Congenital and Perinatal Infections

Dr. Nicolette du Plessis
Paeds ID (2012)

Introduction

- Some infections via placenta during pregnancy
- Some transmitted just before,during or after delivery
- Some transmitted in more than one of these ways
  - Cytomegalovirus
  - Rubella
  - Toxoplasma
  - Syphilis
  - Varicella
  - Herpes simplex
  - Papillomavirus
  - TB
  - Parvovirus
  - Enteroviruses
  - Group B streptococcus
  - Listeria
  - HIV
  - Hepatitis viruses
  - Enteroviruses

2

Common Clinical Features

- Growth retardation
- Hepatosplenomegaly
- Jaundice
  - Elevated conjugated fraction
- Haemolytic anaemia
- Petechiae and ecchymoses
- Microcephaly and hydrocephaly
- Intracranial calcification
- Pneumonitis
- Myocarditis
- Chorioretinitis
- Hydrops

3

Diagnostic Approach

- Incidence of congenital infection
  - 0.5 – 2.5%
  - Significant number asymptomatic
- Need high index of suspicion
- History
- Physical examination
- Total IgM in cord blood
  - Indication for further investigation
- Non specific tests
  - Blood and platelet count, LP, X-ray long bones, CT brain, Ophtalmological examination
- Clues ⇨ Specific tests

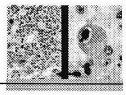
4

Perinatal infections

- Original concept of TORCH:
  - five infections with similar presentations, inc. rash and ocular findings
- These five infections are:
  - Toxoplasmosis
  - Other (syphilis)
  - Rubella
  - Cytomegalovirus (CMV)
  - Herpes simplex virus (HSV)

5

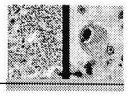
Cytomegalovirus (NB)



- CMV has emerged as the most common congenital viral infection
- Occurs in 0.2 – 2.2% of live births
  - Higher rates in developing countries
- Primary and recurrent infection
  - Risk of damage lower during recurrent infection
  - 5 to 20% primary CMV infection will be symptomatic
  - Mortality rate of almost 30%, and severe neurologic morbidity occurs in 80% of survivors.

6

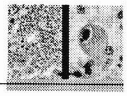
Clinical manifestations



- Asymptomatic infection
  - 90% of infants with congenital CMV infection
  - 15% are at risk:
    - psychomotor, hearing, neurologic, ocular, or dental abnormalities within the first few years of life
  - Sensorineural hearing loss will appear in 5 to 10% of cases

7

Clinical manifestations



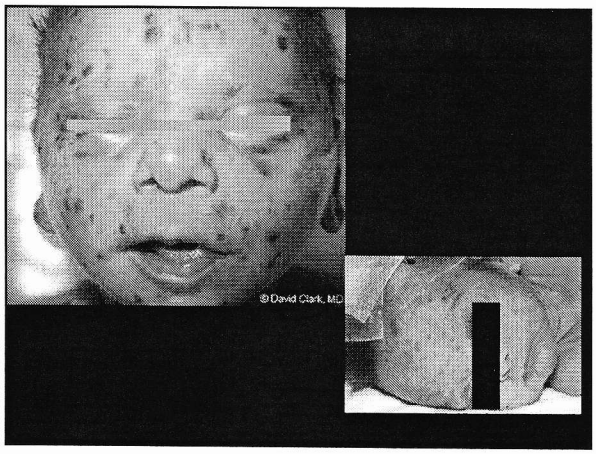
- Symptomatic infection
  - 50%: Isolated splenomegaly, jaundice and/or petechiae
  - 50%: Syndrome of cytomegalic inclusion disease

