Herpes Simplex & Varicella Zoster: Advances in Lesion-causing Pathogen Identification

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We will be discussing

1. Lesion-Causing Herpesviridae Viruses
2. Diagnostic Challenges
3. Platforms for HSV/VZV testing
4. HSV/VZV Case Studies

Lesion-Causing Herpesviridae Viruses

Lesion-causing Herpesviridae viruses

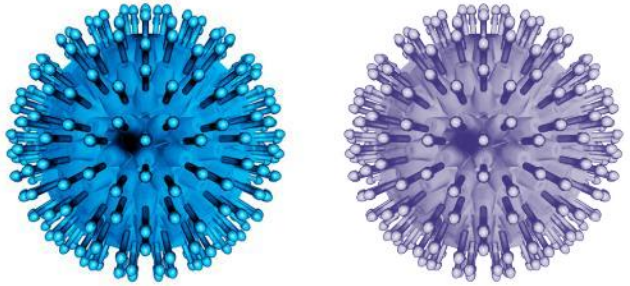
Out of ~130 herpesviruses, only 9 infect humans

Five members of the Herpesviridae virus family are known to be prevalent human pathogens.

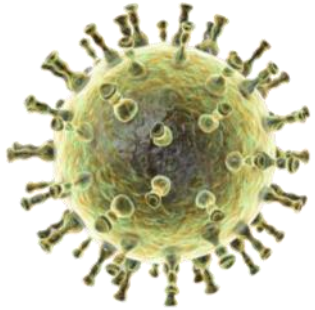
All are capable of producing latent lifelong infections.

Over 90% of adults have been infected with at least one of these viruses.

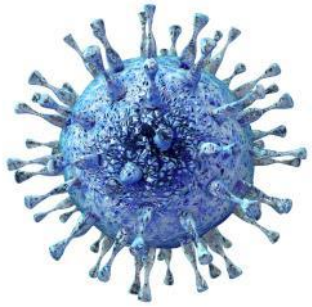
Latent virus exists in almost all who have been infected.



Herpes Simplex Virus 1 & 2 (HSV)



Varicella Zoster Virus (VZV)



Human Cytomegalovirus (HCMV)

Epstein-Barr Virus (EBV)

HSV and VZV are two of the most common causes of primary and latent oral, genital, and cutaneous lesions.

1. Lal H, et al. *N Engl J Med*. 2015;372:2087-2096.
2. Wang S, et al. *Sci Adv*. 2023;9,eadf4904.
3. Herpes Simplex Virus Encephalitis. Accessed Oct 15, 2023. https://www.encephalitis.info/herpessimplexvirusencephalitis
4. Herpesvirus Fact Sheet. Accessed Oct 15, 2023. https://ehs.stanford.edu/reference/herpesvirus-fact-sheet

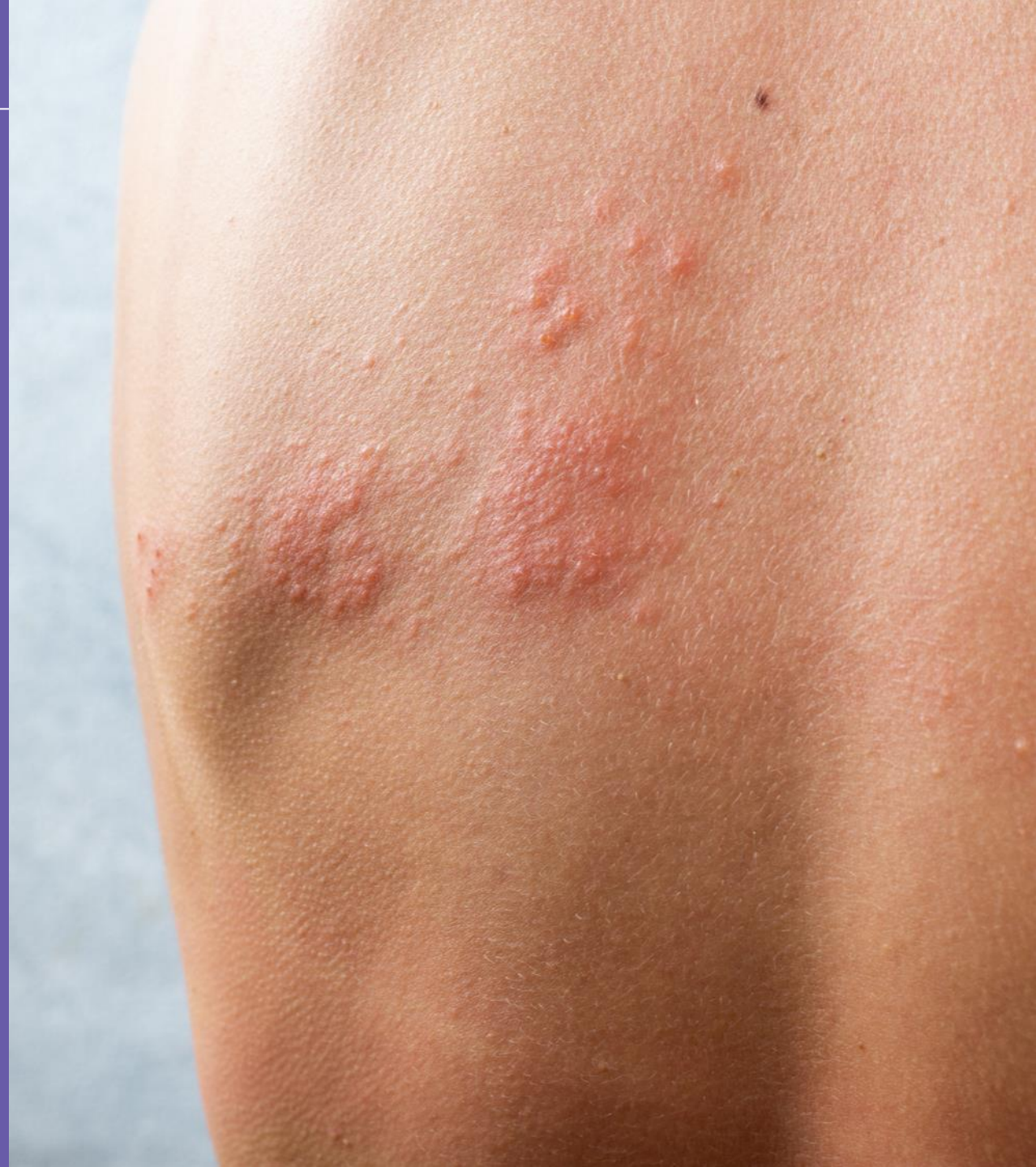
Lesion-causing herpes simplex

- There are two subtypes of HSV
- HSV-1 most commonly affects skin and oral mucous membranes, while HSV-2 lesions are seen in genital mucous membranes
- As a result of oral-to-genital contact, there is an increasing prevalence of HSV-1 in genital lesions and HSV-2 in oral lesions
- Over 66% of individuals under 50 have HSV-1
- HSV-2 is one of the most common sexually transmitted infections with up to 90% of infections unrecognized and undiagnosed
- Early diagnosis and treatment can reduce transmission

1. Wilms L, et al. *JDDG*. 2022;20(10):1327-1351.
2. Saleh D, Yarrarapu SNS, Sharma S. Herpes Simplex Type 1. In: StatPearls. StatPearls Publishing; 2023. Accessed October 15, 2023. https://www.ncbi.nlm.nih.gov/books/NBK482197/
3. Mathew J, Sapra A. Herpes Simplex Type 2. In: StatPearls. StatPearls Publishing; 2023. Accessed October 15, 2023. https://www.ncbi.nlm.nih.gov/books/NBK554427/

