELISA/IMF
Immunohistochemistry	Tissue	Liver, spleen, skin, kidney
RT-PCR	Blood, tissue	
Serology (IgG/IgM)	Serum	ELISA

Bunyaviridae

Structure

- Spherical enveloped particles
  - 90-100 nm
- virus encoded transcriptase
- 2 external glycoproteins
- multipartite - 3 segments of SS RNA
  - antisense

- SS RNA
C=122

Classification

- Genera
  - *Bunyaviruses*
  - *Phlebovirus*
  - *Nairovirus*
  - *Uukuvirus*
  - *Hantavirus*
- Immunologically
  - 35 serogroups
  - 300 types & subtypes

Serious Bunya Virus Diseases

- Crimean Congo Hemorrhagic Fever Virus
- Rift Valley Fever Virus
- La Crosse Virus
- Hanta Virus

Pathogenesis

- Early
  - fever & viremia
- Late
  - encephalitis
  - retinitis
  - renal involvement

Epidemiology

- Determined by distribution of vector and mammalian host
- Humans: accidental dead end hosts

Diagnosis

Presumptive

- febrile illness
- geographic site of exposure
- Sean
- vectors

Confirmation

- virus isolation
- Virus specific IgM
- Rise in antibody titer

Control

- Control Vectors
  - arthropods
  - rodents
- Vaccination
  - Humans: Crimean Congo
  - Sheep & Cattle : Rift Valley

Crimean Congo Hemorrhagic Fever Virus

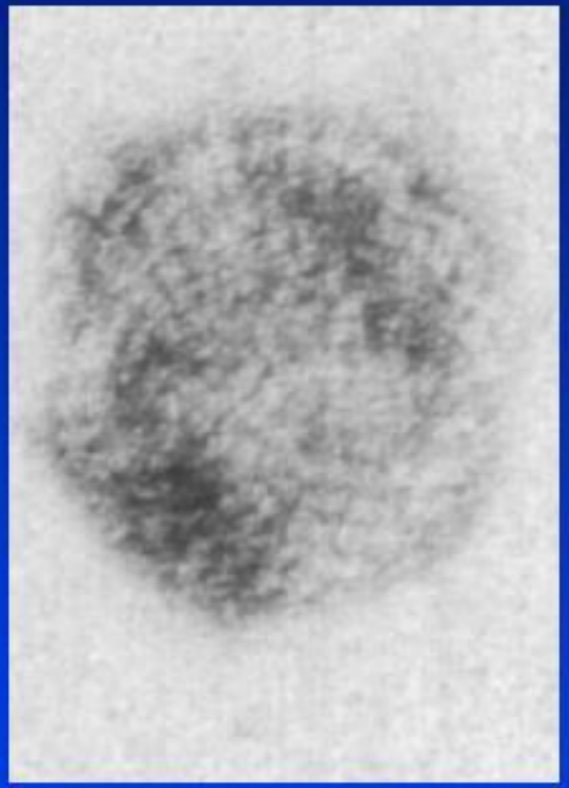
- Headache
- pain in limbs
- bleeding from multiple orifices

Hanta Virus

- Rodents - transmission to humans via aerosolized excretions and bites. A wide variety of biting insects.

Hanta Virus

- Lipid envelope
  - susceptible to most disinfectants.
  - Need to lower pH < 5

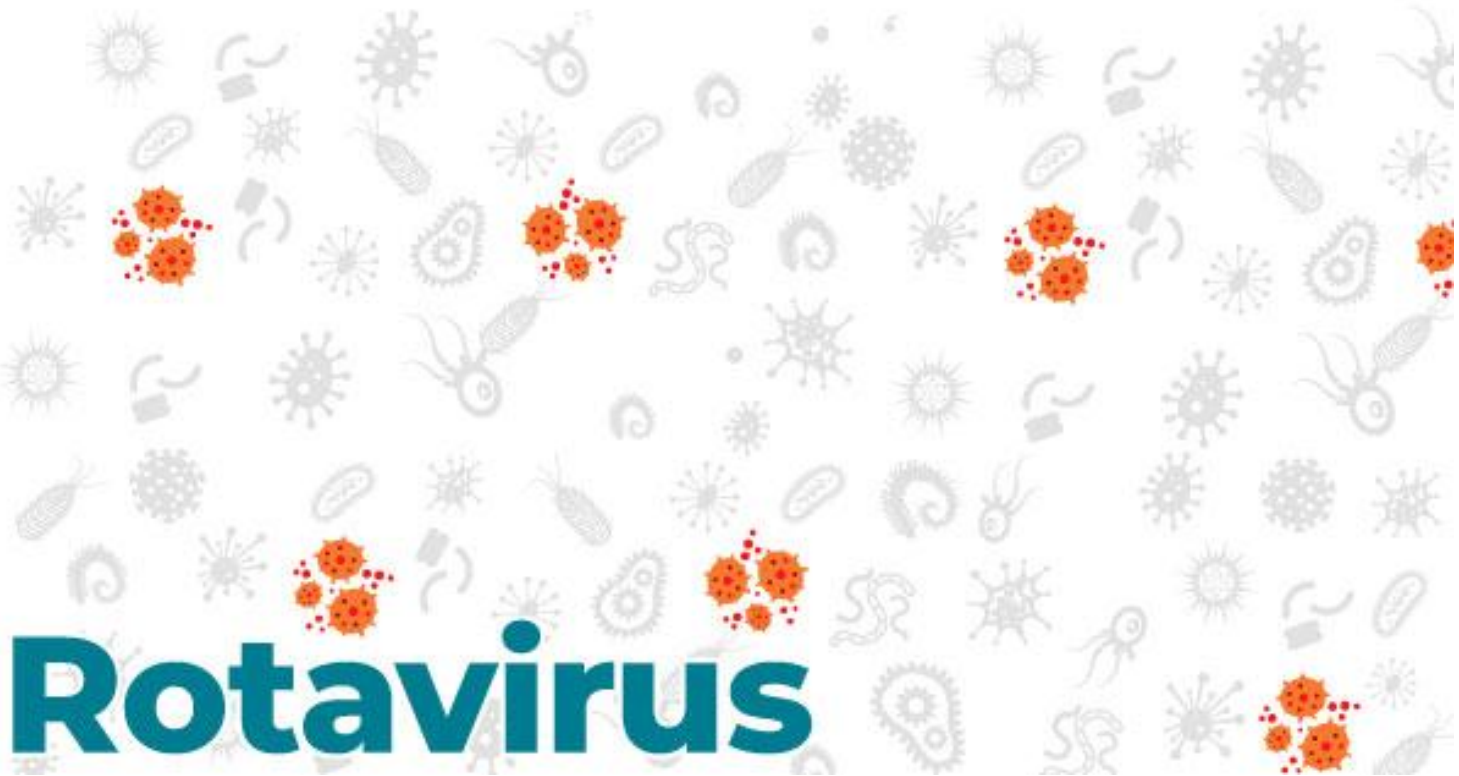


Hanta Virus

- tripartite negative-sense RNA
  - L,>>viral transcriptase
  - M>> envelope glycoproteins
  - >. nucleocapsid protein

