Sections		**HSV-1**	**VZV**
Viral Genome	Genes	~80: 4 diploid (ICP4, 0, 34.5, LAT)	68: 3 diploid (ORFs 62, 63, 64)
	Size	~152kbp	~125kbp
	G+C content	-67%	-47%
	Repeats	-Large repeats for both UL and US	-Large on US only; 88.5bp on UL
	Isomers	4	Mostly 2 with UL region fixed
	miRNA	From LAT region- role not yet clear	No known miRNAs
Viral Proteins	regulation	Regulated Cascade –defined as α, $\beta1$, $\beta2$, $\gamma1$, $\gamma2$	Likely similar, but difficult to define experimentally
	Immediate Early differences	-six genes (ICP0, ICP4, ICP27, ICP22, ICP1.5, ICP47. -All have TAATGARAT motif in IE promoters	-Three genes reported to date -ORF/IE62(ICP4 Eq) ORF/IE4(ICP27 eq) and ORF/IE63 (ICP22 eq) -No ortholog of ICP47. -Only IE62 has TAATGARAT in promoter
	Short Region differences	-gD, an essential protein involved in receptor & entry -gE not required in culture	-No gD, gE is essential- -gE is key receptor binding protein -Missing several HSV equivalents
	Tegument differences	-UL48 (VP16) required in culture: -UL49 not required	-ORF10(VP16 Eq) not required in culture: -ORF9 (UL49 eq) required
Primary Infection	Route of Infection	Spread through direct contact.	Spread via aerosol and inhalation.
	Location of 1^{o} infection	-Epithelia in mucosa, cornea or in epidermal layers of the skin -Usually no viremia	-Epithelial and immune cells in respiratory lymphoid tissues, tonsils -Cell associated viremia -Secondary infection at the sub-dermis
	Spread to neurons	-Usually local only -Accesses neuronal axon termini in skin	-Systemic across entire neuraxis -Same as HSV; may also access neurons during viremia thrugh immune cells
	Innate	TLR-2,3,9 respond to infection	Thought to be the same, but not known
		IFN regulates infection	IFN regulates infection
		NO helps retard viral replication	Role of NO not known
		ICP0 degrades PML and ND10 proteins	Susceptible to PML caging. ORF61 modifies ND10, does not degrade PML

Innate and adaptive immunity	Adaptive T cell response	CD4 and CD8 encounter antigen on DCs and respond to infection	-T cells infected by VZV leading to viral spread. -CD4 and CD8 T cells are VZV specific
	DC	Can infect and reduce presentation to Tcells by DCs	-Can infect and reduce presentation to T cells by DCs
	Humoral Response	Elicit antibodies against broad viral antigens. IgA, IgG and IgM	-Elicit antibodies against broad viral antigens. IgA, IgG and IgM. -Antibodies are used in high risk patients to treat VZV -Antibody has less role on control of infection/latency and reactivation
	Immune Evasion	ICP47 blocks TAP function.	-Does not block TAP function. -Still blocks MHCI and II expression. -Blocks MHCI by ORF66 kinase
		Inhibit IFN responses thru VHS, ICP0, and γ34.5	-Inhibit IFN responses by IE63, IE62 -ORF61 blocks NFkB signaling
		gC blocks complement deposition	No equivalent activity for gC
		Fc binding ability of gE	VZV gE and gI complex to bind Fc
		ICP22, Us5, Us3 and LAT inhibit apoptosis by NK and CD8+ cell mediated lysis	ORF63 blocks apoptosis
Models and Neuronal Latency	Animal modeling	-Most animal models replicate virus -Most show similar disease to humans	-Guinea pig only small natural animal model that replicates virus -No natural model of varicella -No model of reactivated disease
	Location of latency	Sensory ganglia, especially trigeminal ganglia	-Most sensory and autonomic ganglia -Distributed across entire neuraxis
	Load	Generally higher genome load than VZV	About one magnitude lower genome load
Maintenance latency		-Endless Circular episome. -Heterochromatinated state	-Endless circular episome. -Assumed to be Heterochromatinated state
	Latent Gene Expression	-Abundant transcripts from LAT region -LATs processed into miRNAs -LATs block apoptosis	-RNAs for ORFs 4,21,61,10,29,62,63, and 66. - -Reported protein expression is controversial -ORF63 most often reported as expressed

		-Rare protein expression without virus	
	Immune Component	-Drives ganglionic CD8+ immune infiltrate -CD8 may control reactivation events	-No Immune infiltrate yet reported -Cellular immunity maintains latency
reactivation and disease	Occurrence	-May Reactivate frequently -Incidence drops with age -Disease similar to primary infection -At same site as 1^{o} infection	-Reactivated disease usually never or once -Incidence rises with age and declining cellular immunity. -Occurs anywhere on body -Disease clinically different from 1^{o} Infection
	Ganglionic Spread	Involves 1 or few neurons	-Usually intraganglionic spread -Large lesions covering a dermatome.
	Causes of reactivation	Multiple environmental and physiological factors	-Mainly immune senescence or suppression. -Environmental and physiological factors may contribute
	Pain upon reactivation	-Not usually -Some sensory loss with repeated recurrence	-Nearly always neurological involvement -90% of zoster has pain -May develop to post herpetic neuralgia

Table 1: comparison of HSV and VZV with ilustrations of differences and similarities