Lesion-causing varicella zoster

- VZV is known for causing cutaneous lesions in chickenpox and herpes zoster (shingles)
- A varicella vaccine became available in the late 1990s but more than 95% of the adult world population is infected with latent VZV
- 50% of those unvaccinated may develop herpes zoster by 85 years of age
- One month after the onset of herpes zoster, 14% of patients develop postherpetic neuralgia (PHN)
- Early diagnosis and treatment can shorten zoster duration and may reduce the risk of PHN



1. Nagel MA, Gilden D. *Curr Opin Neurol*. 2014;27(3):356-60.
2. Gruver C, Guthmiller KB. Postherpetic Neuralgia. In: StatPearls. StatPearls Publishing; 2023. Accessed October 15, 2023. https://www.ncbi.nlm.nih.gov/books/NBK493198/

HSV prognosis and complications vary depending on manifestation and infection location

HSV-1

- HSV-1 infection follows a chronic course of latency and reactivation
- Most cases of reactivation are mild
- HSV-1 encephalitis
  - 70% of untreated cases are ultimately fatal
- Ocular HSV
  - Globe rupture
  - Corneal scarring
  - Blindness

HSV-2

- May be painful
- Recurrences can be frequent, as often as several times a year
- Increased risk of HIV infection
- Meningitis
  - Aseptic meningitis occurs in 36% of women and 13% of men
- Acute retinal necrosis

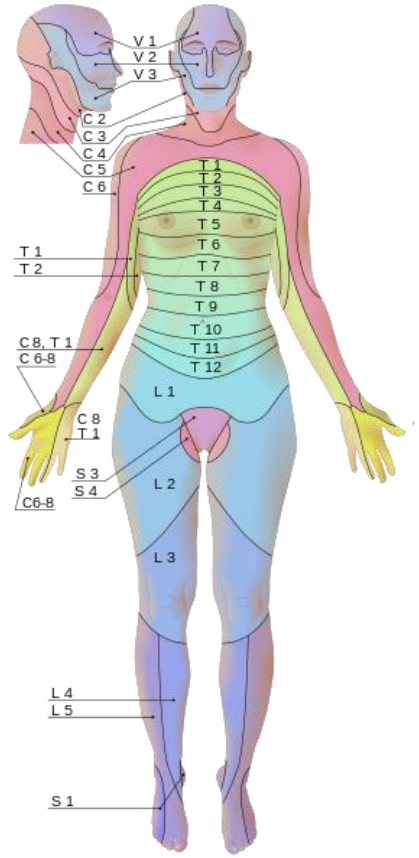
Genital HSV is more transmissible and has a worse prognosis when caused by HSV-2

- Early diagnosis and appropriate antiviral therapy can lead to suppression of viral replication and transmission.
- Abstinence during viral shedding of genital HSV infections can decrease transmission risk.

1. Saleh D, Yarrarapu SNS, Sharma S. Herpes Simplex Type 1. In: StatPearls. StatPearls Publishing; 2023. Accessed October 15, 2023. https://www.ncbi.nlm.nih.gov/books/NBK482197/
2. Mathew J, Sapra A. Herpes Simplex Type 2. In: StatPearls. StatPearls Publishing; 2023. Accessed October 15, 2023. https://www.ncbi.nlm.nih.gov/books/NBK554427/

VZV complications can dramatically impact quality of life

VZV complications depend on the dermatome affected by latent virus reactivation.



General complications

- Paresthesias/dysthesias
- Shock-like sensations
- Secondary bacterial infection
- PHN
- Scarring
- Guillain-Barré syndrome
- Myelitis
- Muscle paralysis
- Meningitis
- Encephalitis

Eye

- Keratitis
- Uveitis
- Optic nerve palsies
- Blindness
- Debilitating pain

Ear

- Hearing loss
- Vertigo

Mouth

- Osteonecrosis
- Tooth loss
- Periodontitis
- Pulp calcification
- Pulp necrosis
- Periapical lesions
- Tooth abnormalities
- Ischemic necrosis

Nair PA, Patel BC. Herpes Zoster. In: StatPearls. StatPearls Publishing; 2023. Accessed October 15, 2023. https://www.ncbi.nlm.nih.gov/books/NBK441824/

Annual costs of HSV and VZV are high

U.S. Annual Direct Healthcare Costs and Lost Productivity

HSV (Genital)[1]

$91 million

VZV (Zoster)[2]

$2.4 billion

Early diagnosis and treatment of HSV and VZV reduce duration and improve outcomes, potentially reducing per-patient healthcare costs[3-4]

1. Chesson HW, et al. *Sex Transm Dis*. 2021;48(4):215-221.
2. Harvey M, et al. *Pain*. 2020;161(2):361-368.
3. Five Things You Should Know About Shingles. Accessed November 12, 2023. https://www.cdc.gov/shingles/5-things-you-should-know.html
4. Almonte-Vega L, et al. *Math Biosc*i. 2020;324:108347.