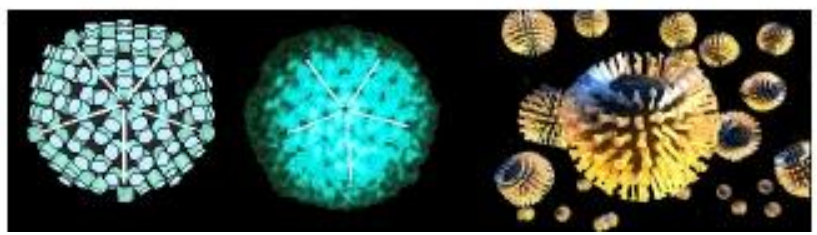
Hantavirus Pulmonary Syndrome

- febrile prodrome
- followed by
  - non-cardiogenic pulmonary edema,
  - hypotension
  - shock


Rotavirus

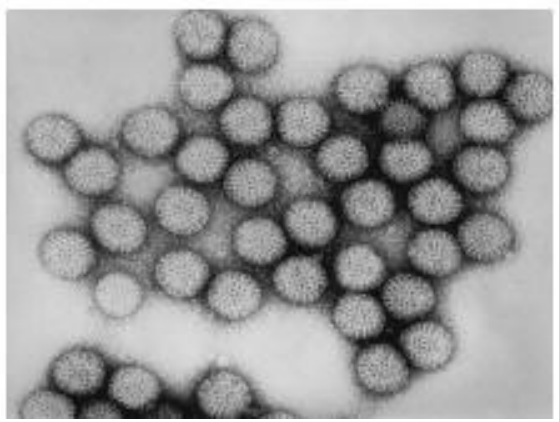
Rotavirus - Structural features

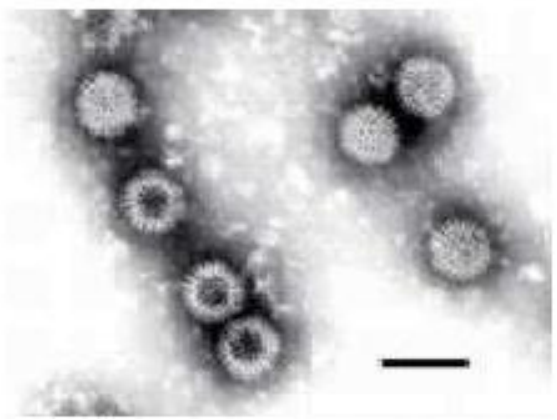
- Reovirus (RNA)
- 60-80nm in size
- Double stranded (ds) RNA
- Non-enveloped virus
- A rotavirus has a characteristic wheel-like appearance when viewed by electron microscopy
  - The name rotavirus is derived from Latin, meaning "wheel"
- Group A is important human pathogen [7 Groups (A to G)]
- 5 predominant strains (G1-G4, G9), account for 90% of isolates
- Strain G1 accounts for 73% of infections



Characters

- The virus is stable in the environment
- Relatively resistant to hand-washing agents
- Susceptible to disinfection
  - 95% ethanol, ‘Lysol’, formalin
- Very stable and may remain viable for weeks or months if not disinfected





Transmission

- Transmission
  - Mainly person to person via fecal-oral route, fomites
  - Poor hygiene
- Food and water-borne spread is possible
- Spread via respiratory route is speculated




Pathogenesis

- Reservoir — Human-GI tract
- Communicability — 2 days before to 10 days after onset

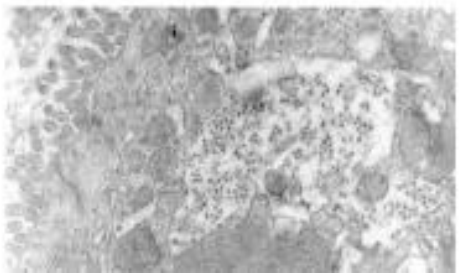
- Entry through mouth
- Replication in epithelium of small intestine
- Viremia uncommon
- Infection leads to isotonic diarrhea

Pathogenicity

- The virus infect the villi of the small intestine
  - Gastric and colonic mucosa are not infected
- Attach with the enterocytes by VP4
- They multiply in the cytoplasm of the enterocytes and damage their transport mechanisms
- Damaged cell may show into lumen of the intestine and release large quantities of virus which appear in the stool
- Viral excretion usually lasts for 2 – 12 days in otherwise healthy patients

Mechanism of diarrhea

- They strip the tips of the villi thus decreasing the surface area and decreasing by more than 50% the specific absorptive capacities of the intestine
- Damaged cells on villi are replaced by non absorbing immature cells
- Watery diarrhea due to net secretion of intestinal fluid and loss of absorptive surface
- Activation of the enteric nervous system
- Role of NSP4 peptide regions as an enterotoxin

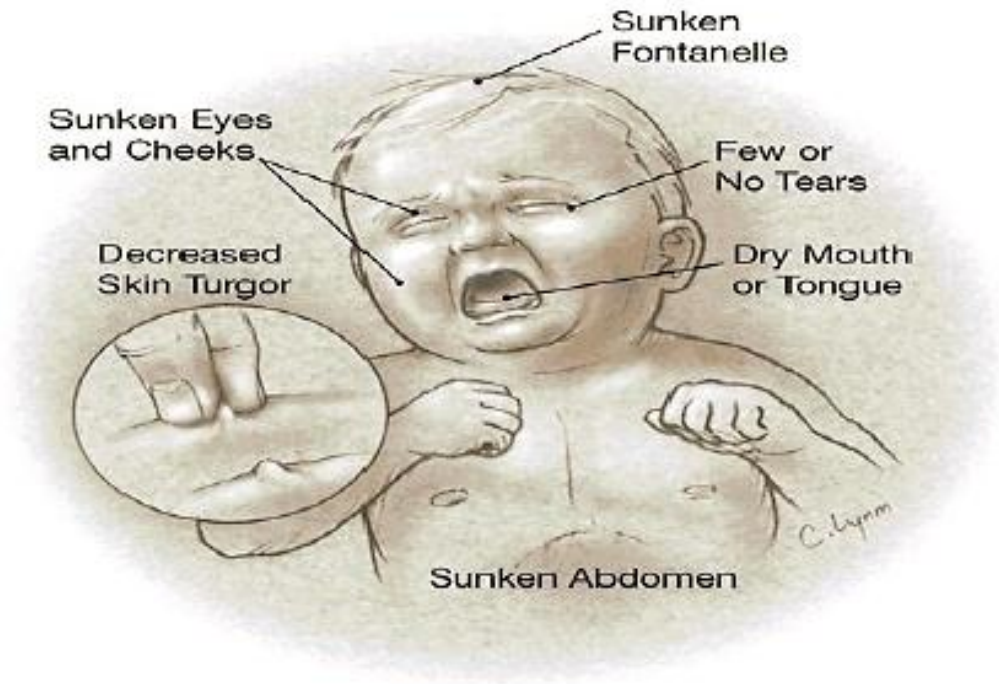


Clinical Features

- Incubation period 1-3 days
- Clinical manifestations depend on whether it is the first infection or reinfection
- Present with
  - Watery diarrhea (no blood or leukocytes)
  - Fever, can be high grade
  - Abdominal pain
  - Vomiting
  - Loss of electrolytes and fluids leading to dehydration
  - May be fatal unless treated

