NPPA
CENTER FOR DERMATOLOGY

Skin Infections: Viruses & Sexually Transmitted Infections

Veronica Richardson
MSN, ANP-BC, DCNP

www.cdnppa.com

Disclosures

- Advisory board:
  - Boehringer Ingelheim (Generalized Pustular Psoriasis),
  - Lilly (Alopecia Areata),
  - Bristol Myers-Squibb (Psoriasis),
  - Dermavant (Psoriasis),
  - Leo (Atopic Dermatitis),
  - Sanofi Regeneron (Atopic Dermatitis)

- All relevant financial relationships have been mitigated.

Learning Objectives

1. Review the common pathogens and epidemiology of viral skin infections
2. Identify differentiating clinical presentations and diagnostics for the accurate diagnosis.
3. Integrate a patient-centered, best-practice approach for disease management, therapeutic interventions, and patient/caregiver education.
4. Explain the pharmacodynamics of medications key in the management of viral and parasitic skin infections.

Viral Skin Infections and STIs

- **Viral**
  - Verruca
  - Condyloma acuminata
  - Molluscum contagiosum
  - Herpes simplex
  - Herpes zoster & post-herpetic neuralgia

- **Other**
  - Syphilis

GOALS OF WART MANAGEMENT: TREAT

- **T:** Test misbehaving warts
- **R:** Reduce risk/Reduce Recurrence/Recognize Risk
- **E:** Eradicate visible lesions
- **A:** Anoscopy if high perianal burden
- **T:** Topicals first in kids

Verruca Vulgaris

- **HPV (>200 genotypes)**
  - Subtypes 6, 11 : benign
  - Subtypes **16, 18, 31, 33, 45, 51, 52, 56, 58, 59, 66, 68: oncogenic**
  - **Higher risk in immunocompromised**
  - HIV, Organ transplant recipients
  - Can lead to squamous cell carcinoma
- Self-limiting, confined to the epidermis BUT TREAT EARLY!
- **Diagnostic Clues**
  - Black dots
  - Disruption of dermatoglyphics
  - Acetowhite test (genital mucosal lesions)

