M&M
Sexually Transmitted Diseases Overview

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Prenatal Testing

- History and Physical
  - Identify Risk Factors

- Testing at first prenatal visit
  - Gonorrhea, Chlamydia, HIV, Syphilis

- Repeat testing in third trimester for those at risk
Chlamydia

- Caused by Chlamydia Trachomatis
  - Obligate intracellular
  - 15 immunotypes
    - D-K : Genital tract infections
    - L1-L3 : lymphogranuloma venereum (genital ulcer disease)
      - Erythromycin base 500mg qid x 21 days
  - Risk Factors
Chlamydia

- Incubation period 1-3 weeks
- Symptoms
  - Infection of the genital tract
  - 50% ♂, 80% ♀ are asymptomatic
  - Mucopurulent cervicitis in ♀ or urethritis in ♂
- Diagnosis
  - Cell culture, Direct fluorescent antibody testing, DNA probe, PCR
Treatment

- Azithromycin 1g PO in a single dose
- Treatment of partner
- No intercourse until completion of treatment
- Repeat testing 3 wks after treatment completion
**Chlamydia**

- *Chlamydophila* (formerly *Chlamydia*) *psittaci* (Psittacosis, Ornithosis)

- *Chlamydophila* (formerly *Chlamydia*) *pneumoniae*

- *Chlamydia trachomatis*
Incubation period

Chlamydial illness IP is variable, depending on type of infection, but usually is at least 1 week.
Chlamydia trachomatis

Clinical Manifestations

Range of clinical manifestations including:

- Neonatal conjunctivitis
- Trachoma
- Pneumonia in young infants
Neonatal conjunctivitis

- Characterized by *ocular congestion*, *edema*, and *discharge* developing a few days to several weeks after birth
- Lasts 1 - 2 wks
- In contrast to trachoma, scars and pannus formation are rare
Neonatal conjunctivitis

Difference from adult type?

Characterized by lack of follicular response, mucopurulent discharge, and propensity to form membranes on palpebral conjunctiva.
Pneumonia
In young infants

→ Afebrile illness of insidious onset occurring between 2 - 19 wks after birth

→ Repetitive staccato cough, tachypnea, and rales are characteristic but not always present

→ CXR: Hyperinflation +/- infiltrates

→ Can be severe
Epidemiology

- Most common reportable ST infection in US
- High rates: Sexually active adolescents & young adults
- Across 27 states, median prevalence among 15-24 y♀-screened in prenatal clinics was 7% (2-20%)
Epidemiology

Oculogenital serovars can be transmitted to newborns:
- 50% born vaginally acquire infection
- & in some infants delivered by C/S
Epidemiology

• Risks:
  ➡ Conjunctivitis 25 - 50%
  ➡ Pneumonia 5 - 20%

• Most commonly infected anatomic site
  ➡ Nasopharynx

• Asymptomatic infection of nasopharynx, conjunctivae, vagina, and rectum can be acquired at birth
Epidemiology

• Nasopharyngeal Cx may remain (+) for 28 months, but spontaneous resolution of vaginal & rectal infection occurs by 16-18 months of age

• Not known to be communicable among infants & children
Diagnostic Tests

• Definitive: Isolating organism in tissue culture and by nucleic acid amplification (NAA) testing in selective circumstances

• Since obligate intracellular → culture specimens must contain epithelial cells, not just exudate
Diagnostic Tests

• Non-culture tests, including EIA, DFA tests, DNA probe tests, and NAA tests, are useful for evaluating:
  → Urethral swab specimens from ♂
  → Endocervical swab specimens from ♀
  → Conjunctival secretion specimens from infants

• NAA tests are useful for evaluating urine specimens from either sex
Diagnostic Tests

• Available NAA tests:
  → PCR (Amplicor)
  → Transcription-mediated amplification (TMA) test (Aptima Combo 2)
  → Strand-displacement amplification (SDA) test (Probe Tec)

• More sensitive than cell culture, DNA probe, direct fluorescent antibody (DFA) tests, or enzyme immunoassays (EIAs), but variable specificity
Diagnostic Tests

If false (+) test (+ DFA test, EIA, DNA probe test, or NAA test )

⇒ Results should be verified by:

1. Culture
2. Second non-culture test different from the first or use of a blocking antibody (e.g., Chlamydiazyme)
When evaluating a child for possible sexual abuse, **Culture of organism** is only acceptable diagnostic test in certain legal jurisdictions.