- First infection after age 3 months generally most severe
  - May be asymptomatic or result in severe dehydrating diarrhea with fever and vomiting
- GI symptoms generally resolve in 3 to 7 days

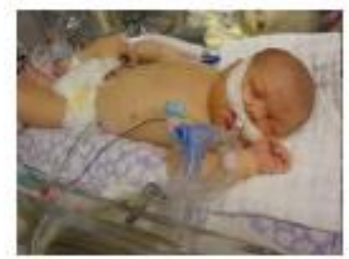
Dehydration - leading cause of morbidity and mortality



Complications

- Severe chronic diarrhea
- Dehydration
- Electrolyte imbalance
- Metabolic acidosis
- Immunodeficient children may have more severe or persistent disease



Immunity

- Antibody against VP7 and VP4, and Secretory IgA probably important for protection
- First infection usually severe
  - First infection usually does not lead to permanent immunity
  - Subsequent infections generally less severe
- Re-infection can occur at any age
- By age 3 years, 90% of the children have serum antibodies to one or more types
- Young children may suffer up to five re-infections by 2 years of age

Diagnosis

- Serology for epidemiologic studies
  - Antigen detection in stool
  - Antibody detection in serum
- Molecular methods
- Electron Microscopy
- Culture
  - Group A Rotaviruses can be cultured in monkey kidney cells
- Histopathology

Serology

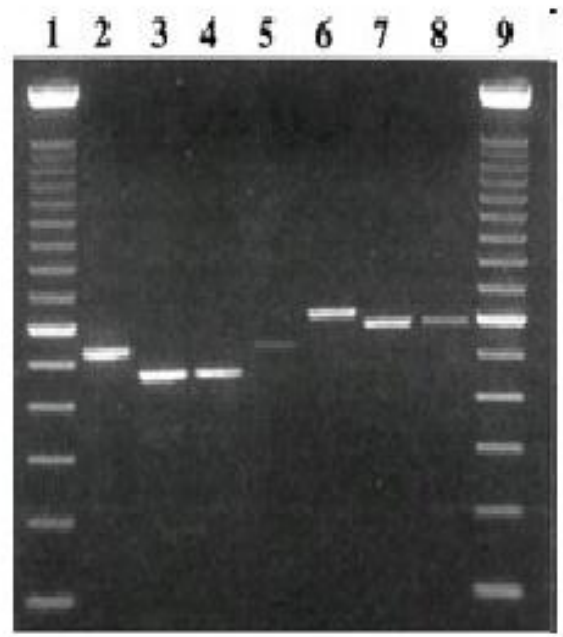
- Antigen detection in stool
  - ELISA, LA (Group A Rotavirus), ICT
- Antibody detection
  - ELISA can detect antibodies and establish rise in titers
- Serology for epidemiologic studies

Microscopy (EM)

- Demonstration of Virus in stool helps in early disease
- Electron Microscopy has made the identification simpler
- Non-Group A viruses also

PCR/Genotyping

- Genotyping is most sensitive method for detection of Rotavirus NA from stool specimens



Treatment

- Treatment of Gastroenteritis is supportive
- Correction of loss of water and electrolytes remain the goal treatment
- Failure for prompt correction of dehydration leads to
  - Acidosis
  - Shock
  - Death
- Lesser deaths if effective fluid replacement therapy is timely initiated

Fluid Replacement

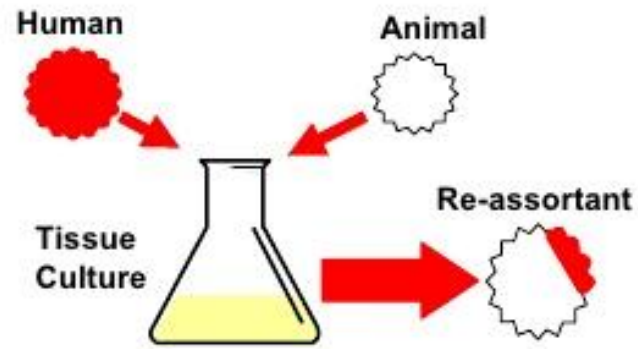
- Management consists of replacement of fluids (ORS) and restoration of Electrolyte balance
- Oral rehydration therapy is highly effective in reducing morbidity and mortality
- Severe dehydration needs parental administration of fluids

Prevention and Control

- In view of fecal-oral route of transmission, significant control measures are
  - Waste water management
  - Safe drinking water supplies
  - Sanitation
- Basic measures
  - Keep your hands clean
  - Wash hands often with soap and warm water after using the toilet, diapering and before preparing or eating food
- Vaccine

Vaccine

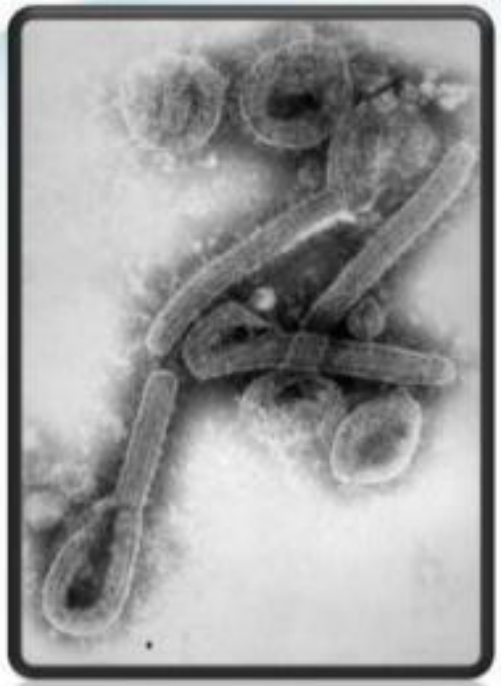
- A live, oral, pentavalent, human-bovine re-assortant vaccine
- Administered at 2, 4, and 6 months of age
  - RotaTeq™
  - Rotarix™



Created by genetic re-assortment of human and bovine antigens

FILOVIRUS

Ébola



Marburg

What is Ebola Virus?

