



## Lecture – 1

# Congenital Infections

Microbiology Team - 430



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## “Transplacental infection”

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

### Congenital infection :

- Mostly **viruses**
- previously known as ( **TORCH** ) ;
  - ✓ **T=Toxoplasma**,
  - ✓ **O=Other**
  - ✓ (Syphilis ,Parvovirus &VZV),
  - ✓ **R=Rubella**,
  - ✓ **C=CMV**,
  - ✓ **H=Herpes** ,**H**epatitis &**H**IV

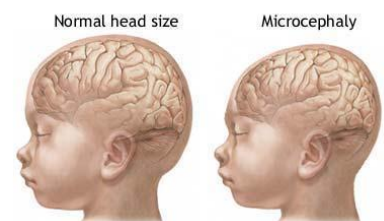
### Risk of congenital infection:

1. Organism (Teratogenicity) (congenital abnormalities)  
*Strong teratogenic effects → like Parvovirus and rubella.*  
*Mild teratogenic effects → like CMV and syphilis.*
2. Type of maternal infection (1<sup>o</sup>= Primary ,recurrent)  
*(1<sup>o</sup> Maternal infection in the first half of pregnancy , poses the greatest risk to the fetus)*
3. Time during pregnancy (1<sup>st</sup>, 2nd, 3rdTrimester)  
*If the infection occurred early in pregnancy, the baby will suffer more.*

### Features of congenital infection (CI) :

1. **Intrauterine growth retardation**  
*(refers to poor growth of a baby while in the mother's uterus during pregnancy.)*
2. **Skin rash**
3. **Microcephaly**
4. **Hepatosplenomegaly [ HSM ]**
5. **Thrombocytopenia**
6. **IgM, Persistent IgG**

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



## Toxoplasmosis

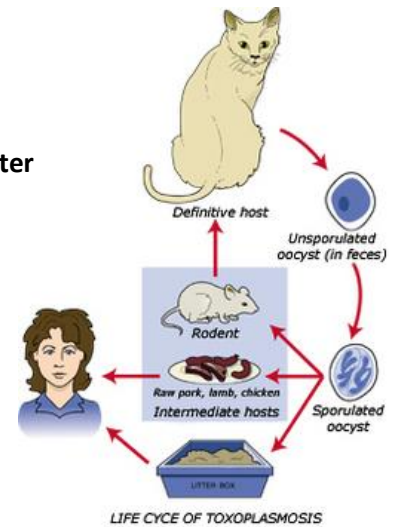
- *Toxoplasma gondii* (Obligate intracellular parasite)
- Definitive host is the domestic cat

### Transmission :

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

### Epidemiology:

- European countries (France, Greece)
- **Usually asymptomatic**  
*but it's dangerous during pregnancy*
- Primary maternal infection in pregnancy
- The rate of transmission of the infection from the mother to the baby is high during the 3<sup>rd</sup> trimester.
- If the infection occurred in the 1<sup>st</sup> trimester it will lead to fetal death.



### Clinical presentation:

- Mostly asymptomatic
- Classic triad of symptoms:
  1. *Chorioretinitis* (inflammation of the choroid and retina of the eye)
  2. *Hydrocephalus*
  3. *Intracranial calcifications*
- Other symptoms include fever, rash, HSM, microcephaly, seizures, jaundice, thrombocytopenia, lymphadenopathy

### Diagnosis

1. Maternal serology IgM/IgA , IgG.
2. Fetal tissue culture, PCR. and Ultrasound
3. Newborn
  1. Serology
  2. Culture
  3. PCR

1. Maternal Serology
2. Neonatal Serology

### Treatment

1. **Spiramycin** [ To the pregnant lady ]
2. **Pyrimethamine** and **sulfadiazine**

### Prevention

- Avoid exposure to contaminated food or water and undercooked meat
- Hand washing

## Syphilis

- Treponema pallidum (spirochete)
- Transmitted via sexual contact
- Mother with primary or secondary syphilis
- Typically occurs during second half of pregnancy

### Clinical features

- Intrauterine death in 25%
- 3 major classifications:
  1. **Fetal**: stillbirth, neonatal death, hydropsfetalis
  2. **Early congenital**: Cutaneous lesions ,HSM, Jaundice, Anemia, **Snuffles**, Periostitis and metaphysial dystrophy, Funisitis
  3. **Late congenital**: **Frontal bossing**, Short maxilla, High palatal arch, **Hutchinson teeth**, 8<sup>th</sup> nerve deafness, Saddle nose , Perioral fissures

