INFECTIONS IN PREGNANCY

CMNRP presentation
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Objectives of the presentation
• Understand the important impact of infections in pregnancy on women and fetuses health
• Review the antenatal management of pregnancy complicated by a TORCH infection
• Review the pregnancy counselling related to TORCH infections

Infections
• Single most common problem encountered by the obstetrician
• Some pose a risk for the mother:
  • Urinary tract infection
  • Endometritis
  • Mastitis
• Some pose a risk for the fetus:
  • Group B streptococcal infection
• Some may cause morbidity for both the mother and the fetus:
  • Human immunodeficiency virus
  • TORCH

TORCH
• Toxoplasmosis
  • Others (Syphilis, Varicella Zoster, Parvovirus B19, Listeriosis, Coxsackie Virus, Hepatitis B)
  • Rubella
  • Cytomegalovirus
  • Herpes

Ultrasound signs of TORCH
• Intracranial calcifications
• Microcephaly
• Hydrocephalus
• Ascites
• Hepatosplenomegaly
• Severe intra-uterine growth restriction (IUGR)

Toxoplasmosis
• Toxoplasma gondii
• Obligate intracellular protozoan parasite
  • Complex life cycle
• 3rd leading cause of food-borne death
• Seroprevalence varies depending on countries:
  • High seroprevalence (> 50%) in France/Africa
  • United States ~ 15% of child-bearing age women
  • 400-4000 cases per year of congenital toxoplasmosis
  • In Canada ~ 20-40% of child-bearing age women...extrapolated data...studies with important biases
  • Up to 59.8% in Nunavik
• Immunity is long lasting
**Toxoplasmosis-Transmission**

- **3 main routes of transmission:**
  - Ingestion of raw or undercooked meats
  - Exposure to oocyst-infected cat feces
  - Vertical transmission (transfusion/organ transplantation)

**Toxoplasmosis-Clinical manifestations**

- Incubation period 5-18 days

- Clinical manifestations:
  - > 90% asymptomatic
  - Influenza-like illness
  - If immunocompromised: encephalitis, pneumonitis, myocarditis, hepatitis

**Toxoplasmosis-Diagnosis**

<table>
<thead>
<tr>
<th>IgM</th>
<th>IgG</th>
<th>Interpretation</th>
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<td>-</td>
<td>-</td>
<td>Absence of infection or extremely recent infection</td>
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<td>+</td>
<td>Old infection (&gt; 1 year ago)</td>
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<td>Recent infection or false-positive result-repeat in 2-3 weeks 4X IgG = recent infection</td>
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- Positive antibody result has to be confirmed by a toxoplasmosis reference laboratory (Montreal, Qc and Palo Alto, CA)
  - IgG avidity:
    - If high: infection at least 5 months before testing

**Toxoplasmosis in pregnancy**

- Highest transmission with primary infection

- 1:8000 pregnancy with clinically significant infection

- Maternal-fetal transmission:
  - 1-4 months following placental colonization by tachyzoites
  - Placenta remains infected for the duration of the pregnancy
  - Act as a reservoir supplying viable organisms to the fetus through the pregnancy
  - Overall risk of transmission 20-50% without treatment
  - Risk of transmission $\downarrow$ with GA but disease severity $\downarrow$ with GA
Toxoplasmosis in pregnancy

<table>
<thead>
<tr>
<th>GA of fetus at maternal seroconversion (weeks)</th>
<th>Risk of congenital infection (%)</th>
<th>Development of clinical signs in the infected offspring (%)</th>
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<td>13</td>
<td>6</td>
<td>61</td>
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<td>26</td>
<td>40</td>
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<td>36</td>
<td>72</td>
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Montoya et al, CID, 2008

Gestational Age at Maternal Seroconversion vs Risk of Toxoplasma gondii Congenital Infection and Development of Clinical Signs in Offspring