- A notoriously deadly virus that causes fearsome symptoms
  - –High Fever
  - –Internal Bleeding
- kills as many as 90% of the people it infects

Introduction

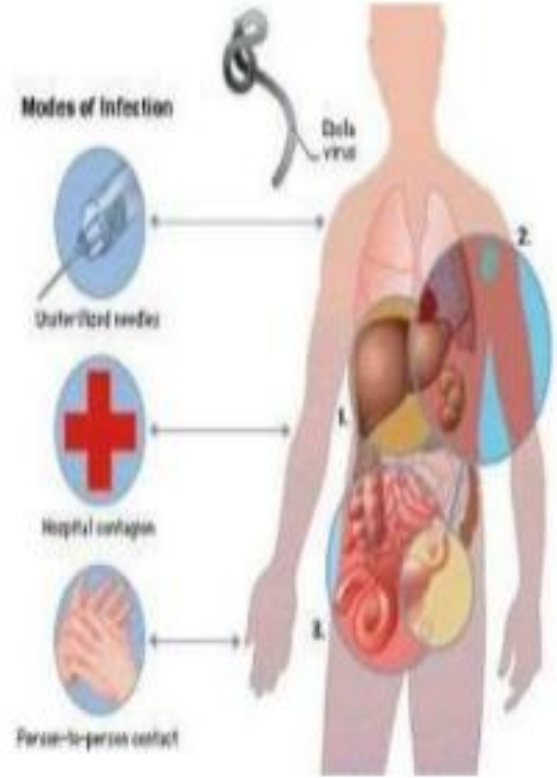
Ebola hemorrhagic fever (Ebola HF) is one of numerous Viral Hemorrhagic Fevers. It is a severe, often fatal disease in humans and nonhuman primates (such as monkeys, gorillas, and chimpanzees.

Structure

- Like all filoviruses, ebolavirions are filamentous particles shape of a shepherd's crook or in the shape of a "U" or a "6", and they may be coiled, toroid, or branched.
- In general, ebolavirions are 80 nm in width, but vary somewhat in length.
- In general, the median particle length of ebolaviruses ranges from 974 to 1,086 nm (in contrast to marburg virions, whose median particle length was measured at 795–828 nm), but particles as long as 14,000 nm have been detected in tissue culture.

MODE OF TRANSMISSION

- Unsterilized needles.
- Sub optical hospital conditions.
- Personal contact.
- Through blood to blood contact.
- Human to human transmission.
- Reusing needles and blood gloves in hospital.



Pathogenesis

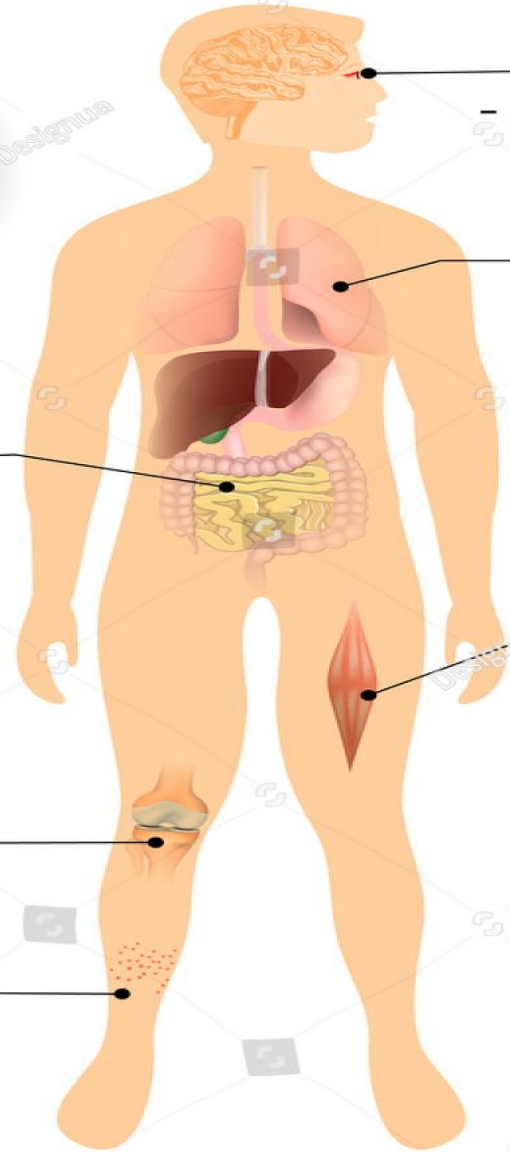
- Endothelial cells, mononuclear phagocytes and hepatocytes are the main targets of infection.
- After infection, a secreted glycoprotein (sGP) known as the Ebola virus glycoprotein (GP) is synthesized.
- Ebola replication overwhelms protein synthesis of infected cells and host immune defenses. The GP forms a trimeric complex, which binds the virus to the endothelial cells lining the interior surface of blood vessels.
- The sGP forms a dimeric protein that interferes with the signaling of neutrophils,which allows the virus to evade the immune system by inhibiting early steps of neutrophil activation.

Pathogenesis

- These white blood cells also serve as carriers to transport the virus throughout the entire body to places such as the lymph nodes, liver, lungs, and spleen.
- The presence of viral particles and cell damage resulting from budding causes the release of cytokines (to be specific, TNF-α, IL-6, IL-8, etc.), which are the signaling molecules for fever and inflammation.
- The cytopathic effect, from infection in the endothelial cells, results in a loss of vascular integrity. This loss in vascular integrity is furthered with synthesis of GP, which reduces specific integrins responsible for cell adhesion to the inter-cellular structure, and damage to the liver, which leads to coagulopathy.

Symptoms of Ebola

Ebola virus



Eye
- bleeding

Respiratory system
- sore throat
- chest pain

Digestive system
- nausea
- diarrhea
- vomiting
- abdominal pain

Muscle
- pain

Joints
- pain

Skin
- rashes

Fever
Headache
Weakness
Internal and external bleeding

Signs and symptoms

- Signs and symptoms of Ebola usually begin suddenly with am influenza-like stage characterized by fatigue, fever, headaches, joint, muscle and abdominal pain.
- Vomiting, diarrhea and loss of appetite are also common.
- Less common symptoms include: sore throat, chest pain, hiccups, shortness of breath and trouble swallowing.
- The average time between contracting the infection and the start of symptoms is 8 to 10 days, but it can vary between 2 and 21 days.
- Skin manifestations may include a maculopapular rash (in about 50% of cases).
- Early symptoms of EVD may be similar to those of malaria, dengue fever or other tropical fevers, before the disease progresses to the bleeding phase.

