Infections in pregnancy – clinical aspects

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In pregnant women, most infections are no more serious than in non-pregnant women of similar age

1. Some infections can be transmitted to the fetus *in utero* or to the infant during or immediately after delivery, with potentially serious sequelae
2. Uncommonly, serious infectious illness in the mother can have non-specific fetal or obstetric effects and lead to miscarriage, premature labour or fetal death; these infections must be treated as any other serious illness
3. More common and a source of anxiety is mild illness or suggestive laboratory findings in the absence of symptoms

- Based on 193 countries, the major causes of neonatal death globally were estimated to be:

1. infections (35%)
2. preterm birth (28%)
3. asphyxia (23%).

(Joy E Lawn 2006)

- Infections are implicated in the pathogenesis of:
  - miscarriage
  - preterm labor
  - prelabor rupture of membranes
- All these in turn are associated with neonatal infections and morbidity.
- Both the direct effect of the infection and the maternal immune response contribute to these eventualities.
- For example, infections that trigger T-helper-1 response can lead to the release of cytokines such as interferon (IFN3)-g, tumor necrosis factor (TNF)-a and interleukin (IL)-2 with activation of killer cells and initiation of preterm labor.

- Intra-amniotic infection due to bacteria in the vaginal flora not only initiate labor but can also cause infections such as septicemia and meningitis in the newborn
- Several host defense mechanisms operate against ascending infections:
  - vaginal acidity
  - cervical mucus
  - intact membranes
  - antibacterial activity of amniotic fluid

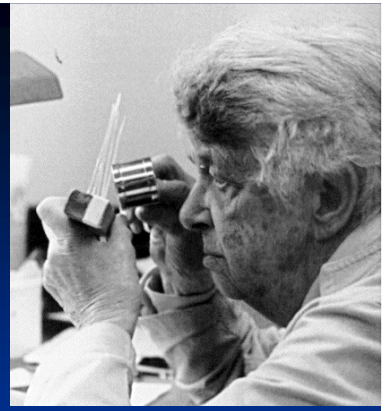
Diagnosing intra amniotic infection

- Intra-amniotic infection is difficult to diagnose on the basis of any single criterion and so diagnosis depends on a set of criteria, the most important clinically being maternal fever and tachycardia and fetal tachycardia
- Increased maternal leukocyte count, fetal biophysical profile examination using ultrasound are also used in diagnosis
- Detection and estimation of surrogate markers:
  - C-reactive protein (CRP)
  - cytokines
  - fetal fibronectin
- The infection may be polymicrobial, but collecting amniotic fluid samples without contamination with normal vaginal flora is cumbersome and may require invasive procedures.
- After membrane rupture many bacteria may enter the amniotic cavity without having caused the rupture.

Organisms causing neonatal sepsis

- Early onset sepsis (24 hours to 7 days postpartum):
  - Streptococcus β-haemolyticus (GBS)
  - E. coli
- Late onset sepsis (later than 7 days postpartum):
  - Coagulase negative Staphylococci (CONS)
  - Streptococcus β-haemolyticus (GBS)
  - Staphylococcus aureus

Streptococcus β-*haemolyticus* of group B of Lancefield (SGB), or *Streptococcus agalactiae*

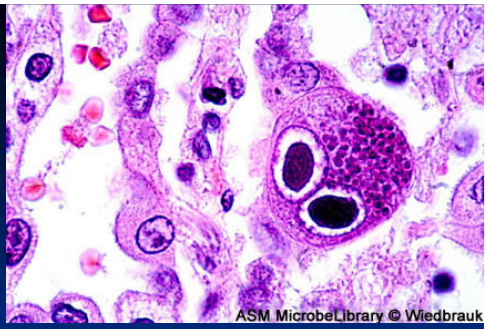


- The prevalence of SGB colonization among pregnant women ranges from 10 to 30%
- SGB disease can occur in three clinical forms:
  - early-onset disease, defined by the development of disease in newborn infants up to the 7th day of life
  - late-onset disease, characterized by occurrence between the 8th day and the 3rd month of life
  - very late-onset disease, occurring after the 3rd month of life
- Prevention: SGB culture for women at between 35 and 37 weeks of gestation – antibiotic therapy if culture is positive

