CONGENITAL INFECTIONS
DEFINITION

• Infections transmitted any time during gestation excluding the last 5 to 7 days
• Common infections acquired in-utero are
  a. CMV
  b. Rubella
  c. Toxoplasma gondii
  d. Treponema Pallidum
  e. Herpes simplex
  f. HIV
DIAGNOSTIC APPROACH

- Maternal History including travel history, blood transfusions
- Obstetric history
- Medical Problems of siblings
- Family history
- Drug use
- Birth weight
- Blood transfusions
CYTOMEGALO VIRUS

• Herpes virus – Family
• Largest DNA genome of any known virus
• Commonest congenital viral infections (50-90%)
• Old age, low socio economic and low educational status
• Viral excretions in the cervix or urine rises during pregnancy from 3% in the first trimester to 50% at term
MODE OF SPREAD

- Primary maternal infection and reactivated maternal infections
- Infants exposed to virus - shed from cervix
- Excreted in Breast milk
- Transfusion related infections
MATERNAL EXPOSURE AND HISTORY

• Child care providers

• 90% of pregnant women – asymptomatic

• Symptomatic - Flu like illness

• Fever, fatigue, headache, myalgia, lymphadenitis, pharyngitis
ETIOPATHOGENESIS

• Infection occurs throughout gestation

• Higher incidence during first trimester

• Only 10% of pregnant women transmit infection to their fetus
LABORATORY EVALUATIONS

• No universal prenatal screening

• Use of IgM antibody testing in mothers and infant – Limitations
  – Mother with reactivation as well as infection may have positive CMV IgM
  – IgM testing has vide variability in accuracy and reproducability

• CMV specific IgG- Discriminate primary from and recurrent infection
PRENATAL DIAGNOSIS

• Isolation of virus by amniocentesis

• A specific nucleic acid test for CMV in amniotic fluid or CVS via PCR
LAB EVALUATION (BABY)

• Detection of virus in organs or culture specimens at birth or within first 2 to 3 weeks of life

• Urine:
  – Sensitive detection is from urine
  – Rapid method of isolation - Shell viral assay

• Blood:
  – Elevation of liver transaminases and thrombocytopenia
  – Peripheral Smear – red cell inclusion bodies (owl’s eye cells)
LAB EVALUATION – CONT..

CT Brain
- Periventricular calcification
- Ventriculomegaly
- Cerebellar hypoplasia
- Neuronal migration disorders

HPE
- Intranuclear inclusion bodies in brain
- Mononuclear cell infiltration and diffuse fibrosis
- Subependymal and periventricular necrosis
TREATMENT

• CMV lacks enzyme thymidine kinase. This feature renders its resistance to antiviral agents like acyclovir.

• Ganciclovir – IV for 6 weeks showed a decreased in viral urine titre
  – Side affects : Neutropenia, Thrombocytopenia
CMV CHORIORETINITIS
MRI BRAIN
PROGNOSIS

• If asymptomatic at birth; have minimal to no sequelae other than potential hearing loss

• If symptomatic at birth
  • Mortality 4 – 30%
  • 90% have late complications
  • Intellectual and developmental impairment
  • Small percentage have chorioretinitis
PREVENTION

• Basic hygiene, Hand washing for pregnant women after contact with urine, diapers, oral secretions and other body fluids

• No role for antiviral therapy during pregnancy

• Vaccines - Progress
RUBELLA

• RNA Virus
• Toga virus family
• German Measles
ETIOPATHOGENESIS

• Transmitted from person to person via respiratory droplet

• Once the oral or nasopharyngeal mucosa are infected, viral replication occurs in both upper respiratory tract and nasopharyngeal lymphoid tissue

• Virus spread contiguously to regional nodes and haematogenously to distant sites

• Fetal infection is presumed to occur during maternal viraemia
ETIOPATHOGENESIS

- Maternal infection can occur from one month before conception to the second trimester

- Classical findings of congenital rubella predominates with onset of maternal infection during first 8 weeks of gestation and is low after 17 weeks of gestation
CLINICAL SPECTRUM

• LBW, Microcephaly, Heart defects (PDA), Cataracts, Hearing loss, Hepatosplenomegaly,

• Skin rashes – Blueberry muffin

• Interstitial pneumonia
Rubella syndrome

Microcephaly  PDA  Cataracts
BLUE BERRY MUFFIN APPEARANCE - RUBELLA
CONGENITAL CATARACT- RUBELLA
INVESTIGATIONS

• Antibody- Ig M titres, rise in paired Ig G titre

• Culture: Isolation of rubella virus cultured from nasal, blood, throat, urine or CSF specimen

