

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

# *Transplacental infections*

( Reproductive Block , Microbiology : 2017)

*BY: DR.MALAK EL-HAZMI*

# **OBJECTIVES;**

- Types of infant infections.
- Major transplacentally transmitted pathogens causing congenital infections .

*Toxoplasma ,  
Treponema pallidum ,  
Parvovirus ,  
Varicella Zoster Virus,  
Rubella virus ,  
Cytomegalovirus.*

**Their major features & epidemiology .**

**Manifestations of congenital infection.**

**Diagnosis of congenital infection.**

**Their Treatment and Prevention.**

# *infant infections*

<b>Classification</b>	<b>Timing of events</b>	<b>Mechanisms</b>
Congenital	In utero	Trans placental
Perinatal	During labour and delivery	Exposure to genital secretions and blood
Neonatal	After birth	Direct contact, breast feeding or nosocomial exposure

# *Congenital infections*

- mostly viruses
- previously known as ( **TORCH**) infections:

**T**= **Toxoplasma gondii**,

**O**=**Others**

(*Treponema pallidum*  
, **Parvovirus & VZV**),

**R**=**Rubella V**,

**C**=**CMV**,

**H**=**Herpes**( **H**epatitis & **H**IV),

# *Congenital infections*

## *Risk of IUI & fetal damage ;*

- Type of org.(teratogenic)
  - Type of maternal inf.(1<sup>o</sup>,R)
  - Time of inf .(1<sup>st</sup>,2<sup>nd</sup> or 3<sup>rd</sup>)
- 
- *1<sup>o</sup> Maternal infection in the first half of pregnancy poses the greatest risk to the fetus*

# *Congenital infections*

## *Common Findings*

- Intrauterine growth retardation(IUGR)
- Hepatosplenomegaly(HSM)
- Thrombocytopenia
- Microcephaly

**Majority of CI (“asymptomatic”) at birth**

Preventative and therapeutic measures ;