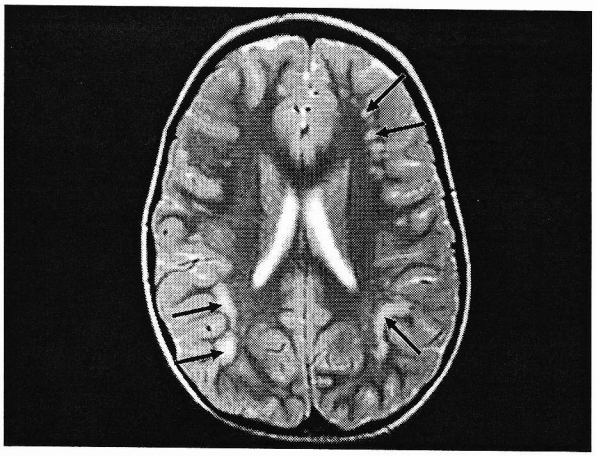
8

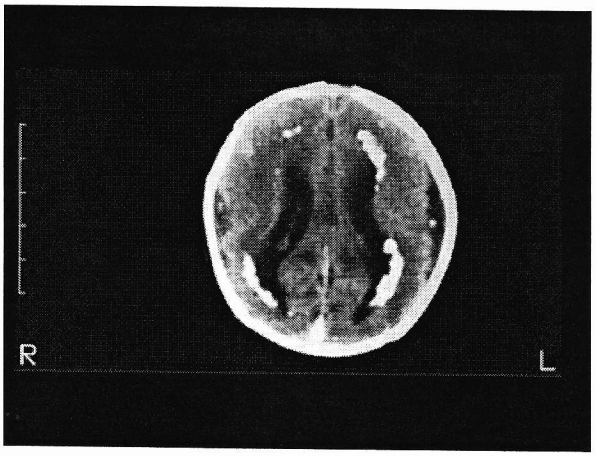
Cytomegalic inclusion disease

- Jaundice — 67%
- Hepatosplenomegaly — 60%
- Petechial rash — 76%
- Multiorgan involvement
  - microcephaly,
  - motor disability,
  - chorioretinitis,
  - cerebral calcifications,
  - lethargy,
  - respiratory distress,
  - seizures
- Thrombocytopenia, hemolytic anemia, elevated transaminases, and elevated direct and indirect serum bilirubin

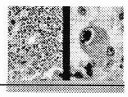
9







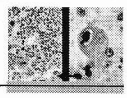
Diagnosis



1. **Rapid culture techniques**
   - CMV culture from throat swab or urine
     - First 3 weeks of life
     - If take after this
       - Not distinguish between neonatal/congenital infection
2. **Polymerase chain reaction**
   - Qualitative versus quantitative
   - CMV Viral loads done more frequently
3. **Serology**
   - Antibody assays
     - IgG crosses the placenta
     - IgM detection
       - Less reliable than isolation, should be confirmed by viral culture

13

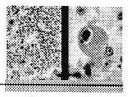
Investigations



- **Confirmation of infection**
- **Identification of disease**
- **Neuroimaging:** cranial ultrasound scan should be carried out as a minimum
- **Ophthalmological evaluation**
- **Audiological testing**

14

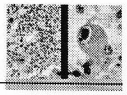
Cytomegalovirus



- Prognosis differ between those with symptoms at birth and not
- If symptomatic at birth – long term complications
  - Cerebral palsy
  - Mental retardation
  - Optic atrophy
  - Sensorineuronal deafness
  - 10% die
- If asymptomatic at birth
  - 90% develop normally
    - 5-15% long term sequelae (deafness)

15

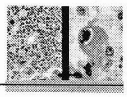
Cytomegalovirus



- Treatment
  - Antivirals
    - Ganciclovir, (foscarnet, cidofovir)
      - Regularly used in immunocompromised and transplant patients
    - Not licensed in pregnancy
      - Teratogenic effects
  - No established treatment
    - Ganciclovir and foscarnet suggested for inhibition of disease progression
    - Results from trials with ganciclovir not great
    - Viral shedding restarts once treatment stopped