1. Snuffles
2. Frontal bossing
3. Hutchinson teeth

### Diagnosis

1. RPR/VDRL: **Non-Treponemal test**
2. MHA-TP/FTA-ABS: **specific treponemal test**
3. **Confirmed if T. pallidum** identified in skin lesions, placenta, umbilical cord, or at autopsy

### Treatment

### Prevention

Penicillin G

- **RPR/VDRL screen in ALL pregnant women** early in pregnancy and at time of birth

## Parvovirus P 19

- Parvovirus P 19
- Causative agent of **Fifth disease(Erythema Infectiosum)**
- Spread by the **respiratory route**, blood and transplacental

### Epidemiology

- Most of the population is eventually infected.
- Half of women of childbearing age are susceptible to infection.
- **Risk of fetal death** highest when infection occurs during the **second trimester of pregnancy**.
- **Minimal risk to the fetus if infection occurred during the third trimesters of pregnancy.**

The baby will die most of the time





### Clinical Features

### Diagnosis

### Treatment

<ul style="list-style-type: none"> <li>Known to cause fetal loss through <b>hydrops fetalis</b>; severe anaemia, <b>congestive heart failure</b> <b>generalized oedema</b> and fetal death</li> <li>No evidence of teratogenicity</li> </ul>	<ul style="list-style-type: none"> <li><b>Serology</b> IgM, persistent IgG</li> <li><b>PCR</b></li> <li><b>US</b></li> </ul> <p><u>This organism doesn't grow in cell culture</u></p>	<ul style="list-style-type: none"> <li>Intrauterine transfusions and administration of <b>digoxin</b> to the fetus.</li> </ul>
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## Neonatal Varicella

- 90% of pregnant women already immune
- Primary infection during pregnancy carries a greater risk of severe disease
- Mild and self-limiting disease in children (Chickenpox)**
- Rare due to vaccination.**

### Clinical Features

- First 20 weeks of Pregnancy
- Up to 3% chance of transmission to the fetus, recognised congenital varicella syndrome; Scarring of skin, Hypoplasia of limbs, CNS and eye defects

### Diagnosis

Test		Pregnant mother and Fetus	Neonate
Direct from the vesicles	<b>Culture</b>	+	+
	<b>DFA</b>	+	+
	<b>PCR</b>	+	+
		Fetal blood and amniotic fluid	
<b>Serology</b>	<b>IGM</b>	+	+
	<b>Rising IgG</b>	+	
<b>US</b> and MRI		+	



### Treatment and Prevention

- Acyclovir** at first signs of **varicella pneumonia**
- Pre-exposure:** **live-attenuated vaccines** before or after pregnancy but not during pregnancy.
- Post-exposure:** **Zoster immunoglobulin** to susceptible pregnant **women and infants** whose mothers develop varicella during the **last 5 days** of pregnancy or the **first 2 days** after delivery and **premature baby**.

## Rubella

- RNA enveloped virus, member of the togaviridae family
- Spread by respiratory droplets and transplacentally

### Epidemiology

- Vaccine-preventable disease
- No longer considered endemic.
- Mild, self-limiting illness
- Infection earlier in pregnancy has a higher probability of affected infant



### Clinical Feature:

- Sensorineural hearing loss (most common)
- Cataracts, glaucoma and cardiac malformations
- Neurologic (less common)
- Others to include growth retardation, bone disease, HSM, thrombocytopenia, "blueberry muffin" lesions "Skin Rash"

### Diagnosis

#### Pregnant mother

#### Infant

<ul style="list-style-type: none"> <li>• Serological diagnosis</li> <li>1. Rubella specific IgM</li> <li>2. Seroconversion compared to booking blood</li> </ul>	<ul style="list-style-type: none"> <li>• Cell culture &amp; RT-PCR (amniotic fluid, chorionic villi) fetus (nasal secretion, throat, urine &amp; blood) newborn</li> <li>• Serological diagnosis</li> <li>• Rubella specific IgM</li> <li>• Persistence &amp; rising titres of anti-rubella IgG Abs in the infants serum beyond 9-12 months of age</li> </ul>
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### Treatment Prevention

- Supportive care only with parent education
- Prevention by immunization
- Maternal screening
- Vaccinate if not immune (avoid pregnancy for three months) .

