Cytomegalovirus in Pregnancy

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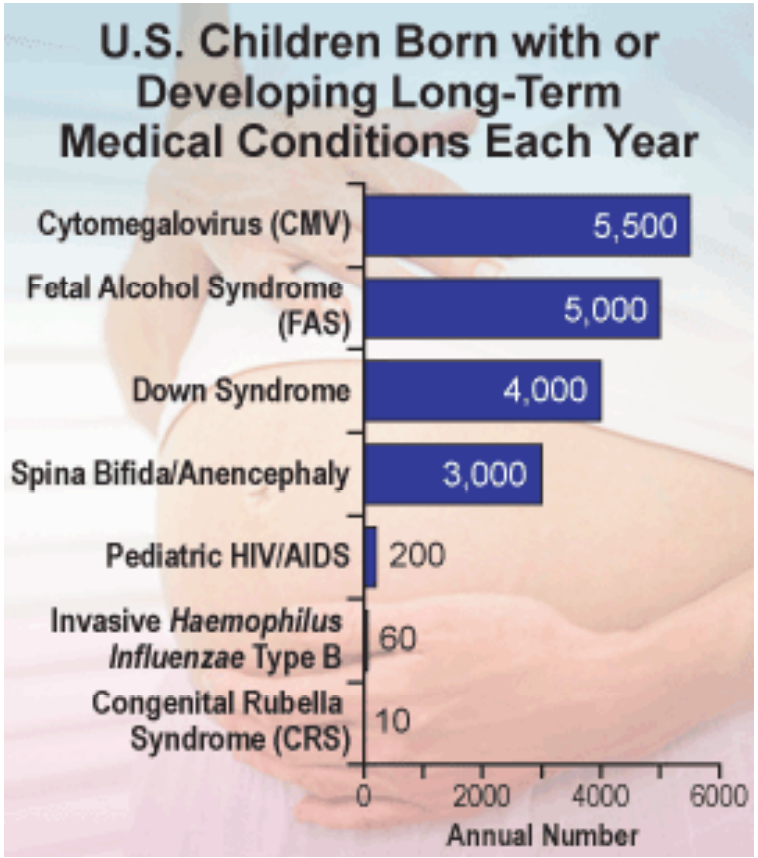
Cytomegalovirus

- Herpes virus
  - Human Subtype
    - Single molecule of double-strand DNA
      - But individual isolates have subtle variations
        - More than 1 strain exists
      - Infection in mother can be
        - Primary
        - Reactivation of latent infection
        - Secondary infection with a different strain