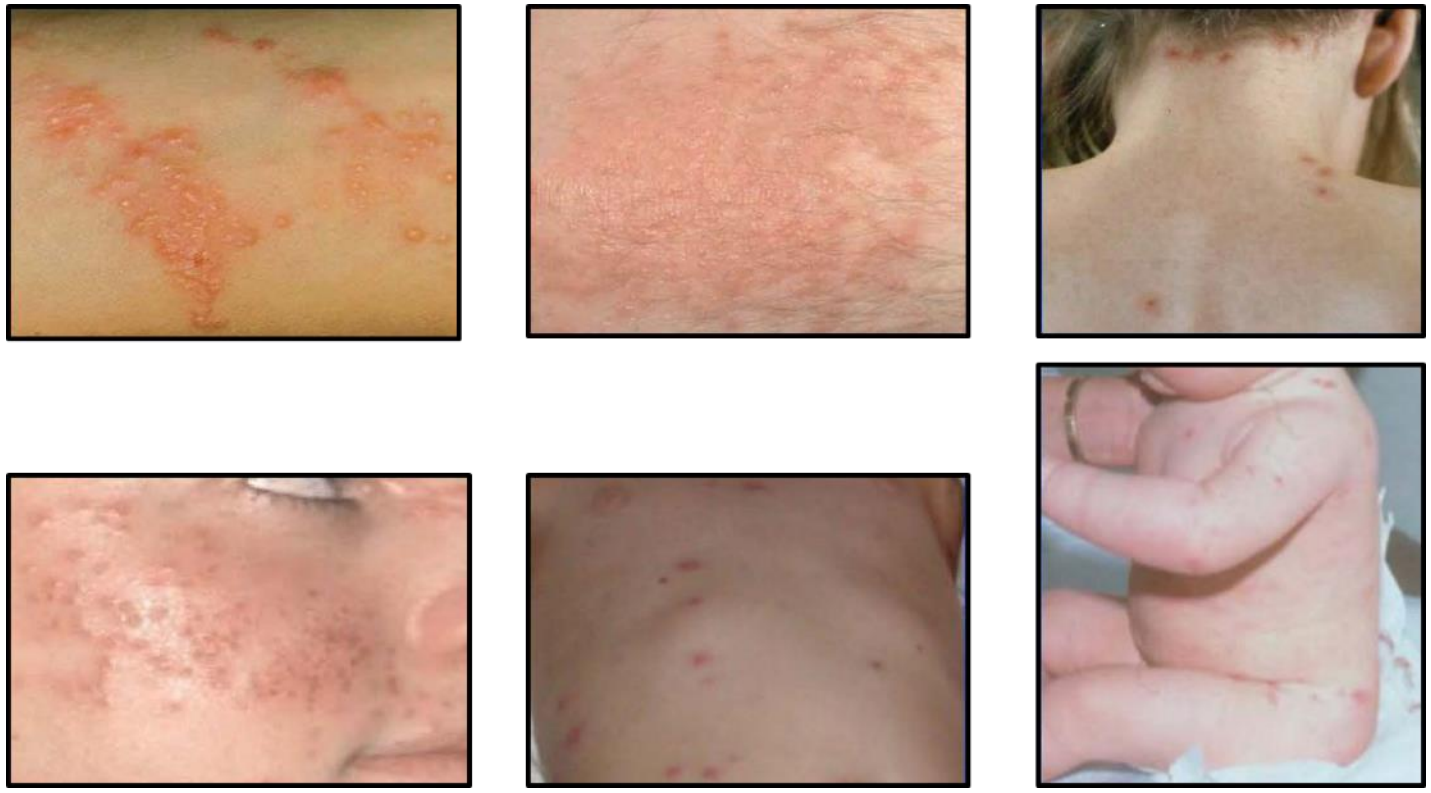
Diagnostic Challenges

Many pathogens and non-pathogenic etiologies may lead to cutaneous, oral, or genital lesions

Lesion-Causing Etiologies	
HSV-1/HSV-2	VZV
Mpox (monkeypox)	Psoriasis
Syphilis	Cellulitis
Chancroid	Insect bites
Lymphogranuloma venereum (LGV)	Dermatitis
Granuloma inguinale (donovanosis)	Folliculitis
Fungal/yeast infections	Ecthyma
Crohn’s disease	Cnidaria envenomation
Behçet's syndrome	Contact stomatitis
Fixed drug eruptions	Lichen striatus

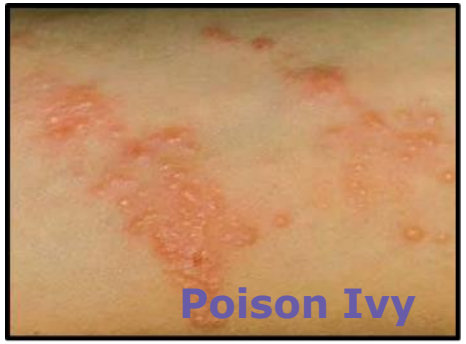
1. Roett M. *Am Fam Physician*. 2020;101(6):355-361.
2. Wilms L, et al. *JDDG*. 2022;20(10):1327-1351.

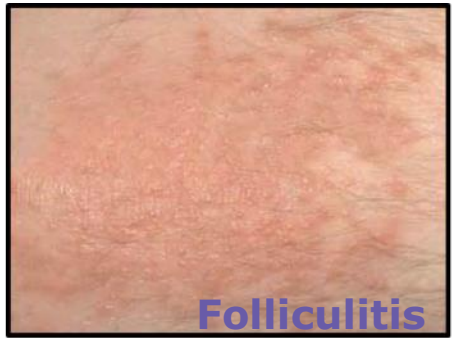
Clinical Diagnosis is Challenging

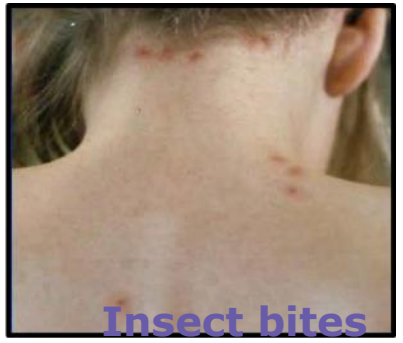


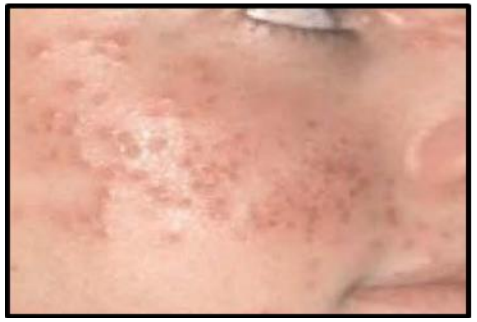
http://www.cdc.gov/chickenpox/index.html
http://www.cdc.gov/vaccines/vpd-vac/varicella/
http://www.cdc.gov/shingles/index.html
http://www.cdc.gov/vaccines/vpd-vac/shingles/

Clinical Diagnosis is Challenging

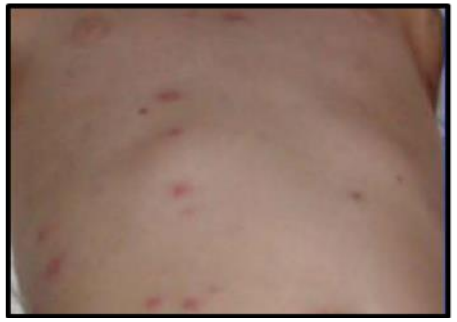








Herpes Simplex



Breakthrough Varicella

http://www.cdc.gov/chickenpox/index.html
http://www.cdc.gov/vaccines/vpd-vac/varicella/
http://www.cdc.gov/shingles/index.html
http://www.cdc.gov/vaccines/vpd-vac/shingles/

Visual clinical diagnosis of lesions often leads to misdiagnosis and unnecessary usage of antibiotics

Genital HSV[2]

- Only 22-82% of visual lesion diagnoses are accurate
- Genital HSV is frequently misdiagnosed
  - Early syphilis
  - Chancroid
  - Granuloma inguinale
  - Lymphogranuloma venereum
- These conditions would normally necessitate antibiotic treatment
- **Unnecessary antibiotics may be prescribed empirically while waiting on confirmatory laboratory tests**

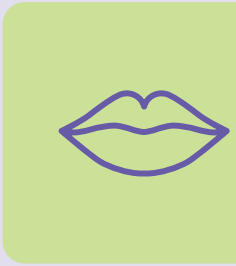
Pediatric Varicella (Chickenpox)[1]

- Visual diagnosis of varicella is often inaccurate
  - 15% of the time in uncomplicated varicella
  - 49% of the time in complicated varicella
- Treatment is also often inaccurately prescribed
  - Antibiotics are recommended 17% of the time
  - Antivirals are recommended 18% of the time
- **Guidelines do not recommend treatment for varicella in most cases**
  - **25% of antibiotics and 69% of varicella antiviral prescriptions are inappropriate**

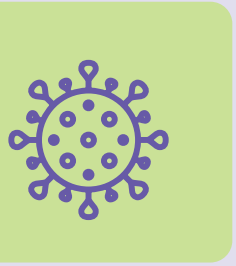
1. Fergie J, et al. *PLoS One.* 2022;17(6):e0269596.
2. Czachor JS. Genital Ulcer Disease. Accessed November 1, 2023. http://antimicrobe.org/new/e16rev.asp

Similar clinical presentations of HSV, VZV, and other lesion-causing pathogens impact diagnosis

Visual differentiation is not possible for most lesion-causing pathogens.



HSV-1 & HSV-2 may not be distinguishable by oral vs. genital lesion patterns.



Atypical presentations are difficult to distinguish.

- VZV in genital dermatomes
- Immunocompromised patients

The only way to definitively determine a diagnosis is through laboratory testing.