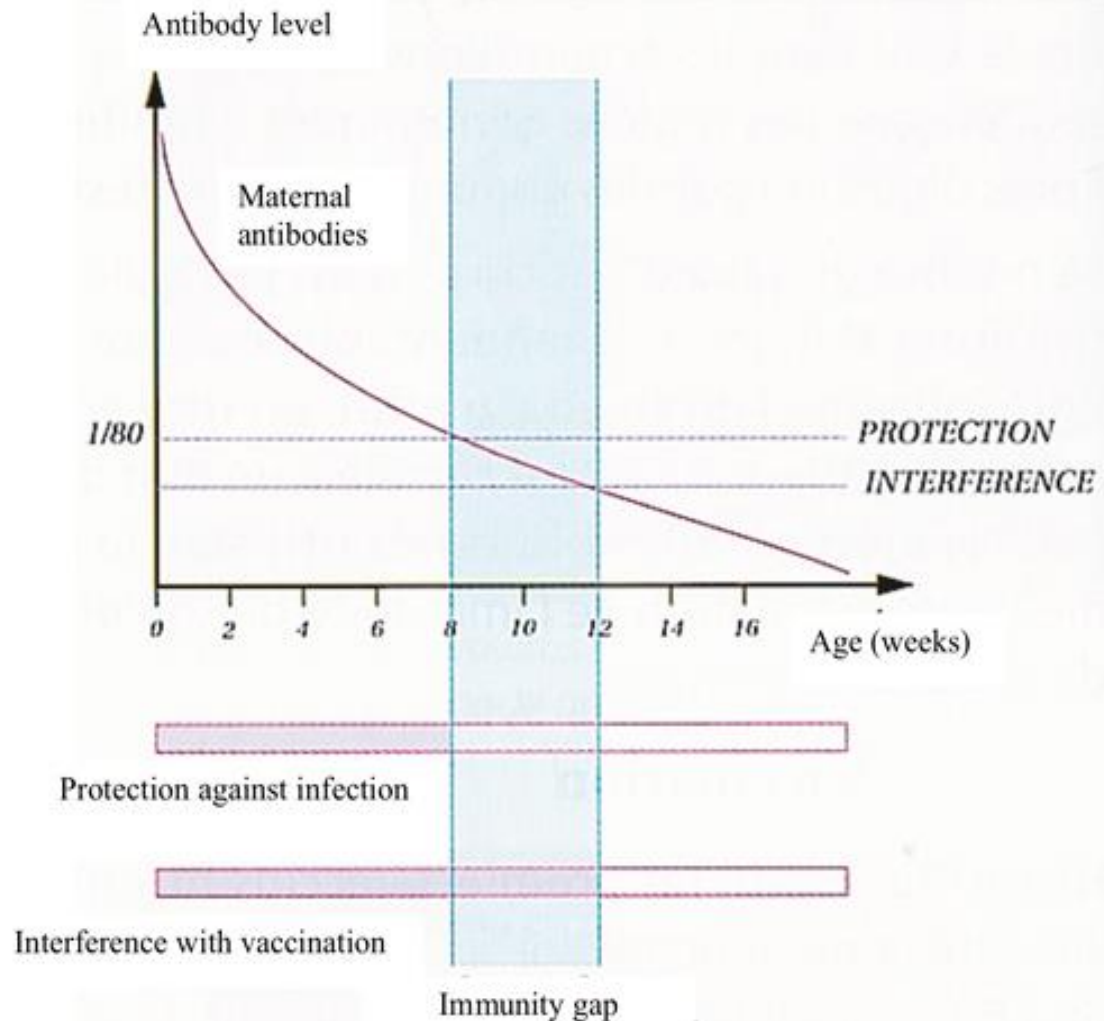
possible for some of the agents

## Neonatal serological Dx;

- IgM antibody

Absence of fetal IgM at birth does not exclude infection

- Persistence of specific IgG antibody >12 ms of age



# *Transplacental infections*

**(TORCH)**

**T = Toxoplasma gondii**

**(*Treponema pallidum*, Parvovirus  
& VZV)**

**R = Rubella V**

**C = CMV**



# Toxoplasma Gondii

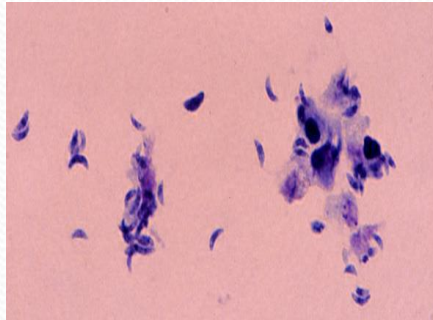
- Obligate intracellular parasite
- Three forms:

## *Oocysts;*



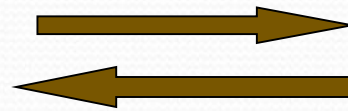
- Shed in cat feces

## *Tachyzoites;*



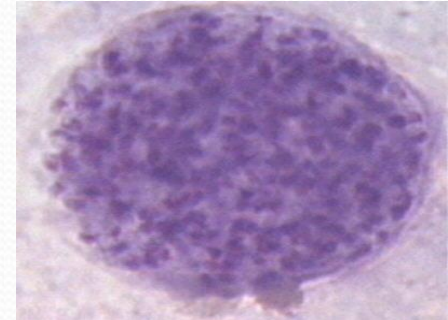
- rapidly dividing forms
- ACUTE PHASE

Immunity +



Immunity -

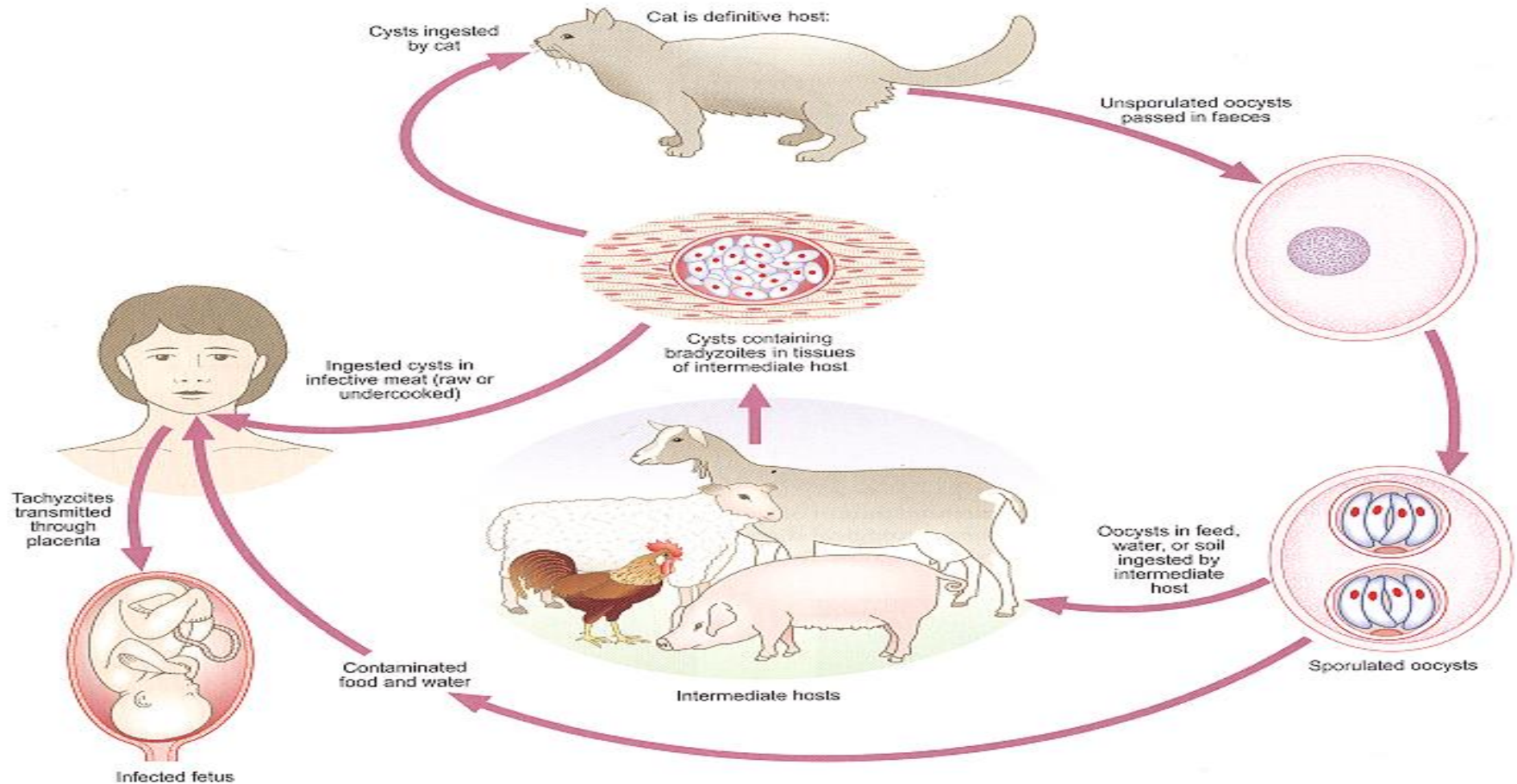
## *Bradyzoites;*



- slowly dividing forms
- CHRONIC PHASE

# Toxoplasma gondii

## Life cycle



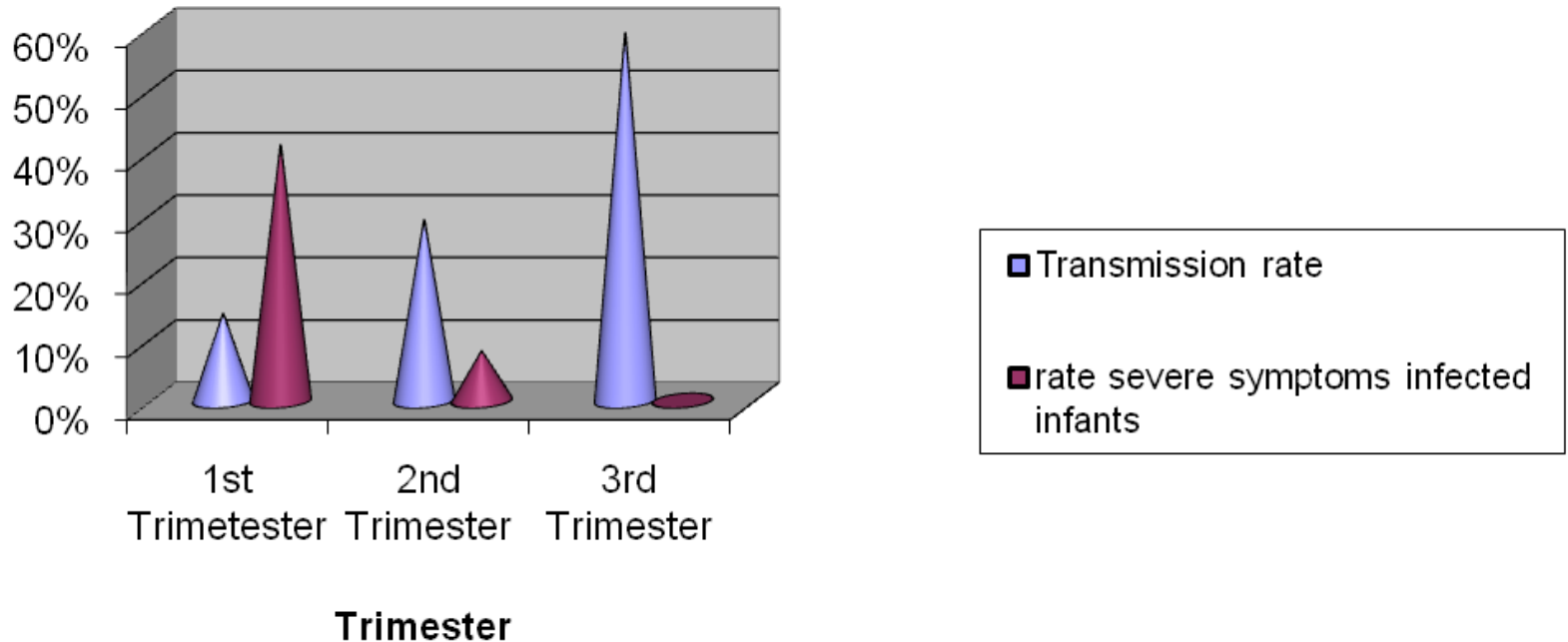
## TRANSMISSION:

- Ingestion of oocyst:  
Contaminated fingers, soil, water
- Ingestion of cyst in undercooked meat.
- Blood transfusion and organ transplant

# *Congenital infection ;*

- Most cases, due to 1<sup>o</sup> maternal inf.
- Rarely, reactivation of a latent inf.

**Transplacental Toxoplasma and Congenital Infection**

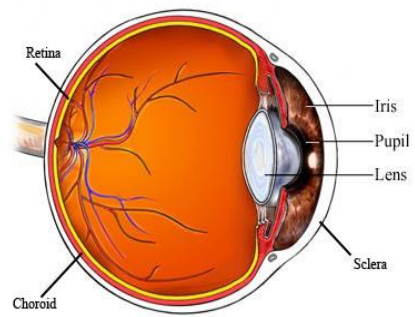


# Congenital infection ;

➤ Most (70-90%) are **asymptomatic** at birth but are still at high risk of developing abnormalities, especially eye (chorioretinitis )/neurologic disease(MR) later.