16

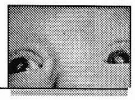
Cytomegalovirus



- Prevention
  - Vaccines not effective
- Screening
  - Antenatal
    - Repeated screening through pregnancy
    - Action if positive?
      - Seen large proportion of asymptomatic infection
  - Neonatal
    - Fewer than 10% of asymptomatic children will develop problems
    - No treatment to offer
    - Does not make sense

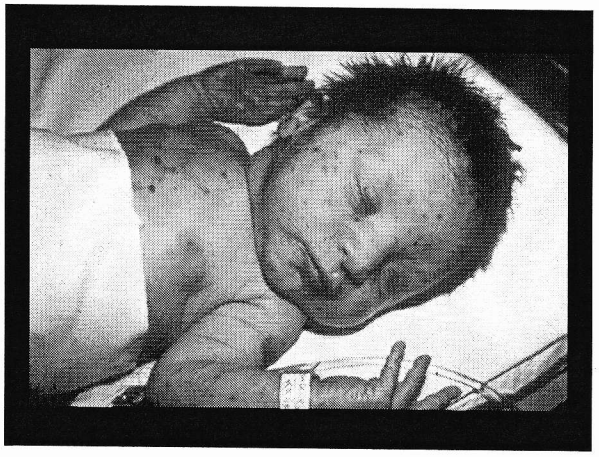
17

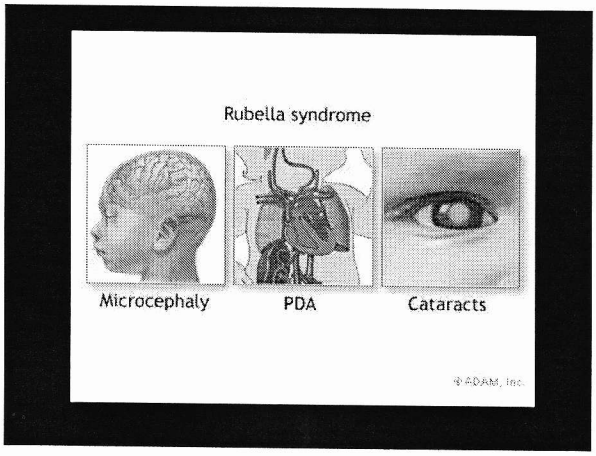
Rubella



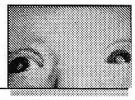
- Maternal rubella within 1 month before conception and through second trimester associated with disease in infant
- Classic findings if infection during first 8 weeks
- Clinical picture **(NB)**
  - *Cataracts, Retinopathy*
  - *Heart disease (PDA or PA hypoplasia)*
  - *Deafness*
  - HSM
  - Thrombocytopaenia
  - Immunological abnormalities
    - Late onset disease

18





Rubella



- Frequency of congenital rubella after maternal infection with rash
  - >80% during first 12 weeks
  - 54% at 13-14weeks
  - 25% at end of second trimester
- Rubella associated defects negligible after 16 weeks
  - Rare cases of deafness
  - Infected infant excretes virus for many months and remain hazard to susceptible individuals

22

Rubella

- Diagnosis
  - Virus isolation
    - Urine,nasal secretions, blood, CSF
    - PCR
  - Serologic testing
    - IgM - fourfold or greater rise in antibody titer or seroconversion between acute and convalescent serum titers
- Prevention
  - Rubella serology in women
  - Vaccine

23

Toxoplasma

- Primary infection during pregnancy
  - 1/3 chance of fetal infection
- Rate of fetal infection is higher when maternal infection occurs in the third compared to the first trimester
- Fetal death or severe congenital infection are more likely from infection during the first trimester.