1. Wilms L, et al. *JDDG*. 2022;20(10):1327-1351.

Similarities and differences between HSV & VZV lesions

	HSV-1	HSV-2	VZV
Clinical presentation (Primary)	• Clustered vesicles on an erythematous base • Vesicles may progress to pustules and ulcerations	• Clusters of macular or papular lesions • Vesicles may progress to pustules and ulcerations	• Clustered blister lesions • Vesicles may progress to pustules with umbilication and scabs
Clinical presentation (Recurrent)	• Recurrent lesions may be milder	• Same grouped presentation as primary lesions • Lesions may be painful	• Grouped papules become ulcerated vesicles • 1-2 contiguous dermatomes • Lesions may be painful
Duration of lesions	18.8 ± 6.5 days	21.5 ± 6.8 days	• Chickenpox: 4-7 days • Zoster: 2-4 weeks
Average time to recurrence	> 6 months	~ 80 days	Years
Average recurrences/year	0.24	3.9	> 1
Primary viral shedding	15%	85%	Yes
Recurrence viral shedding	2%	98%	Yes

1. Gruver C, Guthmiller KB. Postherpetic Neuralgia. In: StatPearls. StatPearls Publishing; 2023. Accessed October 15, 2023. https://www.ncbi.nlm.nih.gov/books/NBK493198
2. Saleh D, Yarrarapu SNS, Sharma S. Herpes Simplex Type 1. In: StatPearls. StatPearls Publishing; 2023. Accessed October 15, 2023. https://www.ncbi.nlm.nih.gov/books/NBK482197/
3. Mathew J, Sapra A. Herpes Simplex Type 2. In: StatPearls. StatPearls Publishing; 2023. Accessed October 15, 2023. https://www.ncbi.nlm.nih.gov/books/NBK554427/
4. Ayoade F, Kumar S. Varicella-Zoster Virus (Chickenpox). In: StatPearls. StatPearls Publishing; 2023. Accessed October 15, 2023. https://www.ncbi.nlm.nih.gov/books/NBK448191/
5. Hook EW. *Med Lab Obs*. 2012;44(7):8-12.

Clinical diagnosis of VZV may need to rule out HSV

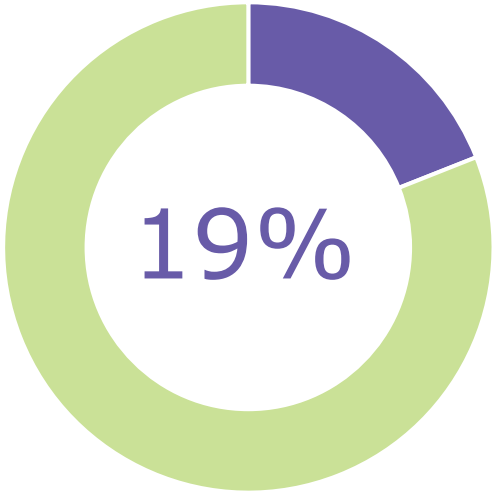
Dermatome distribution of herpes zoster may be distinctive enough to make an accurate clinical diagnosis.[1]

HSV is the primary differential diagnosis for VZV, particularly when the face and genital region are affected.[2]

Molecular assays frequently find HSV in patients with suspected VZV.[2]

HSV : Different risk of transmission and recurrence

HSV is found over 19% of suspected typical VZV cases.[2]



VZV Differential Diagnosis[1]

HSV	Insect bites
Impetigo	Papular urticaria
Contact dermatitis	Candida
Folliculitis	Dermatitis herpetiformis
Scabies	Drug eruptions

1. Centers for Disease Control. Shingles (Herpes Zoster) Diagnostic Testing. Accessed October 20, 2023. https://www.cdc.gov/shingles/hcp/diagnosis-testing.html
2. Nikolic D, et al. *Am J Clin Pathol.* 2019;151(1):122–126.

Recurrent VZV is often HSV

Diagnosis	Percentage
HSV eruption	**56%**
PHN	19%
PHN + Dermatitis	8%
Folliculitis	5%
Actinic keratosis	3%
Contact dermatitis	3%
Herpes zoster	**1%**
Excoriated ulcer	1%
Prurigo nodularis	1%
Fixed drug eruption	1%
Arthropod assault	1%

Recurrent herpes zoster is reported in over **6%** of immunocompromised patients.

Over half of recurrent VZV is **HSV**.

Only **1%** have active VZV lesions.

1. Vangipuram R, et al. *Skin*. 2021;5(1).

HSV-1 & 2 are different

CDC guidelines recommend differentiating between HSV-1 and HSV-2 with molecular testing because they cannot be differentiated visually by region, clustering, or general appearance.

HSV-1 & HSV-2 cannot be differentiated visually.

HSV-1 is 80% less likely to recur within one year.

Recurrent HSV-1 is treated with episodic therapy.

Suppressive therapy for HSV-1 is rare.

HSV-2 can recur up to 12 times per year and episodes are more severe.

HSV-2 has higher rates of viral shedding.

Transmission of HSV-2 occurs most often when a patient is asymptomatic.

Recurrent HSV-2 requires suppressive therapy to prevent transmission.

1. Tan C, et al. *CMAJ*. 2023;195(13):479-482.
2. Myhre J, et al. HSV-1 vs. HSV-2: What Are the Differences? Accessed October 30, 2023. https://www.verywellhealth.com/hsv-1-vs-hsv-2-7092956
3. Bacon TH, et al. *Clin Microbiol Rev*. 2003 Jan;16(1):114-28.

"Clinical diagnosis of genital herpes can be difficult because the self-limited, recurrent, painful, and vesicular or ulcerative lesions classically associated with HSV are absent in many infected persons at the time of clinical evaluation.

If genital lesions are present, clinical diagnosis of genital herpes should be confirmed by type-specific virologic testing from the lesion by NAAT or culture."

CDC
STI Treatment Guidelines. 2021

"Prognosis and counseling depend on which HSV type is present.

Both type-specific virologic and type-specific serologic tests for HSV should be available in clinical settings that provide care to persons with or at risk for STIs.

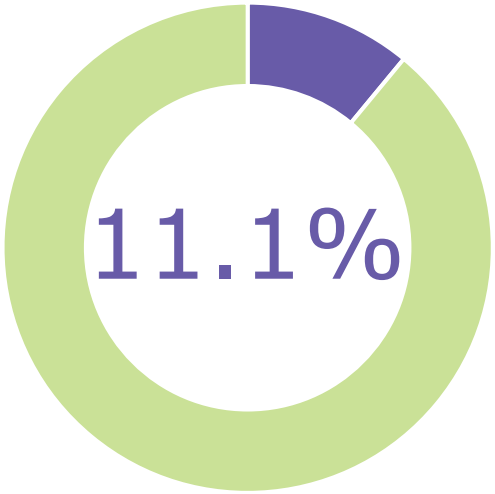
HSV-2 genital herpes infection increases the risk for acquiring HIV twofold to threefold."

CDC
STI Treatment Guidelines. 2021

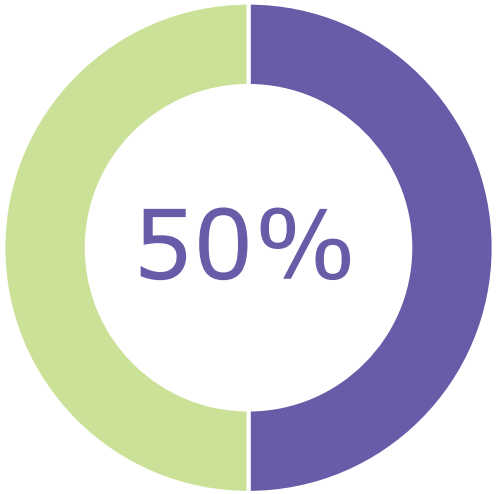
VZV is frequently detected in suspected HSV

- Over 11% of suspected HSV is VZV.
- Most frequent misdiagnosis occurs in facial and genital regions.