➤ **Classic triad :**

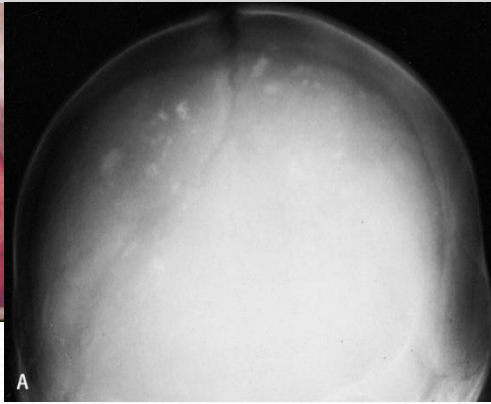
**Chorioretinitis**



**Hydrocephalus**



**Intracranial calcifications**



➤ **Other signs** include ;

rash, HSM, jaundice, LAP, microcephaly, seizures, thrombocytopenia.

➤ **Abortion & IUD.**

# Dx

## • Pregnant mother

- Serology;
  - IgM,
  - IgG
  - IgG avidity
  - IgG seroconversion compared to booking blood.

## Infant

### \*Prenatal Dx;

- Serial U/S
- PCR
- Culture

### \*Postnatal Dx;

- Serology;
  - IgM
  - ↑ IgG or persistently +ve >12 ms
- PCR
- Culture
- Evaluation of infant (ex, neuroimaging)

# Rx

- Spiramycin.
- pyrimethamine & sulfadiazine.

# Prevention

**Avoid** exposure to cat feces;

**Wash** ; - hands with soap and water

- fruits/vegetables,

- surfaces that touched

fruits/vegetables/raw meat.

**Cook** all meats thoroughly



# *Transplacental infections*

(TORCH)

T= Toxoplasma gondii,

O=Other

(Treponema pallidum

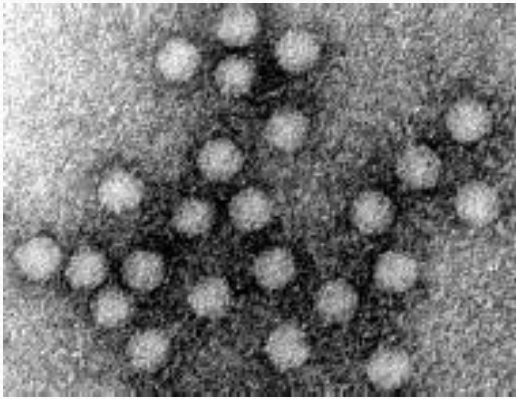
, *Parvovirus* & VZV),

R=Rubella V

C=CMV

# Parvovirus B<sub>19</sub>

## Parvoviridae



non developed V.  
Icosahedral capsid  
& s.s DNA genome.

## Epidemiology:

- Worldwide distribution
- Humans are known hosts
- Transmission
  1. Respiratory route
  2. Blood transfusion
  3. Transplacental route



# Clinical presentation;

## 1.Acquired infection;

\*Immunocompetent host

\*Immunocompromised pts

Erythema infectiosum



## 2.Congenital infection;

# Congenital infection

- Risk of congenital infection is greatest when inf occur in 1<sup>st</sup> 20 wks
- 1. Inf in the 1<sup>st</sup> trimester → IUD (Intrauterine death)
- 2. Inf in the 2<sup>nd</sup> trimester → HF (Hydrops fetalis)
- 3. Inf in the 3<sup>rd</sup> trimester → Lowest risk

➤ Cause fetal loss through hydrops fetalis, severe anaemia, CHF, generalized oedema and fetal death



# Dx

- Pregnant mother;
  - Specific IgM.
  - IgG seroconversion.
- Prenatal Dx;
  - U/S (hydrops)
  - Not grow in c/c.
  - PCR

# Rx:

Intrauterine transfusion

# Prevention:

- Hygiene practice
- No vaccine (TRIAL)

# *Transplacental infections*

(TORCH)

