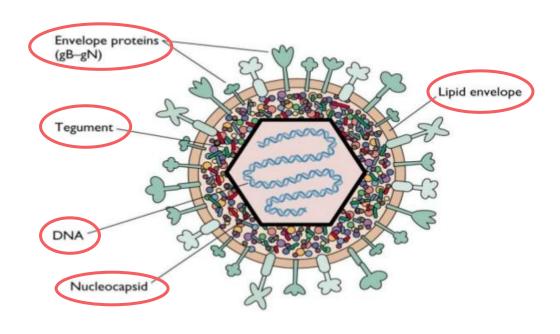


Herpes Simplex Virus (HSV)

- 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)

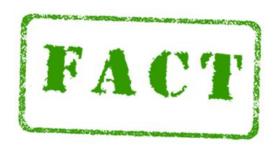


http://www.onlinebiologynotes.com/herpes-simplex-virushsv-structure-genome-mode-transmission-pathogenesis-infection-laboratory-diagnosis-treatment/

Fact or Fiction?

((

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



Epidemiology



http://www.freeworldmaps.net/political.html

• Seroprevalence in Ontario:

o 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)

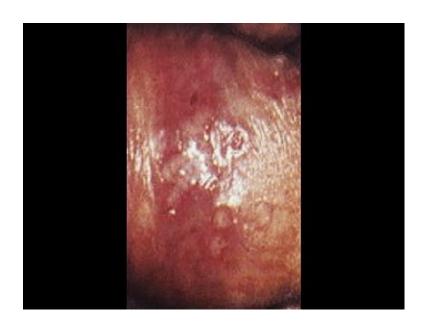
Symptoms: HSV-1

- 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



Infections in Other Parts of the Body

Eyes: Ocular herpes



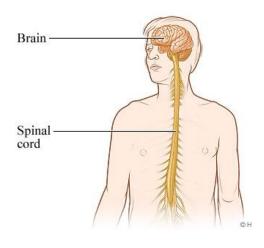
https://eyexan.com/ocular-herpes-causes-symtoms-treatment-virus-eye-infection/

Skin or mucosa: Herpetic whitlow



https://en.wikipedia.org/wiki/Herpetic_whitlow#/media/File:Herpetic_whitlow_in_young_child.jpg

CNS: Encephalitis



https://www.webmd.com/brain/central-nervous-system

(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



HSV-1: Transmission

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

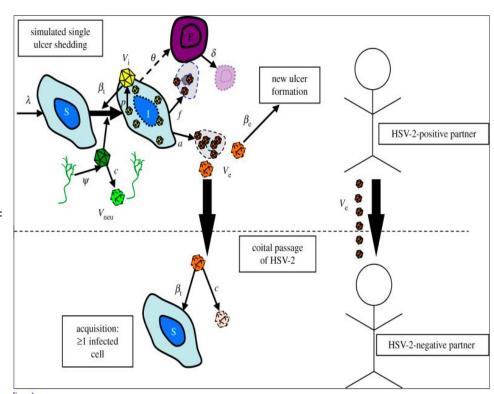
- Nectin-1 & HVEM (cell surface receptors) interacting with viral glycoproteins
- Invades epithelium via basal membrane



https://www.britannica.com/science/herpes-simplex

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





JUST HERPES .com HERPES VIRAL SHEDDING RATES



VIRAL SHEDDING OCCURS ABOUT 20% OF THE TIME.

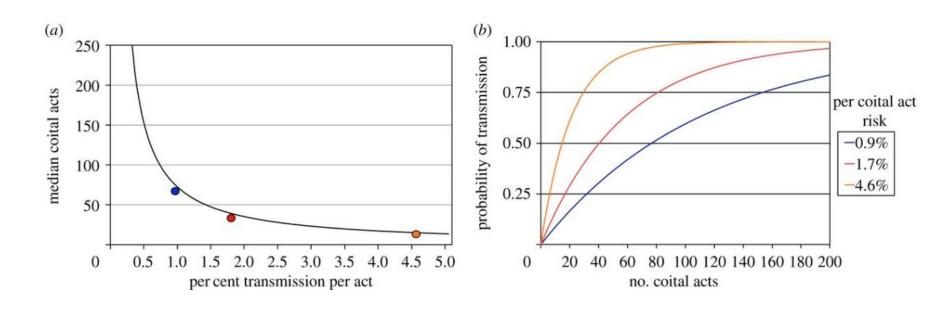
MORE SHEDDING IF:

- 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%.