(On the picture right above: Rebecca Craighill Lancefield (1895-1981))

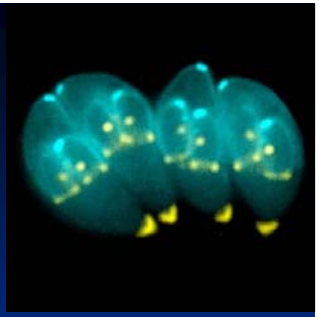
- Infections jeopardizing the fetus with no serious maternal consequences
  - Cytomegalovirus
  - Toxoplasmosis
  - Parvovirus B19
- Infections jeopardizing the fetus with possible maternal complications
  - Rubella
  - Varicella
  - Sexually transmitted infections
  - Malaria

Cytomegalovirus



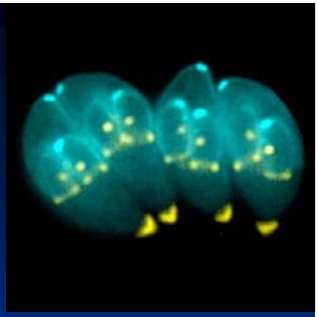
- Cytomegalovirus (CMV) is the leading cause of congenital viral infection, with an incidence of 0.5–3% of live births worldwide.
- Cytomegalovirus is found universally – in every geographic location and in all socioeconomic groups. Its seroprevalence is 50-85 % of adults by age 40.
- Typical clinical symptoms: intrauterine growth restriction, microcephaly, hepatosplenomegaly, petechiae, jaundice, thrombocytopenia, anemia, chorioretinitis
- Long-term neurodevelopmental sequelae include: mental retardation, motor impairment, sensorineural hearing loss and/or visual impairment
- Primary maternal CMV infection during gestation poses a 40% risk of intrauterine transmission

Toxoplasmosis I.



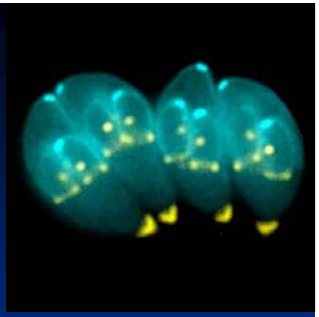
- Approximately 85 percent of women of childbearing age in the United States are susceptible to acute infection with the protozoan parasite *Toxoplasma gondii* (JEFFREY JONES 2003).
- The risk of congenital disease:
  - infection occurs during the first trimester: 10-25 %
  - infection occurs during the third trimester: 60-90 %
- Congenital disease is more severe when infection is acquired in the first trimester.

Toxoplasmosis II.



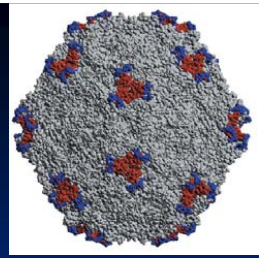
- The classic triad of signs characteristic of congenital toxoplasmosis includes:
  1. chorioretinitis
  2. hydrocephalus
  3. intracranial calcifications.
- Other suggestive symptoms:
  - hepatomegaly
  - microcephaly
  - deafness
  - convulsions

Toxoplasmosis III.



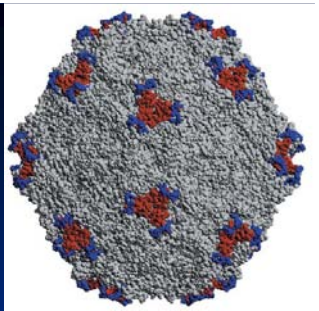
- Detection of *T. gondii–specific IgM antibodies* has been used as an aid in determining the time of infection: a negative IgM test result with a positive IgG result usually indicates infection at least six months previously.
- When a pregnant woman is found to be infected with *T. gondii*, the next step is to determine whether the fetus is infected: *PCR testing of amniotic fluid* is used to diagnose congenital toxoplasmosis.

