CONGENITAL INFECTIONS

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CONGENITAL INFECTIONS

DEFINITION

- Congenital infection
  - infection in utero
  - agents cross the placenta
  - agents infect the developing fetus
  - may or may not cause disease

- Perinatal infection
  - agent infects the newborn at time of delivery
CONGENITAL INFECTIONS
DEFINITION

- Neonatal infection
  - Agent infects the newborn during the neonatal period (the first 28 days of life)
- Asymptomatic infection
  - Infected but not affected
AGENTS CAUSING CONGENITAL INFECTIONS ‘TORCHES’

- Toxoplasmosis
- Rubella
- Cytomegalovirus
- Herpes simplex virus (types 1, 2)
- Syphilis
- Hepatitis B virus
- Hepatitis C virus
- HIV
- Varicella zoster virus (VZV)
- Parvovirus B19
- Enterovirus
CONGENITAL INFECTIONS
Epidemiology

PRIMARY MATERNAL INFECTION
– acquires infection during pregnancy
– more likely to cause infection in fetus
– more likely to cause disease in fetus
  – Toxoplasmosis, CMV, Rubella, VZV, Parvovirus
CONGENITAL INFECTIONS
Epidemiology

SECONDARY MATERNAL INFECTION

- reactivation of old infection
- may result in infection in developing fetus
- less likely to cause disease in developing fetus
- Such as CMV
CONGENITAL INFECTIONS
Epidemiology

OVERALL INCIDENCE
- 1% OF ALL BIRTHS
- 40,000 INFECTIONS PER YEAR
CLINICAL MANIFESTATIONS OF CONGENITAL INFECTIONS

- CNS abnormalities
- Eye abnormalities
- Low birth weight
- Bone marrow suppression
- Hepatosplenomegaly
- Bone lesions
- Cardiac defects
- Pneumonia
- Multiorgan system failure
DIAGNOSIS OF CONGENITAL INFECTIONS

- History: maternal, prenatal, perinatal
- Physical examination
- Placental histology
- Cultures - mother, placenta, newborn
- Serology - mother, cord blood, newborn
- PCR – mother, newborn
SEROLOGY AS A DIAGNOSTIC TOOL

- may or may not be helpful
- positive specific IgM in the neonate confirms the diagnosis
- positive specific IgG in the neonate is consistent with maternal infection
- negative maternal IgG rules out maternal infection
Congenital Cytomegalovirus (CMV)
TRANSMISSION OF CMV INFECTION

- Vertical – mother to infant
- Horizontal through salivary, sexual contact, urine, breast milk, blood transfusions
- Horizontal transmission in DCC
  - Transmission rates up to 70% from infected child to caretaker
  - Child to child transmission rates - 50-80%
CMV CONGENITAL INFECTION
Incidence and Outcomes

- Most common intrauterine infection
- 40,000 infected infants born each year
- Most are asymptomatic at birth
Figure 1. Maternal Risk of Transmitting CMV to the Fetus$^{5,12}$

Risk of Intrauterine Transmission

- Primary: 30%–40%
- Prior Immunity/Recurrent: 0.2%–1.0%
Figure 2. Neonatal Outcomes Following Maternal CMV Infection During Pregnancy

- **Primary maternal infection**
- **Primary immunity/recurrent maternal infection**

<table>
<thead>
<tr>
<th></th>
<th>Symptomatic at Birth</th>
<th>Subsequent Sequelae</th>
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</thead>
<tbody>
<tr>
<td>% Babies With Congenital CMV infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18%</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>0%</td>
<td>8%</td>
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</tbody>
</table>
Clinical Manifestations Of Congenital CMV Disease

- Low birth weight
- Rash - petechiae, purpura, ecchymoses
  - Thrombocytopenia
- Hepatosplenomegaly
- Pneumonia
- Jaundice

- CNS involvement
  - Neurodevelopmental delay and cognitive impairment
  - Microcephaly
  - Chorioretinitis
  - Intracranial calcifications
  - Sensorineural hearing loss
DIAGNOSIS OF CMV INFECTION