HSV-2: Transmission

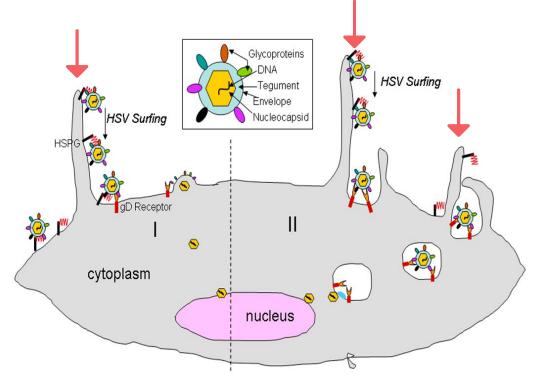


A median of 3.5 sexual acts can result in transmission

HSV-1 & HSV-2: Attachment

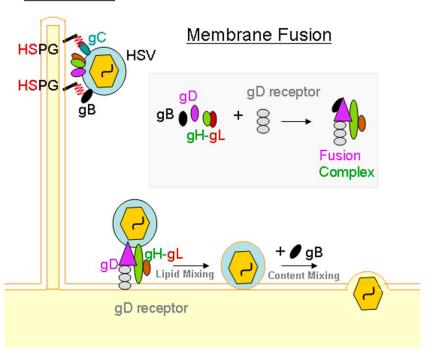
- Fusion of the viral envelope to the plasma membrane
- Endocytic pathway using phagocytosis

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



HSV-1 & HSV-2: Entry

Attachment



- 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

HSV-1 & HSV-2: Post Entry

Nucleocapsids & motor dyenin

Nuclear Membrane

Nucleus

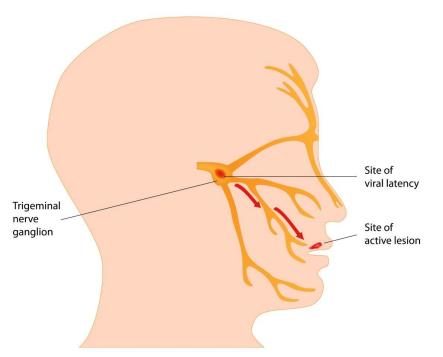
- Nucleocapsids
 dissociate from
 tegument proteins
 to bind to
 microtubule
 dependent motor
 dyenins
- Propels virus towards nuclear membrane

 Virus is uncoated and viral DNA is released into nucleus Once internalized, transcription occurs to infect other cells

(Akhtar & Shukla, 2009)

HSV-1: Neural cells affected

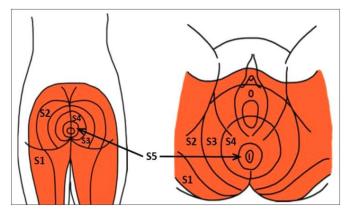
Herpesvirus (type 1) Infection

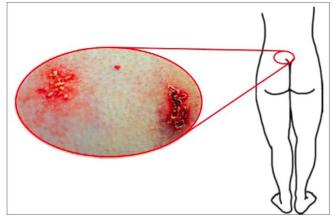


- Latent period: Travels to trigeminal ganglia and sensory neurons
 - A5 and KH10 receptors
- Reactivation: increased expression of lytic cycle genes
 - Physical/emotional stress
 - Tissue damage
 - Fever

HSV-2: Neural cells affected

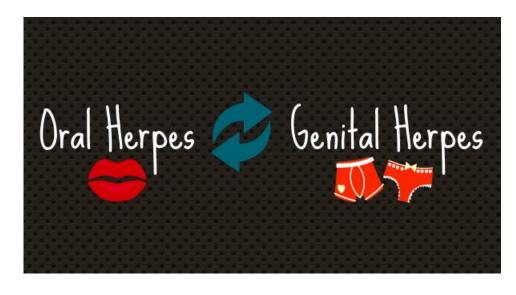
- Latent period: lumbosacral dorsal root ganglia
 - Symptoms below the waist and predominantly in the genital area
- Virus binds to KH10 receptors on these neurons
 - Alters gene expression
- Affected genes: Gprc1g, Gabbr1,
 Kcnab2, and Kcnc1





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

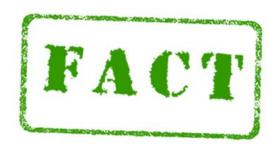


...scary eh?

Fact or Fiction?