Signs and symptoms

- In 40–50% of cases, bleeding from puncture sites and mucous membranes (e.g. gastrointestinal tract, nose, vagina and gums) has been reported.
- In the bleeding phase, which typically starts 5 to 7 days after first symptoms internal and subcutaneous bleeding may present itself through reddening of the eyes and bloody vomit.
- Bleeding into the skin may create petechiae, purpura, ecchymoses and hematomas (especially around needle injection sites).
- Types of bleeding known to occur with Ebola virus disease include vomiting blood, coughing it up or blood in the stool. Heavy bleeding is rare and is usually confined to the gastrointestinal tract.
- In general, the development of bleeding symptoms often indicates a worse prognosis and this blood loss can result in death. All people infected show some symptoms of circulatory system involvement, including impaired blood clotting.
- If the infected person does not recover, death due to multiple organ dysfunction syndrome occurs within 7 to 16 days (usually between days 8 and 9) after first symptoms.

Laboratory diagnosis

Laboratory tests used in diagnosis include:

Timeline of Infection	Diagnostic tests available
Within a few days after symptoms begin	- Antigen-capture enzyme-linked immunosorbent assay (ELISA) testing - IgM ELISA - Polymerase chain reaction (PCR) - Virus isolation
Later in disease course or after recovery	- IgM and IgG antibodies
Retrospectively in deceased patients	- Immunohistochemistry testing - PCR - Virus isolation

Prevention

Quarantine

- Quarantine, also known as enforced isolation, is usually effective in decreasing spread.
- Governments often quarantine areas where the disease is occurring or individuals who may be infected. In the United States, the law allows quarantine of those infected with Ebola.The lack of roads and transportation may help slow the disease in Africa. During the 2014 outbreak, Liberia closed schools.[

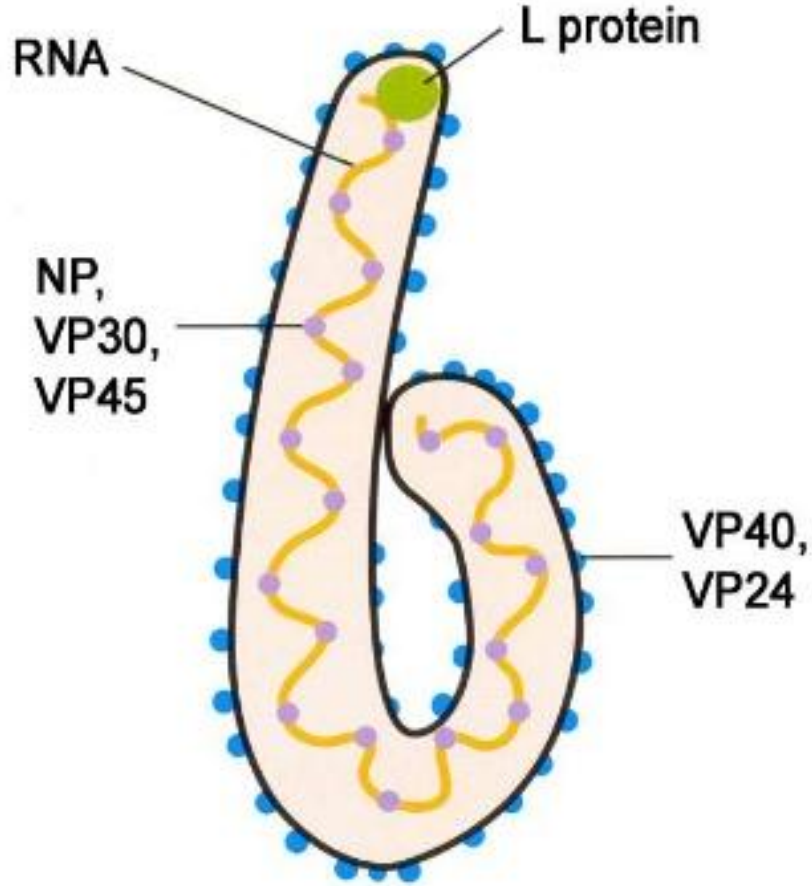
Vaccine

- No vaccine is currently available for humans.
- The most promising candidates are DNA vaccines or vaccines derived from adenoviruses, vesicular stomatitis Indiana virus (VSIV) or filovirus-like particles (VLPs) because these candidates could protect nonhuman primates from ebolavirus-induced disease. DNA vaccines, adenovirus-based vaccines, and VSIV-based vaccines have entered clinical trials

General Characteristics

- Order : Mononegavirales
- Family : Filoviradae
- Genus : Marburgvirus
- Species : Marburg marburgvirus

- Synonyms : Marburg disease, Marburg hemorrhagic fever, African hemorrhagic fever, and green monkey disease.



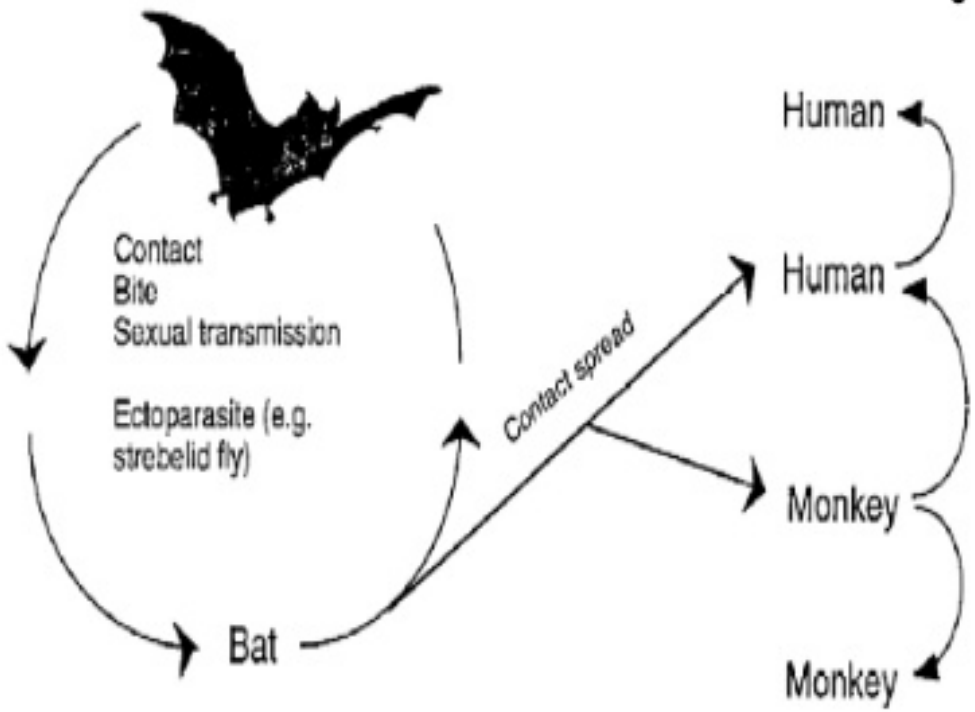
(it has the same structural properties as the Ebola virus)

Morphology

- Marburg is an enveloped, single-stranded, unsegmented, negative-sense RNA virus.
- It has the filamentous structure, can appear shaped like a U, a 6, or spiraled like a snail; and can sometimes be branched.
- They tend to include long noncoding regions at their 3' and/or 5' ends, which probably contributes to the stability of the viral transcript.
- The viral fragment is pleomorphic.
- Complexed with the proteins NP, VP35, VP30, and L.