- **VIRAL ISOLATION FROM URINE OR SALIVA**
- **POSITIVE IgM ANTI-CMV ANTIBODY**
  - 70% positive
- **ACUTE AND CONVALESCENT TITERS**
  - FOURFOLD RISE in CMV IgG SEROLOGY
- **CMV DNA PCR**
- **IN UTERO: CULTURE OR SEROLOGY OF AMNIOTIC FLUID**
TREATMENT and PREVENTION OF CMV INFECTION

- Ganciclovir for severe/disseminated CMV
  - Some benefit in preventing deafness
- CMV immune globulin as adjunctive therapy
  - Investigational
- Early intervention if hearing loss
- Prevention: universal precautions in DCC - infected infants excrete virus in the urine for first 2-3 years of life
- No vaccine yet
CONGENITAL TOXOPLASMOSIS
CONGENITAL TOXOPLASMOsis
Epidemiology

- occurs only when there is primary maternal infection
- source of maternal infection is ingestion of raw meat or contact with cat feces
- 1:1000 to 1:10,000 live births per year in US
- Overall risk of symptomatic infection - 10%
CONGENITAL TOXOPLASMOSIS
Transmission Risk by Trimester

<table>
<thead>
<tr>
<th>Maternal Infection</th>
<th>Newborn</th>
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<tbody>
<tr>
<td>Trimester</td>
<td>infected</td>
</tr>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt;</td>
<td>17%</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt;</td>
<td>25%</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt;</td>
<td>65%</td>
</tr>
</tbody>
</table>
Figure 6-8. Toxoplasma cyst in the placenta of an infected fetus (arrow).
Clinical Presentation of Congenital Toxoplasmosis

- Hydrocephalus
- Microcephaly
- Seizures
- Chorioretinitis
  - blindness
- Diffuse cerebral calcifications
- Jaundice
- Hepatosplenomegaly
SEQUELAE OF CONGENITAL TOXOPLASMOSIS

- Cognitive delay
- Learning disabilities
- Blindness
  - Can cause blindness in adolescent
DIAGNOSIS OF CONGENITAL TOXOPLASMOSIS: Prenatal

- Serology, histology, NAT, imaging
  - Detection of parasite in amniotic fluid or fetal blood
  - *T. gondii* specific IgM or IgA in fetal blood
  - *T. gondii* DNA in amniotic fluid by PCR
  - Serial fetal ultrasound (ie ventricular size)
  - Isolation by mouse inoculation (rare)
DIAGNOSIS OF CONGENITAL TOXOPLASMOSIS: Postnatal

- Ear, eye, and CNS examination
- CT scan of the head
- PCR for DNA detection in WBC, CSF, amniotic fluid
- Toxoplasma IgA or IgM serology
- Persistent Toxo IgG serology >12 mos of age
- Isolation of parasite from placenta, umbilical cord, blood by mouse inoculation
CONGENITAL TOXOPLASMOSIS
DIAGNOSIS

Confirm diagnosis:
- Positive IgM or IgA assay within 1st 6 months of life
- Persistently positive IgG beyond 1 yr of age

Transplacentally acquired IgG disappears by 6 to 12 months of age
Treatment of Congenital Toxoplasmosis

- **Infant**
  - Pyrimethamine plus sulfadiazine
  - Folinic acid supplement
  - Duration of treatment is 1 yr

- **Pregnant woman**
  - If fetal infection is confirmed after 17 wks gestation or if maternal infection acquired in 3rd trimester, treat with pyrimethamine and sulfadiazine
  - Spiramycin for primary infection
Prevention of Congenital Toxoplasmosis

- Identify infection in pregnant woman and treat
- Pregnant women avoid contact with cat litter box
- Pregnant women avoid eating raw meats; cook meats to internal temperature of 150-170 F
- Wash fruits and vegetables
- Wash hands after gardening
- Avoid food contamination with raw meats or soil
CONGENITAL RUBELLA
CONGENITAL RUBELLA SYNDROME (CRS)

- still a problem in spite of vaccination
- 10% of young adults are susceptible
- 25-50% of rubella is asymptomatic
- Reinfection is possible
## RISK OF CONGENITAL RUBELLA INFECTION