## Cytomegalovirus

- **Most common congenital viral infection.**
- Mild, self limiting illness

### Epidemiology

- Transmission can occur with primary infection or reactivation of virus but 40% risk of transmission in primary infection
- Increased risk of transmission later in pregnancy but more severe sequelae associated with earlier acquisition

### Clinical presentation

- 90% are asymptomatic at birth
- Up to 15% develop symptoms later
- Microcephaly, periventricular calcifications, neurological deficits, HSM, petechiae, jaundice, chorioretinitis
- >80% develop long term complications: Hearing loss, vision impairment, developmental delay

### Diagnosis

- Maternal IgG shows only past infection
- **Viral isolation (Culture) from urine or saliva** in 1<sup>st</sup> 3 weeks of life
- Viral load and DNA copies can be assessed by PCR
- Detection of Cytomegalic Inclusion bodies in affected tissue
- Serologies not helpful given high antibody in population

1. Urine Culture
2. Urine PCR

### Treatment Prevention

- **Ganciclovir** in symptomatic infants

## Herpes simplex

- There is two types : HSV1 or HSV2

### Epidemiology

- Primarily transmitted through infected maternal genital tract
- Primary infection with greater transmission risk than reactivation
- Rationale for C-section delivery prior to membrane rupture

### *Clinical presentation*

- **Most are asymptomatic at birth**
- 3 patterns of equal frequency with symptoms between birth and 4wks: Skin, eyes, mouth, CNS disease, Disseminated disease (present earliest)
- Initial manifestations very nonspecific with skin lesions NOT necessarily present

### *Diagnosis*

- **Culture** of maternal lesions if present at delivery
- Cultures in infant
- **CSF PCR**
- Serologies are useless

### *Treatment*

- High dose of **acyclovir**

## *Summary*

- The clinical features of congenital infections are mostly the following; **Intrauterine growth retardation, skin rash**, Microcephaly and Hepatosplenomegaly.
- *Toxoplasmosis* is caused by ***Toxoplasma gondii*** and the **Definitive** host is the domestic cat.
- *Toxoplasmosis* infection is acquired by the ingestion of oocysts in cats' feces, either by eating raw meat or by hand to mouth contact.
- *Syphilis* is caused by ***Treponema Pallidum*** and transmitted by sexual contact.
- *Parvovirus* P 19 is the causative agent of Fifth disease [***Erythema Infectiosum***]
- ***Neonatal Varicella*** causes a mild disease **in children [chickenpox]**, and it's rare due to vaccination.
- *Rubella* is an RNA virus and it spreads by **respiratory droplets and transplacentally, it can be prevented by vaccination.**
- *Cytomegalovirus* is the most common congenital viral infection
- Serology is not helpful in common infections such as CMV, herpes virus because they will appear positive in healthy individuals.
- The rate of transmission of the infection from the mother to the baby is high during the 3<sup>rd</sup> trimester.
- If the infection occurred in the 1<sup>st</sup> trimester it will lead to fetal death.
- There's no screening test for Parvovirus.



	Presentation	Diagnosis	Treatment	Prevention
<b>Toxoplasmosis</b>	1. Chorioretinitis 2. Hydrocephalus 3. Intracranial calcifications	1. Serology 2. Fetal tissue culture 3. PCR	1. Spiramycin 2. Pyrimethamine and sulfadiazine	
<b>Syphilis</b>	1. Snuffles 2. Frontal bossing 3. Hutchinson teeth	1. RPR/VDRL: Non-Treponemal test 2. MHA-TP/FTA-ABS: specific treponemal test	Penicillin G	RPR/VDRL screen in ALL pregnant women
<b>Parvovirus P19</b>	1. hydrops fetalis 2. congestive heart failure 3. generalized oedema	<ul style="list-style-type: none"> <li>Serology</li> <li>PCR</li> <li>US</li> <li>There is <u>NO</u> culture</li> </ul>	Intrauterine digoxin	
<b>Neonatal Varicella</b>	1. Scarring of skin 2. Hypoplasia of limbs 3. CNS and eye defects	1. Culture 2. PCR 3. Serology 4. US	Acyclovir at first signs of <u>varicella pneumonia</u>	-Pre-exposure: live-attenuated vaccines -Post-exposure: Zoster immunoglobulin
<b>Rubella</b>	1. Sensorineural hearing loss 2. Cataracts, glaucoma and cardiac malformations 3. "blueberry muffin" lesions	1. Viral culture from nasal secretions 2. Serologic testing: IgM 3. PCR	Supportive care	immunization
<b>Cytomegalovirus</b>	1. Microcephaly 2. periventricular calcifications 3. Hearing loss	1. Urine and Saliva Culture 2. Urine PCR 3. Serology	Ganciclovir	
<b>Herpes simplex</b>	Skin, eyes, mouth, CNS disease	1. Culture of maternal lesions 2. CSF PCR	acyclovir	