T= Toxoplasma gondii,

O=Other

(Treponema pallidum, *Parvovirus*  
& *VZV*),

R=Rubella V

C=CMV

# Varicella Zoster Virus VZV

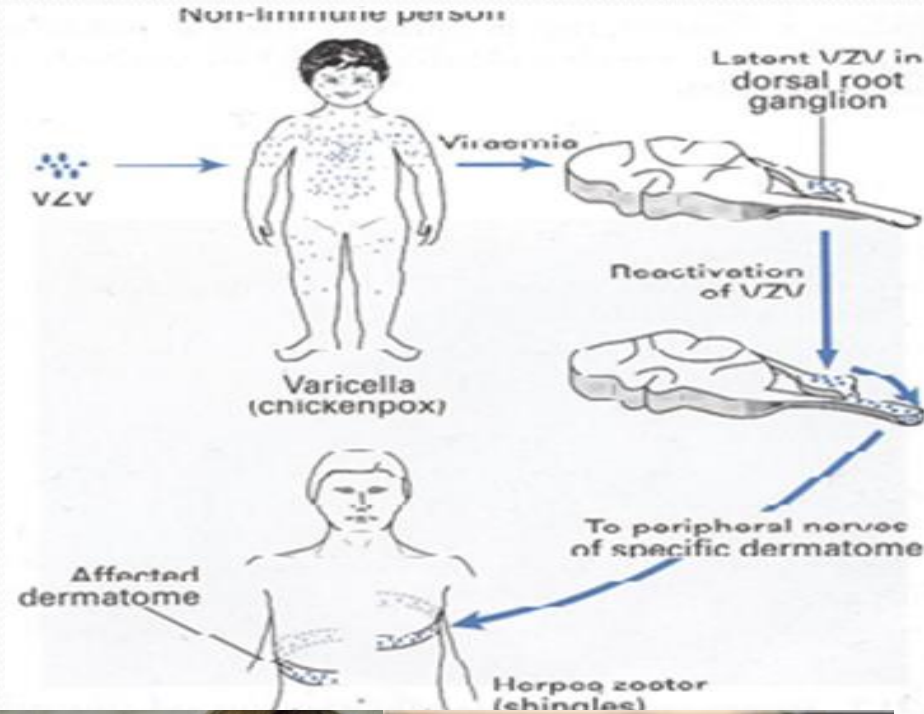
## Herpesviridae

*dsDNA, Enveloped,  
Icosahedral Virus*



## Transmission

- Respiratory route
- Transplacental route



## Clinical presentations

- **Acquired infection ;**
  - ❖ Varicella : Chickenpox:
    - ❖ 1<sup>o</sup> illness
    - ❖ Generalized vesicular rash
  - ❖ Zoster: Shingles:
    - ❖ Recurrent inf
    - ❖ Localized VR
- **Congenital infection ;**



# VZV infection in Pregnancy

- Primary infection carries a greater risk of severe disease, in particular pneumonia.

## Intrauterine infections

### ❖ congenital varicella syndrome ;

- 1<sup>st</sup> 20 weeks of Pregnancy
- The incidence of CVS is ~ 2%
  - Scarring of skin
  - Hypoplasia of limbs
  - CNS defects
  - eye defects



### ❖ Neonatal varicella ;

- < 5 days of delivery → severe disease
- > 5 days before delivery → mild disease

# Diagnosis

VZV

## Pregnant mother

### A. Direct ex:

- Vesicular fluid for virus isolation
- Cells scraping from the base of vesicles



ImmunoFluorescent test (Ag)

- DNA-VZV by PCR

### B. Serological test:

IgM AB

## Infant;

### A. Prenatal Dx

1. U/S
2. VZV DNA in FB or AF or placenta villi
3. VZV IgM in FB.

### B. Postnatal Dx

1. VZV IgM
2. virus isolation
3. VZVDNA in VF or CSF ( CNS inf )

# Rx

- *Acyclovir*

## Prevention;

**Pre exposure;**

Varicella vaccine (LAV)

**Post exposure;**

VZIG

- susceptible **pregnant** women have been exposed to VZV.
- **infants** whose mothers develop **V < 5** to **2** days after delivery.



# *Transplacental infections*

(TORCH)

T = Toxoplasma gondii,

O = Other

(Treponema pallidum, Parvovirus  
& VZV)

R = Rubella V

C = CMV

# Rubella Virus

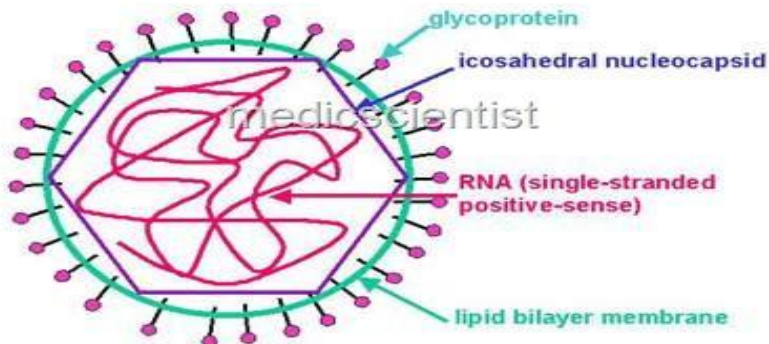
## Togaviridae

❖ SS RNA genome

Icosahedral capsid

Enveloped Virus

RUBELLA VIRUS



## Epidemiology:

- Humans
- Transmission
  - Respiratory route
  - Transplacental route
- A world wide distribution ↓ ed . ?

# Pathogenesis

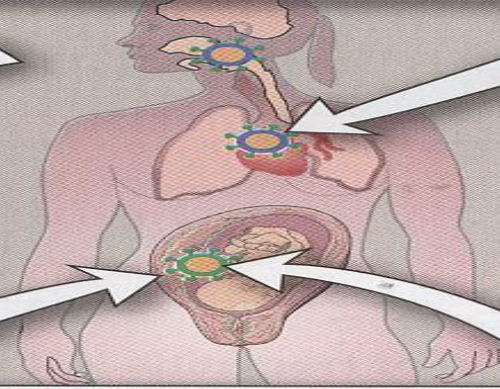
**1**

Rubella enters and infects the nasopharynx and lungs. The virus then spreads to the lymph nodes and reticuloendothelial system.

**2**

The virus is carried in the blood and spreads to other tissues and skin.

  
Rubella  
virus



**3**

In a pregnant woman without protective antibodies, the virus can infect the placenta and spread to the fetus.