<table>
<thead>
<tr>
<th>trimester</th>
<th>infection</th>
<th>symptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>90%</td>
<td>85%</td>
</tr>
<tr>
<td>2nd</td>
<td>50%</td>
<td>20-30%</td>
</tr>
<tr>
<td>3rd</td>
<td>low</td>
<td>5%</td>
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</table>
Clinical Presentation of Congenital Rubella

- Low birth weight
- Cataracts
- Glaucoma
- Retinopathy
- Microphthalmia
- Sensorineural hearing impairment

- CNS: meningoencephalitis, mental retardation
- Bone lesions (osteitis)
- CHD - PDA, PS
- Thrombocytopenia – “blueberry muffin rash”, purpura
- Hepatosplenomegaly
DIAGNOSIS OF CRS

- Rubella specific IgM serum levels
  - also CSF or cord blood
- Viral isolation from lens, stool, urine, blood, CSF, NP
- Rising or stable rubella specific IgG serum levels; four-fold rise
- PCR – blood, CSF
Treatment/Prevention of CRS

- No specific treatment available
- Vaccination with MMR in childhood
  - Antibody induced in 95% after 1 dose
  - 1 dose confers lifelong immunity in 90%
  - 2 dose MMR schedule captures primary vaccine failures
- Knowledge of rubella immune status in child bearing age group
Rubella Exposure during Pregnancy

If pregnant woman has exposure:

- Do serum rubella IgG; if positive, she is immune
- If negative, retest in 4 weeks; if negative again, retest in 6 weeks; if negative, then no rubella infection and no immunity against rubella
- If initial test is negative and follow-up tests are positive, then evidence of acute infection; should be counseled about the risks
CONGENITAL SYPHILIS
CONGENITAL SYPHILIS

- Risk is 70-100% during primary syphilis
- 60-100% risk with secondary syphilis
- 30% with latent syphilis
- If untreated maternal syphilis, 40% of pregnancies result in stillbirths, abortions, perinatal deaths
- Half of infected infants have sequelae, if not treated promptly
Clinical Presentation of Congenital Syphilis

- stillbirth, asymptomatic, or multisystemic
- hepatosplenomegaly, jaundice
- long bone lesions, pseudoparalysis
- low birth weight
- maculopapular rash on soles and palms
- snuffles, mucocutaneous lesions, edema
- lymphadenopathy
- anemia, thrombocytopenia, hemolysis, hemorrhage,
- pneumonitis
LATE MANIFESTATIONS OF CONGENITAL SYPHILIS

Appear after 2 years of age:
- CNS, bones, joints, teeth, skin, eyes
- Hydrocephalus, frontal bossing
- Saddle shape nose, high arched palate
- Short maxilla, Hutchinson’s teeth
- Hearing loss (8th cranial nerve)
- Keratitis
- Perioral fissures
CONGENITAL SYPHILIS DIAGNOSIS

- Maternal and prenatal history
- Physical examination
- Serology - mother and infant
- CSF examination
- Long bone x-rays
- Chest x-ray for pneumonia
Serologic Diagnosis of CS

Screen with non-treponemal tests
- RPR (rapid plasma reagin)
- VDRL (Veneral Disease Research Laboratory)
  - Highly sensitive; low specificity; false positives in collagen vascular disease

Confirm with specific treponemal tests
- FTA-ABS (fluorescent treponemal antibody absorption)
  - FTA-ABS is not 100% specific
- TP-PA (Treponemal pallidum particle agglutination)
  - Treponemal tests remain positive for life
- false positives in other spirochetal diseases
Treatment and Prevention
CONGENITAL SYPHILIS

- Adequate maternal treatment
- Treat infant with IV penicillin
- Follow-up visits and repeat serology
- Treat CNS syphilis
  - Repeat CSF VDRL in 6 months after Rx
  - Retreat if CSF VDRL is still positive at 6 months
CONGENITAL and NEONATAL VARICELLA ZOSTER VIRUS INFECTION
Prevention of Neonatal HSV Infection

- Screen by history during pregnancy and in labor
- Avoid scalp monitors if active lesions
- C-section if ruptured membranes and active cervical/genital lesions
- Treat immediately after birth if primary disease and vaginal delivery; or symptomatic infant
- Obtain surface cultures at 24 hours
  - Rectum, mouth, NP, stool, axillary
  - Treat infant if surface cultures positive
- Caretakers with active lesions avoid mucosal contact (ie kissing baby)
- Continuous rooming-in with mother in private room
HEPATITIS B VIRUS
PERINATAL INFECTION
PERINATAL HBV INFECTION