Toxoplasmosis-Ultrasounds findings

- Classic triad:
  - Chorioretinitis
  - Hydrocephalus
  - Intracranial calcifications

- Ultrasound signs suggesting in utero infection:
  - Microcephaly
  - Severe IUGR

- > 90% of neonates with congenital infection show no sign of infection at birth
  - If no treatment: risk of chorioretinal disease (up to 85%), major neurological abnormalities, psychomotor impairments

Toxoplasmosis-Chorioretinitis

Toxoplasmosis-Management

- Management of pregnancy:
  - Consultation with Maternal-Fetal Medicine

- Amniocentesis if:
  1. Maternal primary infection is diagnosed
  2. Serologic testing cannot confirm or exclude acute infection
  3. Presence of abnormal ultrasound findings

- PCR of the amniotic fluid to identify Toxoplasma gondii (sensitivity 81-90%, specificity 96-100%)

- Timing:
  - > 18 weeks of gestation
  - > 4 weeks after the time of the suspected infection
  - (avoid false-negative result)

- Cordocentesis should no longer be offered
**Toxoplasmosis-Management**

- Universal screening not recommend in pregnant women at low risk
- Serologic screening should be offered to pregnant women at risk of *Toxoplasma gondii* infection
  - Immunosuppressed
  - HIV
  - Ultrasound findings compatible
- Non-pregnant woman diagnosed with an acute disease should be counselled to wait 6 months before attempting to become pregnant
- Treatment of immunocompetent women with previous infection is not necessary

**Toxoplasmosis-Treatment**

- Decreased the risk of congenital infection and late sequelae
- Prophylaxis (maternal infection, fetus not infected):
  - Spiramycin 1g PO q 8h for the duration of the pregnancy if PCR on amniotic fluid is negative
  - Macrolide
    - Concentrate but not readily cross the placenta
    - Should be started if acute infection is suspected without waiting for the result
- Confirmed fetal infection or highly suspected:
  - Pyrimethamine 50 mg PO q 12h X 2 days followed by 50 mg PO daily + sulfadiazine 75 mg/kg PO followed by 50 mg/kg PO q 12h (max 4g daily) + leucovorin (folic acid) 10-20 mg PO daily
  - Potential of teratogenicity in the 1st trimester

**Toxoplasmosis-Prevention**

- Wear gloves and thoroughly clean hands and nails when handling material potentially contaminated by cat feces (sand, soil, gardening)
- Reduce the exposure risk of pet cats by 1) keeping all cats indoor 2) giving domestic cats only cooked, preserved or dry food
- Change litter and get ride of cat feces (with gloves) on a regular basis (q 24h)
- Disinfect emptied cat litter tray with near-boiling water for 5 minutes before refilling
- Eat only well cooked meat
- Freezing meat to at least -20° C/-4° F kills *T. Gondii* cysts

**Parvovirus B19**

- Single-stranded DNA virus
- Erythema infectiosum (Fifth disease)
- Outbreak usually in the spring
  - q 4-5 years
  - Last up to 6 months
- Lifelong immunity
**Parvovirus-Epidemiology**

- 50-65% of women of reproductive age are immune
- Without known exposure 1-3% of pregnant women will develop serologic evidence of infection
- Women at ↑ risk:
  - Mother of preschool and school-age children
  - Workers at day care centers
  - School teachers

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**Parvovirus-Transmission**

- Transmission through:
  - Respiratory secretions
  - Hand to mouth contact
  - Blood product
  - Transplacental

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**Parvovirus-Clinical manifestations**

- Incubation period 4-14 days (up to 20 days)
- Sx:
  - Most asymptomatic
  - Flu-like syndrome
  - “Slapped-cheeks” facial rash
  - Arthralgia (day 15)
  - In children or adult with hemoglobinopathy, can cause transient aplastic crisis

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**Parvovirus-Fetal effects**