• PCR- Detection of virus by reverse transcriptase in specimens from throat swabs, CSF, cataracts
  – Viruses are recovered up to 1 year of life

• Thrombocytopenia, Leukopenia

• Hyperbilirubinemia
TREATMENT

• No specific therapy
• Symptomatic:
  – Anemia – Blood transfusion
  – Seizure control
  – Phototherapy
• Long Term Care: Multi disciplinary approval
  – Psychiatrist
  – O.T.
  – Neurologic and Audiology
• Surgical interventions as needed for cardiac malformation and cataract
PROGNOSIS

• Consequences of fetal rubella infection may not be evident at birth

• Infection in 1\textsuperscript{st} or 2\textsuperscript{nd} trimester may lead to deafness or persistent growth restriction

• Infections in 3\textsuperscript{rd} trimester – IUGR

• Learning deficits and behavioral disturbances

• Neuromuscular development abnormalities like difficulties in balance and gait
PREVENTIONS

• No effective antiviral therapy

• Live attenuated rubella virus vaccines safe and effective

• Recommended for women of child bearing age in women if results of both haemagglutination inhibition antibody test and a pregnancy test are negative
VIRAL HEPATITIS

Hepatitis ‘B’ – Etiopathogenesis

• DNA Virus
• Transplacental leakage of HBeAg – positive maternal blood, a potential source of intrauterine infections
• Infection can occur perinatally during labour or delivery.
CLINICAL MANIFESTATIONS

• Without immunoprophylaxis - development of chronic antigenaemia
• Less commonly manifests as jaundice, fever, hepatomegaly that either recover or leads to chronic active hepatitis.
### INVESTIGATIONS – CONT..

<table>
<thead>
<tr>
<th>Factor to be Tested</th>
<th>Hepatitis B virus Antigen or Antibody</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>Hepatitis B surface antigen</td>
<td>Detection of acutely or chronically infected persons</td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>Antibody to HBsAg</td>
<td>Antigen used in Hepatitis B vaccine Identification of persons who have Determination of immunity after immunization</td>
</tr>
<tr>
<td>HBeAg</td>
<td>Hepatitis B e antigen</td>
<td>Identification of infected persons at increased risk of transmitting HBV</td>
</tr>
<tr>
<td>Anti-HBe</td>
<td>Antibody to HBeAg</td>
<td>Identification of infected persons at lower risk of transmitting HBV</td>
</tr>
<tr>
<td>Anti-HBc</td>
<td>Antibody to HBcAg</td>
<td>Identification of persons with acute, resolved, or chronic HBV infection</td>
</tr>
</tbody>
</table>
TREATMENT

• Infants born to mother known to be HBsAg Positive
• First dose Vaccine within 12 hours along with HBIG.
• Second dose 1 to 2 months
• Third dose within 6 months
HERPES SIMPLEX

• Two Types
  - HSV I
  - HSV II
INCIDENCE

• 20% - 45%
• 1:3500 – 10,000
• Primary genital herpes infection in a pregnant mother – 33% to 50%
• Recurrent maternal infection- 1% to 3%
• Acquire infection from maternal genital tract at the time of delivery
CLINICAL SPECTRUM

• Multiple system involvements-
  Liver, Lungs, Adrenal glands, Skin, CNS, Eyes

• Three groups
  – Skin – Grouped vesicles around flat irregular ulcers within erythematous base
  – CNS – Poor feeds, lethargy, convulsions, irritability
  – Disseminated - Jaundice, Hypotension, DIC, Shock

• Very difficult to differentiate from bacterial sepsis and hence differential diagnosis for any neonate with fever during first 2 weeks of life
HERPES SIMPLEX
INVESTIGATIONS

• Virus isolated from
  – Blood, conjunctiva, respiratory secretions urine and CNS
  – Mothers genital tract
  – Scraping of skins vesicle may show giant, multinucleated cells
• Demonstration of viral antigen in cytologic smears by EIA and DFA staining provide rapid results.
• CSF- PCR
• In disseminated disease – ALT elevated
INVESTIGATIONS – CONT..

• CT and MRI Brain- Loss of gray matter and white matter differentiation and features of encephalitis
  * Dilated ventricles
  * Intracranial Calcification
  * Cystic degeneration
  * Parenchymal echogenecity

• EEG - Abnormal
TREATMENT

• Acyclovir 60mg / kg/ day. IV q8th hourly for 2 to 3 weeks.