24

Toxoplasma

- Asymptomatic at birth in 70 – 90% of cases
- Visual impairment, learning disabilities or mental retardation
  - Months to years later
- Signs at birth
  - Maculopapular rash
  - Generalized lymphadenopathy
  - Hepatosplenomegaly
  - Jaundice
  - Thrombocytopaenia
- *Classic triad: chorioretinitis, hydrocephalus, and intracranial calcifications* ***(NB)***

25

Toxoplasma

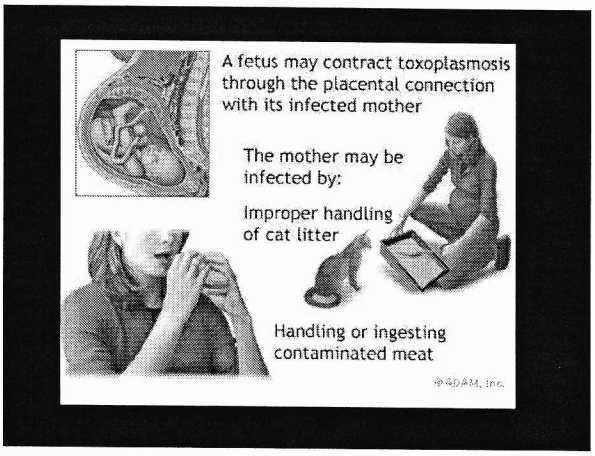
- Neurological signs **(NB)**
  - Intracranial calcifications
  - Chorioretinitis
  - Hydrocephalus
  - Mental retardation
  - Seizures
  - Spasticity
  - Palsies
  - Deafness
- Risk of developing signs before three years of age inversely related to gestation at maternal infection

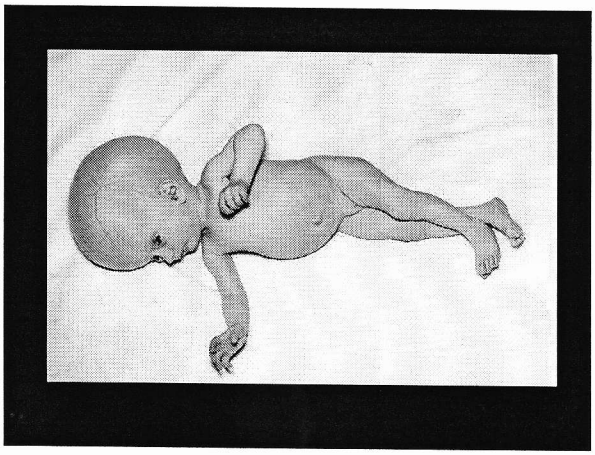
26

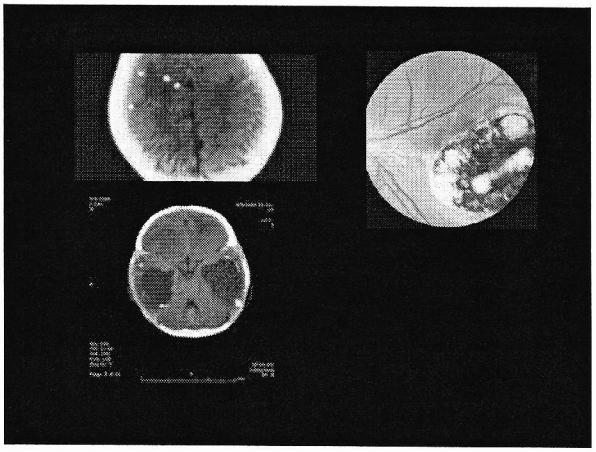
Toxoplasma

- Treatment
  - Pyrimethamine and sulfadiazine, spiramycin, sulfadoxine, folic acid
  - 6 months to 2 years
- Neonatal screening
  - Guthrie card
    - Toxoplasma IgM
    - 85% of infected infants identified

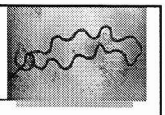
27





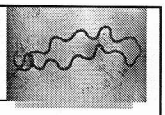


Syphilis (**NB**)



