Oral Herpes

by Nghia Nguyen

Etiological agent - *Simplexvirus herpes simplex virus 1 (HSV-1)* is from the family *Herpesviridae*. (2) Although there are others in the family, HSV-1 and HSV-2 (genital herpes) are most common. The infections are usually non-life threatening but can lead to other serious complications (9)

Transmission: primarily transmitted through oral-to-oral direct contact with virus living in sores, saliva, and surfaces around the mouth region. It can also be contracted by oral-to-genital contact to cause genital herpes. (1)

Reservoir: Infected adolescents and adults. HSV-1 and 2 infections are life-long, can be latent or full blown overt disease. HSV-1 do not survive for prolonged periods in the environment; requires inoculation of fresh virus-containing body fluid of infected person into susceptible tissue of uninfected person; may be transmitted during primary or reactivation infections; often the person shedding virus is asymptomatic. (2)

Specific characteristics (2)

- **Taxonomy**: *Alphaherpesvirus* subfamily of family *Herpesviridae*
- One of the leading viral disease, only second to cold and flu.
- Double stranded DNA enveloped virus with a genome of around 150 kb.
- The genome of HSV-1 and HSV-2 share 50 - 70% homology. They also share several cross-reactive epitopes with each other. There is also antigenic cross-reaction with VZV.
- Man is the only natural host for HSV

Herpes Simplex Virus is usually acquired through direct contact like kissing infected lesion or body fluid (saliva). They target mucoepithelial cells and remain dormant till activation. HSV-1 comprised of an envelope (herpes glycoproteins that infect), capsid (contains capsomeres), tegument (initiates replication), and genome (double stranded DNA, encode enzymes). (9)

During the latency period, HSV does not have an envelope so it remains ineffective or dormant. [10] This “neurotropism” characteristic of HSV makes latency possible. (9) After the primary infection, the virus remains in neural tissue but it extends away from the cell’s central nerve for a secure place to stay without being lost.(9)

Specific tests for identification:
There are several methods for identifying HSV virus and distinguish them from each others. The first way is to look at the lesions around the mouth (1)

- **Smears** - Cells may be obtained from the base of the lesion (called a Tzank smear) and histochemistry performed. Can be seen in the smears as multinucleated giant cells and contain Cowdry type A inclusion bodies. (8)
- **Direct Detection** - Electron microscopy of vesicle fluid - rapid result but cannot distinguish between HSV and VZV (8)
- **Immunofluorescence** of skin scrappings - can distinguish between HSV and VZV (11 Harvey)
- **PCR** - now used routinely for the diagnosis of herpes simple encephalitis (3 webmd)
- **Virus Isolation** - HSV-1 and HSV-2 are among the easiest viruses to cultivate. It usually takes only 1 - 5 days for a result to be available. (1)
- **Serology** - Not that useful in the acute phase because it takes 1-2 weeks for before antibodies appear after infection. Used to document to recent infection. (8)

**Signs and Symptoms:**

Symptoms of oral herpes include painful blisters or open sores called ulcers in or around the mouth. There can be multiple blisters on or around affected areas -- usually the mouth, genitals, or rectum. The blisters break, leaving tender sores. (3)

Oral herpes infection is mostly asymptomatic, and the majority of people with HSV-1 infection are unaware they are infected. Sores on the lips are commonly referred to as “cold sores.” Infected persons will often experience a tingling, itching or burning sensation around their mouth, before the appearance of sores. (8)

After initial infection, the blisters or ulcers can periodically recur. The frequency of recurrences varies from person to person. (9) Following primary infection, 45% of orally infected individuals will experience reactivation. The actual frequency of recurrences varies widely between individuals (9)

**Historical Information:**

HSV is said to have infected human populations as far back as the middle ages and antibodies developed and evolved to deal with the herpes virus. Its origin have been traced back to east asia. The name *Herpes* comes from the Latin *herpes* which, in turn, comes from the Greek word *herpein* which means to creep (2)

