NCPTS
National Cervical Pathology Training Service

GENITAL HERPES

Notes updated: 03.07.14

Definition

- Genital tract infection with herpes simplex virus types 1 (HSV-1) or 2 (HSV-2).
- Both viruses can cause the same clinical syndromes although mostly HSV-1 causes orolabial lesions and HSV-2, genital herpes virus infections.
- Mild infrequent symptoms that often go unnoticed, is common.
- Episodes of genital pain/itching/burning lasting 3-5 days interspersed with symptom-free periods, is typical for the symptomatic group. First episode usually most severe.
- Painful shallow anogenital ulcers typically seen. Usually appear 4-7 days after first exposure.
- May be fever/malaise/myalgia/headache/dysuria/vaginal discharge.
- **First episode primary infection:** herpes virus infection with no HSV-1 or HSV-2 antibodies.
  First episode non-primary infection: HSV-2 infection with HSV-1 antibodies or vice versa.
  First recognised recurrence: HSV-1 or HSV-2 infection with same virus antibodies.
  Recurrent genital herpes: reactivation of latent herpes simplex virus.
- HSV-1 can also cause gingivostomatitis and orolabial ulcers. HSV-2 can cause ocular herpes. Both can cause encephalitis.

Prevalence

- One of most common sexually transmitted diseases. NZ studies:
  - 50-70% of NZ adults seropositive for HSV-1 (i.e. all HSV-1 infections including oral).
  - 11% of 26 year-olds in Dunedin cohort study were seropositive for HSV-2.
  - 25% of Auckland Sexual Health patients were positive for HSV-2.
- First episode: HSV-2: 70% and HSV-1: 30%. Recurrent disease usually HSV-2.
- 20% asymptomatic, 60% “unrecognized symptomatic”, 20% “recognised symptomatic”.

Diagnosis

- Cytopathic cell changes may be seen in cervical smears.
- Virological confirmation and typing should be attempted in all patients.
  - Viral culture from a swab: reported as “positive/negative” and typed for HSV 1 and HSV 2.
  - PCR may be useful in selected cases e.g. recurrent disease with negative culture
  - Type-specific serology indicates exposure to HSV-1 or HSV-2 in the past. Used in selected clinical situations.

Prognosis

Sequelae includes:

- neonatal herpes simplex infection
- opportunistic infection in the immunocompromised
- recurrent genital tract ulceration
- psychosocial morbidity
- neurological complications: aseptic meningitis, urinary retention (spinal cord involvement)

Treatment

- Aim to prevent transmission, reduce morbidity of first infection, reduce recurrence risk
- Many people with genital herpes are underdiagnosed and therefore undertreated
- Treatment offered if present within 72 hours of onset of symptoms. Also other cases such as severe disease, recurrent episodes. Many patients will not require treatment.
- Antiviral management may be episodic oral therapy or continuous to prevent recurrences

- Three drugs: aciclovir, famciclovir and valaciclovir. All prevent virus replication by inhibiting viral DNA synthesis

Clinical comment: Dr Rosemary Ikram, Microbiologist

"Diagnosis: PCR is commonly used to diagnose Herpes simplex virus infections. Typing of the virus is performed at the same time. Culture may be performed, and is the "gold standard", however most laboratories have moved to PCR. Culture is less sensitive because it requires the virus to replicate. Some laboratories use EIA (enzyme immunoassay) for HSV. This test is less sensitive and specific than the above, and the virus is not typed."

References:

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   www.nzdoctor.co.nz/sexual-health-guidelines
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4. The Australian Herpes Management Forum www.ahmf.com.au
5. Cunningham A et al. Prevalence of infection with herpes simplex virus types 1 and 2 in Australia: a nationwide population based survey *Sex Transm Infect* 2006;82: 164-168
6. Whitley RJ et al. Herpes simplex viruses. *Clin Infect Dis* 1998;26:541-553
7. Smith J et al. The management of herpes simplex virus infection in pregnancy. *Br J Obstet Gynaecol* 1998;105:255-268
8. Kimberlein DW et al. Clinical Practice: Genital herpes. *NEJM* 2004:350(19):1970-77
9. College of American Pathologists Practical Guide to Gynecologic Cytopathology. David Wilbur and Michael Henry Pub CAP Press 2008

