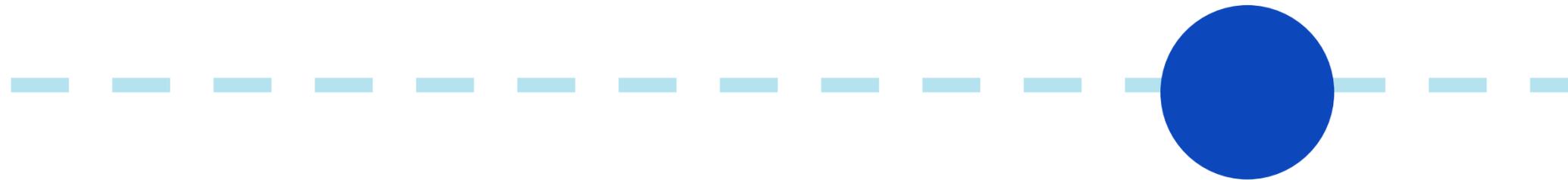


Infection in Pregnancy, Congenital Viral Infections



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Learning outcomes:



At the end of the lecture, the students should be able to:

- Identify viral infections in pregnancy
- Describe different modes of transmission.
- List causative viruses, outcome, and prevention of congenital infections.
- Describe the structure, transmission, pathogenesis, clinical syndromes, latency, reactivation, diagnosis and treatment of CMV.
- Identify morphology, clinical significance, transmission and laboratory diagnosis of Parvovirus B19.
- Recognize the morphology, clinical significance, transmission, laboratory diagnosis and prevention of Rubella virus.

Lecture Outline:

1. Identification of congenital infections
2. List causative viruses, mode of transmission, sequela, prevention
3. Cytomegalovirus
4. Parvovirus B19
5. Rubella virus



Case scenario:

A 35-year-old woman during her second pregnancy experienced no complication until 10 weeks of gestation.

Routine CMV serologic tests were performed. CMV immunoglobulin (IgG) and CMV-(IgM) were demonstrated in both samples obtained during 10th and 14th weeks of gestation.

Questions:

- **What are the confirmatory tests that should be done?**
- **What are the modes of transmission of this virus?**

Viral infections in pregnancy are major causes of maternal and fetal morbidity and mortality.

The clinical manifestations vary depending on:

- **Viral agent** (Some viruses results in congenital malformation).
- **Gestational age at infection:** the early is the infection, the more dangerous is the outcome.

Mode of transmission: Infections that develop in the neonate can be transmitted through:

Prenatal (Trans-placental)

Through placenta

Perinatal

(from vaginal secretions or blood)

Postnatal

(from breast milk or other sources)

Early in life

Causative agents:

Infections causing congenital defects are described with “TORCH”

– **T** (Toxoplasma), **O** (Others), **R** (Rubella), **C** (Cytomegalovirus), **H** (Herpes).

– **Parvovirus B19 (B19V).**

– Varicella-zoster virus (VZV).

– Adenovirus.

– Human immunodeficiency virus (HIV).

– Zika virus.

– Hepatitis E virus.

Outcomes

Spontaneous abortion.

Premature birth.

Intrauterine growth retardation (IUGR).

Abnormalities in the **CNS**, the **skeletal** and **endocrine** systems, and the internal organs (e.g., **cardiac** defects, **vision** and **hearing** loss).

Prevention:

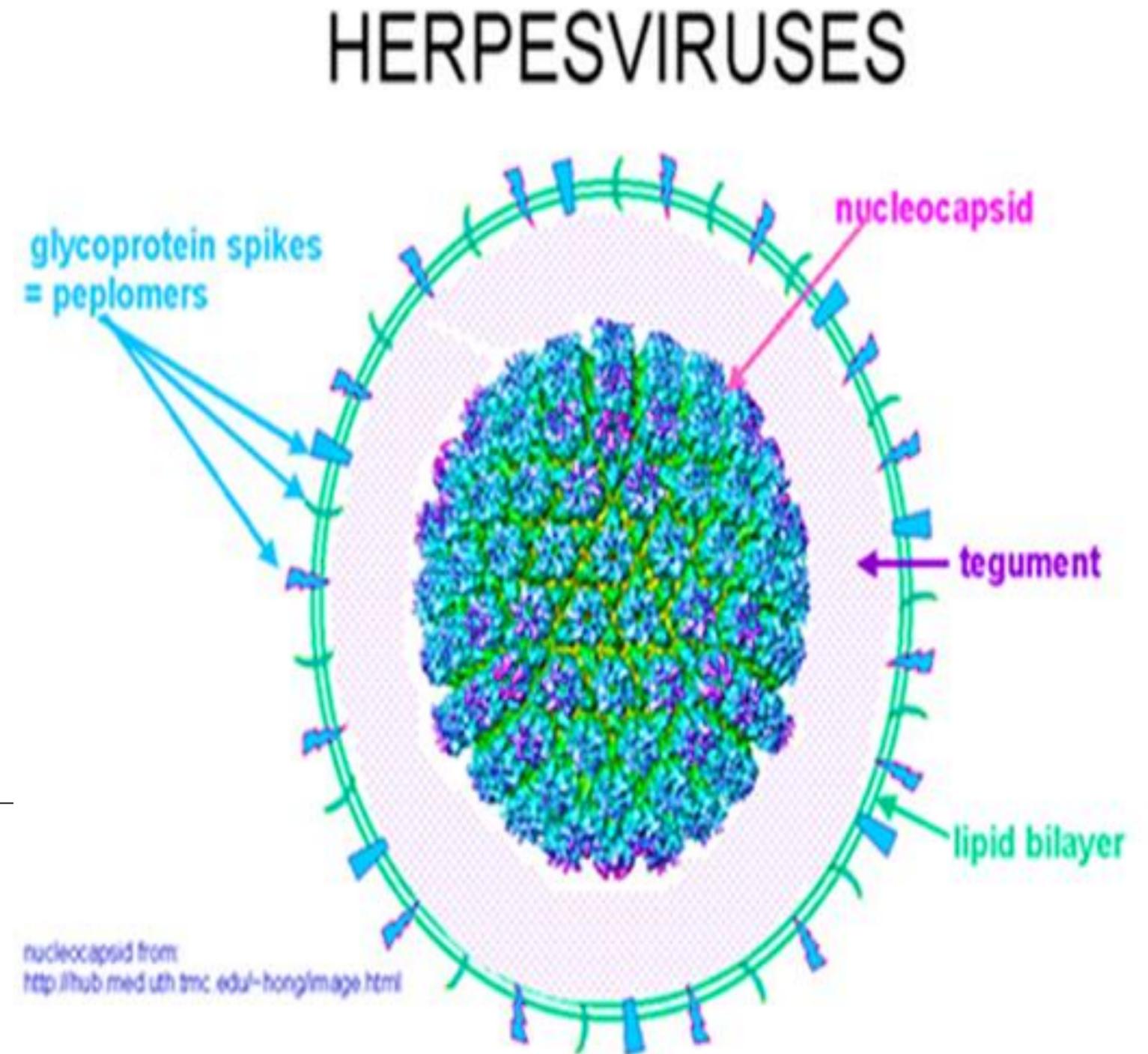
General Measures:

- **Hygiene** measures (washing hands).
- Do **not sharing** drinking glasses or eating utensils with young children.
- **Avoid kissing** young children on the mouth or cheek.
- Affected infants require regular **follow-ups** to monitor for hearing loss, ophthalmological abnormalities, and developmental delays.

Specific Measures: Primary (vaccination for varicella and rubella (prior to pregnancy)).

Classification of human Herpes viruses

- **Eight** human herpesvirus species are known.
- All have the ability to enter a **latent** state following **primary** infection and to be **reactivated** at a later time.