- Transmission rate 17-33%
- Risk of adverse fetal outcome
  - Before 12 weeks: 5-10%
  - 12-20 weeks: ≤ 5%
  - After 20 weeks: ≤ 1%
- Spontaneous abortion, intrauterine fetal demise, anemia, thrombocytopenia
- No congenital anomalies

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**Parvovirus-Fetal effects**

- Hydrops
  - Secondary to:
    1. Fetal anemia: virus crossing the placenta – virus attaches to the i antigen on red blood cells - suppress erythropoiesis - severe anemia – hypoxia – high output cardiac failure
    2. Fetal viral myocarditis - same i antigen on fetal myocardial cells

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**Parvovirus-Management**

- SOGC Guidelines, 2002

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**INFECTIONS IN PREGNANCY**
INFECTIONS IN PREGNANCY

Parvovirus-Management

- Management of hydrops
  - Tertiary care center
  - MFM specialist
  - Cordocentesis...mortality 11%
    - Fetal hemoglobin, reticulocyte count
    - +/- intrauterine transfusion
  - Vs expectant management...mortality 26-30%
  - If term or near-term: consider delivery

  *Due to myocarditis: degree of hydrops may not correspond to the Hb level*

Parvovirus-Diagnosis

- Maternal Dx:
  - IgM IgG Interpretation
    | IgM | IgG | Interpretation |
    |-----|-----|----------------|
    | -   | -   | Susceptible    |
    | -   | +   | Prior immunity |
    | +   | -   | Acute infection (within previous 7 days) |
    | +   | +   | Subacute infection (> 7 days and < 120 days) |

- Dx of fetal infection:
  - PCR amniotic fluid: not required for all suspected or confirmed maternal infections
  - False negative before 22 weeks (fetus does not make its own IgM)

Parvovirus-Prognosis

- Usually excellent long-term prognosis
- Possibility of delayed psychomotor development
  *Nagel et al. Obst Gynecol, 2007*
- 3rd trimester ultrasound recommended: growth and cerebral anatomy
- Long-term surveillance for neurologic problems

Syphilis

- *Treponema pallidum*-spirochete
  - Incubation 21 days (10-90 days)

Syphilis-Epidemiology

- 80% of women with syphilis are in the reproductive age group
- Congenital syphilis:
  - 10.1 cases per 100,000 live-born infants
  *Center for Disease Control 2008*
- Risk factor for syphilis in pregnancy:
  - Poverty
  - Use of illicit drugs
  - STI
  - Sex worker
  - Living in an area with high syphilis morbidity
  - HIV
Syphilis - Transmission

- Sexual contact
  - 50-60% transmission after a single exposure to an infected individual with early syphilis
- Vertical

Syphilis - Clinical manifestations

- Different stages:
  - Primary syphilis
    - Chronic, painless ulcer with raised/indurated margins
    - Regional lymphadenopathy (often bilateral)
    - Often missed in women
  - Secondary syphilis
    - Systemic process; fever, lymphadenopathy
    - Generalized maculopapular rash involving palms/soles/mucous membranes
    - Condyloma lata
  - Latent syphilis
    - Asymptomatic infection
    - Positive serology/negative physical exam
    - Early (within 1 year) vs late
  - Tertiary syphilis
    - Involves central nervous system, cardiovascular system, skin/subcutaneous tissues
      - 1/3 if untreated patient

Syphilis - Screening

- 1st prenatal visit
- Repeat in high risk group: 28 weeks and in labor
- 2 type of serologic testing:
  - Treponemal antibody tests: FTA-ABS, TPPA, MHA-TP
  - Nontreponemal antibody tests: VDRL, RPR
- Dark-field microscope or direct fluorescence antibody tests of lesion exudates or tissue

Syphilis - Diagnosis

- Usual algorithm in pregnancy:
  - VDRL
    - If positive: confirmation with a treponemal test