- If not available, some experts support using NAA testing if a positive result can be verified by another NAA test.
- The EIA and DFA test should not be used in infants because of low sensitivity and specificity.
Diagnostic Tests

- S. antibody concentrations are difficult to determine.
- In children with pneumonia, an acute serum titer of *C. trachomatis*-specific (Ig) M of 1:32 is diagnostic.
- However, most available serologic tests in US are based on EIAs and might not provide quantitative "titer-based" result.
Diagnostic Tests

- Diagnosis of genitourinary chlamydial disease in a child, adolescent, or adult should prompt investigation for other ST infections, including syphilis, gonorrhea, hepatitis B and HIV

- In the case of an infant → Evaluation of mother is advisable
Treatment Chlamydial Conjunctivitis

- Oral erythromycin base or ethylsuccinate (50 mg/kg/day in 4 divided doses) X 14 days

- Oral sulfonamides may be used after the immediate neonatal period for infants who do not tolerate erythromycin

- Topical Ax of conjunctivitis is ineffective & unnecessary

- Because erythromycin efficacy Ax is ~ 80%, 2nd course may be required, and f/u is recommended
Association?

- Infantile hypertrophic pyloric stenosis (IHPS) reported in infants < 6 wks
- Risk of IHPS with other macrolides (e.g., azithromycin) is unknown
- Because confirmation still require additional investigation and alternative therapies are not as well studied $\rightarrow$ AAP continues to recommend use of erythromycin
  - However, inform parents!
Treatment Chlamydial Pneumonia

- Oral azithromycin
  (20 mg/kg once daily X 3 days)
- Erythromycin base or ethylsuccinate
  (50 mg/kg/ day in 4 divided doses) X14 days
- Oral sulfonamide is an alternative for infants who do not tolerate macrolides
Treatment
Chlamydial Pneumonia

- Can be simply avoided by screening pregnant women to detect and treat *C trachomatis* infection before delivery

- A diagnosis of *C trachomatis* infection in an infant should prompt treatment of mother and her sexual partner(s)
Treatment
Chlamydial Pneumonia

• Infants born to mothers known to have untreated chlamydial infection are at high risk of infection

• However, prophylactic antimicrobial treatment is not indicated, because the efficacy of such treatment is unknown
Treatment
Chlamydial Pneumonia

- Infants should be monitored clinically to ensure appropriate treatment if infection develops.
- If adequate follow-up cannot be ensured, some experts recommend that preemptive therapy be considered.
The recommended topical prophylaxis with silver nitrate, erythromycin, or tetracycline for all newborn infants for prevention of gonococcal ophthalmia will **not prevent** neonatal chlamydial conjunctivitis or extraocular infection.

**YET** the chances of developing it was found to be rare.
Gonococcal Infections
Gonorrhea

- Caused by Neisseria gonorrhoeae
- Risk Factors
- Incubation period 1-14 days after sexual contact
- Symptoms: skin and mucous membranes
  - More often symptomatic
  - Urethritis, cervicitis, salpingitis, PID, proctitis, conjunctivitis, pharyngitis
Gonorrhea

- Diagnosis
  - Gram Stain
    - Highly sensitive for urethral infections
      - Intracellular gram negative diplococci in pairs within leukocytes
  - Culture
    - Specific culture of a swab from the site of infection
  - PCR testing
Treatment

– Ceftriaxone 125mg IM in a single dose

– Cefixime 400mg PO in a single dose

– PLUS treatment for Chlamydia

– Partner treatment
Disseminated Gonococcal Infection

• Symptoms:
  – Rash, fever, arthralgias, migratory polyarthritis, septic arthritis, endocarditis
  – Susceptibility increased if primary mucosal infection occurred during menstruation or pregnancy

