Herpes Simplex Virus: Localized Disease

Background
1. Definition
   - Superficial localized infection caused by HSV
   - Primary infection:
     - Individuals w/no preexisting antibodies to HSV
   - Recurrent infection:
     - Individuals w/preexisting antibodies to HSV or prior hx of HSV infection
2. General information
   - HSV is a member of herpesvirus group
   - Dz in children comes in 2 distinct types
     - Localized
     - Cause of Neonatal sepsis
   - Occurs as 2 antigenic types- HSV1 and 2
     - HSV1 most commonly assoc w/infection of mucous membranes of mouth, lips, eyes
     - HSV2 most assoc w/localized genital infections but also can cause neonatal sepsis
   - All local herpes virus infections share characteristic of becoming latent after primary infection
     - Virus may subsequently reactivate periodically
   - Site of latency is dorsal root ganglia for both HSV1 and HSV2
   - Reactivation may occur from stimulus like fever, stress, UV light, other

Pathophysiology
1. Pathology of localized dz
   - Characteristic lesion is vesicle on skin or ulcer on mucous membrane
   - Usually involves only epidermis in superficial infections
   - Invaded epithelial cells are destroyed by virus and inflammatory response of host
     - Sparing an intact superficial cornified layer that covers vesicle
     - This layer is absent in ulcer
   - Cells invaded by virus
     - Coalesce to form multinucleated giant cells
     - Undergo nuclear degeneration
     - Ballooning and intranuclear inclusions
2. Incidence/ prevalence
   - Lifetime risk of HSV1 very high
   - HSV2: 20-30% in age group of 15-29 yo
3. Risk factors
   - Local dz
     - Race
       - Not directly related to race
       - Varies w/race d/t difference in prevalence of poverty, access to health
       - Higher among African Americans than Caucasians
     - Sex: infection rates of males = females
• Age
  • 20% of children by age of 5 are seropositive for HSV1
  • HSV2 more prevalent in adolescent population
• Lifetime risk for genital herpes directly correlated w/number of sexual partners
• Incubation period for primary infection is 2-20 days w/average of 6 days

4. Morbidity/ mortality
  o Localized infections have 0% mortality
  o HSV infection of eyes can cause blindness
  o Herpetic ulcers
    • Expose dermis
    • Which then becomes a more ready surface to transmit or accept other sexually transmitted disease (if exposed)
    • Or become secondarily infected by bacteria

Diagnostics
1. History
  o Symptoms
    • Onset:
      • Usually acute h/o previous herpes infection
    • Location:
      • Oral mucosa, skin, eyes, perioral region, vagina, penis, anus are the most common sites
    • Duration:
      • Varies from 5-7 days for mild infections to 10-14 days for more severe infections
    • Associated symptoms:
      • Fever, irritability, anorexia, sore mouth, regional lymphadenitis, local pain
      • Asymptomatic shedding from other infected people usual mode of transmission
        • Those w/genital infection particularly benefit from hearing this
  o Past hx
    • Hx of previous herpes infection
    • Hx immunocompromise
  o Social hx: sexual hx for genital herpes
2. Physical exam
  o Herpetic Gingivostomatitis
    • Most common clinical presentation of first episode
    • Abrupt onset
    • Fever, listlessness
    • Inability to eat or drink
    • Gingivitis, gums maybe swollen, red, bleed easily
    • Occasional episodes of drooling
    • Vesicular lesions on tongue, buccal mucosa, palate, lips, face
    • Anterior cervical lymphadenitis maybe present
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3. Diagnostic tests

3.1 Laboratory

- Viral culture: best dx method, time taking
- Viral PCR: often preferred initial method due to quick results
- Serology showing rise in antibody titers

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- Histological evidence of multinucleated giant cells and intranuclear inclusion bodies
- Tzanck smear: low sensitivity
  - Other studies
    - Blood cultures
    - Urine culture
    - Fluid from eyes, nose and mucous membranes should be obtained if involved

**Differential Diagnosis**

1. Acute Herpetic Gingivostomatitis
   - Herpangina: coxsackie or enteroviruses most likely
   - Streptococcal pharyngitis
   - Thrush
2. Acute Herpetic Vulvovaginitis
   - Ammoniacal dermatitis w/secondary infection
   - Gonorrheal and monilial vulvovaginitis
   - Impetigo
   - Foreign body
   - Trichomonas
   - Vaginal candidiasis
3. Eczema Herpeticum
   - Eczema w/secondary bacterial infection
   - Varicella
   - Eczema vaccinatum
4. HSV skin lesions can be confused with Varicella Zoster infection
5. Acute Herpetic Keratoconjunctivitis
   - Conjunctivitis
     - Haemophilus
     - Pneumococci
     - Staphylococci
     - Adenovirus
     - Picorna virus
     - Influenza virus

**Therapeutics**

1. Mainly supportive care for mucocutaneous oral lesions
   - Avoid dehydration
   - Encourage fluid intake
2. Acyclovir
   - IV: 10mg/kg iv q8 hrs for extensive oral lesions maybe considered
   - PO: 15mg/kg 5x per day can be used if tolerated for children between 1-6 yrs to shorten duration
3. Tx of genital dz depends on if it is initial, recurrent or suppressive in intent
   - See individual drugs for details
4. For initial genital herpes in adolescents
   - Acyclovir 200mg five x/day OR
   - Valacyclovir 1000mg BID for 5 days OR
   - Famciclovir 250mg q8 hrs for 5 days
     - Valaciclovir and famicyclovir not recommended in children
5. Topical trifluridine for herpetic keratoconjunctivitis w/ophthalmology referral
   - Infants less than 1 month should receive IV acyclovir and close follow up
6. Other tx options w/less proven benefit may incl
   - L-Lysine and aspirin orally
   - Licorice root (glycyrrhiza glabra), lemon balm, aloe or zinc applied topically
7. Pts may well respond to an initial dx of genital herpes w/anger, disbelief or depression
   - It is useful to have printed educational materials to aid this discussion
   - Schedule a follow-up exam for discussion in near future

**Prevention/ Screening**
1. Avoid contact w/oral secretions of infected individual
2. Avoid sexual contact w/partner w/active genital herpes
3. Routine serological screening for HSV in asymptomatic adolescents and adults is not recommended

**References**

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