Vector

- The natural reservoir for the virus is unknown. Epidemiologists have tested bats, monkeys, spiders and ticks for the virus, but were not able to acquire definitive data. Common factors indicate that the natural reservoir is part of rural Africa.



- Secondary spread of the disease is via contact with infected persons or contact with blood, secretions, or excretions of infected persons. The virus may continue to be shed in the patient's semen for up to 3-4 months after illness. Sexual transmission of the disease did occur in one instance in Germany.

PATHOGENICITY/TOXICITY

- A rare, severe hemorrhagic fever in humans and non-human primates characterized by a sudden onset with high fever, chills, headache, myalgia, and maculopapular rash, possibly followed by vomiting, chest pain, sore throat, abdominal pain, and diarrhea.

- Symptoms become increasingly severe and may include inflammation of the pancreas, jaundice, severe weight loss, delirium, shock, liver failure, massive hemorrhage, and multi-organ dysfunction. Marburg disease has a fatality rate of approximately 25 %.

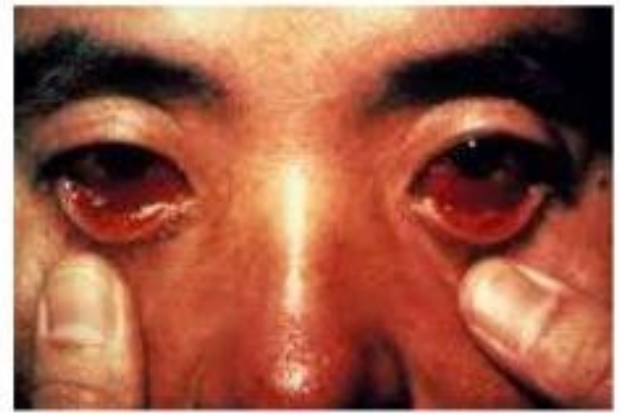
Mechanism

- As with Ebola, the exact mechanism of Marburg is unknown. However, virion surface spikes are made soley of large glycoprotein. It is presumed that, as with other negative-strand RNA viruses, these surface spikes bind to receptors on the host cell and mediate entry into susceptible cells.

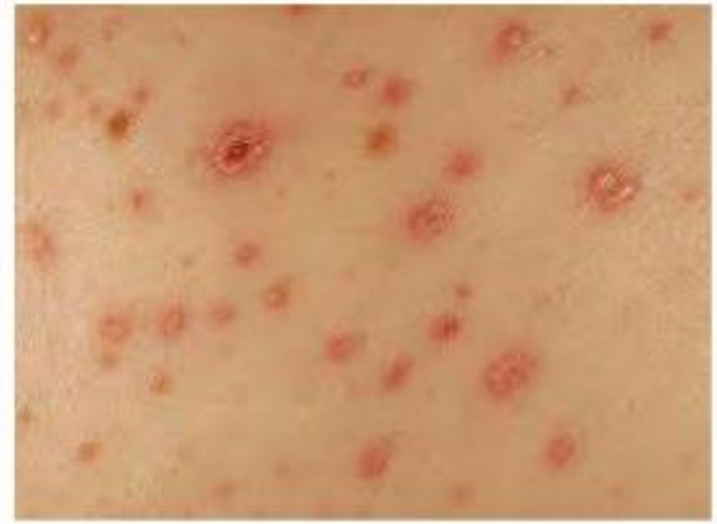
- The Marburg virus has 22 potential *N*-linked glycosylation sites on its surface. Viral replication takes place in the cytoplasm, and envelopment is the result of budding preformed nucleocapsids. Systemically, the virus involves the liver, lymphoid organs, and kidneys.

- *Incubation period* : Usually 5-7 days, but can range from 3-10 days.

Symptoms



- Fever / Severe headache
- Joint and muscle aches
- Chills /Weakness
- Nausea and vomiting.
- Diarrhea (may be bloody)
- Red eyes.
- Raised rash.
- Chest pain and cough.
- Stomach pain.
- Severe weight loss.



- Bleeding, usually from the eyes, and bruising (people near death may bleed from other orifices, such as ears, nose and rectum)

Diagnosis

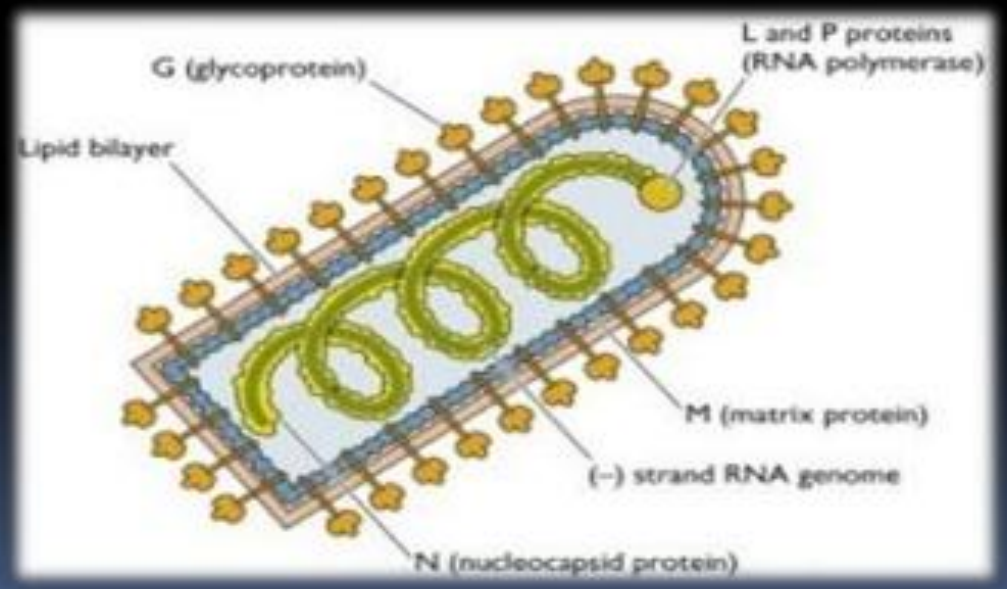
- For patients presenting with Marburg symptoms, initial possible diagnoses can include malaria and tyhpoid fever.
- As with Ebola, diagnosis of Marburg virus is confirmed by IgG ELISA, although IgM ELISA can be used to distinguish acute infections from old infections. IFA results can be misleading.
- Electron microscopy is useful in diagnosing filovirus infection, but does not help distinguish Marburg from Ebola.