• Treatment
  – Ceftriaxone 1g IM or IV q 24 hours
    • Continue until symptoms have resolved for 24-48 hours then switch to PO cefixime 400mg po bid
Etiology

*Neisseria gonorrhoeae* is
gram (-)
Oxidase (+)
diplococcus
Clinical Manifestations

In children, gonococcal infections occur in 3 distinct age groups
Clinical Manifestations

1 Newborns

• Infection *usually involves eyes*
Clinical Manifestations

Newborns

Other include:

- Scalp abscess (which can be associated with fetal monitoring)
- Vaginitis
- And disseminated disease with bacteremia, arthritis, or meningitis
Clinical Manifestations

- May occur in genital tract and almost always is sexually transmitted
- Vaginitis is most common manifestation
- Gonococcal urethritis in prepubertal ♂ is uncommon
- Anorectal and tonsillopharyngeal infection also can occur in prepubertal children
Clinical Manifestations

Sexually active adolescents

- As in adults, gonococcal infection in ♀ often is asymptomatic.
- Common clinical syndromes are vaginitis, urethritis, endocervicitis, and salpingitis.
Clinical Manifestations

Sexually active adolescents

• In ♂, infection often is symptomatic, and the primary site is the urethra

• Infection of rectum and pharynx can occur alone or with genitourinary tract infection in either sex

• Rectal and pharyngeal infections often are asymptomatic
Epidemiology

• Occur only in humans

• Source of organism is exudate & secretions from infected mucosal surfaces

• Communicable as long as person harbors organism

• Transmission: Intimate contact, such as sexual acts, parturition, and rarely, household exposure in prepubertal children
Epidemiology

• Sexual abuse should be considered strongly when genital, rectal, or pharyngeal colonization or infection are diagnosed in prepubertal children beyond newborn period

• In 2004, there were 330,132 new cases reported in US

• Reported incidence of infection is highest in ♀ 15 - 19 y and in ♂ 20 - 24 y

• Concurrent infection with *Chlamydia trachomatis* is common
Gonococcal Isolate Surveillance Project (GISP) — % of \textit{N. gonorrhoeae} isolates obtained from homosexual attending STD clinics, 2003–2006
Diagnostic Tests

• Microscopic examination of Gram-stained smears of exudate from eyes, vagina of prepubertal girls, male urethra, skin lesions, synovial fluid

• When clinically warranted, CSF may be useful in the **initial evaluation**

• Identification of gram (-) intracellular diplococci in these smears can be helpful
Diagnostic Tests

• Can be cultured from normally sterile sites, such as blood, CSF, or synovial fluid, using nonselective chocolate agar

• Selective media that inhibit normal flora and nonpathogenic *Neisseria* organisms are used for culture from nonsterile sites, such as the cervix, vagina, rectum, urethra, and pharynx
Diagnostic Tests

- Caution when interpreting the significance of the isolation of *Neisseria* organisms, because it can be confused with other *Neisseria* species that colonize the genitourinary tract or pharynx.

- At least 2 confirmatory bacteriologic tests involving different principles (e.g., biochemical, enzyme substrate, or serologic) should be performed.
Diagnostic Tests

- Nucleic acid amplification (NAA) tests are highly sensitive and specific when used on urethral, endocervical swab, and urine specimens.

- Include PCR, transcription-mediated amplification (TMA), and strand-displacement assays.
Sexual Abuse
Legal Aspect

- In all prepubertal children beyond newborn period and in nonsexually active adolescents, sexual abuse must be considered unless proven otherwise.
- Genital, rectal, and pharyngeal secretion cultures.
- All gonococcal isolates from Pt should be preserved.
Sexual Abuse
Legal Aspect

• Nonculture gonococcal tests including Gram stain, DNA probes, enzyme immunoassays, or NAA testing of oropharyngeal, rectal, or genital tract specimens in children cannot be relied on for diagnosis because false (+) results can occur

• If culture is not available, some experts support use of NAA testing on vaginal swabs when (+) result can be verified by a different NAA test
Other sexually transmitted diseases, such as *C. trachomatis* infection, syphilis, hepatitis B virus infection, and HIV should be tested for.
Treatment

• Because of penicillin- and tetracycline-resistant *N gonorrhoeae* prevalence, extended-spectrum cephalosporin (e.g., ceftriaxone, cefixime) is recommended as initial therapy for children.