**4**

The classic triad of rubella symptoms in affected neonates is:

**Cataracts**



**Deafness**



**Cardiac abnormalities**

# Clinical manifestation:

## ➤ *Acquired infection ;*

Ex. Maculopapular rash  
(Rubella = German measles)

## ➤ *Congenital infection;*

Normal  $\longrightarrow$  CRS  $\longrightarrow$  IUD

- Risk of acquiring congenital rubella infection varies and depends on gestational age of the fetus at the time of maternal infection.

### gestational age

- 0-12 wks
- 13-16 wks
- >16 wks

### risk to fetus

70%  
20%  
Infrequent

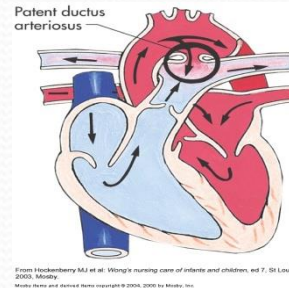
# Congenital Rubella Syndrome

## Triad of abnormalities

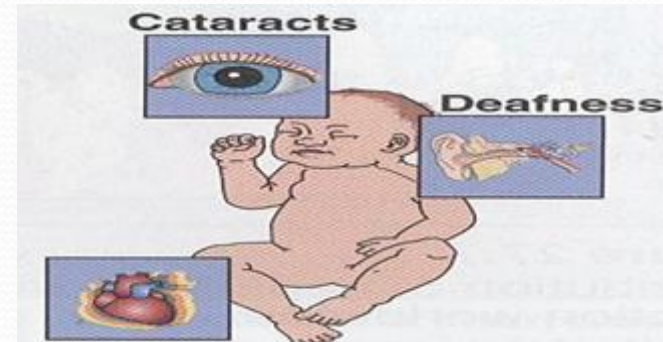
- Sensorineural hearing loss\*
- Cataracts and glaucoma
- Cardiac malformations (patent ductus arteriosus)
- Neurologic defects
- Others

growth retardation,  
bone disease,  
HSM, thrombocytopenia,  
“blueberry muffin” lesions

## Affecting ears , eyes & heart



From Hackberry MJ et al. Wong's nursing care of infants and children, ed 7, St Louis, 2003, Mosby.  
Walter de Gruyter and de Gruyter Verlag. Copyright © 2004, 2000 by Mosby, Inc.



“Blueberry muffin” spots

# Dx;

## Pregnant mother

- Serological diagnosis
- 1. Rubella specific IgM
- 2. IgG seroconversion

## Infant

### \*Prenatal Dx;

- U/S
- Culture
- PCR

### \*Postnatal Dx;

- Serology;
  - IgM
  - IgG or persistently +ve >9-12 ms
- Culture
- PCR

## Prevention:

- Rubella vaccine ;(LAV)
- Routine antenatal screening:  
Rubella specific IgG

Non-immune women → vaccination  
( avoid pregnancy for 3 months).

# *Transplacental infections*

(TORCH)

T = Toxoplasma gondii,

O = Other

(Treponema pallidum, Parvovirus  
& VZV),

R = Rubella V

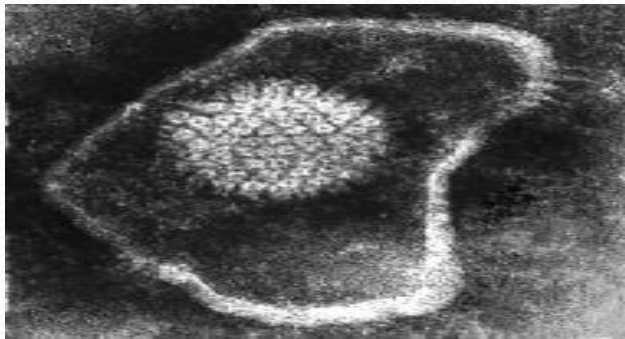
C = CMV



# Cytomegalovirus CMV\*

## Herpesviridae

*dsDNA, Enveloped,  
Icosahedral Virus.*



Establishes in latent form

↓  
reactivation

↓  
Recurrent inf

## Epidemiology

*Human, worldwide.*

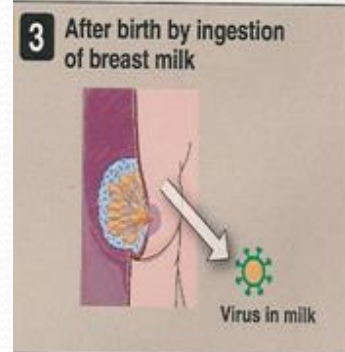
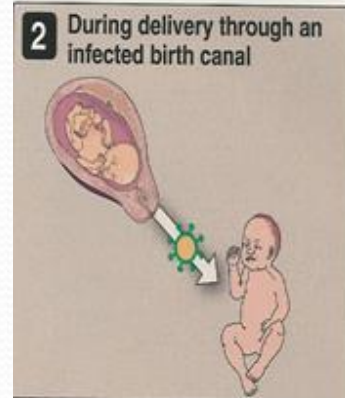
### *Transmission(tn)*

#### *1- Horizontal tn*

- Young children: saliva
- Later in life: sexual contact
- Blood transfusion  
& organ transplant