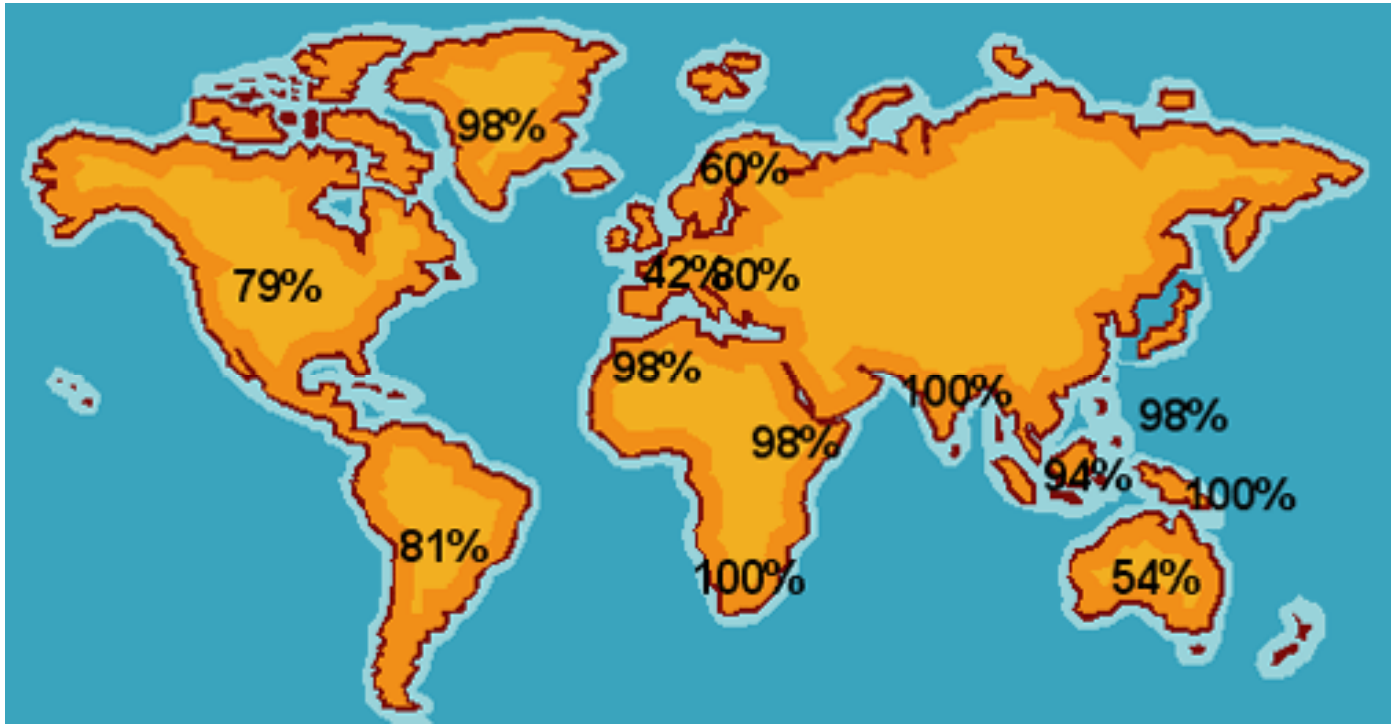
Cytomegalovirus

Commonest congenital viral infection in the world



Cytomegalovirus (CMV) Disease, CDC, 2009

Cytomegalovirus



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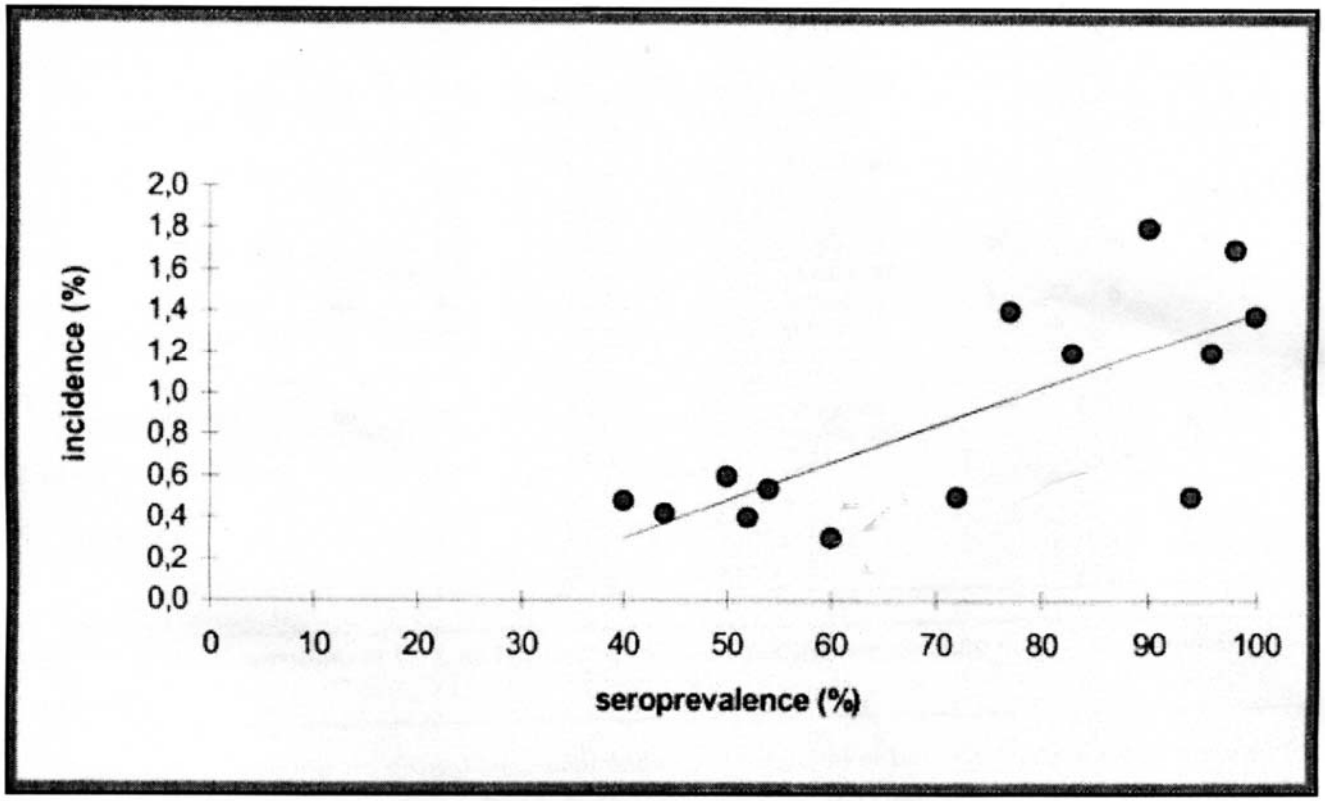