• Occasional isolates of quinolone-resistant *N gonorrhoeae* have been isolated in many parts of the US.
Treatment

- **IV cephalosporins:**
  - Ceftriaxone approved for infections of all sites
    25-50 mg/kg IV or IM
  - Cefotaxime approved only for gonococcal ophthalmia

- **Gonococcal urethritis and cervicitis in older adolescents:** PO cefixime, ciprofloxacin, ofloxacin, and levofloxacin

- Fluoroquinolones are not recommended for < 18 y
Treatment

• All patients should be evaluated for concurrent syphilis, hepatitis B virus, HIV, and *C trachomatis* infections

• Children treated with ceftriaxone do not require f/u cultures unless they remain in an at-risk environment, but if treated with other regimens, f/u culture is indicated
Specific recommendations

For management and antimicrobial therapy:

- Infants with clinical evidence of ophthalmia neonatorum, scalp abscess, or disseminated infections should be hospitalized

- Infants with gonococcal ophthalmia should be hospitalized and evaluated for disseminated infection (sepsis, arthritis, meningitis)

- Tests for concomitant infection with *C trachomatis*, congenital syphilis, & HIV should be performed
Specific recommendations

- Recommended therapy for ophthalmia neonatorum: *ceftriaxone given once*
- Should receive eye irrigations with saline solution immediately and at frequent intervals until discharge is eliminated
- Topical antimicrobial treatment *alone is inadequate*
For disseminated Infections

① Recommended therapy for arthritis & septicemia
   ➡️ Ceftriaxone or Cefotaxime for 7 days

② Recommended therapy for meningitis
   ➡️ Ceftriaxone or Cefotaxime for 10-14 days
Specific recommendations

- Results of maternal HB S.Ag should be confirmed
- Mother and her partner(s) also need appropriate examination and management for *N gonorrhoeae*
Specific recommendations

For children beyond the neonatal period and in adolescents

➔ Recommendations for treatment of gonococcal infections, by age and weight, are given in following tables
### Uncomplicated Gonococcal Infection: Treatment of Children Beyond the Newborn Period and Adolescents