Syphilis - Perinatal transmission

- Frequency of transmission increases as gestation advance but severity of infection decreases
- Frequency of transmission decrease with stage of disease:
  - Primary or secondary: 50%-50% perinatal death
  - Early latent: 40%-20% perinatal death
  - Late latent: 10%
  - Tertiary: 10%
  - 70-100% of infants born to untreated mother will be infected compared to 1-2% born from adequately treated mother

Sheffield et al, AJOG 2002
Syphilis-Congenital syphilis

- Fetal:
  - Miscarriage
  - Stillbirth
  - IUGR
  - Prematurity
  - Hepatosplenomegaly

- Placental findings:
  - Hydrops placentalis
  - Chronic villitis
  - Perivillous fibrous proliferation
  - Necrotizing fusinitis
  - Acute chorioamnionitis

Syphilis-Congenital syphilis

- EARLY congenital syphilis:
  - 2/3 asymptomatic at birth
  - Development of active disease in 3-8 weeks
  - Maculopapular rash-desquamation/vesicle
  - Snuffles (flu-like syndrome with nasal discharge)
  - Mucous patch in the oral pharyngeal cavity
  - Hepatosplenomegaly/jaundice
  - Lymphadenopathy
  - Pseudoparalysis of Parrot due to osteochondritis
  - Chorioretinitis
  - Iritis

  - If untreated or incompletely treated: will progress to LATE CONGENITAL SYPHILIS

Syphilis-Congenital syphilis

- LATE congenital syphilis:
  - Hutchinson teeth
  - Mulberry molars
  - Interstitial keratitis
  - Deafness
  - Saddle nose
  - Rhagades
  - Saber shins
  - Neurologic manifestations (MR, hydrocephalus, general paresis, optic nerve atrophy, Clutton joint)

Syphilis-Maternal tx

- Penicillin-GOLD STANDARD
  - Effective to treat the mother, prevent fetal transmission and treat infected fetus
  - Optimal dose still under debate
  - General consensus:
    - Primary, secondary and early latent syphilis: benzathine penicillin G 2.4 million units IM X 1
    - Late latent syphilis or latent syphilis of unknown duration: benzathine penicillin G 7.2 million units total (3 doses of benzathine penicillin G 2.4 million units IM q week)

  - Walker, Cochrane Collaboration, 2010
  - CDC 2006

  - If allergy: desensitization followed by penicillin tx

Syphilis-Maternal tx

- Jarisch-Herxheimer reaction
  - Following the tx with penicillin
  - Acute febrile reaction
    - Headache-myalgia-rash-hypotension
    - Release of large amounts of treponemal lipopolysaccharide from dying spirochetes and an increased in circulatory cytokines levels
    - May be more common in HIV-positive women
    - Supportive care
    - May precipitate preterm labor and nonreassuring fetal heart rate tracings (30%)

Varicella-Epidemiology

- Highly contagious DNA virus (herpes family)

- Common childhood disease
  - Usually mild infection in child
  - Mortality rate 0.4/million in US

- More 90% antenatal population are seropositive for VZV IgG antibody

- Primary maternal VZV infection
  - 2-3/1000 pregnancies
  - 700-1050 cases/year in Canada
### Varicella-Transmission
- Respiratory droplets
- Direct personal contact with vesicular fluid

### Varicella-Clinical manifestations
- Incubation period 10-21 days
- Disease infectious 48 hours before the rash appears and continuous to be infectious until the vesicles crust over
- Primary infection
  - Fever, malaise
  - Maculopapular disseminated pruritic rash

### Varicella-Exposure
- Significant exposure:
  - Direct contact ≥ 1 hour with an infectious person while indoors
  - Hospital contact:
    - Sharing the same room
    - Prolonged, direct, face-to-face contact with an infectious person

### Varicella-Management
- Antenatal varicella immunity status should be documented:
  - History of previous infection
  - Vaccination
  - VZV serology
- Non-immune pregnant women should be aware of the risk
- Possible exposure to varicella in a pregnant woman with unknown immune status:
  - Serum testing
    - If negative or unavailable within 96 hours: VZIG