Classification of Herpesviruses:

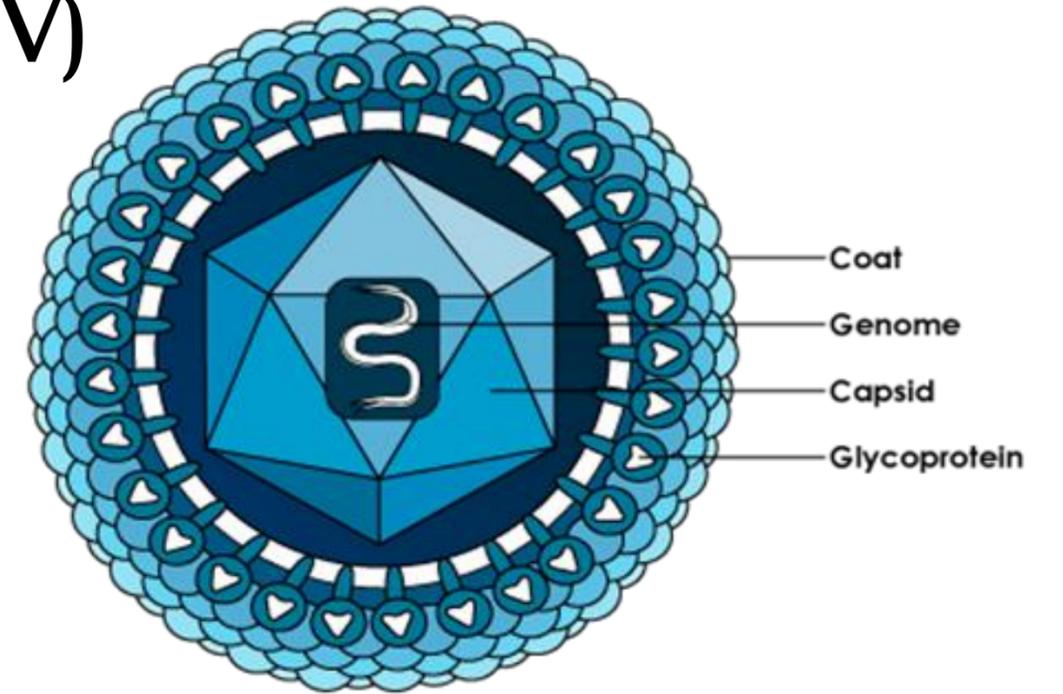
They have been divided into three subfamilies:

| Alpha herpesvirinae | Beta herpesvirinae | Gamma herpesvirinae |
|---|-------------------------|-----------------------------|
| Herpes simplex virus types 1 (HSV-1 or HHV-1) | Cytomegalovirus (HHV-5) | Epstein-Barr virus (HHV-4). |
| Herpes simplex virus | HHV-6 | HHV-8 |
| Varicella – Zoster virus | HHV-7 | |

Cytomegalovirus (CMV)

Structure:

- Virion: icosahedral
- Genome: Double stranded DNA, linear
- Envelope: Contains
- Glycoprotein spikes.



Transmission and pathogenesis:

| Early in life: | Later in life: |
|---|--|
| Trans-placental Within birth canal Via breast milk. | Saliva (most common route). Sexually. Blood transfusion. Organs transplant. |

Clinical Significance:

A) Primary infection:

In healthy individuals may cause:

- **Asymptomatic infection** with intermittent shedding in saliva and urine.
- **Infectious mononucleosis like syndrome:** similar to EBV infection but heterophil antibodies negative.

Infection of immunodeficient patients:

Hepatitis and pneumonia are common, In AIDS, (diarrhea and retinitis may occur).

Congenital infections: the most common intrauterine viral infection:

In-utero, it causes: abortion, still birth or cytomegalic inclusion disease: (Mental retardation, microcephaly, blindness and deafness).

Perinatal infection from the birth canal or from the milk: usually subclinical infection.

B) Latency and Reactivation:

Latency is established in **monocytes, macrophages** and **kidney**. Reactivation: repeated episodes of asymptomatic virus **shedding** over prolonged periods of times.

Laboratory diagnosis:

| Direct Detection: | | Indirect Detection: |
|--|--|---|
| <p>1. Fluorescent antibody & histological staining of inclusions in giant cells in body fluids and in tissue.</p> <p>2. PCR for detection of CMV nucleic acid in tissues or body fluid as CSF, blood, saliva, urine.</p> | <p>3. Virus isolation in cell culture: CPE is 2-3 weeks (Typical swollen and translucent cells with intranuclear inclusion bodies (Owl's eye) appearance.</p> | <p>Serological test to detect rising IgG titer or IgM.</p> |

Diagnosis of CMV during pregnancy:

- Mother:

Positive **IgM**

PCR.