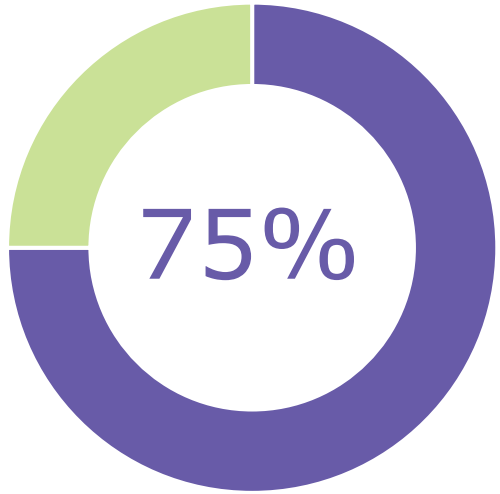
VZV is found in over 11% of suspected HSV cases.



50% of these cases are in genital regions.



75% are not suspected to be VZV due to presentation.



1. Nikolic D, et al. *Am J Clin Pathol.* 2019;151(1):122–126.
2. Granato PA, et al. *J Clin Virol*. 2016;84:87-89.

Important differential diagnosis in patients with suspected HSV lesions and have been not vaccinated for varicella

HSV and VZV treatment efficacy is dependent on accurate timely diagnosis

HSV and VZV have different treatments for primary outbreaks, recurrences, and viral suppression.

Dosages differ depending on viral type, outbreak severity, and health status of the patient.

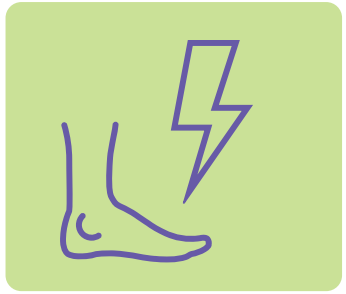
	HSV-1	HSV-2	VZV (Chickenpox)	VZV (Zoster)
Initial outbreak	▪ Acyclovir* ▪ Famciclovir ▪ Valacyclovir	▪ Acyclovir* ▪ Famciclovir ▪ Valacyclovir	▪ Oral or IV acyclovir if at risk for moderate to severe disease or immunocompromised	▪ Acyclovir ▪ Valacyclovir ▪ Famciclovir ▪ Brivudin
Recurrence	As needed	Episodic recurrences and viral suppression • Acyclovir* • Famciclovir • Valacyclovir	None	▪ Acyclovir ▪ Famciclovir ▪ Consider vaccination if over 50 or immunocompromised
Most effective treatment window	24 hours	24 hours	24 hours	72 hours

* In unresponsive cases, resistance should be considered. Foscarnet or cidofovir are alternatives for acyclovir resistance.

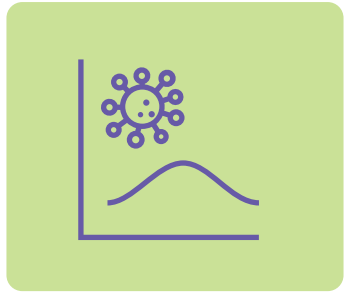
1. Johns Hopkins ABX Guide, Herpes Simplex Virus. Accessed November 1, 2023. https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540242/all/Herpes_Simplex_Virus
2. CDC STI Treatment Guidelines, 2021. Accessed November 1, 2023. https://www.cdc.gov/std/treatment-guidelines/herpes.htm
3. Treatment. Accessed November 1, 2023. https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/varicella-chickenpox#treatment
4. Five Things You Should Know About Shingles. Accessed November 1, 2023. https://www.cdc.gov/shingles/5-things-you-should-know.html
5. Patil A, Goldust M, Wollina U. Herpes zoster: A Review of Clinical Manifestations and Management. *Viruses*. 2022;14(2):192. doi:10.3390/v14020192

Early diagnosis and treatment of VZV limits pain associated with zoster outbreaks and neuropathic sequelae

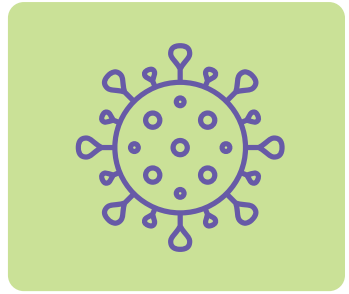
Antiviral treatment for zoster is most effective in the first 72 hours of symptoms.



Reduces pain



Improves lesion resolution and reduces new lesions



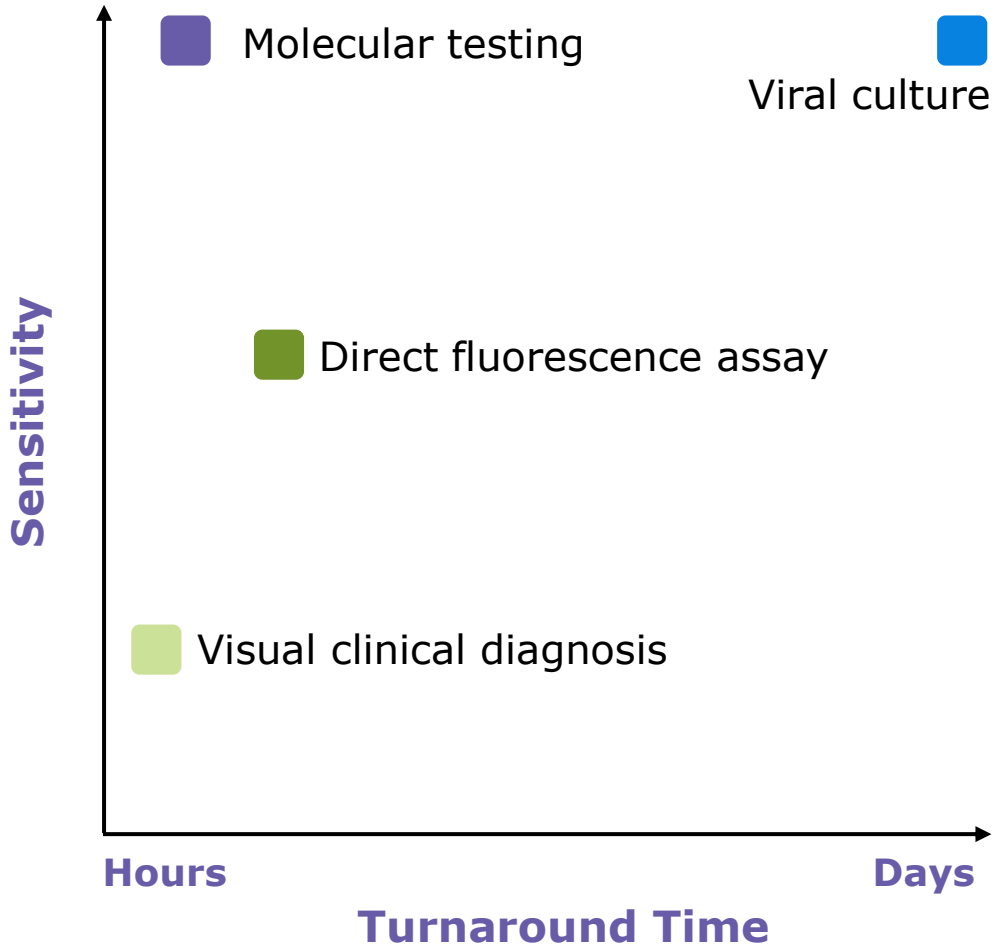
Reduces viral shedding

Some studies suggest early antiviral treatment and early supplemental pain management of zoster may reduce progression to PHN and its severity.