<table>
<thead>
<tr>
<th>Disease</th>
<th>Prepubertal Children Who Weigh &lt;100 lb (&lt;45 kg)</th>
<th>Disease</th>
<th>Patients Who Weigh ≥100 lb (≥45 kg) and Who Are 8 Years or Older</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncomplicated vulvovaginitis, cervicitis, urethritis, proctitis, or pharyngitis</td>
<td>Ceftriaxone, 125 mg, IM, in a single dose OR Spectinomycin, 40 mg/kg (maximum 2 g), IM, in a single dose PLUS Azithromycin, 20 mg/kg (maximum 1 g), orally, in a single dose OR Erythromycin, 50 mg/kg per day (maximum 2 g/day), orally, in 4 divided doses for 14 days</td>
<td>Uncomplicated endocervicitis, urethritis, proctitis, or pharyngitis</td>
<td>Ceftriaxone, 125 mg, IM, in a single dose OR Ciprofloxacin, 500 mg, orally, in a single dose OR Cefixime, 400 mg, orally, in a single dose OR Cefpodoxime, 400 mg, orally, in a single dose OR Ofloxacin, 400 mg, orally, in a single dose OR Levofloxacin, 250 mg, orally, in a single dose PLUS Azithromycin (1 g, orally, in a single dose) OR Doxycycline (100 mg, orally, twice a day for 7 days)</td>
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</tr>
</tbody>
</table>
| Disseminated gonococcal infection (e.g., arthritis-dermatitis syndrome) | Ceftriaxone, 50 mg/kg per day (maximum 1 g/day), IV or IM, once a day for 7 days  
PLUS  
Azithromycin or erythromycin, orally | Disseminated gonococcal infections | Ceftriaxone, 1 g, IV or IM, given once a day for 7 days  
PLUS  
Azithromycin or erythromycin, orally  
OR  
Cefotaxime, 1 g, IV, every 8 hours for 7 days |
| Meningitis or endocarditis                  | Ceftriaxone, 50 mg/kg per day (maximum 2 g/day), IV or IM, given every 12 h; for meningitis, duration is 10-14 days; for endocarditis, duration is at least 28 days  
PLUS  
Azithromycin or erythromycin, orally | Meningitis or endocarditis | Ceftriaxone, 1-2 g, IV, every 12 h; for meningitis, duration is 10-14 days; for endocarditis, duration is at least 28 days  
PLUS  
Azithromycin or erythromycin, orally |
| Conjunctivitis                              | Ceftriaxone, 50 mg/kg (maximum 1g), IM, in a single dose                                                   | Epididymitis                                | Ceftriaxone, 250 mg, IM  
PLUS  
Doxycycline, 100 mg, orally, twice daily for 10 days |
|                                             |                                                                                                              | Conjugunctivitis                           | Ceftriaxone, 1 g, IM, in a single dose  
PLUS  
Azithromycin or erythromycin |

**Complicated Gonococcal Infection: Treatment of Children Beyond the Newborn Period and Adolescents**
Control Measures

Neonatal Ophthalmia

• For routine prophylaxis of infants immediately after birth:
  → 1% solution silver nitrate
  → or 1% tetracycline
  → or 0.5% erythromycin oint. is instilled into each eye

• Subsequent irrigation should not be performed
• Topical antimicrobial agents are less likely to cause a chemical irritation than silver nitrate
Control Measures

**Neonatal Ophthalmia**

Infants born to mothers with gonococcal infections

↓

When prophylaxis is administered correctly, infants rarely develop gonococcal ophthalmia

However as it can occasionally occur → Newborn should receive single dose ceftriaxone

125 mg IV or IM

(Preterm & LBW = 25 - 50 mg/kg)
Herpes Simplex
Herpes

- Herpesviridae, a double-stranded DNA virus
- Classification of Infection
  - Primary
  - Non-Primary First
  - Recurrent
- Incubation period is 3-7 days
  - Constitutional symptoms:
    - fever, headache, malaise, myalgia
  - Local symptoms:
    - pain, itching, dysuria, vaginal/urethral discharge, tender lymphadenopathy
Herpes

- Unique biological properties
  - Neurovirulence (capacity to invade and replicate in the nervous system)
  - Latency (establishment and maintenance of infection in the nerve cell ganglia)
  - Reactivation
Herpes

- Clinical features
  - Vesicles on external genitalia, labia majora/minora, introitus
    - In moist areas the vesicles can rupture leaving tender ulcers
  - Cervix: ulcerative or necrotic cervical mucosa
  - Ulcerative lesions persist from 4-15 days until crusting and re-epithelialization occurs
**Herpes**

**Diagnosis**

- Cell culture
- Serology
- Histological appearance of the lesion
  - Multinucleated giant cells and epithelial cells containing eosinophilic intranuclear inclusion bodies as demonstrated on Tzank smear
Specific Treatments

- **First clinical episode**
  - Acyclovir 400mg po TID x 7-10days

- **Recurrent genital herpes**
  - Suppressive therapy (frequent recurrence >9 per year)
    - Acyclovir 400mg po bid
    - Valacyclovir 500mg po qday
  - **Beginning at 36 weeks**

- **Severe disease**
  - IV acyclovir recommended for patients with severe disease or complications such as disseminated infection, pneumonitis, CNS symptoms
    - Acyclovir 5-10mg/kg q 8 hours for 2-7 days
Obstetrical Management

• History and Physical

• Vaginal Delivery:
  – No lesions and No symptoms

• Cesarean Delivery:
  – Lesions or Symptoms

• PPROM
• Invasive procedures
Primary Prevention of STDs

• Changing at-risk sexual behaviors

• Routine sexual histories from patients
  – Address risk reduction

• Counseling
  – respect, compassion, non-judgmental attitude
...how to do that

• **Use open ended questions**
  – Tell me about any new sexual partners you’ve had since your last visit?
  – What has your experience with condoms been like?

