



Southern African HIV Clinicians Society

3rd Biennial Conference

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Sandton Convention Centre
Johannesburg

HSV

**Our Issues, Our Drugs,
Our Patients**

www.sahivsoc.org
www.sahivsoc2016.co.za

HSV

Herpes Simplex Virus

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“The oldest and strongest emotion of mankind is fear, and the oldest and strongest kind of fear is fear of the unknown”

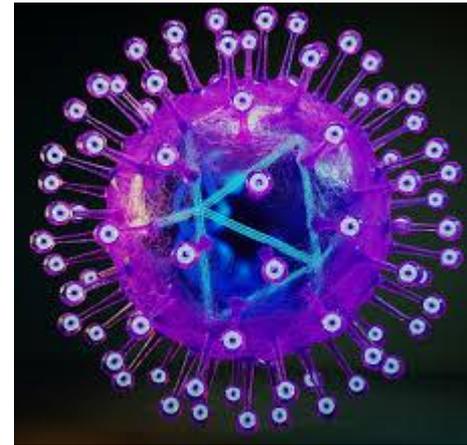
— H.P. Lovecraft, Supernatural Horror in Literature



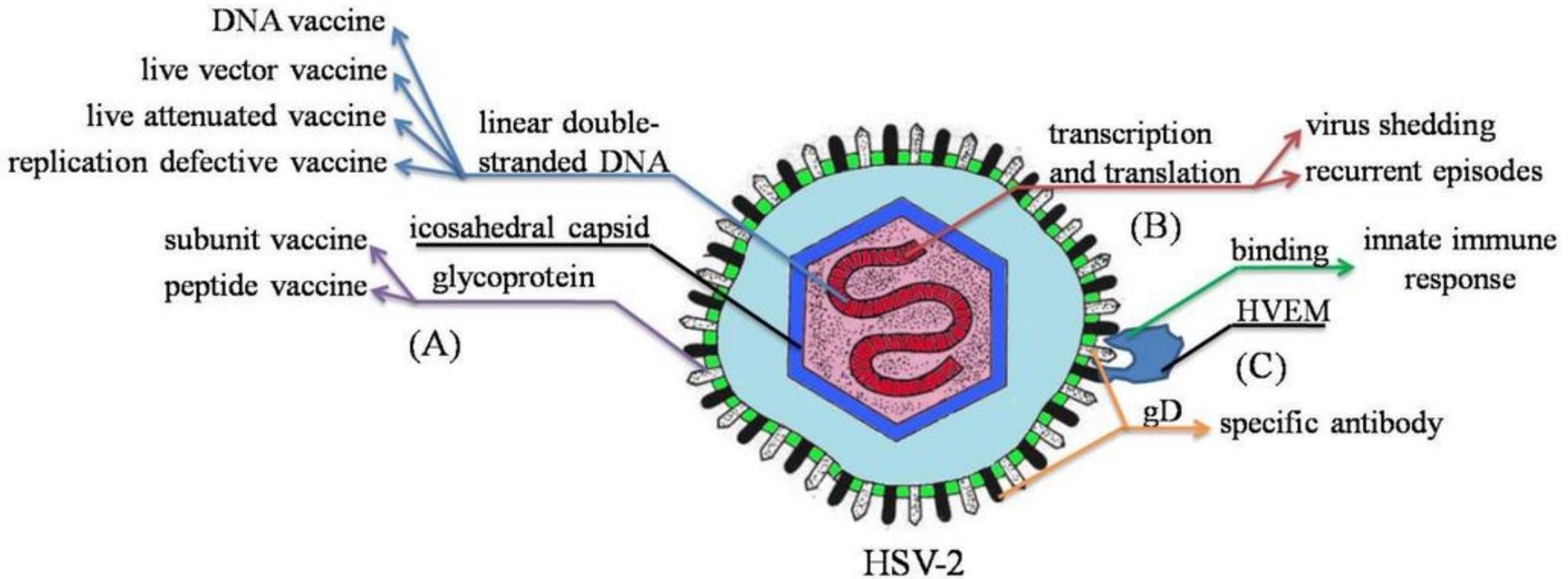
2016

Brief overview

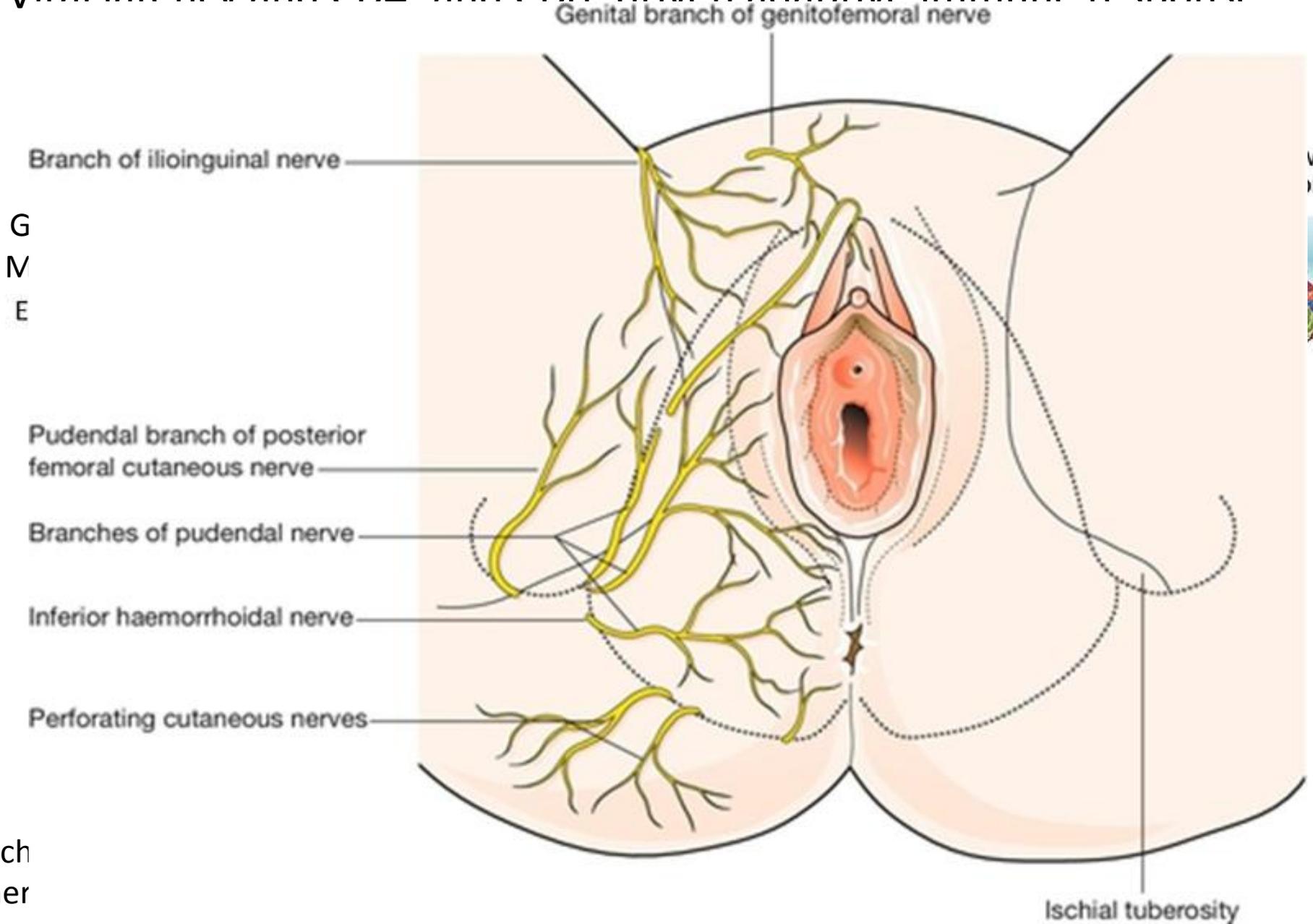
- Virology
- Epidemiology
- Disease spectrum
- Diagnosis
- Treatment strategies
- Vaccine development
- Summary/Take home message



HSV 2 virus



Viral latency and CD4- and CD8- driven adaptive immune response



Sch
her

Epidemiology

- worldwide distribution, even in remote areas
- HSV-1 very widespread Africa, Asia ~100 % HSV-1 antibody pos.
Europe, North America 80-100% lower socio-economic status
Europe, North America 30-50% in higher socioeconomic groups
- HSV-2 Africa has a high prevalence rate (30 to 74 %)
Women > men
- Antibodies to HSV-2 appear with puberty, correlating with sex
- Herpes is predominant cause for genital ulcers
85% of genital herpes is caused by HSV-2
75% of sexual partners of infected individuals will get HSV
HIV and other STI are cofactors in infection
- Prevention of transmission:
Consistent condom use and male medical circumcision