1. Five Things You Should Know About Shingles. Accessed November 12, 2023. https://www.cdc.gov/shingles/5-things-you-should-know.html
2. Xing X, et al. *Pain Physician.* 2020;23:65-72.
3. Lancaster T. *BMJ Evidence-Based Med.* 2000;5:144.

Multi-plex Platforms for HSV/VZV

Accuracy of laboratory testing has improved with molecular assays



Visual clinical diagnosis is often inaccurate.

Tzanck smears and direct fluorescence assays (DFA) have low sensitivity.

Viral culture, while accurate, may take two weeks or longer.

Serological testing is not recommended due to lack of sensitivity for active infection.

Guidelines now recommend molecular testing for improved sensitivity.

1. Nath P, et al. *Infect Dis Rep*. 2021;13(2):518-539.

Molecular detection improves sensitivity and specificity for HSV

Technique	Sensitivity	Specificity	Turnaround Time
Tzanck smear	84%	-	60-90 min
Viral culture	100%	-	5-14 days
Direct fluorescence assay	61%	90–100%	60-90 min
Molecular assays (PCR, RT-PCR, HDA)	92.7-100%	93.4-100%	1-4 h

1. Nath P, et al. *Infect Dis Rep*. 2021;13(2):518-539.

Molecular testing of VZV zoster provides sensitivity over other methodologies

Technique	Sensitivity	Turnaround Time
Tzanck smear	75%	60-90 min
Viral culture	46-75%	7-14 days
Direct fluorescence assay	88%	60-90 min
Molecular assays (PCR, RT-PCR, HDA)	97-100%	1-4 h

1. Dollard S, et al. *J Infect Dis*. 2022;226(4):S450-455.
2. Levin MJ, et al. *Clin Microbiol*. 2016;4(3):10.1128.

FDA-cleared IVDs for HSV and VZV

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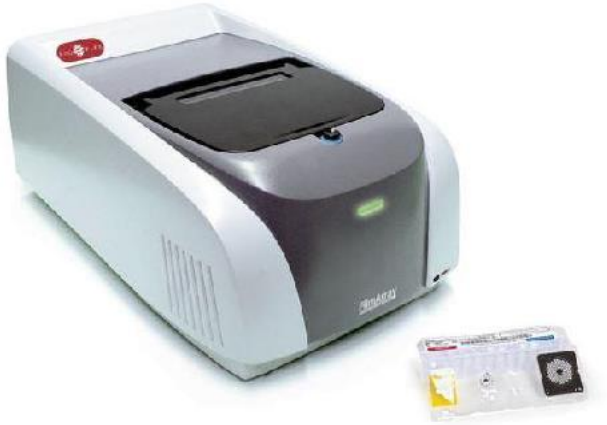


Meningitis/Encephalitis Panel
14 bacterial/viral/yeast pathogens
Sample type: CSF

QuidelOrtho™

Solana HSV 1+2/VZV Assay
Savanna HSV 1+2/VZV Assay
Lyra HSV 1+2/VZV Assay
Sample type: Cutaneous and mucocutaneous swabs

DiaSorin Molecular

Simplexa HSV 1 &2 Direct
Simplexa VZV Direct
Sample types: CSF
Cutaneous and mucocutaneous swabs

Multiplex molecular testing with results in less than an hour for HSV & VZV perform better than culture and DFA for lesion specimens

	HSV Culture	VZV DFA
HSV Sensitivity (%)	71.1	NA
HSV Specificity (%)	93.2	NA
VZV Sensitivity (%)	NA	71.4
VZV Specificity (%)	NA	100

1. Nikolic D, et al. *Am J Clin Pathol.* 2019;151(1):122–126.

	Molecular HSV 1+2/VZV Assay			
	Simplexa HSV 1&2 Direct (Diasorin)	Simplexa VZV Swab Direct (Diasorin)	Savanna (QuidelOrtho)	Solana (QuidelOrtho)
	~60 Mins	~60 Mins	~24 Mins	50 Mins
HSV 1 Sensitivity (%)	98.8		99.1	100
HSV 1 Specificity (%)	97.6		97.6	97.0
HSV 2 Sensitivity (%)	99.3		96.4	98.0
HSV 2 Specificity (%)	97.6		99.4	96.3
VZV Sensitivity (%)		98.0	100	100
VZV Specificity (%)		99.2	99.9	97.3

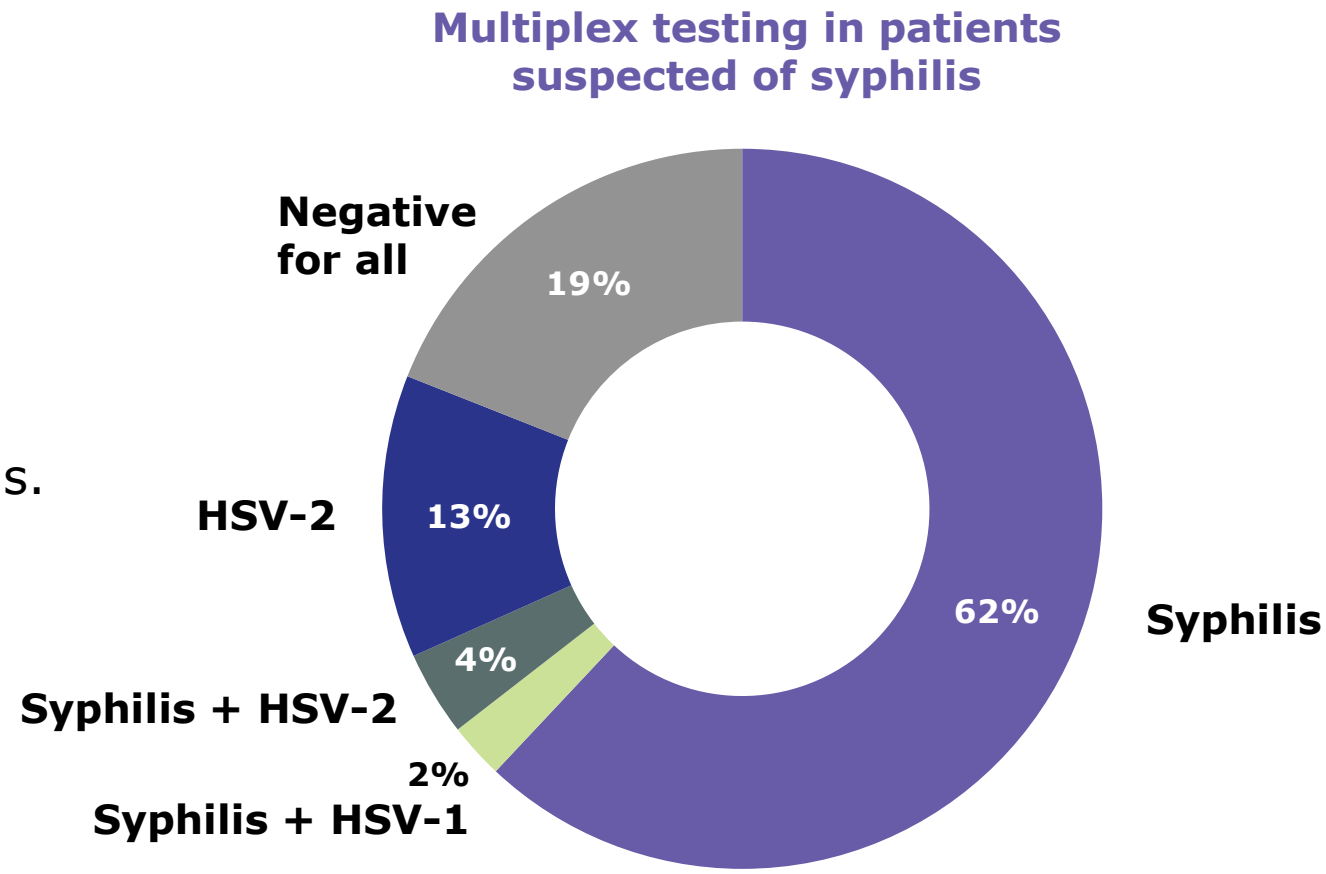
combined prospective and retrospective data for cutaneous and mucocutaneous specimens