Fig. 1. Correlation between seroprevalence of CMV antibodies and incidence of congenital CMV infections.

WHO. 2004

Infection in pregnancy

- Primary infection in pregnancy
  - 0.5-4% of women
    - Rates only an estimate (infection usually silent)
    - Commonest source :- infants and children
    - Highest in women with low socioeconomic status or living in developing world
- Recurrent infection in pregnancy
  - Rates unknown

Coll et al, J Perinat Med. 2009;37(5):433-45.

Cytomegalovirus

- In pregnancy, CMV
  - Infects uterine wall and adjacent placenta, and causes fetal infection.
  - Replicates in placenta, causes inflammation resulting in dysfunction and abnormal fetal growth.
  - Virus replicates in the fetal tissue and causes cell destruction.

Cytomegalovirus in Pregnancy

- Evidence of CMV infection in 0.2 – 2.2% of fetuses
  - 30 – 50% in primary infection
  - 2 -5x rate after recurrent infection
  - Risk to fetus highest if infection in the first trimester
    - No risk if infection occurs 2 weeks before conception

Coll et al, J Perinat Med. 2009;37(5):433-45

Congenital infection - consequences

- Consequences in the fetus are not dependant on whether infection from primary or recurrent infection.
  - 10-15% symptomatic at birth
    - Hepatosplenomegaly, jaundice, low platelets, petechae, anaemia, IUGR, seizures, chorioretinitis, optic atrophy, intracranial anomalies, pneumonitis
    - 22-60% will get hearing loss

Congenital infection - consequences

- Consequences not dependant on whether infection from primary or recurrent infection.
  - 10-15% symptomatic at birth
  - 85-90% asymptomatic at birth,
    - 5-25% will show signs of infection in childhood (hearing loss +/- other neurological).