• Herpetic conjunctivitis -Tropical ophthalmic antiviral therapy.
PROGNOSIS

• Mortality 20% with treatment
• Neurological abnormality develops later in 5% group
• In CNS disease 4% to 14% with antiviral therapy and survivors have long term neurological sequelae
• In Disseminated Disease 80% dies
• In skin involvement recurrent crops of skin vesicles for several years
• More than 3 episode of recurrent infection in first 6 months of life – Poor neurological outcome
PREVENTION

• Mother with active genital herpes simplex intention at time of delivery – LSCS

• 30% - 50% chance if delivered Vaginally
TOXOPLASMOSIS

• Protozoan parasite
• Cat – Definitive host
• **Etiopathogenesis**- Possible route of transmission from animals to human are direct contact with cat faeces, ingestion of uncooked meat containing infective cyst and ingestion of contaminated fruits or vegetables
• Congenital infection results from placental infection and subsequent haematogenous spread to fetus
### NATURAL HISTORY

- Approximately 40% babies born to mothers who acquire toxoplasmosis during pregnancy are infected
  - I Trimester: - 15%
  - II Trimester: - 30%
  - III Trimester: - 60%
- Severity of clinical manifestation greater if acquired in early in pregnancy.
CLINICAL MANIFESTATIONS

• Classical triad
  – Chorioretinitis
  – Intracranial calcifications
  – Hydrocephalus

• Chorioretinitis - Strabismus in infants and Defect in visual acuity

• Intracranial calcification involves - Caudate nucleus, Choroid plexus, Meninges and Subependymal areas

• Hydrocephalus - Periaqueductal & periventricular
DIAGNOSIS

• Isolation of T.gondii from body fluids and tissues
• Isolated from
  – Placenta
  – Amniotic fluid
  – Fetal blood by cordocentesis
  – Umbilical cord blood
  – Infant peripheral smear
  – CSF
• Inoculation requires as long as 4 – 6 weeks for demonstration of parasite
DIAGNOSIS – CONT.

• Serology
  – T. gondii specific IgG antibodies - Sabin feldmen dye test
  – Enzyme Linked Immuno Filtration Assay (ELIFA)
    – discriminates IgG of maternal origin and fetal origin
TREATMENT

In pregnant women with acute toxoplasmosis

• For 1st 21 weeks of gestation if fetus is not infected
  – Spiramycin 1 gm Q8H, without food

• If fetal infection confirmed after 18 week of gestation
  – Pyrimethamine 100 mg / day for 2 two days, followed by 50 mg / day till delivery
  – Sulfadiazine 75 mg / kg / day BD for 2 days, followed by 100 mg / kg / day till delivery
  – Leucovorin 10 – 20 mg QID till delivery
TREATMENT – CONT..

Congenital toxoplasmosis

- Pyrimethamine 2 mg / kg / day BD for 2 two days, followed by 1 mg / kg / day for 2 – 6 months and then thrice a week for 1 year
- Sulfadiazine 100 mg / kg / day for 1 year
- Leucovorin 10 – 20 mg QID for 1 year
- Corticosteroids 1 mg / kg / day until resolution of CNS infection or Chorioretinitis
PROGNOSIS

• 1\textsuperscript{st} and 2\textsuperscript{nd} trimester - still birth and perinatal deaths secondary to severe fetal infections

• Long term follow up – High risk for ophthalmologic, neurodevelopmental audiological impairment
PREVENTION

• Avoidance to exposure with cat faeces and raw meet.

• Pregnant women advised to wear gloves when carrying cat litter box or gardening and wash hands.
SYMPHILIS

• Causative organism: Treponema pallidum

• Pathogenesis:
  – Introduction of Treponema through an abrasion in the skin or mucous membrane or by Transplacental transmission
  – Transplacental transmission may take place at any time during gestation

• Only 50% are clinically symptomatic at birth
PATHOLOGY

• Enters the fetal blood stream directly
• No chancre and local lymphadenopathy
• Liver flooded with organisms which then penetrate all other organs
• Principals sites of predilection are liver, skin mucus membrane of lips and anus, bones and CNS
• In lungs - Pneumonia alba
DIAGNOSIS

• Earliest sign : “SNUFFLES”
  – Nose becomes abstracted and begins to discharge clear fluid at first and then purulent

• Cutaneous lesions- 2\textsuperscript{nd} week
  – Sparse copper coloured rounded or oval, Iris shaped and circinate desquamative lesions seen in the perioral and perianal regions
  – Palms and soles involved but rashes replaced by diffuse reddening thickening and wrinkling
  – Mucocutaneous junction
  – Lips – Thickened roughened and tend to weep
DIAGNOSIS – CONTD..