- HBV is transmitted *perinatally* if the mother is HBsAg positive (i.e. chronic carrier)

- HBV transmitted through **blood/body fluids**
RISK OF PERINATAL HBV

- Up to 90% of babies born to HBsAg positive mothers become chronic carriers
- Most are asymptomatic for the first few decades of life
- Up to 25% of chronic carriers develop chronic liver disease or hepatic cancer
DIAGNOSIS OF PERINATAL HBV INFECTION

Evaluate maternal serology - HBsAg, anti-HBs, HBeAg, Anti HBc

- A chronic carrier is HBsAg positive but never develops anti-HBs antibody
Prevention of Neonatal HBV Infection

- HBV screening (HBsAg) during pregnancy
- Avoid unsafe sex and intravenous drug use
- Universal HBV immunization of infants
  - Vaccinate adolescents if not immunized
- If mother is HBsAg positive or unknown, give HBIG + HBV vaccine to newborn within 12 hours of birth (95% effective)
- HBV vaccine at birth, 1 and 6 months of age
Hepatitis C Infection

- Vertical and horizontal transmission
- Similar to HBV perinatal infection
- Perinatal transmission risk in US is 5%
- Seroprevalence among pregnant women in US is 1-2%
- Asymptomatic infection
- <10% of infants later develop chronic hepatitis and <5% develop cirrhosis
Hepatitis C Infection Diagnosis in Infants

- No specific IgM available
- HCV IgG antibody persists for 12-15 months of age
- HCV qualitative RT-PCR for diagnosis
- If symptomatic, do liver enzymes and quantitative RNA PCR (viral load)
Prevention of HCV Perinatal Infection

- No immunoprophylaxis is available
- No vaccine is available
- Routine screening of pregnant women is not recommended
- Screen high risk pregnant women (IDU, multiple partners, HIV infected)
CONGENITAL VZV INFECTION

- Placental transmission
- Rare because adults have VZV antibodies
- Results in embryopathy
  - Limb atrophy
  - Scarring of the skin
  - CNS and eye abnormalities
NEONATAL VZV INFECTION

IF MOTHER DEVELOPS VARICELLA WITHIN 5 DAYS OF DELIVERY, THE NEWBORN CAN DEVELOP DISSEMINATED DISEASE, INCLUDING PNEUMONIA AND ENCEPHALITIS.

THIS IS ASSOCIATED WITH HIGH MORBIDITY AND MORTALITY.
TREATMENT/PREVENTION OF NEONATAL AND CONGENITAL VARICELLA

- Congenital VZV - no treatment available
- Neonatal VZV – treat with IV acyclovir
- Prevention
  - if mother develops rash within 5 days of delivery
  - give varicella zoster immunoglobulin (VZIG) to newborn
HERPES SIMPLEX VIRUS
NEONATAL HSV INFECTION

- Infection occurs during delivery
- 75% due to HSV-2
- Premature infants are at higher risk
- Intrauterine infection is rare
- Source of postnatal infection - hand, nipple, mouth of caregiver
Risk of HSV Neonatal Infection

- Incidence of infection is low
- < 1% of all pregnant women shed HSV at delivery
- 33-50% transmission risk in primary infection; less than 5% in secondary infection
- > 75% of infants with HSV infection are born to women with no hx or clinical findings of HSV
Neonatal Herpes
Genital Herpes
Genital Herpes
Clinical Presentation of Neonatal HSV Infection

- Occurs in 2nd or 3rd week of life; 3 types.
- **SEM**: Mucocutaneous vesicular lesions of the skin, eye and mucous membrane
- Localized **CNS** disease - seizures; high morbidity and mortality
- **Disseminated** disease - liver, CNS, blood, multiple organ system; high mortality
Diagnosis of Neonatal HSV Infection

Maternal Source

- Maternal acute and convalescent HSV IgG serology
- Maternal cervix – viral culture
- Maternal cervix - giant cells seen on PAP smear
Neonatal HSV Infection
Diagnosis