Coll et al, J Perinat Med. 2009;37(5):433-45

Congenital infection - consequences

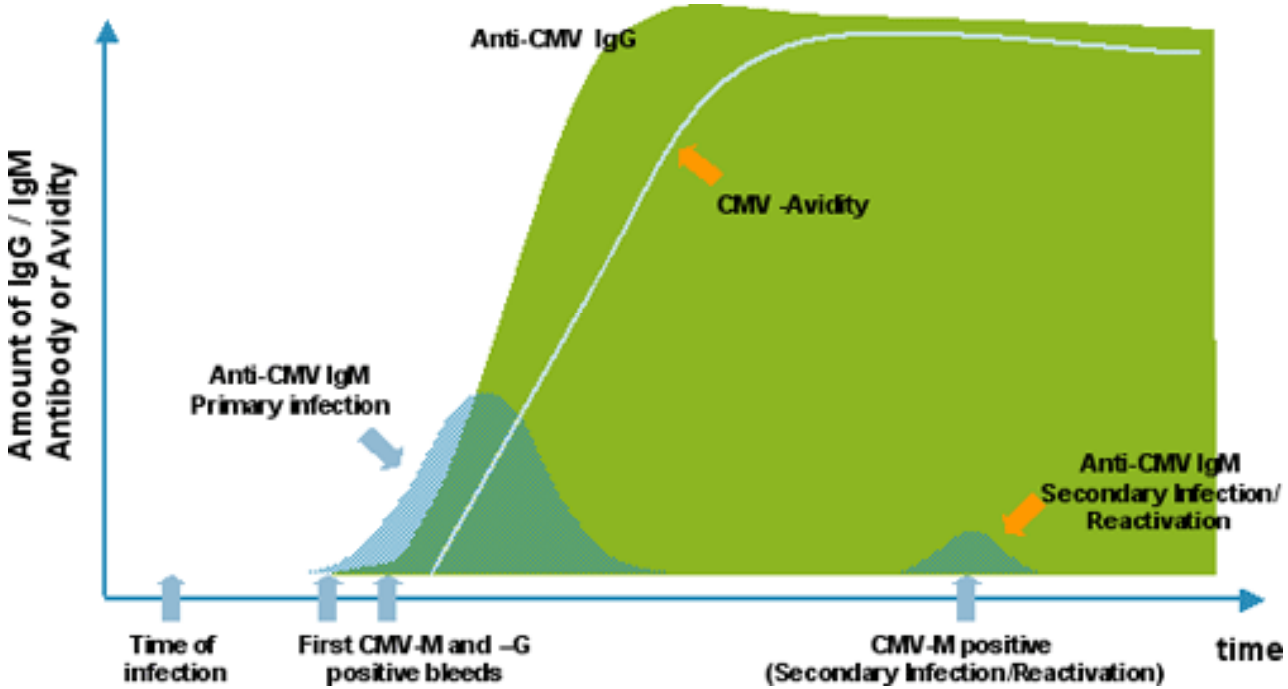
- Follow up must be for 48 months to ensure all pathology is found

Diagnosis

- Primary infection in mother mostly assymptomatic
  - About 10% will be symptomatic
    - fever, feel unwell, muscle aching, lymph node enlargement,
    - Less commonly pneumonia, hepatitis
    - Blood tests:- Raised lymphocytes, low platelets, abnormal liver function tests
    - Illness lasts 7-21 days but viral excretion persists long after blood tests return to normal

Diagnosis of primary infection

- Rising CMV specific IgM and Low avidity of the IgG



Cytogalovirus (CMV) Disease, CDC, 2009

Diagnosis of primary infection

- Rising CMV specific IgM and
  Low avidity of the IgG
  - NB - IgM may stay positive for life so
  - Presence of IgM is NOT a marker of recent disease.

- Viral culture of urine or saliva
  - Fibroblast culture
- PCR for DNA in saliva or urine

Detection of Fetal Infection

Cytomegalovirus

- After evidence of primary infection, fetal infection diagnosed by
  - PCR of amniotic fluid
    - Up to 100% detection of fetal infection if done at least 6 weeks after onset of maternal infection or at 21-23 weeks
  - (Fetal thrombocytopenia + IgM)
    - Ultrasound will detect possible fetal infection in up to 45%

Benoist et al Ultrasound Obstet Gynecol. 2008 Dec;32(7):900-5.

Cytomegalovirus

- Not all infections will be severe
  - Role of ultrasound is to detect those fetuses that have severe infection
- Early pregnancy
  - Abnormal Nuchal translucency

Benoist et al, BJOG. 2008 Jun;115(7):823-9.