### Varicella-Maternal impact
- Mortality rate higher compared to general population
  - Due to respiratory complications
- 5-10% will develop pneumonitis
  - Risk factors: cigarette smoking and more 100 skin lesions
  - Develop day 4 or later
  - High rate of intubation and mechanical ventilation

### Varicella-Fetal impact
- Congenital
  - Maternal infection during the 1st half of pregnancy-transplacental infection
    - 0.4% under 13 weeks
    - 2% between 13-20 weeks
### Varicella-Ultrasound findings
- Asymmetric limb shortening or malformations
- Chest wall malformations
- Intestinal and hepatic echogenic foci
- IUGR
- Polyhydramnios
- Fetal hydrops
- Fetal demise
- Cerebral anomalies:
  - Ventriculomegaly
  - Hydrocephalus
  - Microcephaly with polymicrogyria
  - Porencephaly
- Ocular lesions (not seen on ultrasound: congenital cataract and microphthalmos)

### Varicella-Neonatal impact
- Peripartum exposure/neonatal infection:
  - Sx of maternal infection less than 5 days before delivery to 2 days after
  - Fulminant infection
  - Potential of disseminated visceral and central nervous system disease
  - Commonly fatal
- 30-40% of infected newborn if VZV immunoglobulin given to the mother
  - Number of complications reduced

### Varicella-Treatment of exposed women
- VZ immunoglobulin
  - ↓ infection rate if administered within 72-96 hours after exposure
  - Protection last 3 weeks
  - 125 units / 1 kg IM (max 625 units)
- PRINCIPAL INDICATION: susceptible pregnant women to reduced maternal risks
  - ↓ risk of fetal infection:
    - 1373 women with varicella
    - 9 cases of congenital varicella (maternal varicella before 20 weeks)
    - No case reported in 97 women who received VZIG
- Enders et al, Lancet, 1994
- Adverse reactions:
  - Local discomfort at the injection site - 1%
  - GI Sx, malaise, headache, rash, respiratory Sx - 0.2%
  - Angioneurotic oedema, anaphylactic shock - <0.1%
  - Patient consent required-blood product

### Varicella-Treatment of infected women
- Significant varicella infection:
  - Acyclovir 800 mg PO 5 times daily
  - Severe complications: iv acyclovir 15 mg/kg q 8h X 5-10 days
  - Ideally started within 24-72 h of the onset of the rash
  - Consider admission to the hospital
- Acyclovir:
  - Inhibit replication of human herpes virus including VZV
  - Crosses the placenta-can be found in fetal tissues, cord blood and amniotic fluid
  - No adverse event related to pregnancy
  - Not a prophylaxis to exposed women during pregnancy

### Varicella-Vaccine
- Attenuated live-virus vaccine (Varivax)
  - Recommended for all non-immune woman in pre-pregnancy or post-partum
  - Not recommended during pregnancy
  - 58 vaccine-exposed pregnancies
  - No case of congenital varicella syndrome
  - No other congenital malformation
  - Termination of pregnancy is not recommended if inadvertent vaccination during pregnancy

### Rubella
- RNA virus
- 4/100 000 per year
- 10-20% of US women remain susceptible to rubella
- Transmission by respiratory droplets
- Lifelong immunity
Rubella-Clinical manifestations

- Incubation period 12-23 days
  - Infectious period from 7 days before to 5-7 days after rash onset
- Asymptomatic in 25-50% of cases
- Rash: begins on the face and spreads to trunk and extremities
  - Resolve within 3 days in the same order in which it appeared
- Polyarthritis-polyarthralgia 60-70% adolescent and adult women
  - 1 week after the rash

Rubella-Diagnosis

- Diagnosis of rubella infection:
  - Fourfold rise in rubella IgG titer between acute and convalescent serum specimens
  - Positive serologic testing test for rubella-specific IgM antibody
  - Positive rubella culture (clinical specimen from the patient)
- Serologies:
  - Ideally within 7-10 days after rash onset
  - Repeat 2-3 weeks later