#### *2- Vertical tn*

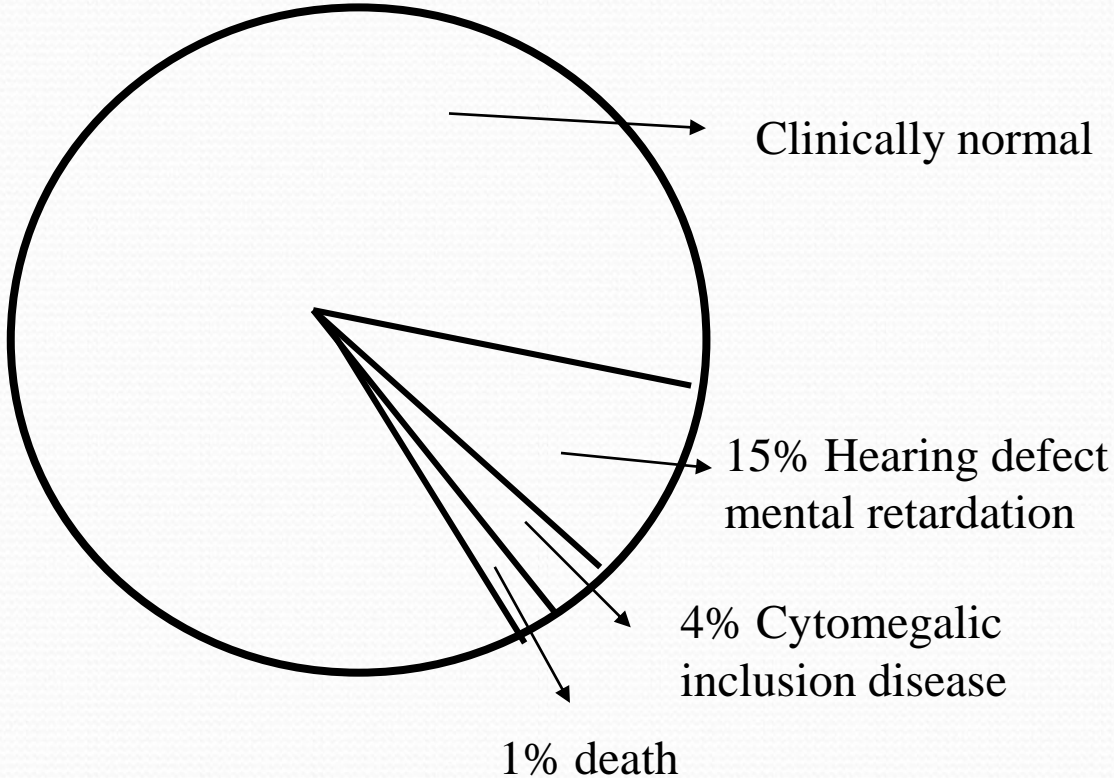
↓                      ↓  
1° CMV inf .      Recurrent CMV inf  
(~40%)                      (~1%)



# Congenital Infections:



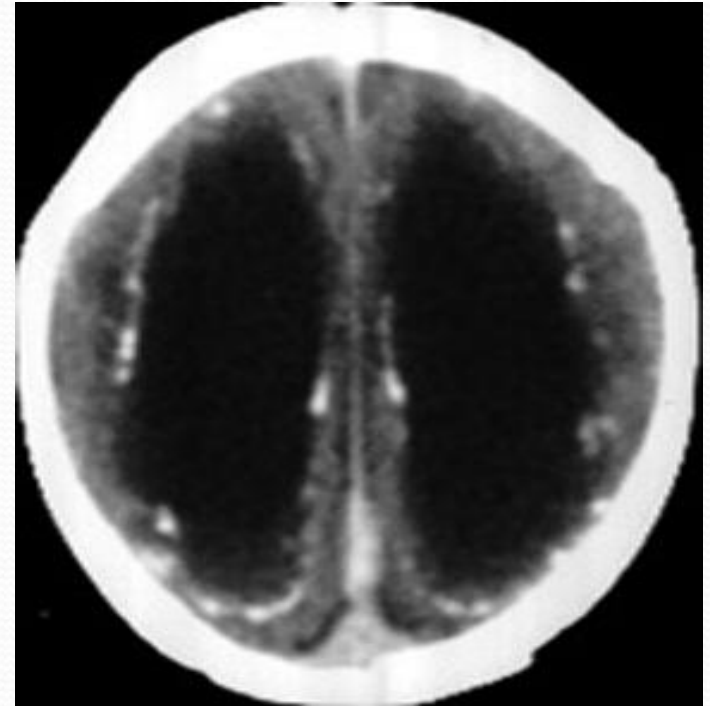
Blueberry muffin” spots



# *Cytomegalic Inclusion Disease;*

- CNS abnormalities - **microcephaly**, periventricular **calcification**.
- Eye - chorioretinitis
- Ear - sensorineural deafness
- Liver – HSM and jaundice.
- Lung - pneumonitis
- Heart - myocarditis
- **Thrombocytopenic** purpura

Ventriculomegaly & calcifications of congenital CMV



# Dx.

- Maternal :

Serology ;

- CMV IgM
- CMV IgG
- CMV IgG avidity

- Prenatal :

- *Ultrasound*
  - CMV specific IgM
  - culture
  - PCR

- Postnatal:

by *isolating CMV or detection of its genome* in first 3 wks of life.

Body fluid : urine, saliva, blood.