Treatment & prevention

- Supportive therapy (there is no specific treatment for Marburg hemorrhagic fever. However, the virus itself is sensitive to lipid solvents, detergents, commercial hypochlorite disinfectants, and phenolic disinfectants. The virus can also be destroyed by ultraviolet and gamma radiation.

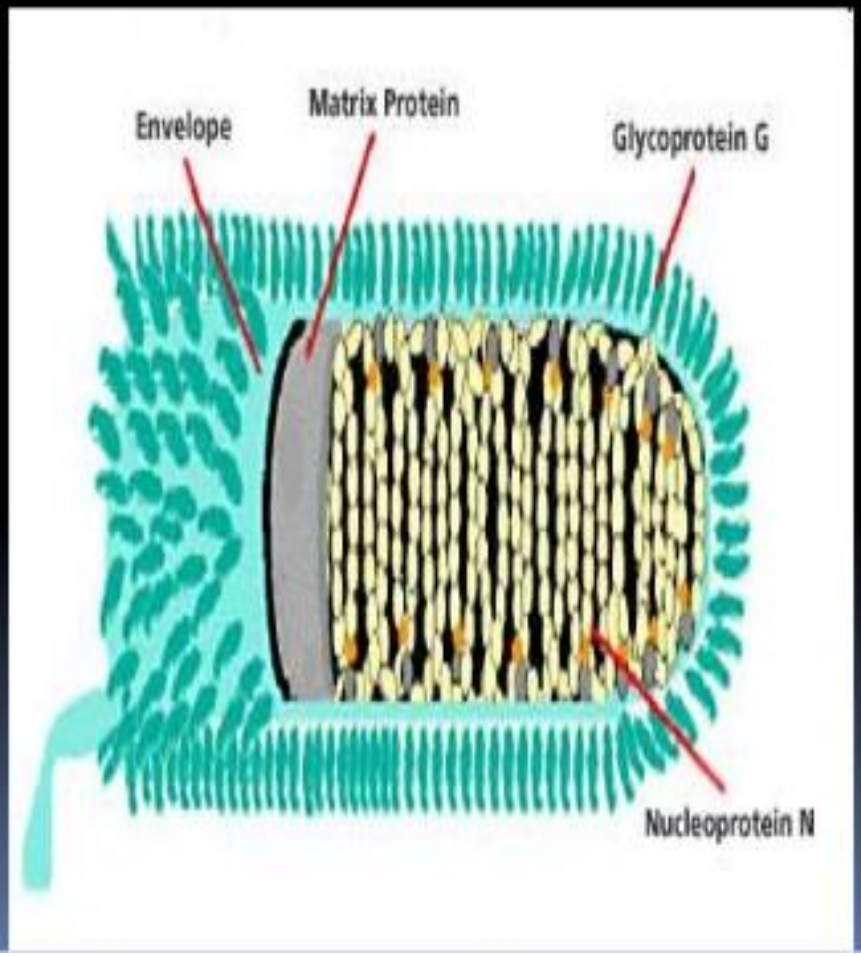
- Vaccine. None. As with exposure to other filoviruses, exposure to Marburg does not confer subsequent immunity. The antibody response in convalescent patients does not neutralize or protect against subsequent infection by Marburg virus.

RHABDO VIRUS



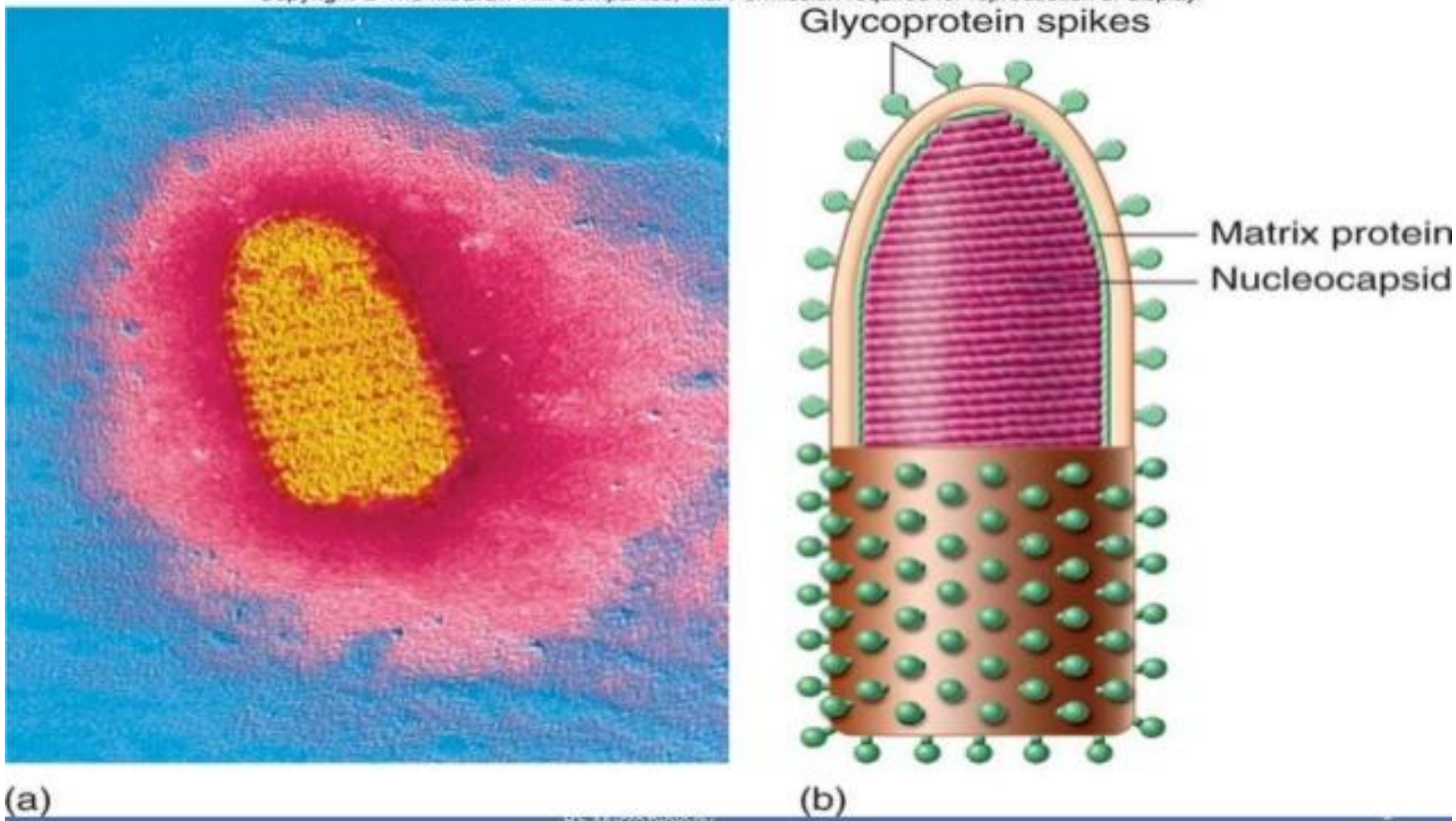
RhabdoVirus

- Single stranded ,linear ,negative sense ,non segmented RNA
- These are enveloped
- Bullet shaped virus
- Multiply in cytoplasm