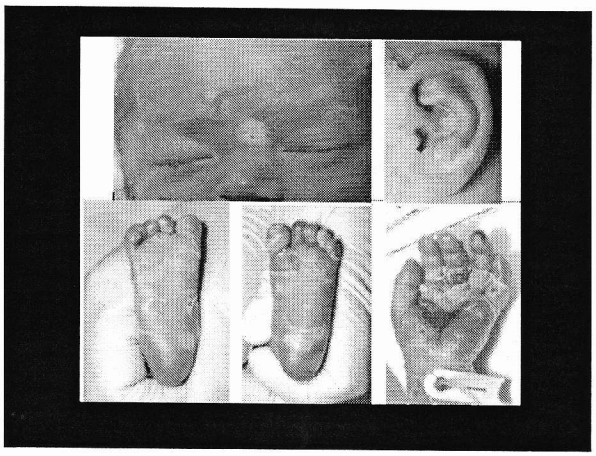
- Infection with *Treponema pallidum:*
  - stillbirth, hydrops fetalis, or prematurity and associated long-term morbidity
- Transplacental transmission can occur at any time during gestation but typically occurs during the second half of pregnancy.
- Women with primary or secondary syphilis are more likely to transmit the disease to their fetuses than are those women with latent (not clinically apparent) disease

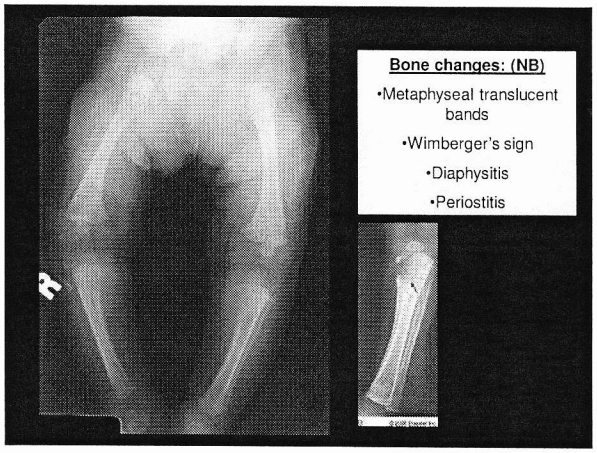
Clinical manifestations



- Early congenital syphilis
  - First 2 years of life
  - Common neonatal presentation
    - Cutaneous lesions, palms and soles; if ulcerative in nature, they are **highly contagious**.
    - Hepatosplenomegaly
    - Jaundice
    - Osteochondritis
    - Lymphadenopathy, pneumonia and myocarditis less often
    - May not become apparent until 2 – 12 weeks of age

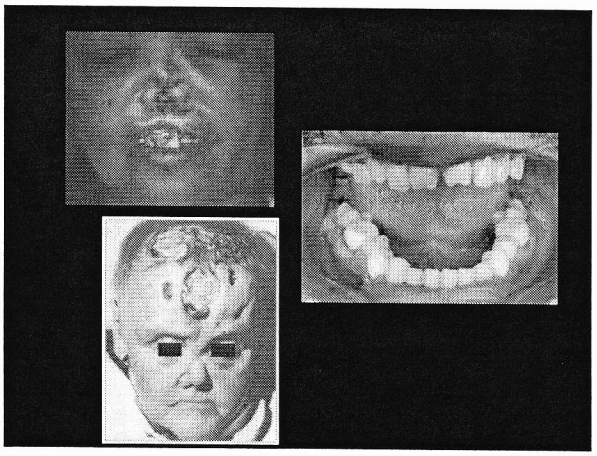
33





Clinical manifestations

- Late congenital syphilis
  - After 2 years of life
  - Late findings can include
    - frontal bossing,
    - short maxilla,
    - high palatal arch,
    - Hutchinson triad (Hutchinson teeth [blunted upper incisors], interstitial keratitis, and eighth nerve deafness),
    - saddle nose,
    - and perioral fissures