Primary genital HSV infection - Clinical course

- Prodrome: 2-5 days after infection patient experiences burning and tingling in genital area
- 3-7 days after infection patient will develop very painful vesicular and ulcerated lesions. Many patients will have difficulty urinating due to pain. Median duration women: 20 days, men: 16 days.
- In addition to the painful lesions patients can develop malaise, fever, inguinal adenopathy
- Aseptic meningitis may also develop one week after the lesions appear:
- Patients will have fever, severe headache and stiff neck, usually resolves within one week without treatment

Chronic genital HSV in HIV

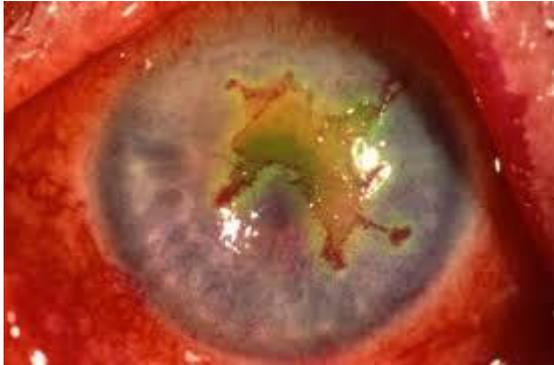


recurrent lesions