Cytomegalovirus – Fetal anomalies

- Site of fetal anomalies
  - Central nervous system
  - Cardiovascular
  - Gastrointestinal
  - Severe IUGR

Cytomegalovirus

- Disease progression:-
  - Marked fetal ascites
    - Related to fetal liver dysfunction
    - Hepatomegaly often present
  - Cardiomegaly
    - May be associated with pericardial effusion and SVT
    - May resolve with time
    - Resolution does not relate to the disease severity

Benoist et al Ultrasound Obstet Gynecol. 2008 Dec;32(7):900-5

Cytomegalovirus

- Disease progression:-
  - Marked fetal ascites and cardiomegaly
  - Hyperechogenicity of bowel

Cytomegalovirus

- Disease progression:-
  - Marked fetal ascites and cardiomegaly
  - Hyperechogenicity of bowel
  - Intracranial anomalies
    - Periventricular echogenicity
    - Periventricular calcification
    - Linear calcification of basal ganglia and thalamus

Cytomegalovirus

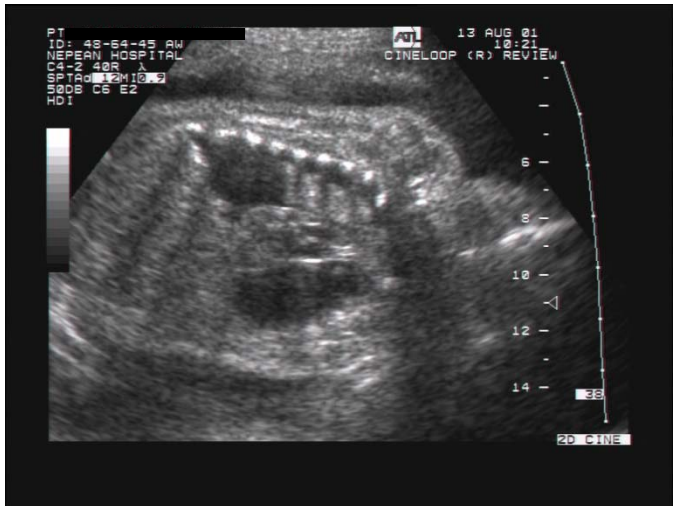
- Disease progression:-
  - Marked fetal ascites and cardiomegaly
  - Hyperechogenicity of bowel
  - Intracranial anomalies
  - Placental hypertrophy
  - Calcification
    - Liver and parenchyma (lung, abdomen)

Cytomegalovirus

- Disease progression:-
  - Marked fetal ascites and cardiomegaly
  - Hyperechogenicity of bowel
  - Intracranial anomalies
  - Placental hypertrophy
  - Calcification
  - Cerebral atrophy
    - Ventricuolmegaly, microcephaly

Cytomegalovirus

- Disease progression:-
  - Marked fetal ascites and cardiomegaly
  - Hyperechogenicity of bowel
  - Intracranial anomalies
  - Placental hypertrophy
  - Calcification
  - Cerebral atrophy
  - IUGR
  - +/-Hydrops
    - May resolve with time



Cytomegalovirus

- Detailed ultrasound
  - Anomalies of the eye
    - Chorioretinitis
    - Cateracts
    - Microphthalmos

Cytomegalovirus

- Anomalies develop over time
  - A normal scan at 21 -22 weeks at the time of a positive PCR does not mean that the fetus will not be affected.
  - Negative PCR at 21 -22 weeks or > 6 weeks after maternal infection indicates no fetal infection in over 98%.
  - Given that many fetuses will not be severely affected after maternal CMV infection, common belief is that termination should only be offered for severe ultrasound changes

Benoist et al, BJOG. 2008 Jun;115(7):823-9.

Cytomegalovirus

- Commonest ultrasound anomalies in severe infection
  - Ascites
  - Large placenta – 32%
  - Polyhydramnios
  - Intracranial and hepatic calcifications
    - 42%
  - Cardiac anomalies
    - 37%

Benoist et al, BJOG. 2008 Jun;115(7):823-9.

Cytomegalovirus

- Twins
  - Rate of infection unaffected
    - 30-50% of pregnancies
  - Type of twins does not affect rate of infection
    - 30% 1 twin affected
    - 70% both affected.

Cytomegalovirus

- Treatment
  - Early results with CMV hyperimmune globulin to prevent hearing loss promising
    - 100U/Kg IV
  - Antiviral agents decrease viral load at delivery but do not appear to decrease neonatal disease.
  - Vaccine is awaited