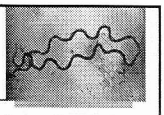


Syphilis

- A presumptive diagnosis, which results in treatment, is made if the newborn has a positive serologic test for syphilis and any of the following:
  - Compatible findings on physical examination
  - CSF abnormalities including positive VDRL, increased white blood cell count (WBC), or elevated protein
  - Osteitis on radiography of long bones
  - Placentitis
  - Nontreponemal test fourfold higher than the maternal result on the same test
  - Positive FTA-ABS IgM antibody

38

Syphilis



- Symptomatic infant of untreated/inadequately treated mother **(NB)**
  - 10-14 days of uninterrupted pen G IV or
  - 10 days of procaine pen G 1x/d for 10 days IMI
- **Asymptomatic infants**
  - LBW, Inadequately treated mothers
    - Treat as for symptomatic infants
  - Term appropriately grown infants
    - Mothers had any number of injections more than 1 month before delivery
      - No risk, no investigations, no follow up
  - Term appropriately grown infants
    - Mothers had no injections before delivery/ only in last month
      - 4% chance for occult syphilis
      - One dose of Benzathine penicillin IM

39

Herpes Simplex

- Incidence of neonatal HSV infection
  - 1/3000 – 1/20 000 births
- Transmitted to infant by
  - Birth through infected birth canal
    - 75% HSV-2, 25% HSV-1
  - Ascending infection
  - Intrauterine
    - Very rare, Congenital defects
  - Postnatal
    - Mother, caregiver, infected infant via caregiver
- Risk of transmission
  - Primary infection in mother: 33 – 50%
  - Reactivation in mother: < 5%

40

Herpes Simplex

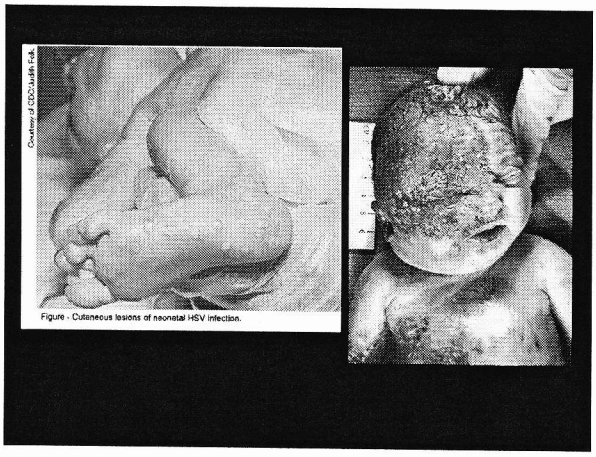
- 1/3 Disseminated disease
  - Liver and Lungs
- 1/3 Localized CNS disease
- 1/3 Disease of skin, eyes and mouth
- Suspect in sepsis syndrome with negative cultures, severe liver dysfunction
- High morbidity and mortality
- Initial symptoms may appear any time between birth and 4 weeks of age
  - Disseminated disease earliest onset

41

Herpes Simplex

- Diagnosis
  - PCR (esp CSF), Culture, Histology of lesions
- Treatment
  - Parenteral Acyclovir 14 - 21days
- Prevention
  - C/S if clinically apparent HSV, within 6 hours after rupture of membranes
  - Cultures of babies born to mothers with active herpes
  - ?Role for prophylactic therapy if mother primary infection
  - Observation for up to 6 weeks

42



Tuberculosis (**NB**)

- Perinatal tuberculosis acquired via several routes
  1. Transplacental spread via umbilical vein
  2. In utero aspiration of amniotic fluid
  3. Ingestion of amniotic fluid during birth process