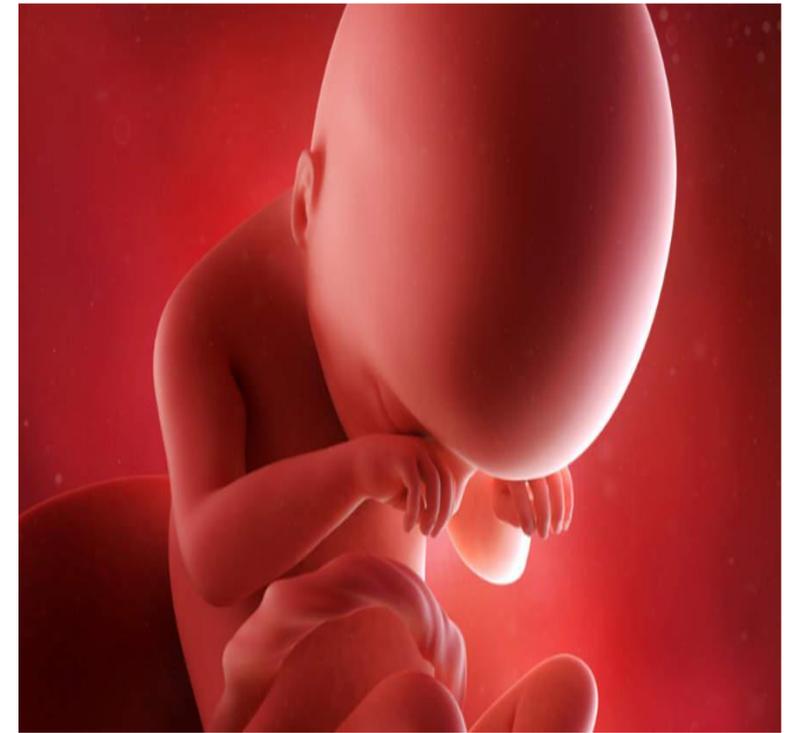
- Fetus:

Amniotic fluid sample is taken and CMV is demonstrated either by **PCR** or isolation on **tissue culture.**

Prevention and treatment:

Prevention: General preventive measures for intra-uterine viral infections.

Treatment: **Ganciclovir**: is effective in immunocompromised patients.



Parvoviruses

- **Structure:**

Virion: icosahedral

Genome: **Single** stranded DNA, linear

Non-enveloped

- **Clinical Significance:**

Dependo-viruses:

They require helper virus for their replication which usually an adenovirus (e.g. Adeno-associated virus).

Autonomous parvoviruses:

They are capable of independent replication (e.g. human parvovirus **B19**).

Human B19

- Human B19 virus targets **immature** cells of the erythroid lineage (**RBCs**).

Diseases caused:

- Transient **aplastic crisis** in patients with sickle cell disease.
- **Erythema infectiosum** (fifth disease or slapped cheek disease).
- A common **childhood** disease.
- Associated with bright red **rash** of the cheeks.
- Exacerbation of rash by **sunlight**, **heat** and **stress**.



Hydrops fetalis



- Hydrops fetalis and fetal death:
 - ✓ Due to severe **anemia** if Infection occurs during pregnancy
 - ✓ May leads to **miscarriage** (spontaneous abortion) if occurs **before 20th week** of gestation.
 - ✓ Or **stillbirth after 20th week** of gestation.

Laboratory diagnosis: PCR

Prevention:

- The best approach is to recommend all pregnant women to **avoid contact with children** with current symptoms of infection.
- The risk to the fetus is reduced by:
 - ✓ Correct **diagnosis** of the anemia (by ultrasound scans)
 - ✓ Correct **treatment** (blood transfusions).



MCQ:

Which of the following viruses targets immature cells of erythroid lineage (RBCs)?