- By
  - Standard tube culture method
  - Shell vial assay
  - PCR

*Histology;*

- Detection of Cytomegalic Inclusion Bodies in affected tissue

*Serology;* CMV IgM



Intranuclear I B [Owl's -eye]

# Rx

- **Symptomatic** infants → ? Ganciclovir .
- **Asymptomatic** infants → not recommended .

## Prevention !?

*Education about CMV  
& how to prevent it  
through hygiene;  
hand washing*

*Vaccine is not available  
(TRIAL)*



# OBJECTIVES;

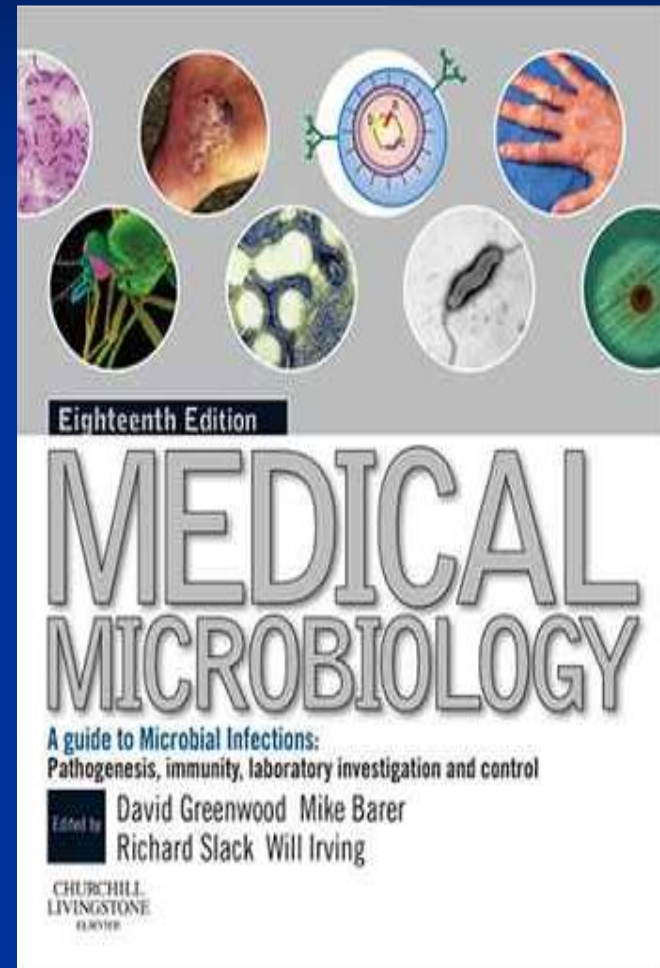
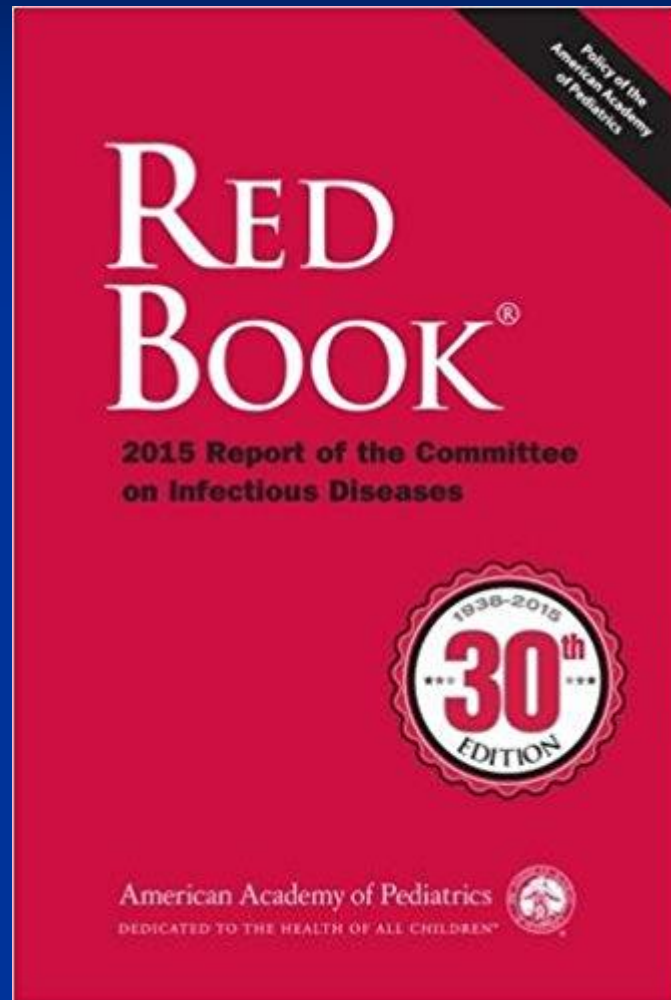
Upon completion of this lecture, the students should be able to

- To recognize the different types of **infant infections**.
- To know major **transplacentally transmitted pathogens** causing congenital infections .

*(Toxoplasma , TP ,ParvoV , VZV, Rubella V & CMV.)*

- *To describe their **structure***
- To know their major **epidemiology** features
- *To describe **clinical manifestations** of their congenital infections*
- To illustrate different **laboratory diagnosis** of maternal and congenital infection
- To know their **treatment** and **preventive** measures.

# Reference books



# فضل العلم

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