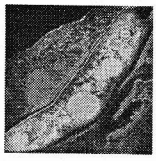
Postnatal

1. Inhalation soon after birth from mother or someone else
2. Ingestion of infected breast milk

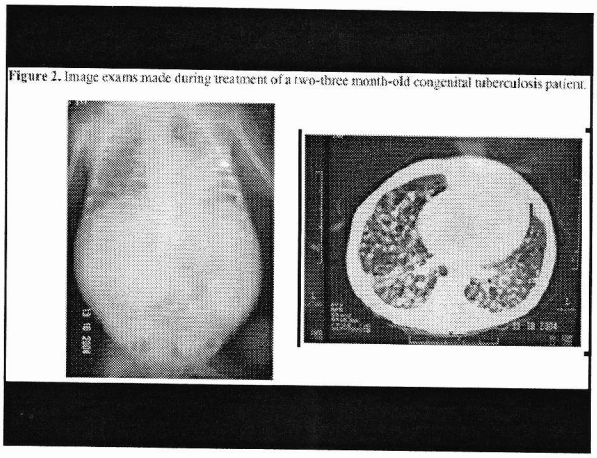
45

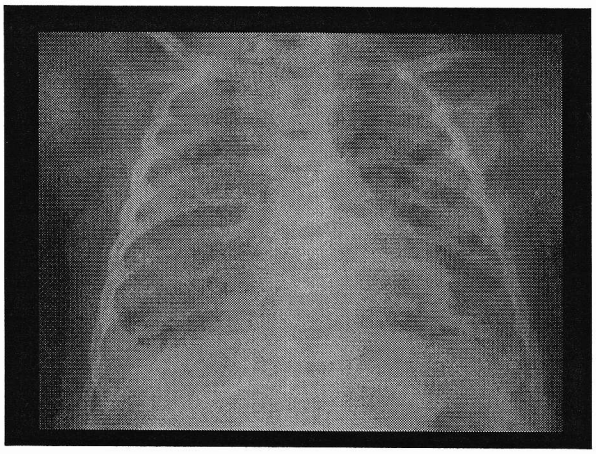
Tuberculosis

- Diagnosis difficult, often delayed
  - Skin test very rarely positive
  - Need to demonstrate TB bacilli
    - Gastric aspirates
    - Middle ear fluid
    - Lymph node biopsy
    - Blood culture
    - NPA or tracheal aspirates
    - BMA, skin or lung biopsy
  - Examination of the placenta
- Treatment
  - Response slow



46





Papillomavirus

- Clinical infection in females
  - Overt 1-3%
  - Subclinical infection 13 – 34%
- Juvenile onset papillomatosis/Recurrent respiratory papillomatosis
- Symptoms **(NB)**
  - Changing voice, hoarseness
  - Respiratory distress and stridor
- Location of papillomata
  - Vocal cords, epiglottis, subglottis
  - Entire larynx, bronchial tree, lungs
  - Single or multiple
- Treatment difficult

49

Parvovirus B19

- Overall risk of infection in fetus low
- Hydrops fetalis/Congenital anaemia **(NB)**
  - Virus replicating in bone marrow
  - Myocarditis secondary role
- No congenital abnormalities

50

Varicella

- Congenital infection
  - 0.5 – 3/1000 pregnancies
  - Congenital infection in 2% of second trimester varicella
- Fetal consequences
  - LBW
  - Skin lesions
    - Pale, yellow in distribution of dermatoma
    - Scarring
  - Limb hypoplasia
  - Other bones like scapula may be involved
    - ?Consequence of atrophy after denervation

51

Varicella

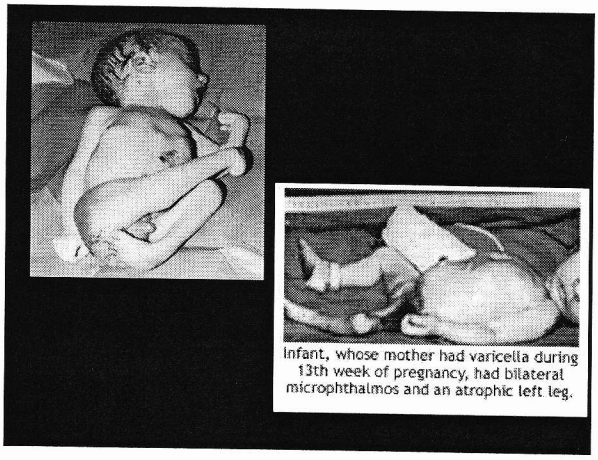
- Neurological abnormalities
  - Mental retardation
  - Microcephaly
  - Cortical atrophy
  - CNS calcifications
  - Ventriculomegaly
  - Paralysis
  - Atrophy of limbs
  - Deafness