"

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



Treatments for HSV

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



http://www.slate.com/articles/health_and_science/medical_examiner/2016/09/the_zika_vaccine_could_convince_anti_vaxxers_of_vaccines_necessity.html

Treatment for Genital Herpes

- Medications
 - Acyclovir
 - Valacyclovir (Valtrex)
 - Famciclovir (Famvir)
- Genital Herpes can reoccur
- Two treatment strategies
 - Episodic Treatment
 - Suppressive Therapy



http://nursingcrib.com/drug-study/acyclovir-drug-study/



https://www.dokteronline.com/en/famvir-famciclovir



http://hsvtype1.com/valacyclovir-hcl.html

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



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





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.)





Preventative Measures



(American Academy of Dermatology, 2018)

References

Akhtar, J., & Shukla, D. (2009). Viral entry mechanisms: cellular and viral mediators of herpes simplex virus entry. The FEBS journal, 276(24), 7228-7236.

American Academy of Dermatology. (2018). Herpes Simplex: Tips for Managing. American Academy of Dermatology Association. Retrieved from https://www.aad.org/public/diseases/contagious-skin-diseases/herpes-simplex#tips

Crooks, R., & Baur, K. (2014). Our Sexuality. Belmont, CA: Jon-David Hague.

DerSarkissian, C. (2016). Oral Herpes. WebMD. Retrieved from https://www.webmd.com/a-to-z-quides/oral-herpes#3-6

Danziger, P (2016). Could A Zika Virus Break the Vaccine Stalemate? Slate. Retrieved from http://www.slate.com/articles/health and science/medical examiner/2016/09/the zika vaccine could convince anti vaxxers of vaccines necessity.html

Dokter Online (2018). Famvir. Doktoronline.com. Retrieved from https://www.dokteronline.com/en/famvir-famciclovir

Elion, G. B. (1982). Mechanism of action and selectivity of acyclovir. The American journal of medicine, 73(1), 7-13.

Fatahzadeh, M., & Schwartz, R.A. (2007). Human herpes simplex virus infections: Epidemiology, pathogenesis, symptomatology, diagnosis, and management. Journal of the American Academy of Dermatology, 57(5), 737-763.

Genital Herpes Overview .(2018). STD Check. Retrieved from https://www.stdcheck.com/herpes-2.php

Heldwein, E.E., & Krummenacher, C. (2008). Entry of herpesviruses into mammalian cells. Cellular and Molecular Life Sciences, 65(11), 1653-1668.

Herpes simplex virus. (2017). World Health Organization Retrieved from http://www.who.int/mediacentre/factsheets/fs400/en/# hsv1

Herpes Simplex. (2018). American Academy of Dermatology Association. Retrieved from https://www.aad.org/public/diseases/contagious-skin-diseases/herpes-simplex#symptoms

Howard, M., Sellors, J. W., Jang, D., Robinson, N. J., Fearon, M., Kaczorowski, J., & Chernesky, M. (2003). Regional distribution of antibodies to herpes simplex virus type 1 (HSV-1) and HSV-2 in men and women in Ontario, Canada. *Journal of clinical microbiology*, 41(1), 84-89.

Jane, D. (2011). Acyclovir-Drug Study. Nursingcrib. Retrieved from http://nursingcrib.com/drug-study/acyclovir-drug-study/

John Hopkins University. (2018). Oral Herpes. John Hopkins Medicine. Retrieved from https://www.hopkinsmedicine.org/healthlibrary/conditions/adult/infectious diseases/Oral Herpes 22,OralHerpes

Just Herpes. (2015). Herpes Viral Shedding: The Research and the Rates. Just Herpes. Retrieved from http://justherpes.com/facts/herpes-viral-shedding/

Karki, G. (2018). Herpes simplex virus(HSV): Structure and genome, mode of transmission, pathogenesis, infection, laboratory diagnosis and treatment -. Retrieved from http://www.onlinebiologynotes.com/herpes-simplex-virushsv-structure-genome-mode-transmission-pathogenesis-infection-laboratory-diagnosis-treatment/

Kramer, M. F., Cook, W. J., Roth, F. P., Zhu, J., Holman, H., Knipe, D. M., & Coen, D. M. (2003). Latent herpes simplex virus infection of sensory neurons alters neuronal gene expression. Journal of virology, 77(17), 9533-9541.

References (cont)

eone, P. & Corey, L. (2005). Genital herpes: prevalence, transmission, and prevention. Retrieved from: https://www.medscape.org/viewarticle/502718 3

LeVay, S., & Baldwin, J. I. (2009). Human sexuality. Sunderland, Mass: Sinauer Associates.

Liu, T., Khanna, K.M., Carriere, B.N., & Hendricks, R.L. (2001). Gamma Interferon Can Prevent Herpes Simplex Virus Type 1 Reactivation from Latency in Sensory Neurons. Journal of Virology, 75(22), 11178-11184.