- a) Human parvovirus B19
- b) CMV
- c) Rubella
- d) HSV
- e) HHV-6

Rubella virus

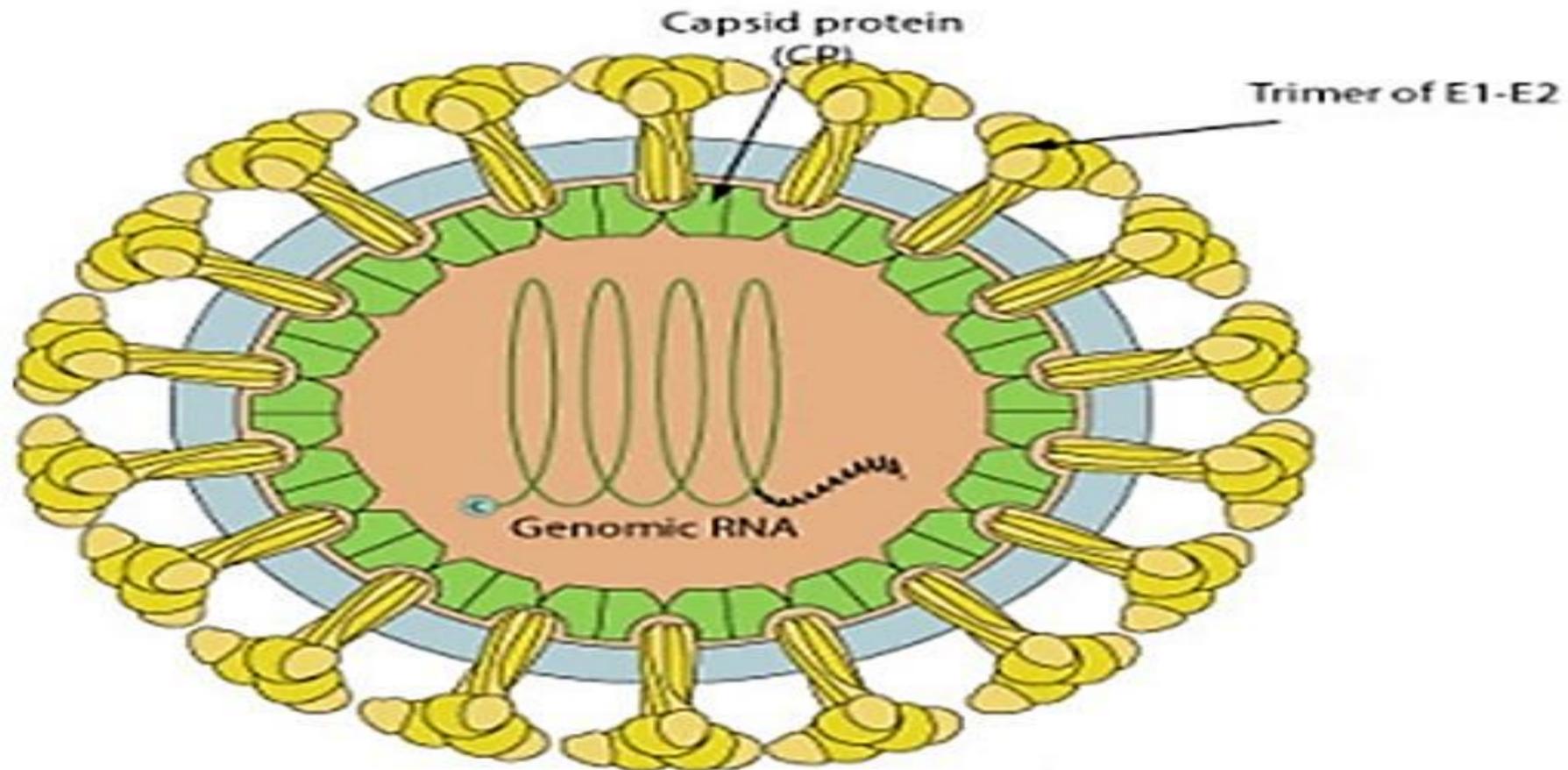
Structure:

Virion: icosahedral nucleocapsid. Spherical shape.

