Herpes Simplex Virus

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Herpes Simplex Virus (HSV)

- Ancient Greek: ‘creep’ or ‘crawl’
- Most commonly infectious to humans: HSV-1 and HSV-2
- Structure
  - Double Stranded DNA
  - Icosapentahedral capsid
  - Tegument
  - Envelope (Lipid, protein)

(Whitley & Roizman, 2001)

Fact or Fiction?

“Increasing the number of sexual partners puts individuals at greater risk of acquiring HSV”

FACT
Epidemiology

- **Seroprevalence in Ontario:**
  - HSV-1: 51.1% and HSV-2: 9.1%

- **Globally:**
  - HSV-1: 67% and HSV-2: 11.3%

- **In America:**
  - Prevalence of HSV-2 infection has decreased from 21% to 16% from 1990 to 2010

- **Risk factors:**
  - Socioeconomic status
  - Geographical location/population
  - Number of sexual partners
  - Mother-fetus transmission

(Howard et al., 2003), (LeVay & Baldwin, 2012), (WHO, 2015), (Looker et al., 2015)
Symptoms: HSV-1

- Blisters/open sores in or around the mouth
- Majority of infections are asymptomatic and initially acquired through childhood
- Episodic infections
Symptoms: HSV-2

- Genital/anal blisters or ulcers
- Mostly transmitted through sexual contact
- Mostly asymptomatic
- Initial infection can be accompanied with fever, body aches, swollen lymph nodes
- Episodic infections
  - More mild

(Herpes simplex, 2005)
Infections in Other Parts of the Body

**Eyes:** Ocular herpes

**Skin or mucosa:** Herpetic whitlow

**CNS:** Encephalitis

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(Crooks, & Baur, 2014), (Whitley, Kimberlin, & Prober, 2007)
Fact or Fiction?

“You will not transmit HSV to a sexual partner if you are not exhibiting symptoms”

FICTION
HSV-1: Transmission

- Contact with mucosal surfaces/abraded skin on lips, mouth, skin above waist, or infected saliva (shedding)
- Close nonsexual contact

- Nectin-1 & HVEM (cell surface receptors) interacting with viral glycoproteins
- Invades epithelium via basal membrane

(Whitley & Roizman, 2001), (Nahmias, Keyserling & Lee, 1989), (Heldwein & Krummenacher, 2008), (Thier et al., 2017)
**HSV-2: Transmission**

- **Shedding** of a lesion in the genitals onto a mucosal surface during sex
- Most often during **asymptomatic reactivation**
- Increased viral load + >3mm lesion = high transmission

(Schiffer, Mayer, Fong, Swan, & Wald, 2014)
VIRAL SHEDDING OCCURS ABOUT 20% OF THE TIME.

MORE SHEDDING IF:

- Asymptomatic shedding is higher within the first three months of a first outbreak.
- Asymptomatic shedding is higher in genital herpes cases caused by HSV-2 than those caused by HSV-1.
- For seven days after an outbreak has cleared up, there is a higher likelihood of asymptomatic shedding.
- In people who have had outbreaks before, there is more shedding.

LESS SHEDDING IF:

- The rate of shedding decreases after the first year of infection.
- Daily antivirals are shown to reduce shedding by more than 90%.

Read the data and research at: justherpes.com/facts/herpes-viral-shedding
HSV-2: Transmission

A median of 3.5 sexual acts can result in transmission

(Schiffer, Mayer, Fong, Swan, & Wald, 2014)
HSV-1 & HSV-2: Attachment

1. Fusion of the viral envelope to the plasma membrane
2. Endocytic pathway using phagocytosis

- Attachment via filopodia membrane protrusions to heparan sulphate proteoglycans (HSPG)
- HSV SURFING

(Akhtar & Shukla, 2009)
HSV-1 & HSV-2: Entry

- Binding of glycoprotein-D to Nectin-1 (HSV-1 & 2) and Nectin-2 (HSV-2)
  - Conformational change
- Multi-glycoprotein complex
- Cellular membranes fuse
  - Lipid mixing
- Viral nucleocapsid and tegument proteins released into host’s cytoplasm