- **Viral isolation** from newborn >48 hrs old
  - Vesicles, mouth, NP, eyes, urine, blood, stool, rectum, CSF
  - Tzank is not recommended – low sensitivity

- **PCR on CSF** of newborn (negative cx)

- **Rapid Ag detection** (EIA) or DFA (antibody) staining of vesicle scrapings – less sens than cx

- **EEG, CT scan** - temporal lobe focus
Treatment of Neonatal HSV Infection

- Intravenous antivirals (i.e. acyclovir) - add topical antiviral for eye
- Duration is 14 days for skin, eye, mouth and 21 days for CNS
- Early treatment (25% mortality in disseminated disease)
- Most with HSV encephalitis survive but have sequelae
Group B *beta hemolytic streptococcus*
- GBS and *Ecoli* are the 2 most common bacteria in neonatal sepsis

*Enterovirus*

*Parvovirus B19*

*Listeria monocytogenes*
Group B Beta Hemolytic Streptococcal Infection in the Newborn

- Incidence is 0.5 per 1000 live births
- Mortality is 1-2%; higher in premature
- Early onset is < 7 days of age. (EOGBS)
- Late onset is >7 days of age.
- Causes sepsis and meningitis.
- Serotype III is most common in late onset and meningitis
Clinical Presentation of EOGBS Infection

- fever or hypothermia
- nausea, vomiting, diarrhea
- poor feeding
- decreased activity, irritability
- jaundice, hepatomegaly
- respiratory distress
- pallor, mottling
DIAGNOSIS IN EOGBS DISEASE

- SEPSIS WORK-UP
  - blood culture
  - complete blood count and differential
  - urinalysis and urine culture (straight catheterization)
  - chest x-ray
  - CSF examination
RISK FACTORS FOR EOGBS DISEASE

- Maternal vaginal/rectal GBS colonization
- History of previous infant with GBS disease
- GBS bacteruria during pregnancy
- Preterm labor < 37 weeks
- Maternal fever during labor
- Prolonged rupture of membranes ≥ 18 hours prior to delivery
TREATMENT/PREVENTION OF EOGBS DISEASE

Intrapartum antimicrobial prophylaxis (IAP) indicated (prompt use of antibiotics for high risk mother at least 4 hours prior to delivery):
- Previous infant with invasive GBS disease
- GBS bacteruria during pregnancy
- Positive GBS screening culture during pregnancy
- Unknown GBS status plus one of the following:
  - Delivery at <37 weeks
  - Ruptured membranes ≥ 18 hours PTD
  - Intrapartum maternal fever ≥ 100.4°F
TREATMENT/PREVENTION OF EOGBS DISEASE

- Identify high risk mothers during pregnancy and treat prior to delivery
- Treat baby with signs of sepsis with IV ampicillin and gentamicin (synergistic)
  - IV ampicillin given 4 hours prior to delivery
- No vaccine is currently available
NEONATAL ENTEROVIRAL INFECTION

- SEPSIS- LIKE ILLNESS
- LIVER, CNS, CARDIAC, BONE MARROW
- DX BY CSF DNA PCR and VIRAL ISOLATION
- SUPPORTIVE TREATMENT
NEONATAL HUMAN PARVOVIRUS B19 INFECTION

- Fetal infection leads to stillbirths, abortions or hydrodrops fetalis
- Risk of fetal death is 2-6% with greatest risk in 1st trimester
- No specific treatment
- Supportive care
NEONATAL LISTERIA

- Causes stillbirths, abortions, sepsis
- Transmitted vertically or horizontally
- Ascending or intrauterine placental infection
- Sources of Listeria include dairy products, cattle, sheep, soil
- Newborn presents with sepsis, granulomatosis infantisepticum – pale nodules, meningitis
Treatment/Prevention of Neonatal Listeriosis

- Treat newborn with IV antibiotics (ampicillin and gentamicin)
- Pregnant women should avoid eating unpasteurized dairy products, soft cheeses, undercooked meats
HOST DEFENSES IN THE NEWBORN

- Has no IgG at birth except IgG from mother
- Makes IgM; reaches adult levels in 2-3 months
- CMI at adult levels within weeks of birth
- Immature immune system overall