Genome: positive-sense, single stranded **RNA**

Enveloped with hemagglutinin-containing spike-like projections.

Belongs to **Togaviridae** family



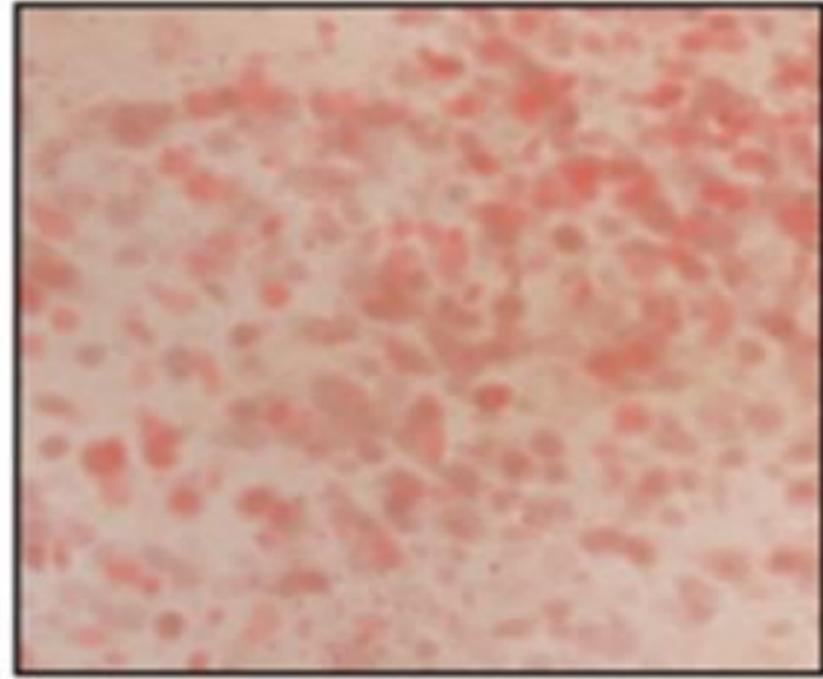
Transmission:

- The virus is transmitted via **respiratory** droplets.
- Initial replication of the virus occurs in the **oropharynx** and local **lymph nodes**.
- From there it spreads via the **blood** to the **internal organs** (including placenta and skin).
- I.P. **14-25** days after infection, patient is infectious for most of this time.

Clinical Significance

The disease is characterized by:

- 1- In 95% of adolescent patients** 14-25 days (average: 18 days) after infection:
 - Characteristic pink continuous maculopapular rash appears.
 - Posterior auricular lymphadenopathy are characteristic of the disease
- 2- In children**, a mild febrile illness - less severe than measles.
- 3- In adults other than pregnant women**: symptoms are rare.



Rash

Congenital rubella syndrome:

- Virus crosses **placenta** and multiplies in the **fetus**.
- Up to **85%** of infants infected **in the first trimester** of pregnancy get congenital rubella syndrome (**CRS**) with **low birth weight, deafness, CNS involvement, cardiac abnormality, eye abnormality and abortion**.
- The **earlier** in pregnancy infection occurs, the **worse** the prognosis becomes.
- Fetus is **persistently** infected (presumably due to immature immune response) and continues to excrete virus after birth (a risk to doctors, nurses and other patients).



Microcephaly



PDA



Cataracts

Prevention and control:

MMR vaccine:

- Trivalent live attenuated vaccine (MMR)
- Usually given by **IM injection**.
- It is given at **12 – 15 months**.
- A single dose of the MMR vaccine gives around 90% protection against measles and mumps and 95-99% against rubella.
- (For women infected during 1st trimester of pregnancy, therapeutic abortion is recommended).



MCQ:

Which of the following is a mode of transmission of rubella?

a) Mosquitos

b) Transplacental

c) Perinatal Rare

d) Breast milk

e) Sexually

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- **What are the confirmatory tests that should be done?**
- **What are the modes of transmission of this virus?**

References

Brooks, G. F., Jawetz, E., Melnick, J. L., & Adelberg, E. A. (2013). *Jawetz, Melnick, & Adelberg's medical microbiology*. New York: McGraw Hill Medical.