chronic persistent lesion

Herpetic eye lesions



Herpetic eye ulcer stained with fluorescent dye

Herpes necrotizing stromal keratitis

metaherpetic ulcer

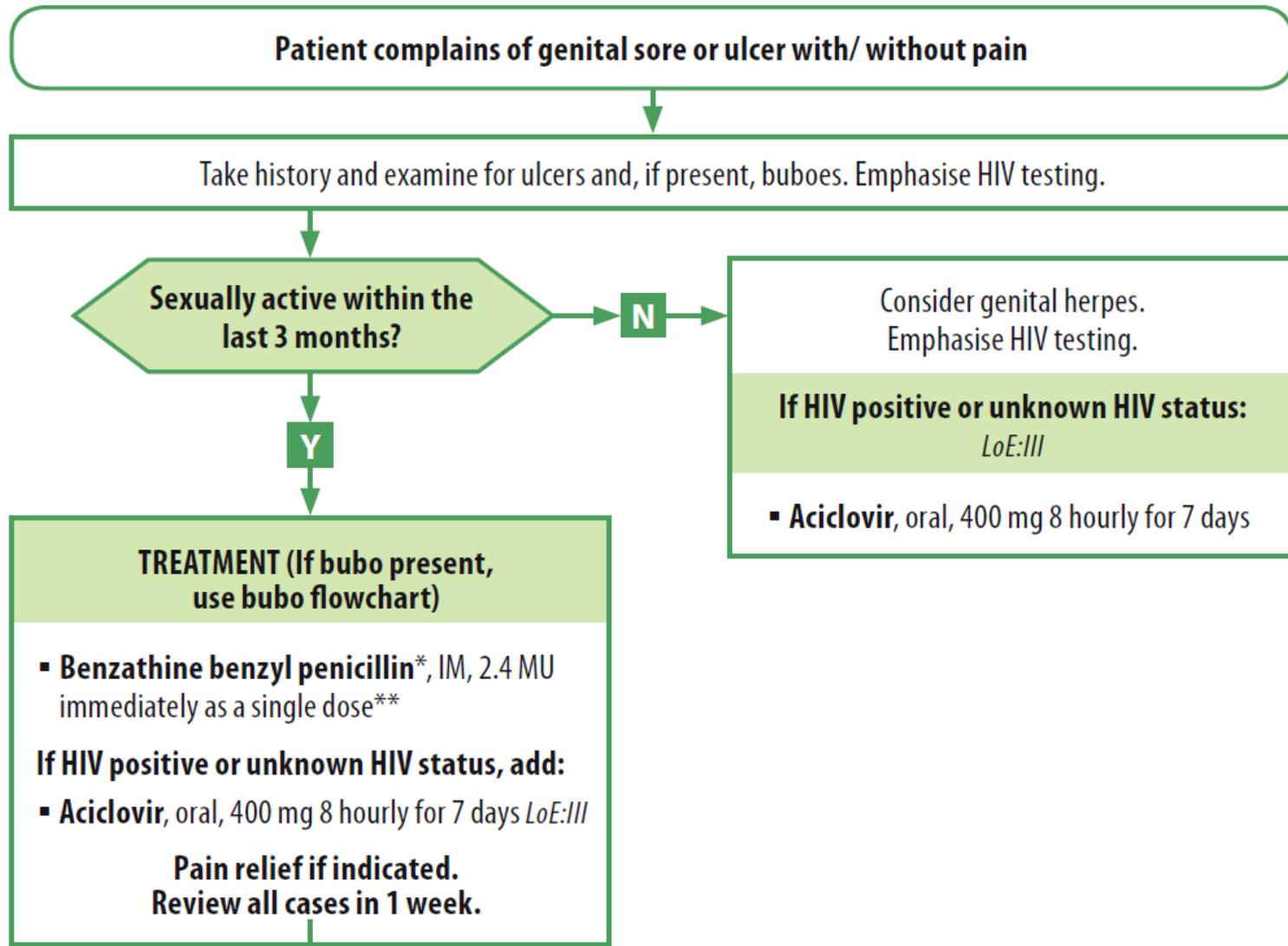
Diagnosis of genital herpes

- Ask about symptoms of STIs
- Clinical: Looking for vesicles, ulcerations etc.
(yes, taking the underwear off)
- PCR: secretion/swab in viral transport medium:
HSV I or II

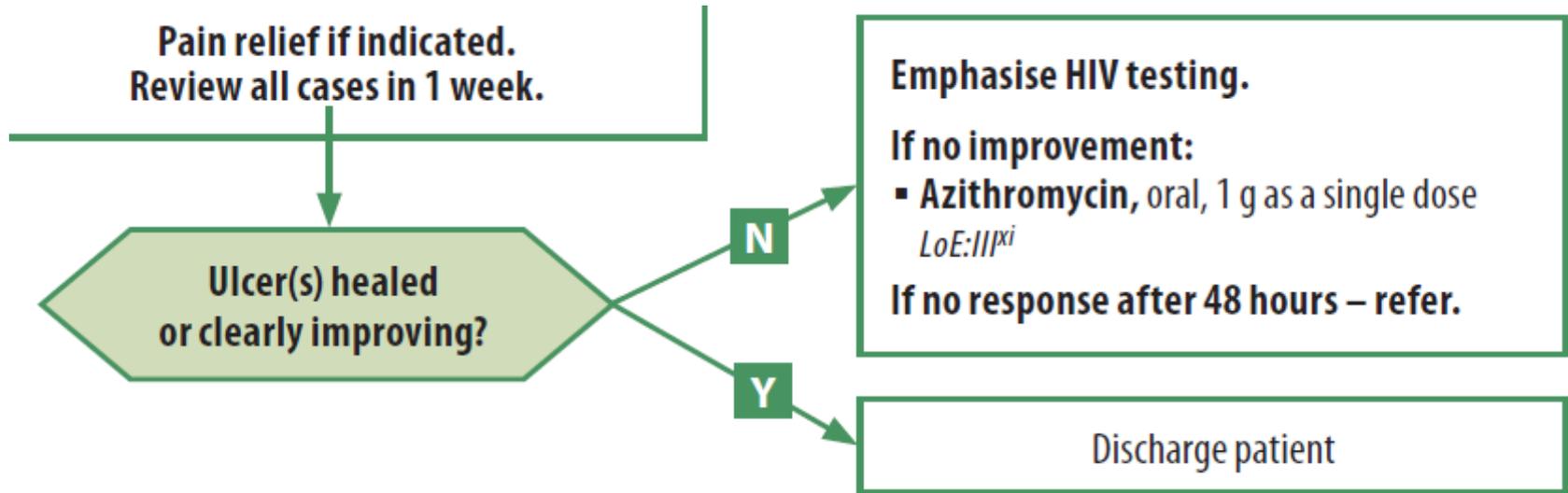
caveat: very sensitive: asymptomatic/by-stander shedding

- Cytology/histology: microscopic viral inclusion bodies
- *Serology: IgM (IgG)*
- *Viral culture (research)*

Genital ulcer syndrome Flowchart DOH 2015



Genital ulcer syndrome Flowchart DOH 2015 cont.