• **Use understandable language**
  – Have you ever had a scab on your vagina or labia

• **Normalize conversation**
  – Some of my patients have difficulty using a condom with every sexual activity...What about your experiences?
Eliciting Information

- Partners (male/female/both; how many)
- Prevention of pregnancy
- Protection from STDs
- Practices (to understand your risk for an STD, I need to understand which kind of sex you have; vaginal/oral/anal)
- Past history of STDs
Prevention

- Abstinence/Reduction of number of partners
  - Most reliable

- Male condoms
  - Highly effective
    - (failure often secondary to inconsistent and incorrect use rather than actual breaking)
    - Use a new condom with every sex act

- Female condoms
(1) Disseminated disease involving multiple organs, mostly liver and lungs → ~1/3rd + has earliest age of onset (~1st week)

(2) Localized CNS disease → ~1/3rd + manifests latest

(3) Or disease localized to skin, eyes, and mouth → ~1/3rd + between 2nd & 3rd wks
Neonatal Clinical Manifestations

- Can be clinical overlap among disease types
- Initial signs can *occur anytime* (birth & 4 wks)
- In many neonates with disseminated or CNS disease, skin lesions do not develop or appear late
Neonatal Clinical Manifestations

• Absence of skin lesions → Difficult diagnosis

• Disseminated infection should be considered with:
  - Sepsis syndrome
  - Negative bact. Cultures
  - Severe liver dysfunction
  - Unexplained fever, irritability, & abnormal CSF
  - Seizures
• Asymptomatic HSV infection is common in older children but rarely, if ever, in neonates

• Usually severe, with high M & M rates, even with antiviral therapy

• Recurrent skin lesions (1st 6 months) are common in survivors and can be associated with CNS sequelae
Herpes Simplex Ophthalmia

- Rare in neonates
- Can be associated with significant M&M
- Edema, conjunctival injection, and tearing usually begin within 1st 2 wks
- May be followed by keratitis or kerato-uveitis
Most primary HSV infections are asymptomatic.
Clinical Manifestations

Beyond Neonatal Period

**Gingivostomatitis**
- Most common C/F beyond neonatal period
- Usually HSV type 1
- Characterized by fever, irritability, tender submandibular adenopathy, and ulcerative enanthem involving gingiva and mm of mouth, often with perioral vesicular lesions

**Genital herpes**
- Most common manifestation in adolescents & adults
- Caused by HSV 2, but HSV 1 appears to be increasing in frequency
- Characterized by vesicular or ulcerative lesions of ♂ or ♀ genital organs, perineum, or both
Clinical Manifestations

Beyond Neonatal Period

- When symptomatic, recurrent herpes labialis HSV-1 manifests as single or grouped vesicles in perioral region, usually on vermilion border of lips (cold sores)

- Symptomatic recurrent genital herpes manifests as vesicular lesions on penis, scrotum, vulva, cervix, buttocks, perianal areas, thighs, or back
Clinical Manifestations

Beyond Neonatal Period

• When symptomatic, recurrent herpes labialis HSV-1 manifests as single or grouped vesicles in perioral region, usually on vermilion border of lips (cold sores)

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HSV encephalitis

- Can result from primary or recurrent infection

- Usually associated with fever, alterations in state of consciousness, personality changes, seizures, and focal neurologic findings

- Encephalitis *commonly* has an acute onset with a fulminant course ⇒ coma and death if untreated