- Radiograph of Bones-
  - a. Osteochondritis
  - b. Periostitis
  - c. Epiphyseal dislocation and metaphyseal changes consistent with congenital syphilis
Confirmation by

1. Dark field visualisation of treponema in scraping from any lesions or any body fluids

2. Characteristic bone changes on X-ray

3. Positive serological tests for syphilis.
<table>
<thead>
<tr>
<th>Stages of Syphilis</th>
<th>Drug</th>
<th>Route</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early &lt;1 year duration</td>
<td>Benzathine</td>
<td>IM</td>
<td>2.4 million single dose repeat in one week</td>
</tr>
<tr>
<td>Primary, Secondary or early latent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latent &gt; 1 year duration</td>
<td>Benzathine</td>
<td>IM</td>
<td>2.4 million weekly x 3 weeks</td>
</tr>
<tr>
<td>Neurosyphilis</td>
<td>Aqueous</td>
<td>IV</td>
<td>3 – 4 million every 4 hours x 10 – 14 days</td>
</tr>
<tr>
<td></td>
<td>Procaine</td>
<td>IM</td>
<td>2.4 million daily x 10 – 14 days</td>
</tr>
<tr>
<td></td>
<td>Probenecid</td>
<td></td>
<td>500mg orally QID x 2 weeks</td>
</tr>
</tbody>
</table>

TREATMENT IN PREGNANCY
RECOMMENDED TREATMENT OF THE NEWBORN WITH SYPHILIS

Aqueous Penicillin G

50,000 unit/kg/dose every 12 hours during first 7 days and every 8 hours thereafter for a total of 10 – 14 days
<table>
<thead>
<tr>
<th>S.L.No</th>
<th>Patient Category</th>
<th>Follow – up procedures</th>
</tr>
</thead>
</table>
| 1     | Patients receiving diagnosis of congenital syphilis | • Reagin testing every 2 – 3 months for the first 15 months and then every 6 months  
      |                                               | • Treponemal antibody test after 15 months of age                                       
      |                                               | • Repeat cerebrospinal evaluation 6 months                                               
      |                                               | • Careful developmental evaluation, vision testing, and hearing testing before 3 years   |
| 2     | Patients receiving treatment in utero or at birth | Reagin testing at birth and then every 3 months until test is negative.                
      |                                               | Treponemal antibody test after 15 months of age.                                         |
| 3     | Women receiving treatment for                 | Reagin testing monthly until delivery, then every 6 months until test result is negative |
## COMMONLY USE TERMS DESCRIBING HIV INFECTION STATUS

<table>
<thead>
<tr>
<th>Common – Usage Term</th>
<th>Usual meaning</th>
<th>Technical Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV – Positive</td>
<td>Infected with HIV</td>
<td>Anti-HIV, antibodies in blood</td>
</tr>
<tr>
<td>HIV – Negative</td>
<td>Not infected with HIV</td>
<td>No detectable HIV antibody</td>
</tr>
<tr>
<td>HIV-DNA PCR-Negative</td>
<td>Not infected with HIV older than 1 month</td>
<td>High sensitive testing No HIV DNA detected</td>
</tr>
<tr>
<td>HIV-DNA PCR-Positive</td>
<td>Individual is infected with</td>
<td>HIV-DNA detected</td>
</tr>
</tbody>
</table>
# Laboratoy Evaluation of HIV Exposed Infant

<table>
<thead>
<tr>
<th></th>
<th>HIV-1 Antibody Test</th>
<th>HIV-1 Culture</th>
<th>HIV-1 DNA PCR</th>
<th>HIV-1 RNA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>What it does</strong></td>
<td>Detects the antibody</td>
<td>Detects the replicating HIV</td>
<td>Detects the integrated proviral DNA</td>
<td>Detects Viral RNA</td>
</tr>
<tr>
<td><strong>What Result means</strong></td>
<td>Sero reversion to negative at 12 – 18 confirms negative PCR. Gold standard in infection status</td>
<td>If result is positive infant is infected</td>
<td>If result is positive infected. If result is negative at least twice not infected</td>
<td>Quantitative results reflects HIV-1 activity</td>
</tr>
<tr>
<td><strong>When performed?</strong></td>
<td>Starting at 12 months. Every 6 months until result negative</td>
<td>Replaced by PCR</td>
<td>First 48 hours then 4 – 6 weeks 3 months 6 months</td>
<td>Quantify viral replication and disease activity</td>
</tr>
</tbody>
</table>
Thank You