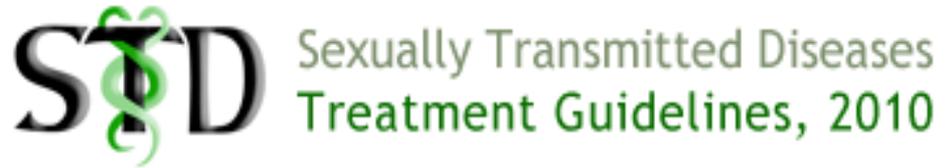


Refer.

Where to?

What is the next health professional going to do?

US guidelines



If lesions persist or recur in a patient receiving antiviral treatment, HSV resistance should be suspected and a viral isolate should be obtained for sensitivity testing (184). Such persons should be managed in consultation with an HIV specialist, and alternate therapy should be administered. All acyclovir-resistant strains are resistant to valacyclovir, and the majority are resistant to famciclovir. Foscarnet, 40 mg/kg IV every 8 hours until clinical resolution is attained, is frequently effective for treatment of acyclovir-resistant genital herpes. Intravenous cidofovir 5 mg/kg once weekly might also be effective. Imiquimod is a topical alternative, as is topical cidofovir gel 1%, which is not commercially available and must be compounded at a pharmacy. These topical preparations should be applied to the lesions once daily for 5 consecutive days.

Clinical management of antiviral resistance remains challenging among HIV-infected patients, and other preventative approaches might be necessary. However, experience with another group of immunocompromised persons (hematopoietic stem-cell recipients) demonstrated that persons receiving daily suppressive antiviral therapy were less likely to develop acyclovir-resistant HSV compared with those who received episodic therapy with outbreaks (185).



Practical tips:

Discuss with an infectious diseases specialist:

Give Acyclovir in higher doses for longer!

800 mg 5 x daily for 2-4 weeks (or admit for IV therapy)

If improving: (opinion gained from reading case reports)

Continue with 400 mg TDS for 4-12 weeks

Then 2nd prophylaxis: 400 mg BD for 6 months

If not improving:

Off-label use of Imiquimod (Aldara):

**Topical Imiquimod Treatment of Aciclovir-resistant Herpes Simplex Disease
Case Series and Literature Review**

Nicky Perkins, Mitzi Nisbet, Mark Thomas Sex Transm Infect. 2011;87(4):292-295.



Jacobs, elife, March 7, 2015

Radical Vaccine Design Effective Against Herpes Viruses

- Herpes simplex virus infections are an enormous global health problem and there is currently no viable vaccine.
- 30 years of futile HSV vaccine search using the very immunogenic and abundant gD glycoprotein
- Breaking from this approach, Howard Hughes Medical Institute (HHMI) scientists at Albert Einstein College of Medicine have created a genetic mutant lacking that protein. This viral mutant is non infective and produces a different immune response.
- In Mouse model 100% effective and serum from vaccinated mice convey passive immunity in unvaccinated mice.
- In a few years hopefully human trials
- Watch this space, if effective, Nobel price waiting



Table 3. Key points regarding herpes simplex virus type 2 (HSV-2) coinfection in HIV-infected persons.

- Most HIV+ with HSV-2 coinfection are asymptomatic.
- genital HSV-2 infection in patients with HIV-1 coinfection ranges from extensive, deeply ulcerated, necrotic and chronic lesions to small, unrecognized mucosal or epithelial fissures or ulcers.
- HSV-2 infection has been associated with increased risk of HIV acquisition and transmission.
- HAART alone does not reduce the rate of asymptomatic mucosal HSV-2 shedding and, therefore, potential infectivity for HSV-2.
- HSV-2 suppression with antiviral drugs has been demonstrated to reduce both plasma and genital HIV-1 levels in persons co-infected with HIV and HSV-2 and, therefore, may have public health benefits.
- Despite increasing use of suppressive acyclovir therapy, there has not been an increase in the detection of acyclovir-resistant HSV-2 isolates.
- **Intermittent treatment of HSV in HIV+ may increase risk for developing acyclovir resistance.**

Strick LB HIV/AIDS 2006

Thank you to my boss, Prof MYS Moosa, my colleagues and patients for all they have taught me and to the organisers for inviting me to speak!



2016