(Akhtar & Shukla, 2009)
HSV-1 & HSV-2: Post Entry

Nucleocapsids & motor dyenin
- Nucleocapsids dissociate from tegument proteins to bind to microtubule dependent motor dyenins
- Propels virus towards nuclear membrane

Nuclear Membrane
- Virus is uncoated and viral DNA is released into nucleus

Nucleus
- Once internalized, transcription occurs to infect other cells

(Akhtar & Shukla, 2009)
HSV-1: Neural cells affected

Herpesvirus (type 1) Infection

- **Latent period:** Travels to trigeminal ganglia and sensory neurons
  - A5 and KH10 receptors

- ** Reactivation:** increased expression of lytic cycle genes
  - Physical/emotional stress
  - Tissue damage
  - Fever

(Nicoll, Proença, & Efstathiou, 2012), (Whitley & Roizman, 2001), (Margolis, Imai, Yang, Vallas, & Krause, 2007)
HSV-2: Neural cells affected

- **Latent period:** lumbosacral dorsal root ganglia
  - Symptoms below the waist and predominantly in the genital area
- **Virus binds to KH10 receptors on these neurons**
  - **Alters gene expression**
- **Affected genes:** Gprc1g, Gabbr1, Kcnab2, and Kcnc1

(Vassantachart & Menter, 2016)
HSV-1 & HSV-2: Crossover

- HSV-1 can cause genital herpes and HSV-2 can cause oral herpes
  - Oral sex
- Process of **shedding of lesions**
- HSV-1 binds to A5 and KH10 receptors
- HSV-2 binds to KH10
  - Located in **both** trigeminal ganglia and lumbosacral dorsal root ganglia

...scary eh?

(STDcheck, 2015), (Margolis, Lmai, Yang, Vallas, Krause, 2007)
Fact or Fiction?

“"It is possible to live with HSV infection throughout one’s lifetime with proper treatment/management"

FACT
Treatments for HSV

- Currently incurable
- HSV vaccine research is ongoing
- Current methods focus on:
  - Prevention
  - Reduction of discomfort
  - Increasing healing process during outbreak

(Crooks, & Baur, 2014)
Treatment for Genital Herpes

- Medications
  - Acyclovir
  - Valacyclovir (Valtrex)
  - Famciclovir (Famvir)

- Genital Herpes can reoccur

- Two treatment strategies
  - Episodic Treatment
  - Suppressive Therapy

(Crooks, & Baur, 2014)
Genital Herpes

Episodic Treatment

- Immediately after onset
- Reduces severity and duration of lesion pain
- Does not reduce risk of HSV transmission
- Only effective when taken within one day of lesion onset

Suppressive Therapy

- Daily
- Reduces the recurrence rate by 70%-80%
- Decreases risk of transmission

Increased quality of life for patients receiving Suppressive Therapy over Episodic Treatment

(Crooks, & Baur, 2014), (Wish, 2017) (Centers for Disease Control and Prevention, 2015)
Management of Genital Herpes

- Drink more fluids to dilute the acid in the urine to reduce burning sensation during urination
  - Don’t drink cranberry juice (acidic)
- Keep blisters dry and clean

(Crooks, & Baur, 2014), (Arshi, 2015)
Treatments for Oral Herpes

- Topical anesthetics to relieve pain
  - Lidocaine (Dilocaine, Nervocaine, Xylocaine, Zilactin-L)

- Oral or IV medication
  - Only for those with weakened immune systems (e.g. infants younger than 6 weeks old, people with severe diseases, etc.)

(DerSarkissian, 2016), (WebMD, 2018), (MEDQUIK, 2018)
Preventative Measures

- Avoid direct physical contact.
- Do not share items that could transmit the virus.
- Wash hands thoroughly.
- Avoid sexual intercourse with infected partners during an episode.
- Use a latex condom to lower the risk of transmission.

(American Academy of Dermatology, 2018)
References


References (cont)