**Virulence Factors:**

HSV-1 is highly contagious, prevalent and spread easily. (1) They enter the host by interacting with the glycoproteins on the surface of the enveloped virus with receptors of the host. The enveloped particle will fuse and create an opening or pore, that the virus use to enter. (2) Then the HSV virus evades the immune system through interference with MHC class I antigen presentation on the cell surface, by blocking TAP transporter (2 wiki). Antibodies to HSV antigens can be detected within 4 - 8 days (IgM IgG IgA) viral antigens are presented on dendritic cells and macrophages to CD4+ Th1 cell lysis of the Infected cells ----CD4+ T-cells, CD8 + T-cells, NK cells (8)

During the primary infection, HSV spreads locally and a short-lived viraemia occurs, whereby the virus is disseminated in the body. Spread to the to craniospinal ganglia occurs. The virus then establishes latency in the craniospinal ganglia. (9) The exact mechanism of latency is not known, it may be true latency where there is no viral replication or viral persistence where there is a low level of viral replication. (9)

**Control/Treatment:**

Treating the herpes virus is a lifelong battle and cannot be fully removed. The main strategy is to take antiviral and disrupt the replication cycle. (2) The best way to
prevent HSV is to avoid contact, and washing with soap helps. Also avoid oral sex as it easy to get oral herpes from this practice.

**Drugs:** Antiviral medications disrupts virus ability to replicate

- **Acyclovir:** drug of Choice, safe and effective, widely tested. (4)
- **Valacyclovir:** new, higher bioavailability (3-5x) greater than that of acyclovir. More expensive, oral route only. Test trials have shown that it is safe and well tolerated. (5)
- **Famciclovir:** new antiviral medication, oral form of penciclovir, a purine analog similar to acyclovir, bioavailability is 77% and the drug is quickly converted to its active form. The intracellular half-life is 10 times longer than acyclovir. (6)
- A topical anesthetic such as viscous lidocaine (Dilocaine, Nervocaine, Xylocaine, Zilactin-L) may be prescribed to relieve pain associated with oral blisters and lesions (12)

**Vaccine:** There have been many attempts to create a successful vaccines for the herpes virus but no success to date (13). However, Professor Ian Frazer developed an experimental vaccine designed to prevent new infections, and to treat those who already have the infection. In February 2014, it was announced that Frazer's new vaccine against genital herpes has passed human safety trials in a trial of 20 Australians. Further research is required to determine if the vaccine can prevent transmission. (13)

**Current outbreaks / cases locally (with prevalence/incidence):**

Statistical studies suggest that about 80%-90% of people in the U.S. have been exposed to HSV-1 and about 30% have been exposed to HSV-2. (3) In the US, 57.7% of the population is infected with HSV-1 and 16.2% are infected with HSV-2. Among those HSV-2-seropositive, only 18.9% were aware they were infected. During 2005–2008, the prevalence of HSV-2 was 39.2% in blacks and 20.9% in women.( 2)

**Current outbreaks/cases globally (with prevalence/incidence):** An estimated 3.7 billion people under age 50 (67%) have HSV-1 infection globally (7) The number was highest in Africa, South-East Asia and Western Pacific, reflecting large population size. The estimated worldwide prevalence of HSV-1 infection among 0–49 year olds in 2012 was 67% averaged across all ages Prevalence increased with age, and was high across all regions, but highest in Africa (87% overall prevalence) and lowest in the Americas (40–50%) in 2012 (7)

**Incident:** The total number of new infections of HSV-1 in 2012 was estimated to be 118 million. Again, the number was highest for those regions where population size was highest: Africa, South-East Asia and Western Pacific. Most HSV-1 infections occurred during the first five years of life in Africa and South-East Asia, with virtually no new infection in adulthood. Around two thirds of HSV-1 infections occurred in those aged 0–5 years in Eastern Mediterranean, half in Western Pacific, and one-third in Europe. By contrast, around half of new HSV-1 infections in the Americas occurred in those aged 15–49 years (7)

**Work Cited:**