- CSF pleocytosis with lymphocytes predominance and some RBC
HSV encephalitis

- HSV infection can also cause meningitis with nonspecific C/F, that usually are mild and self-limited.
- Usually associated with genital HSV-2 infection.
- Unusual CNS manifestations of HSV: Bell palsy, atypical pain syndromes, trigeminal neuralgia, ascending myelitis, and postinfectious encephalomyelitis.
Epidemiology

HSV infections are ubiquitous and are transmitted from people who are symptomatic or asymptomatic with primary or recurrent infections.
Epidemiology

Neonatal

- Incidence: 1/3000 – 1/20 000 live births
- More likely preterm
- Intrauterine infections causing congenital malformations rare
Epidemiology

*Neonatal* Transmission

- Mostly during birth through infected genital tract
- Ascending infection (sometimes with apparently intact membranes)
- Other less common: Postnatal transmission from parent or other caregiver, from nongenital infection (e.g., mouth or hands)
Epidemiology

Neonatal

Risk at delivery from mother with primary genital infection

↓

33% - 50%

Risk from mother shedding HSV from reactivated infection

↓

< 5%
• Distinguishing between primary and recurrent HSV in ♂ by history or PE may be impossible

• Primary & recurrent infections may be asymptomatic
> 3/4 of infants who contract HSV infection have been born to ♀ who had no history or C/F suggestive of active HSV infection during pregnancy
Epidemiology

Neonatal

• Best outcome in terms of M&M is observed among infants with disease limited to skin, eyes, and mouth

• Although most neonates treated for HSV encephalitis survive, most suffer substantial neurologic sequelae
Diagnostic Tests

• HSV grows readily in cell culture

• Cytopathogenic effects are seen 1-3 days after inoculation
Diagnostic Tests

- Cultures (-) by day 15 → likely to continue (-)

- CSF cultures from HSV encephalitis usually (-)

- PCR assay often detect HSV DNA in CSF from Pt with HSV encephalitis
  ➔ Diagnostic method of choice

- Histologic examination and viral culture of brain tissue specimen obtained by biopsy
  ➔ Most definitive method
Diagnostic Tests

• Serologic testing (HSV-1/HSV-2) is not useful in neonates

• Several glycoprotein G (gG)-based type-specific assays have been approved by US FDA
  → Sensitivities for detection of HSV-2 abs 80% - 98%, and false (-) may occur early after infection
  → Specificities >96%; false (+) can occur, especially in Pt with low likelihood of HSV infection

⇒ Therefore, repeat testing or confirmatory test (e.g., an immunoblot assay if initial test was an enzyme-linked immunosorbent assay) may be indicated
Diagnostic Tests

• Rapid diagnostic techniques available: Direct fluorescent Ab staining of vesicle scrapings or enzyme immunoassay detection of HSV Ag
  → Are specific but slightly less sensitive than culture

• Histologic examination of lesions (multinucleated giant cells & eosinophilic intranuclear inclusions)
  e.g. Tzanck test has low sensitivity and is not recommended
How to diagnose?

Swabs of mouth, nasopharynx, conjunctivae, & rectum and specimens of skin vesicles, urine, stool, blood, & CSF should be obtained for culture

↓

(+) cultures > 48 hrs after birth indicate viral replication suggestive of infection rather than contamination after intrapartum exposure
Dilemma

- Differentiating primary genital infection from recurrent HSV infection in mother → helpful for assessing risk of HSV infection in infant, but distinction may be difficult.

- First-episode clinical infections are not always primary infections.
  How? ☞ Often, primary infections are asymptomatic, in which case the first symptomatic episode will represent a reactivated recurrent infection.
In selected instances, serologic testing can be useful:

- e.g.: if a woman with herpetic lesions has no detectable HSV Abs, she is experiencing a primary infection.

- Assessment of seropositive♀ necessitates differentiation of HSV-1 from HSV-2 Abs.