Parvovirus B19



- Most persons (usually children: erythema infectiosum or fifth disease) with parvovirus B19 infection are asymptomatic or have mild, nonspecific, cold-like symptoms
- The virus is highly infectious and spreads mainly through respiratory droplets.
- The virus also may cause acute or persistent arthropathy and papular, purpuric eruptions on the hands and feet ("gloves and socks" syndrome) in adults.
- Parvovirus B19 infection can trigger an acute cessation of red blood cell production, causing transient aplastic crisis, chronic red cell aplasia, *hydrops fetalis, or congenital anemia*.
- It has been noted that 3–19% of pregnant women will serologically convert to IgM positive on exposure to parvovirus B-19, with a 33% vertical transmission rate.
- Although the virus can be contracted in any trimester, the second trimester seems to carry the highest risk of fetal loss

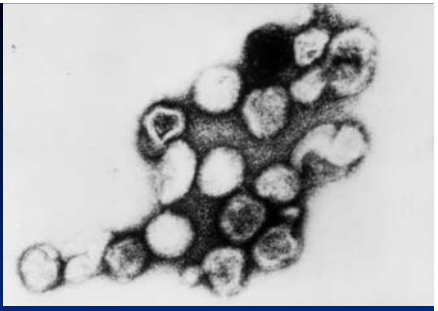
Parvovirus B19



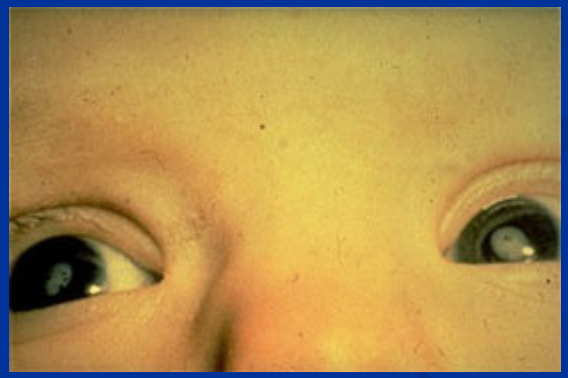
- To test a fetus for possible infection, a polymerase chain reaction (PCR) is performed on a sample of the amniotic fluid (sensitivity >97%, specificity 79–99%).
- Fetal cord blood sample is not widely used because of the associated 1% fetal loss rate, and also because the IgM does not often appear in the fetal circulation until after 22 weeks' gestation.
- The fetal death rate is highest if infection occurs before 20 weeks' gestation, reaching approximately 10%, and it declines rapidly as the fetus ages.
- Routine prenatal screening for parvovirus B19 is not advised.
- If the fetus shows evidence of hydrops, the only treatment option is intrauterine blood transfusion to correct the associated anemia

Sir Norman McAlister Gregg australian ophtalmic surgeon showed in 1941 that maternal rubella infection in early pregnancy caused birth defects. His findings were however not immediately accepted among the medical profession and it was not until 1961 that scientists were able to isolate the rubella virus.

Rubella infection

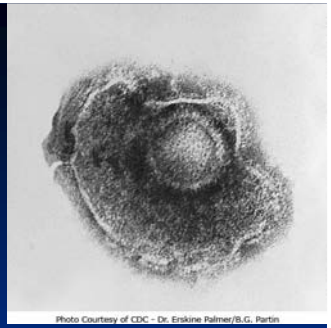


- The earlier in gestation the maternal infection occurs, the more severe is the damage to the fetus
- Maternal infection during the first 8 weeks after the last menstrual period results in nearly all fetuses becoming infected and up to 100% of infected fetuses developing congenital defects:
  - congenital heart disease
  - *congenital cataract*
  - deafness
  - microcephaly
  - mental retardation