2. Package Insert. Simplexa HSV 1&2 Direct. Diasorin
3. Package Insert. Simplexa VZV Swab Direct. Diasorin
4. Package Insert. Savanna HSV 1+2/VZV. QuidelOrtho
5. Package Insert. Solana HSV 1+2/VZV. QuidelOrtho

Multiplex molecular testing can rule out viral lesion causes, diagnose co-infection, and improve antimicrobial stewardship

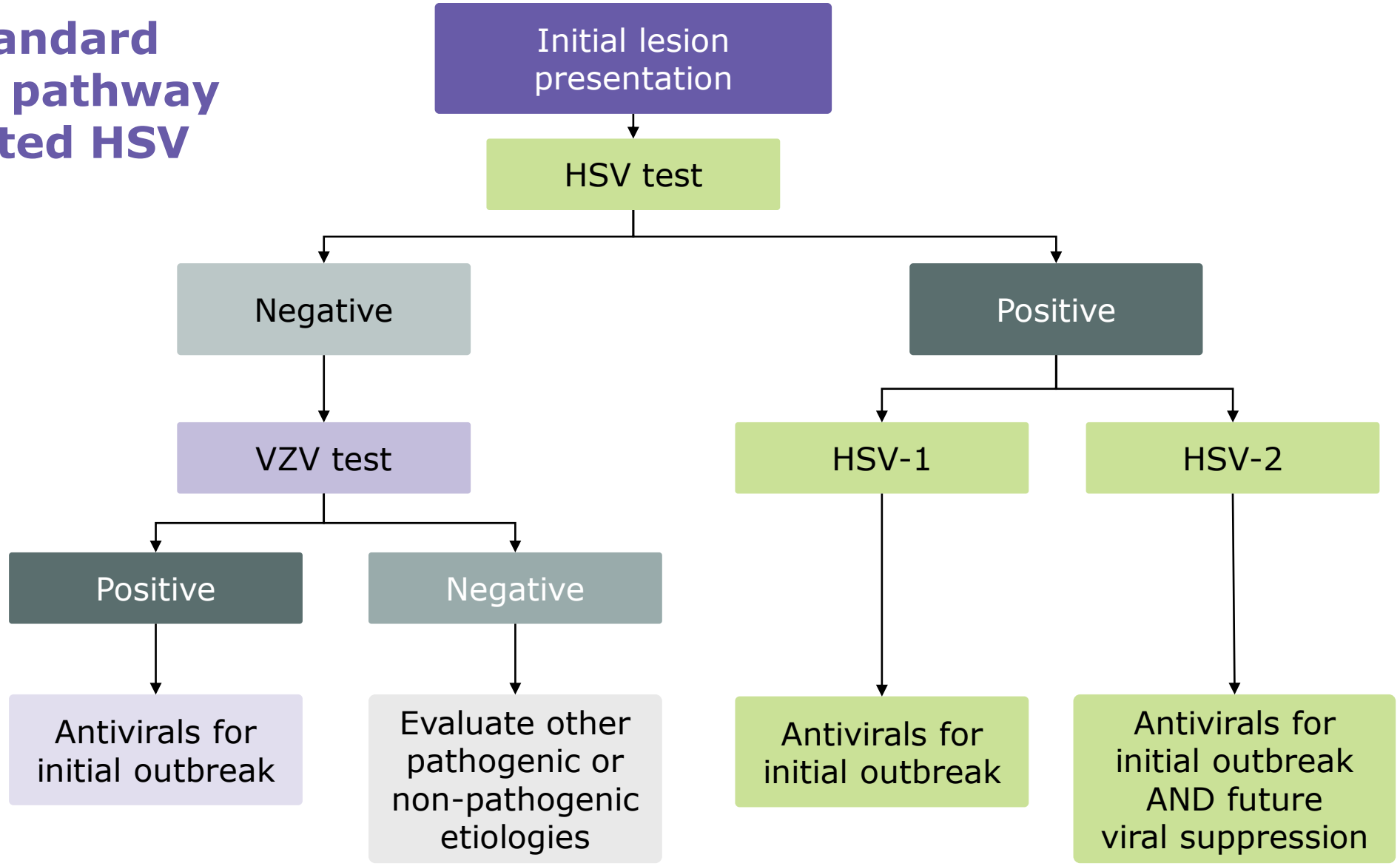
Multiplex molecular testing can confirm bacterial or viral etiologies.

Determining a viral cause can reduce inappropriate antibiotics for viral infections.