Looker, K. J., Magaret, A. S., Turner, K. M., Vickerman, P., Gottlieb, S. L., & Newman, L. M. (2015). Global estimates of prevalent and incident herpes simplex virus type 2 infections in 2012. PloS one, 10(1), e114989.

Margolis, T. P., Imai, Y., Yang, L., Vallas, V., & Krause, P. R. (2007). Herpes simplex virus type 2 (HSV-2) establishes latent infection in a different population of ganglionic neurons than HSV-1: role of latency-associated transcripts. Journal of virology, 81(4), 1872-1878.

MedlinePlus. (2018). Herpes-oral. U.S. National Library of Medicine. Retrieved from https://medlineplus.gov/ency/article/000606.htm

Mertz, G. J., Benedetti, J., Ashley, R., Selke, S. A., & Corey, L. (1992). Risk factors for the sexual transmission of genital herpes. Annals of Internal Medicine, 116(3), 197-202.

Nahmias, A.J., Keyserling, H., & Lee, F.K. (1989). Herpes Simplex Viruses 1 and 2. Viral Infections of Humans. New York: Plenum Publishing Corporation.

Nicoll, M.P., Proenca, J.T., & Efstathiou, S. (2012). The molecular basis of herpes simplex virus latency. FEMS Microbiology Reviews, 36(3), 684-705.

Payne, W.A., Hahn, D.B., & Lucas, E.B. (2013). Understanding Your Health. New York, NY: McGraw-Hill.

Pettersson, N. (2013). Valacyclovir HCl. hsvtype1.com. Retrieved from http://hsvtype1.com/valacyclovir-hcl.html

Pierce, J.M. What is the difference between HSV1 & HSV2? Oral and Genital Herpes. The STD Project. Retrieved from https://www.thestdproject.com/what-is-the-difference-between-hsv1-hsv2-oral-and-genital-herpes/

Public Health. (2018). Clinics & Services. Hamilton. Retrieved from https://www.hamilton.ca/public-health/clinics-services

Schiffer, J. T., Mayer, B. T., Fong, Y., Swan, D. A., & Wald, A. (2014). Herpes simplex virus-2 transmission probability estimates based on quantity of viral shedding. Journal of The Royal Society Interface, 11(95), 20140160.

Shui, J.W., & Kronenberg, M. (2013). HVEN: An unusual TNF receptor family member important for mucosal innate immune responses to microbes. Gut Microbes, 4(2), 146-151.

Smith, J. S., & Robinson, N. J. (2002). Age-specific prevalence of infection with herpes simplex virus types 2 and 1: a global review. The Journal of infectious diseases, 186(Supplement 1), S3-S28.

STDcheck. (2015). Getting Genital Herpes from Oral Herpes & Vice Versa. Exposed. Retrieved from https://www.stdcheck.com/blog/getting-genital-herpes-from-oral-herpes-vice-versa/

Taylor, S. (2018). Herpes Simplex. healthline. Retrieved from https://www.healthline.com/health/herpes-simplex

References (cont)

Thier, K., Petermann, P., Rahn, E., Rothamel, D., Bloch, W., & Knebel-Morsdorf, D. (2017). Mechanical Barriers Restrict Invasion of Herpes Simplex Virus 1 into Human Oral Mucosa. Journal of Virology, 91(22), e01295-17.

U.S. Department of Health & Human Services. (2015). Genital HSV Infections. Centers for Disease Control and Prevention. Retrieved from https://www.cdc.gov/std/tg2015/herpes.htm

Vassantachart, J. M., & Menter, A. (2016). Recurrent lumbosacral herpes simplex virus infection. Baylor University Medical Center Proceedings, 29 (1), 48-49.

Wald, A. (2004). Herpes simplex virus type 2 transmission: risk factors and virus shedding. Herpes: the journal of the IHMF, 11, 130A-137A.

Wald, A. (2006). Genital HSV-1 infections. Sexually Transmitted Infections, 82(3), 189-190. http://doi.org/10.1136/sti.2006.019935

Whitley, R., Kimberlin, D. W., & Prober, C. G. (2007). Pathogenesis and disease.

Whitley, R. J., & Roizman, B. (2001). Herpes simplex virus infections. The Lancet, 357(9267), 1513-1518.

WHO (2015). Globally, an estimated two-thirds of the population under 50 are infected with herpes simplex virus type 1. Retrieved from http://www.who.int/mediacentre/news/releases/2015/herpes/en/