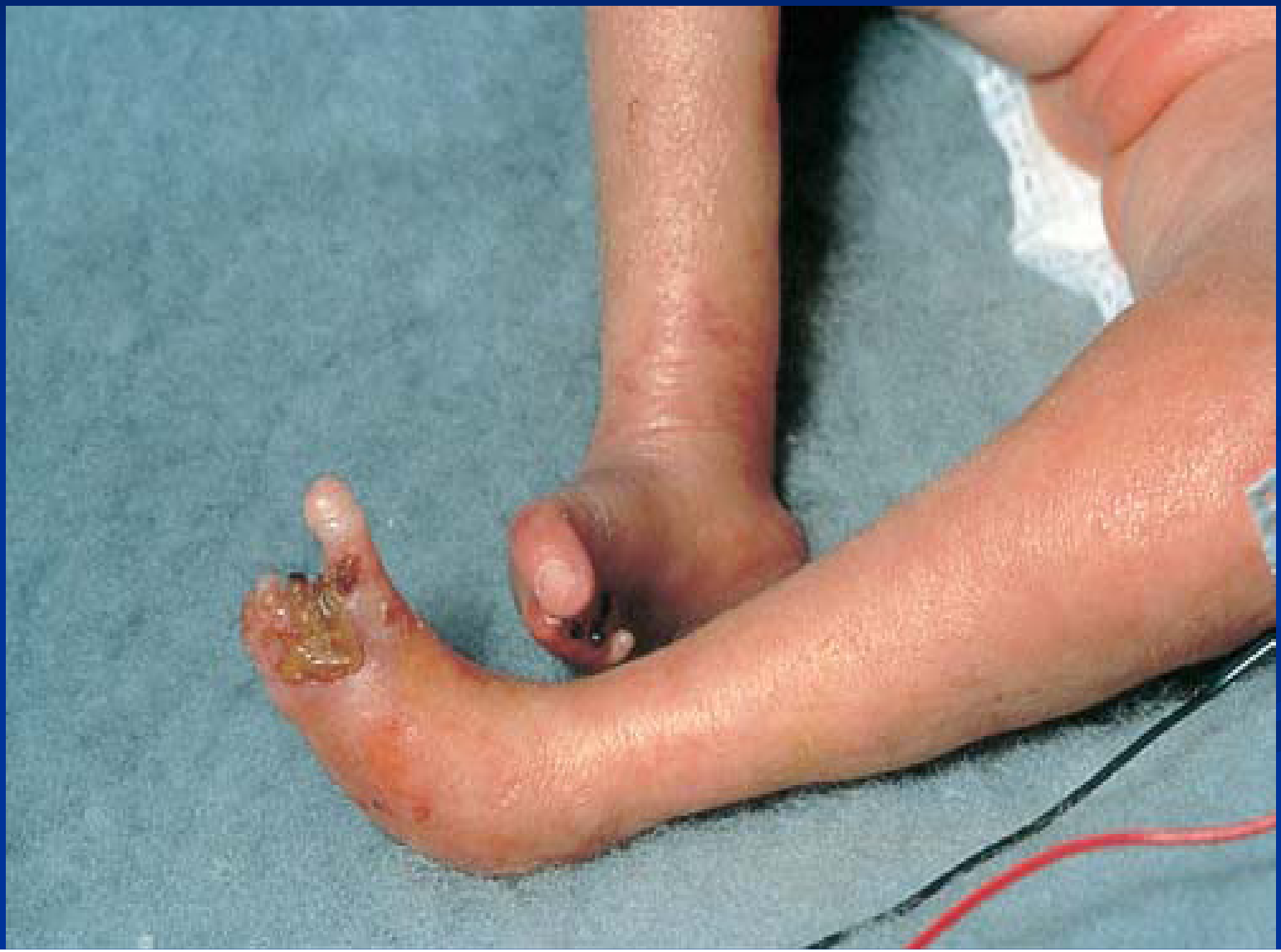
- The risk of fetal infection and the severity of congenital abnormalities decreases after the first trimester; after 17 weeks gestation, the risk of developing any defects is low

Varicella – zoster virus



- Varicella - zoster virus (VZV) is spread by respiratory transmission or direct contact with infectious lesions
- At any stage during pregnancy, severe maternal chickenpox may cause intrauterine death
- Varicella infection in the first and second trimesters may lead to the congenital varicella syndrome
- When infection occurs in the first half of pregnancy, the risk of congenital varicella syndrome is about 2%
- The characteristic symptoms:
  - skin lesions in dermatomal distribution
  - neurologic defects
  - eye diseases
  - skeletal anomalies
- About 30% of infants born with these lesions die in the first months of life

Bilateral lower-limb deformities in an infant whose mother had varicella at 12 weeks' gestation. (Gwendolyn L Gilbert 2002)