Rubella-Congenital Rubella Syndrome

- Hematogenous transmission through the placenta
- Fetal infection:
  - 1st trimester: 80%
  - 2nd trimester: 25%
  - 27-30 weeks: 35%
  - > 36 weeks: 100%
- Risk of congenital defect:
  - < 11 weeks: 90%
  - 11-12 weeks: 33%
  - 13-14 weeks: 11%
  - 15-16 weeks: 24%
  - 16-20 weeks: < 1%
  - > 20 weeks: 0%

Rubella-Neonatal manifestations

- Audiologic anomalies (60-75%)
  - Sensorineural deafness
- Cardiac defect (10-20%)
  - Supravalvular pulmonary stenosis
  - Patent ductus arteriosus
  - Ventricular septal defect
- Central nervous system (10-25%)
  - Mental retardation
  - Microcephaly
  - Meningoencephalitis
Rubella-Neonatal manifestations

- Ophthalmic defects (10-25%)
  - Retinopathy
  - Cataracts
  - Microphthalmia
  - Pigmentary and congenital glaucoma
- Others
  - Thrombocytopenia
  - Hepatosplenomegaly
  - Radiolucent bone disease
  - Characteristic purpura (Blueberry muffin appearance)

Rubella-Congenital Rubella Syndrome

- Guarded prognosis:
  - 50% of child will need to attend schools for hearing-impaired
  - 25% will need some special schooling
  - 25% will be able to attend regular school
- TOP should be offered

Rubella-Treatment

- Supportive treatment
- Immunoglobulins?
  - No data to support the use to decrease the fetal response to disease
  - CDC recommend limiting its use to women with known rubella exposure who decline pregnancy termination

Rubella-Vaccine

- Vaccine:
  - Live attenuated
  - Potential to cross the placenta and infect the fetus
  - NO report of Congenital Rubella Syndrome in the offspring of women inadvertently vaccinated during early pregnancy
  - Termination of pregnancy NOT RECOMMENDED
  - Potential risk → women are advised not to become pregnant for a period of 28 days after immunization
  - Can be given postpartum to women who breastfeed

Rubella-Prevention

1. Universal infant immunization to decrease the circulation of the virus
2. Using MMR vaccine in catch-up campaigns
3. Ensuring that girls are immune before they reach child-bearing age
4. Screening to determine the antibody status of all pregnant women
5. Postpartum immunization
6. Screening for immunity and vaccination, if necessary, of all health care personnel
7. Immunize all immigrant

INFECTIONS IN PREGNANCY

Rubella-Neonatal manifestations

- Late manifestations:
  - Diabetes mellitus
  - Thyroiditis
  - Growth hormone deficit
  - Behavioural disorder
Cytomegalovirus infection
- DNA virus (herpesvirus family)
- Remain latent in host cells after the initial infection
- Several strains of CMV
- Secondary infection:
  - Reactivation of an endogenous latent virus (most frequent)
  - Reinfection with a new viral strain
- Not highly contagious; require close personal contact

CMV-Epidemiology in pregnancy
- Most common cause of intrauterine infection
  - 0.2-2.2% live births
  - Common cause of sensorineural hearing loss and mental retardation
- Seroconversion in 1-4% of pregnancies
  - Low socioeconomic status or poor personal hygiene

CMV-Transmission
- Transmission:
  - Contaminated saliva/urine
  - Sexual contact
  - Transfusion of infected blood/transplantation of infected organ
- Vertical:
  - Transplacental: more important consequences
  - During delivery through contaminated genital tract secretion
  - Breastfeeding

CMV-Clinical manifestations
- Incubation period: 28-60 days
- Asymptomatic vs mild symptoms of flu-like illness in immunocompetent patients