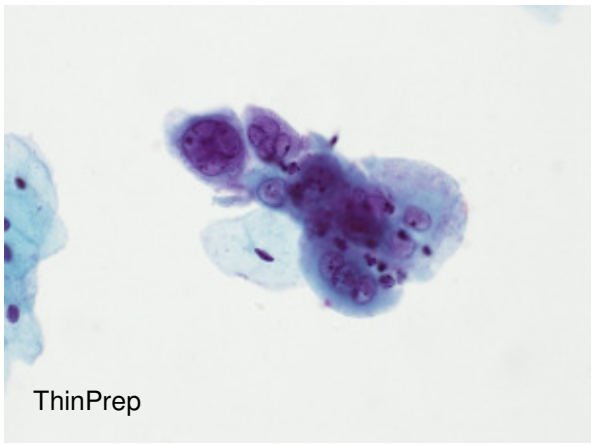
HERPES: IDENTIFICATION BY CYTOLOGY

- Causes cytopathic effects in squamous cells: multinucleation with nuclear molding, ground-glass chromatin and nuclear enlargement. Mononucleated cells also show nuclear enlargement and ground-glass chromatin.
- May see typical intra-nuclear inclusions surrounded by a clear halo
- Associated ulceration, necrosis and epithelial cell regeneration can result in marked reactive changes in epithelial cells
- Increased numbers of single isolated herpetic cells can be misinterpreted as HSIL
- Differential Diagnosis: Reactive endocervical cells can be large and multinucleated. If also slightly degenerate, the nuclei can appear washed out and mimic the ground glass appearance of herpes.

Bethesda 2001 Terminology:

There are cellular changes consistent with Herpes simplex virus

CYTOPATHIC CELL CHANGES OF HERPES SIMPLEX INFECTION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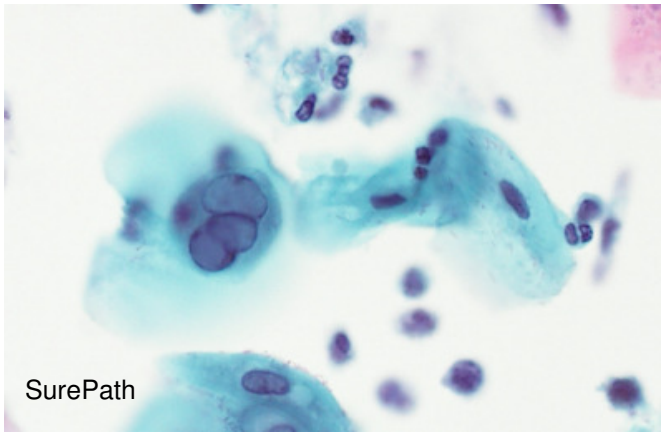
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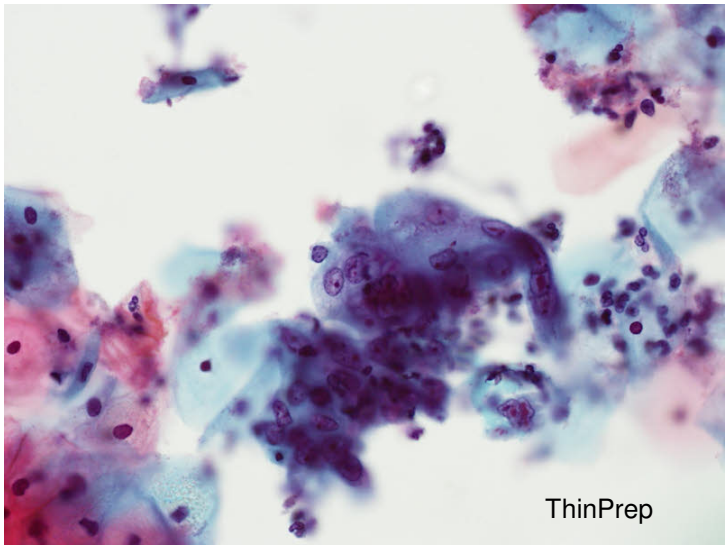
The “ground-glass” appearance in nuclei is due to the accumulation of intra-nuclear viral particles causing margination of nuclear chromatin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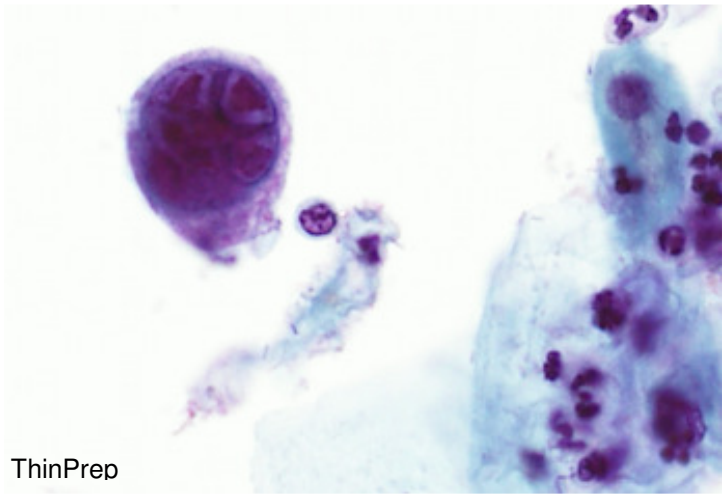
Large multinucleated epithelial cells with molded nuclei are usually a prominent feature. Intranuclear inclusions are also present.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Dense eosinophilic intra-nuclear inclusions (“Cowdry bodies”) surrounded by a clear zone may be present.

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