Prevalence of selected sexually transmitted infections (STI) in pregnant women in developing countries

(Mullick et al. 2005)

STI	Prevalence
Syphilis	2.4-17.0 %
Chlamydia trachomatis	5.3-21.5 %
Gonorrhoea	2.0-20.0 %
Bacterial vaginosis	9.0-48.5 %
Trichomoniasis	9.9-27.5 %
Herpes simplex virus	6.7-53.4 %
HIV	15-42.5 %

Pregnancy outcomes following maternal sexually transmitted infections

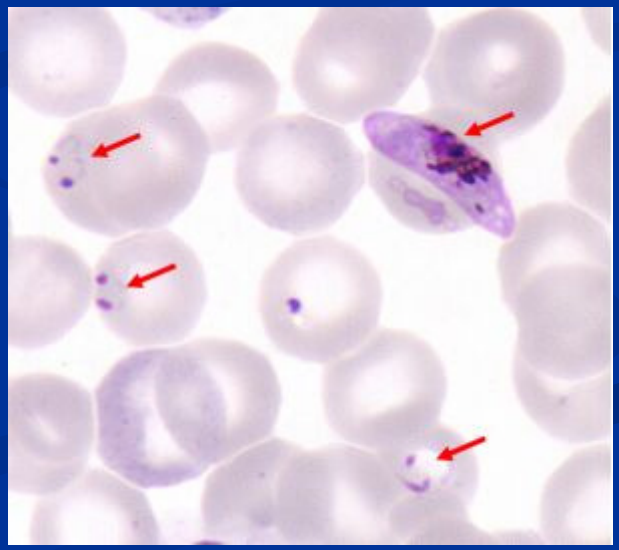
- Neonatal herpes:
  - pulmonary disease, seizures, fever, intracranial findings, a high fatality rate
  - transmission rate: 5-50%
- Gonococcal infection:
  - preterm delivery, premature rupture of the membranes, LBW, postpartum endometritis, gonococcal ophtalmia neonatorum
- Chlamydia infection:
  - preterm delivery, premature rupture of the membranes, LBW, infant pneumonia, ophthalmia neonatorum
- Trichomonas infection:
  - preterm delivery, LBW
- Bacterial vaginosis:
  - preterm birth, LBW, premature rupture of the membranes, postpartum sepsis, spontaneous miscarriage
- Syphilis:
  - stillbirth, LBW, preterm birth, congenital infection

Ureaplasma urealyticum

- ureaplasmal colonization of the *lower genital tract* is *not associated* with adverse pregnancy outcome
- ureaplasmal infection of the *chorioamnion* have been implicated in:
  - infertility
  - spontaneous abortion
  - stillbirth
  - premature birth
  - low birth weight
  - increased perinatal morbidity and mortality
- U. urealyticum is the single most common microorganism isolated from the central nervous system and lower respiratory tract of newborn infants

Malaria in pregnancy

- women living in endemic areas are considered to have some immunity and malarial infections are usually asymptomatic or with less severe symptoms
- the disease is almost always symptomatic, and potentially lethal, in non-immune patients particularly gravid females
- pregnant women attract at least twice as many mosquitoes as non-pregnant patients
- possible pregnancy complications:
  - preterm delivery
  - IUGR
  - spontaneous abortion
  - stillbirth
  - eclampsia
  - postpartum hemorrhage
  - puerperal fever
  - maternal/fetal death



Screening of infections

- Universal screening of pregnant women for syphilis at the first prenatal visit is recommended
- All women at increased risk for sexually transmitted infections, including those younger than 25 years, should be screened for chlamydial, ureaplasmal infection and gonorrhea
- Routine screening of all pregnant women for bacterial vaginosis is recommended
- SGB culture for women at between 35 and 37 weeks of gestation is recommended
- Human immunodeficiency virus testing is recommended in all pregnant women
- All patients and their partners should be asked about a history of genital and orolabial herpes simplex virus infection
- All pregnant women should be screened for rubella if testing was not performed before conception – vaccination!
- All women of childbearing age should be asked about their history of chickenpox – vaccination!
- Routine screening for toxoplasmosis, cytomegalovirus, or parvovirus infection is not recommended

Thank you for your attention!