CMV-Congenital infection
- Probability of intrauterine transmission
  - Following primary infection: 30-40%
  - Congenitally infected infants:
    - 10-15% will have Sx at birth
    - IUGR, microcephaly, hepatosplenomegaly, petechia, jaundice, chorioretinitis, thrombocytopenia, anemia
    - 20-30% of mortality mostly related to DIC, hepatic dysfunction, bacterial superinfection
    - 80% of survivors have major morbidity
    - 85-90% will NOT have Sx at birth
    - 5-15% of them will develop sequelae: sensorineural hearing loss, delay in psychomotor development, visual impairment

CMV-Congenital infection
- Probability of intrauterine transmission
  - Following secondary infection: 1%
  - Most do not have Sx at birth
  - 5-10% risk of long term sequelae (hearing loss, visual deficits, mild developmental delays)
INFECTIONS IN PREGNANCY

**CMV-Prenatal Dx**

- **Diagnosis of a primary infection in pregnancy:**
  - Appearance of CMV-specific IgG antibody in a previously seronegative woman OR
  - Detection of specific IgM antibody associated with low IgG avidity

- **Recurrent infection:**
  - IgG without IgM antibodies before pregnancy AND
  - Significant rise of IgG titer (X 4) with or without the presence of IgM antibodies AND
  - High IgG avidity

**CMV-Dx of fetal infection**

- Ultrasonographic findings:
  - IUGR
  - Cerebral ventriculomegaly
  - Microcephaly
  - Intracranial calcifications
  - Ascites/pleural effusion
  - Hydrops fetalis
  - Oligohydramnios/polyhydramnios
  - Hyperechogenic bowel
  - Liver calcifications

  **Helpful! But not diagnostic**
  Observed < 25% of infected fetuses

**CMV-Prognostic markers**

- Major limitations:
  - Positive amniocentesis result do not discriminate between infants who will have Sx at birth and those who will not
  - Severity of sonographic anomalies can help
  - But absence of anomalies does not guarantee a normal outcome

- **If fetal infection:**
  - Ultrasounds q 2-4 weeks
  - Role of fetal MRI?
  - Role of quantitative CMV DNA in the amniotic fluid-to be determined...

  Goebelbau et al, J Clin Microbiol, 2009

**CMV-Prenatal tx**

- **No effective therapy**

- **Multicenter prospective cohort study**
  - N=157
  - CMV+ in the amniotic fluid
  - 5/157 received IV CMV hyperimmune globulin (200 U/kg)
  - 102 had intrauterine growth restriction (IUGR) at birth
  - 16 had abnormal cranial bone development
  - 11 had brain calcifications
  - 7 had liver calcifications

- **Prevention group**
  - 37 received IV CMV hyperimmune globulin (200 U/kg)
  - 100 had IUGR at birth
  - 6 did not receive immunoglobulins
  - 37 had intrauterine growth restriction
  - 14 had abnormal cranial bone development
  - 12 had liver calcifications
  - 7 had brain calcifications

- **Termination of pregnancy should be discussed**


**CMV-Prenatal Dx**

- **CMV isolation in the amniotic fluid = GOLD STANDARD**
  - High sensitivity and specificity
  - Culture/PCR
  - At least 7 weeks after the onset of maternal infection
  - After 21 weeks of gestation
  - Result in 16-24 hours

  **No consensus whether or not it is recommended in recurrent infection…fetal risk low but several cases with severe sequelae reported in the literature…may be considered**

**CMV-Prenatal Dx**

- **Diagnosis of a primary infection in pregnancy:**
  - Appearance of CMV-specific IgG antibody in a previou sly seronegative women OR
  - Detection of specific IgM antibody associated with low IgG avidity

SOGC Guidelines, 2010
CMV-Postnatal tx

- Ganciclovir/valganciclovir treatment of neonates?
- Hearing improvement

Stronati et al, Curr Drug Metab, 2012

CMV-Prevention

- CMV-negative blood products when transfusing pregnant women or fetuses
- Careful hand washing techniques after handling infant diapers and toys