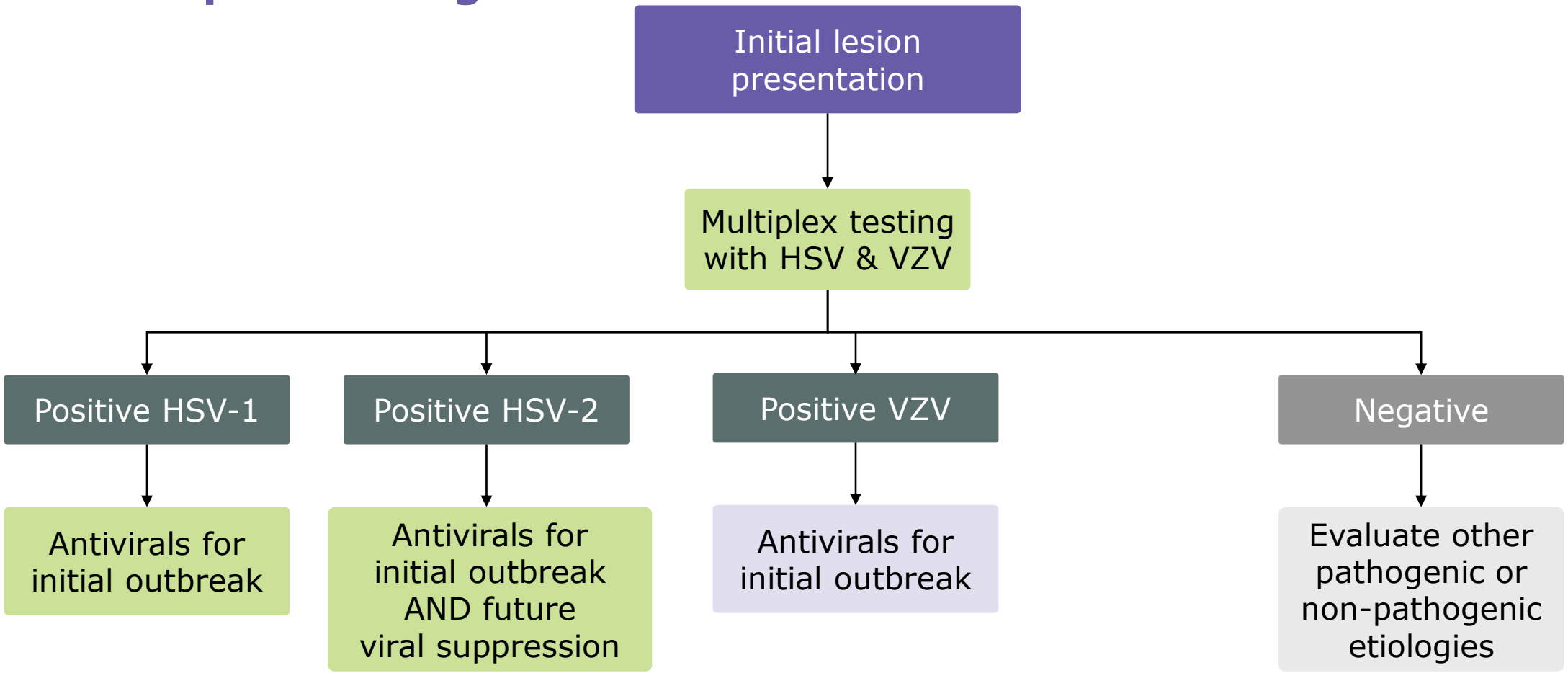


1. Eguiluz M, et al. *Open Forum Infect Dis.* 2023;10(10):ofad483

Current standard diagnostic pathway for suspected HSV



Diagnostic algorithm for suspected HSV or VZV with multiplex testing



Case Studies

Case Study:
Genital lesions in middle-aged adult

Patient: Mary, a 47-year-old woman presented with a cluster of vulvar lesions for 48 hours.

Mary reported a previous history of oral HSV with rare outbreaks but no genital infection. Mary had varicella when she was a child.

Mary informed providers she was sexually active with a new boyfriend but was using condoms. She had not noticed him having any oral lesions.

Diagnosis: Clinical diagnosis of genital herpes.

Treatment: Acyclovir 400 mg orally 3 times/day for 7 days.

Testing: A sample was sent for molecular testing to determine HSV type per CDC guidelines.

Diagnosis: Molecular tests were negative for HSV-1 and HSV-2.

Follow-up molecular multiplex testing was positive for VZV.

Treatment: Acyclovir was increased to 800 mg 5 times/day for 7 days.

Outcome: After 7 days, lesions were healing and there was no need for continued treatment.

Final Diagnosis:

VZV

Visual evaluation and recent sexual history led to an initial diagnosis of HSV.

VZV does not indicate suppressive therapy or transmission risk.

1. CDC STI Treatment Guidelines, 2021. Accessed December 13, 2023. https://www.cdc.gov/std/treatment-guidelines/herpes.htm.
2. Patil A, Goldust M, Wollina U. *Viruses*. 2022;14(2):192.

Case Study:
Genital lesions in college student

Patient: Mark, a 20-year-old college student presented with a cluster of three ulcerated penile lesions for 3 days.

Mark reported no previous history of oral HSV or other genital lesions. He was unvaccinated for varicella as were his siblings. He reported childhood varicella at the age of 4.

Mark informed providers of consistent sexual activity with infrequent usage of condoms.

Diagnosis: Clinical diagnosis of genital herpes.

Treatment: Acyclovir 400 mg orally 3 times/day for 7 days.

Testing: A sample was sent for molecular multiplex testing to determine HSV type per CDC guidelines.

Diagnosis: Molecular multiplex testing was positive for HSV-1 and negative for HSV-2 and VZV.

Treatment: Continued oral acyclovir for primary infection.

Outcome: After 7 days, lesions were healing. Suppressive therapy was put on hold pending determination of rate of recurrence.

Education was provided on HSV-1 transmission.

Final Diagnosis:

Primary genital HSV-1

Mark's treatment was directly affected by HSV type.

Suppressive therapy for HSV-1 genital herpes is only recommended for frequent recurrences.

1. CDC STI Treatment Guidelines, 2021. Accessed December 13, 2023. https://www.cdc.gov/std/treatment-guidelines/herpes.htm

Case Study:
Facial lesions in a patient with a history of HSV

Patient: Ronald, a 69-year-old man presented with a skin eruption on the right side of his face for 5 days.

Ronald reported previous oral HSV with recurrent outbreaks every 2 years and childhood varicella.

Diagnosis: Clinical diagnosis of Kaposi varicelliform with secondary bacterial infection.

Treatment: Oral acyclovir and levofloxacin for 2 days.

Ronald presented to outpatient clinic after lack of improvement. He had crusted lesions on the right side of the face and small vesicles below his lip and on his trunk and extremities.

Testing: Standard laboratory testing showed slightly elevated C-reactive protein, but no immunological dysfunction. Coagulase-negative staphylococci were present.

Differential diagnosis included HSV, disseminated VZV, and impetigo.

Diagnosis: Molecular testing was positive for HSV-1 and VZV from multiple sample sites.

Treatment: Acyclovir 750 mg/day and cefcapene pivoxil 300 mg/day for 7 days.

Outcome: After 7 days, facial swelling had improved, and all vesicles were resolving.

Final Diagnosis:

Disseminated VZV

Reactivation of HSV-1

Ronald was diagnosed with both HSV-1 and VZV, indicating monitoring for PHN or possible HSV recurrences.

1. Kobayashi T, et al. *Case Rep Dermatol.* 2014;6(1):5-9.

Case Study: Neonatal lesions

Patient: Marcus, day 4 neonate presented to level 2 NICU for ongoing fever and suspected sepsis.

Diagnosis: Clinical diagnosis of neonatal sepsis.

Treatment: Empiric antibiotics

Marcus continued to have feverish episodes (>38°C) for 6 days after admission.

Testing: Blood, cerebrospinal fluid (CSF) and urine cultures were negative for bacterial infection. Initial C-reactive protein. Low lymphocyte counts indicated a possible viral infection.

Testing: COVID-19 was negative. ALT was high.

Toxoplasmosis, congenital cytomegalovirus, rubella and HSV serum screens were negative.

Diagnosis: On day 5, two tiny red crusted lesions were noted on the back of Marcus's scalp.

Treatment: Empiric acyclovir pending PCR results.

Outcome: PCR confirmed HSV-1. Acyclovir was continued for 3 weeks and Marcus was discharged after a 23-day stay in the NICU. HSV prophylaxis was continued for a year.

Final Diagnosis:

Disseminated HSV-1

Mother's antenatal serology was normal. Both mother and her partner denied any history of genital herpes or cold sores. There were no ulcers during pregnancy or at delivery.

1. Badawy MK, et al. *BMJ Case Rep*. 2021;14:e241405.

Summary

Due to symptom and presentation overlap, lesion-causing pathogens are often difficult to differentiate via clinical observation alone.

- Inaccurate diagnoses
- Inaccurate prescribing of antimicrobial agents
- Treatment resistance

Molecular multiplex assays permit rule out of most major viral lesion-causing pathogens, leading to reduced transmissions and complications and improved patient outcomes.

Thank you
Questions??