52

Varicella

- Eye abnormalities
  - Choreoretinis
  - Microphtalmia
  - Cataracts
  - Corneal opacities
  - Optic atrophy
  - Strabismus
- GI tractus
  - GER, duodenal stenosis, jejenal dilatation, microcolon
- Mortality
  - 40-100%

53



Infant, whose mother had varicella during 13th week of pregnancy, had bilateral microphthalmos and an atrophic left leg.

Varicella

- Perinatal infection **(NB)**
  - *Mom with infection 5 days before delivery and 2 days after birth*
    - 31% mortality
  - If earlier infection, transfer of antibodies across placenta

55

Varicella

- *Management of perinatal infection*
  - Hyperimmune immunoglobulin
  - Monitor for 14 days
    - Delayed presentation
  - Attack rate 50%
  - No prophylactic acyclovir
  - If varicella develops
    - Acyclovir IV for 7 days

56

Varicella

- Postnatal varicella
  - Rare
  - No more severe than childhood varicella
  - Preterms treated with Acyclovir

57

Neonatal Sepsis

- Organisms
  - Group B streptococcus, E.coli
  - After three days
    - Nososcomial
      - *K. pneumoniae*
      - *P aeruginosa*
      - *E. faecalis*
      - *S. epidermidis*
        - Prematures
      - *Acinetobacter*
      - Fungi

58

Neonatal Sepsis

- Diagnosis
  - History of risk factors
    - Chorioamnionitis, PROM, UTI
  - Clinical examination
    - Lethargy, vomiting, respiratory distress, hypotonia, poor perfusion etc.
  - Special investigations
    - Blood count and differential count
      - Leucopaenia, increased number of immature cells
    - CRP – serial measurements
    - IL 6, Expensive, not specific for infection
    - Procalcitonin, ?exact role

59

Neonatal sepsis

- Diagnosis
  - Blood cultures
    - 81-82% positive in babies who died of infection
    - Volume NB
  - LP
    - If suspicion of meningitis or blood cultures positive
  - Urine
    - If underlying renal problem or positive dipstix

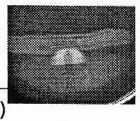
60

Neonatal sepsis

- Treatment
  - General measures
    - Supportive care
      - Transfusions, fluids, inotropes, warming, glucose,exchange transfusion may be of help
  - Antibiotic treatment
    - Penicillin/Ampicillin plus aminoglycoside
    - Penicillin and cefotaxime in suspected meningitis
      - Discontinue one once culture result available
    - Nosocomial infection
      - Know your unit
        - Carbapenem/Vancomycin/ Antifungals

61

Group B Streptococcus



- Invasive disease in young children **(NB)**
  - Early onset disease
    - Within 24 hours (0-6days)
    - Signs of systemic infection
      - Respiratory distress, apnea, shock,pneumonia, meningitis (less often)
  - Late onset disease
    - 3-4 weeks of age (7days-3months)
    - Occult bacteremia or meningitis
  - Case fatality ratios 5%-8%
    - Higher in preterms
  - Transmission shortly before or during delivery

64

Group B Streptococcus

- Diagnosis
  - Blood culture
  - Culture of CSF, pleural or joint fluid
- Treatment
  - Initially Penicillin and Aminoglycoside
  - Pen G only when culture available
    - Meningitis higher dosage
    - Second LP to document response?
  - Sepsis without focus
    - 10 days
  - Meningitis
    - 14 days

65

Summary

- High index of suspicion necessary to diagnose congenital infections
- Clinical features and basic investigations will give you clues
- Simple things like hand washing and breastmilk will decrease sepsis

66