CMV-Screening

- Routine screening is still a debated issue
- Should be used only in women who develop influenza-like Sx during pregnancy or following detection of sonographic findings suggestive of CMV
- Seronegative health care and child care worker may be offered serologic monitoring during pregnancy

CMV-Prevention

- CMV-negative blood products when transfusing pregnant women or fetuses
- Careful hand washing techniques after handling infant diapers and toys

Herpes Simplex Virus

- Raising prevalence of HSV genital infection
- HSV-2 seropositivity in Canadian women 7.1-28.1%

Patrick et al, Sex Trans Disease, 2001

- Neonatal HSV:
  - 1/17 000 in Canada
  - 1/3 500 in US

HSV-Vertical transmission

- Congenital infection (1-5%)
  - In utero acquisition
- Neonatal HSV
  - Acquisition of infection through exposure to the virus from maternal genital tract (85%)
  - Iatrogenic/familial transmission after birth from oral/skin lesion (10-15%)
  - Manifestation > 48 hours after delivery

HSV-Diagnosis

- Viral culture = Gold standard
  - Vesicular fluid ideally
- HSV antibodies
  - IgG assays specific to the respective glycoprotein G of each type
  - Role in making the diagnosis of genital herpes is controversial
HSV-Antenatal management

- Important to make the distinction whether the infection is primary, 1st episode non-primary or recurrent disease

- Primary infection in pregnancy:
  - Risk greatest in the 3rd trimester
  - Infants delivered in the absence of protective passive IgG from the mother
  - 30-50% risk of neonatal infection
  - Caesarean section recommended

  1st-2nd trimester
  - Rare cases of in utero infection
  - Ultrasound features: microcephaly, IUGR, hepatosplenomegaly, intrauterine fetal demise

- Recurrent HSV
  - If lesion at the time of vaginal birth: 2-5% risk of neonatal infection
  - If no lesion: 0.02-0.05% risk of neonatal infection (asymptomatic shedding)
  - Suppressive treatment recommended at 36 weeks’ gestation
    - ↓ risk of viral shedding
    - ↓ clinical herpes lesions
    - ↓ need for C-section at time of labour

  [Brock et al, JAMA 1990]

  - Acyclovir 400 mg PO tid or 200 mg PO qid
  - Valacyclovir 500 mg PO bid

  □ Consider earlier start if risk of preterm birth
  □ Caesarean section if lesion or prodrome at time of delivery
  - Ideally within 4 hours of ROM

HSV-Antenatal management

- PPROM
  - Suppressive treatment
  - Breastfeeding contraindicated ONLY if active lesion on the breast

HSV-Neonatal manifestations

- 3 levels of the disease:
  1. Skin, eyes and mouth infection
     - Rarely fatal
     - Up to 38% may have neurologic sequelae
     - Whitley et al, J Infectious Disease, 1988
  2. Central nervous system infection
     - Encephalitis +/- skin, eyes and mouth infection
  3. Disseminated disease
     - 90% mortality if untreated

  [AAP 1997]

- If suspicion: pediatric consultation highly recommended
  - Intravenous acyclovir ASAP (CPS Guidelines 2006)
  - ↓ mortality (58% → 16%) and neurological sequelae
  - Whitley et al, NEJM 1991

HSV-Prevention

- Benefit to prevent neonatal disease not proven for routine HSV serology in pregnancy

- Type-specific HSV discordant couple (pregnant women seronegative and partner positive)
  - Advice about the risk of transmission
  - Abstinence is the most effective strategy to prevent HSV acquisition
  - ...antiviral suppression to the partner with genital HSV (in conjunction with condom use)...

Conclusion

- TORCH infection can be potentially devastating for the fetus and the newborn

- Importance of early detection in order to administer the appropriate treatment
Thank you

References

- Creasy and Resnik, Maternal-Fetal Medicine, Principles and Practice, Sixth Edition, 2009
- SOGC Guidelines