- Currently, only assays based on detection of type-specific glycoprotein G make this distinction reliably.
Treatment

Neonatal

IV acyclovir

➔ Treatment of choice for neonatal HSV infections

• Acyclovir should be administered to all neonates with HSV infection, *regardless* of manifestations and clinical findings after obtaining cultures.
Acyclovir therapy should be initiated if any of the culture or PCR results are positive, CSF findings are abnormal, or HSV infection otherwise is suspected strongly.
Treatment
Neonatal

• Acyclovir dosage: 60 mg/kg/day Q 8hr IV
  X 14 days if disease limited to skin, eyes & mouth
  X 21 days if disease disseminated or involves CNS

• Infants with ocular involvement should receive topical ophthalmic drug (1% trifluridine, 0.1% iododeoxyuridine, or 3% vidarabine) as well as IV antiviral therapy
Treatment

**Neonatal**

- Approximately 25% with disseminated disease die despite antiviral therapy
- Disease relapse of skin, eyes, mouth, and CNS can occur after cessation of treatment
- The optimal management of these recurrences is not established
Because risk to infants exposed to HSV lesions during NSVD varies from < 5% to 50% ➔ Decision to treat asymptomatic exposed infant empirically with IV acyclovir is controversial.
As infection rate with active recurrent genital herpes infections is < 5%, most experts would not treat infants empirically with acyclovir.

The infant's parents or caregivers, however, should be educated about S&S of neonatal HSV infection.
Treatment

Neonatal

• For primary genital infection, the risk of infection may exceed 50% = High infection rate

➤ Some experts recommend empiric acyclovir treatment at birth after HSV cultures have been obtained

➤ Others would obtain HSV cultures 24-48 hours after delivery and initiate acyclovir only if HSV is recovered from these cultures
The accuracy of viral cultures for predicting neonatal infection in infants whose mothers were treated with antiviral medication during pregnancy is not known.
In General

Infant whose mother has known, recurrent genital infection, whether active lesions were present at time of delivery or not, should be observed carefully for signs of infection.
In General

Infants born by C/S delivery to mothers with herpetic lesions should be observed carefully, with laboratory studies performed as recommended for potentially exposed infants born by NSVD

➔ Antiviral therapy should be initiated if culture results from infant are (+)
### Recommended Therapy for Herpes Simplex Virus Infections

<table>
<thead>
<tr>
<th>Infection</th>
<th>Drug</th>
</tr>
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<tbody>
<tr>
<td>Neonatal</td>
<td>Acyclovir</td>
</tr>
<tr>
<td>Keratoconjunctivitis</td>
<td>Trifluridine OR Iododeoxyuridine OR</td>
</tr>
<tr>
<td></td>
<td>Vidarabine</td>
</tr>
<tr>
<td>Genital</td>
<td>Acyclovir OR Famciclovir OR Valacyclovir</td>
</tr>
<tr>
<td>Mucocutaneous (immunocompromised or primary gingivostomatitis)</td>
<td>Acyclovir OR Famciclovir OR Valacyclovir</td>
</tr>
<tr>
<td>Acyclovir-resistant (severe infections, immunocompromised)</td>
<td>Foscarnet</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>Acyclovir</td>
</tr>
</tbody>
</table>
Isolation?

Neonates *with HSV infection* → Should be hospitalized and managed with contact precautions if mucocutaneous lesions are present.
Neonates *exposed* to HSV during delivery:

- Should be managed with contact precautions during incubation period
- ? contact precautions unnecessary if born by C/S, provided membranes ruptured for < 4 hrs
- Risk of HSV infection in infants born to mothers with H/O recurrent genital herpes who have no genital lesions at delivery is low, and special precautions are not necessary
Recommendations

Breastfeeding is acceptable if no lesions are present on the breasts and if active lesions elsewhere on the mother are covered.
Management of exposed asymptomatic infants who were born vaginally to mothers with active genital lesions can be categorized according to type of maternal infection as follows:

① Mother with primary infection
② Mother with known recurrent lesions
③ Mother whose status (primary vs. recurrent) is unknown
④ Mother who has no apparent genital lesions but a positive HSV culture of vagina or cervix
References

- Red Book – Infectious Diseases. 2006
Thank you for listening!