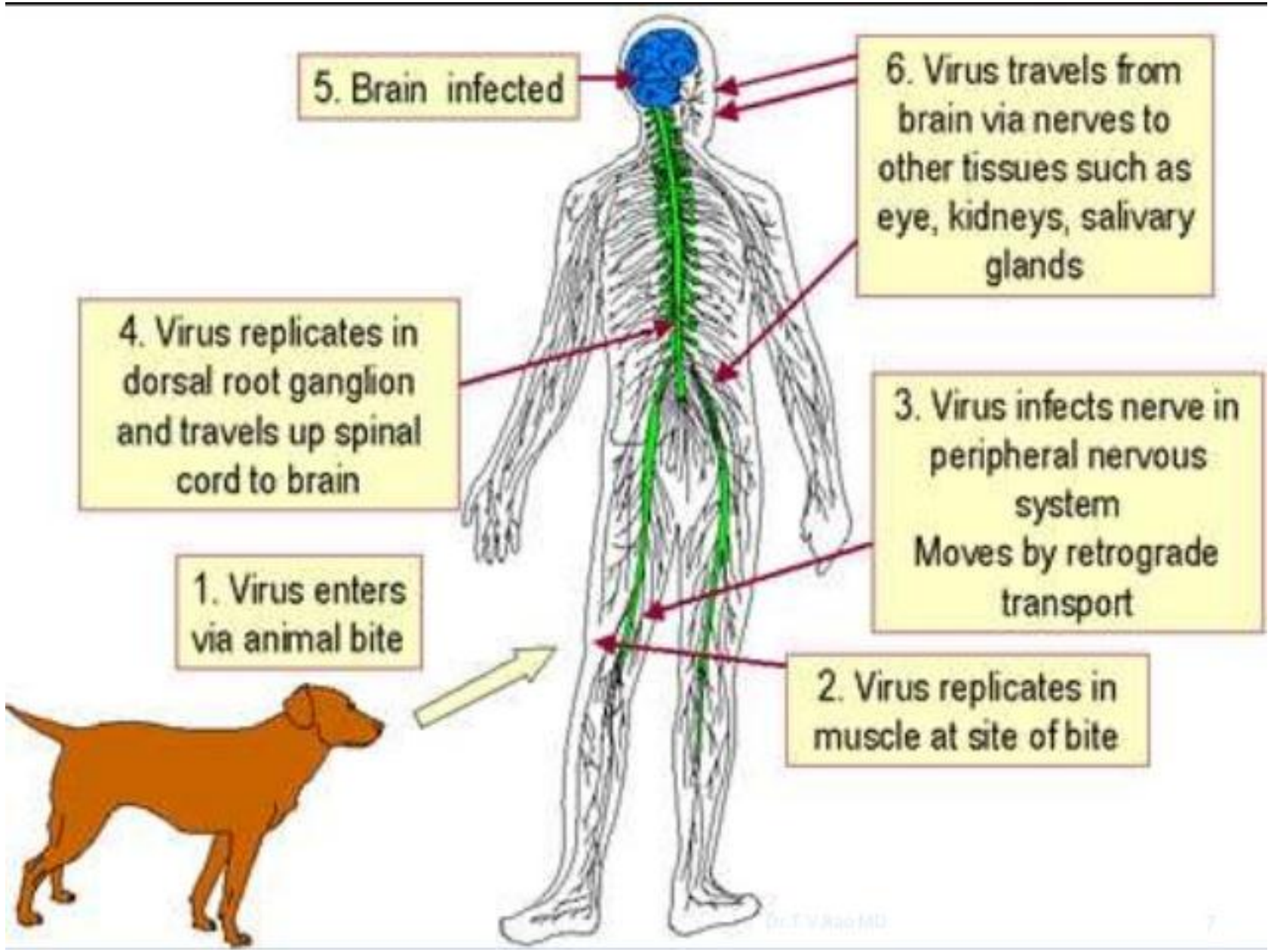
Structure of the rabies virus

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



Pathogenesis of Rabies

- Bite by Rabid dog or other animals
- Virus are carried in saliva virus deposited on the wound site.
- If untreated 50% will Develop rabies.
- Rabies can be produced by licks and corneal transplantation.
- Virus multiply in the muscle ,connective tissue, nerves after 48 – 72 hours.
- Penetrated nerve endings.


5. Brain infected
6. Virus travels from brain via nerves to other tissues such as eye, kidneys, salivary glands
4. Virus replicates in dorsal root ganglion and travels up spinal cord to brain
3. Virus infects nerve in peripheral nervous system
Moves by retrograde transport
1. Virus enters via animal bite
2. Virus replicates in muscle at site of bite

Symptoms

- Headache, fever, sore throat
- Nervousness, confusion
- Pain or tingling at the site of the bite
- **Hallucinations**
  - Seeing things that are not really there
- **Hydrophobia**
  - "Fear of water" due to spasms in the throat
- **Paralysis**
  - Unable to move parts of the body
- Coma and death

Clinical Findings

- Bizarre behavior.
- Agitation
- Seizures.
- Difficulty in drinking.
- Patients will be able to eat solids
- Afraid of water - Hydrophobia.
- Even sight of sound disturbs the patient.
- But suffer with intense thirst.
- Death in 1 -6 days.
- Respiratory arrest / Death / Some may survive.

Diagnosis

- Based on the history
- Signs and symptoms
- Clinical examination
- Detection of antigen by taking skin biopsy using immunofluorescence.
- Virus isolation from saliva & other secretions.
- CSF analysis, MRI and CT scan.
- ELISA
- RT-PCR
- direct Fluorescent Antibody (DFA) testing
- Negri bodies

Prevention

- Vaccination of susceptible animal species, particularly dogs and cats, will control this zoonotic disease.

Rabies PEP — Vaccination

- Previously unvaccinated persons get 4 doses
  - Days 0, 3, 7, and 14
  - 5th dose dropped from vaccine schedule last year
  - Intramuscular injections