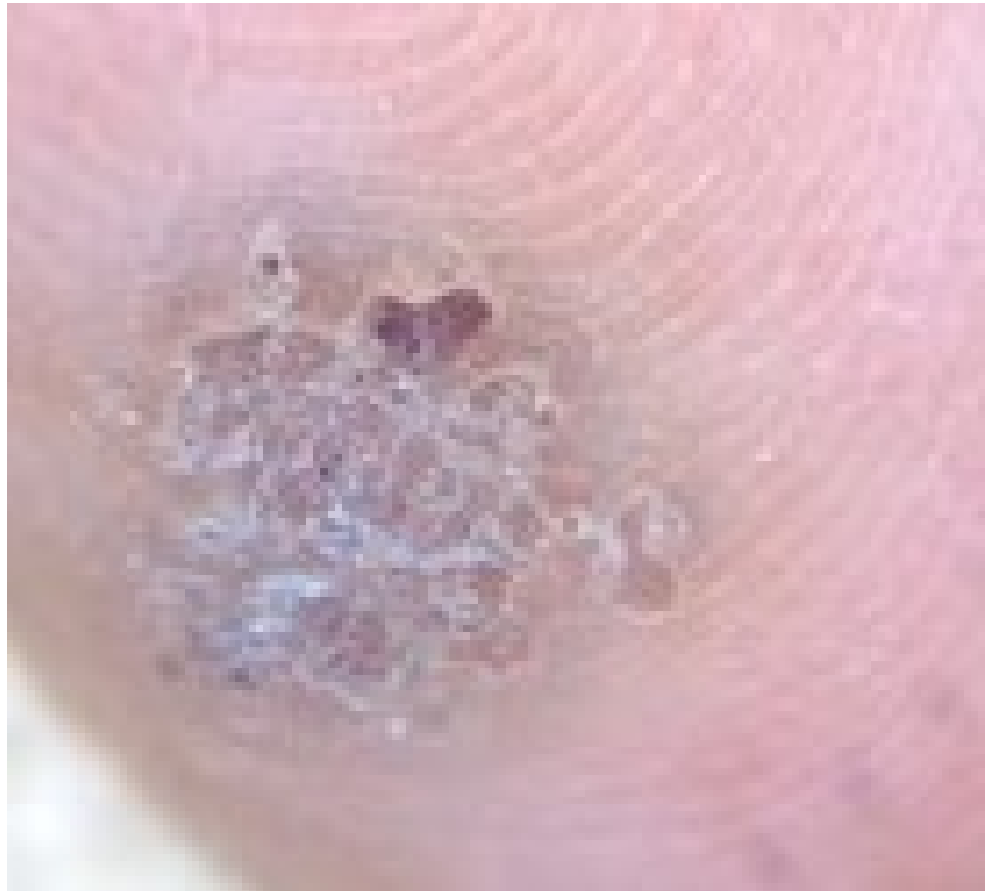
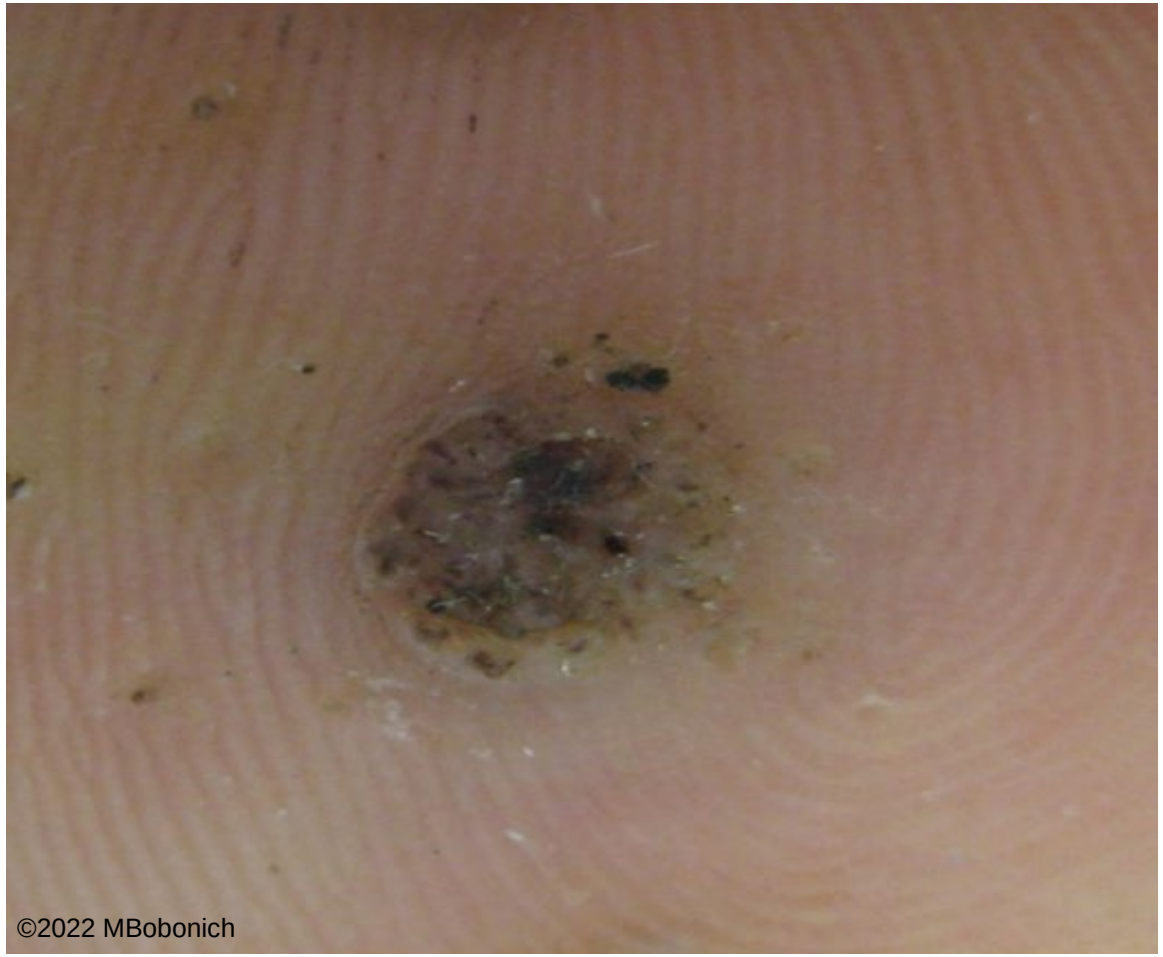
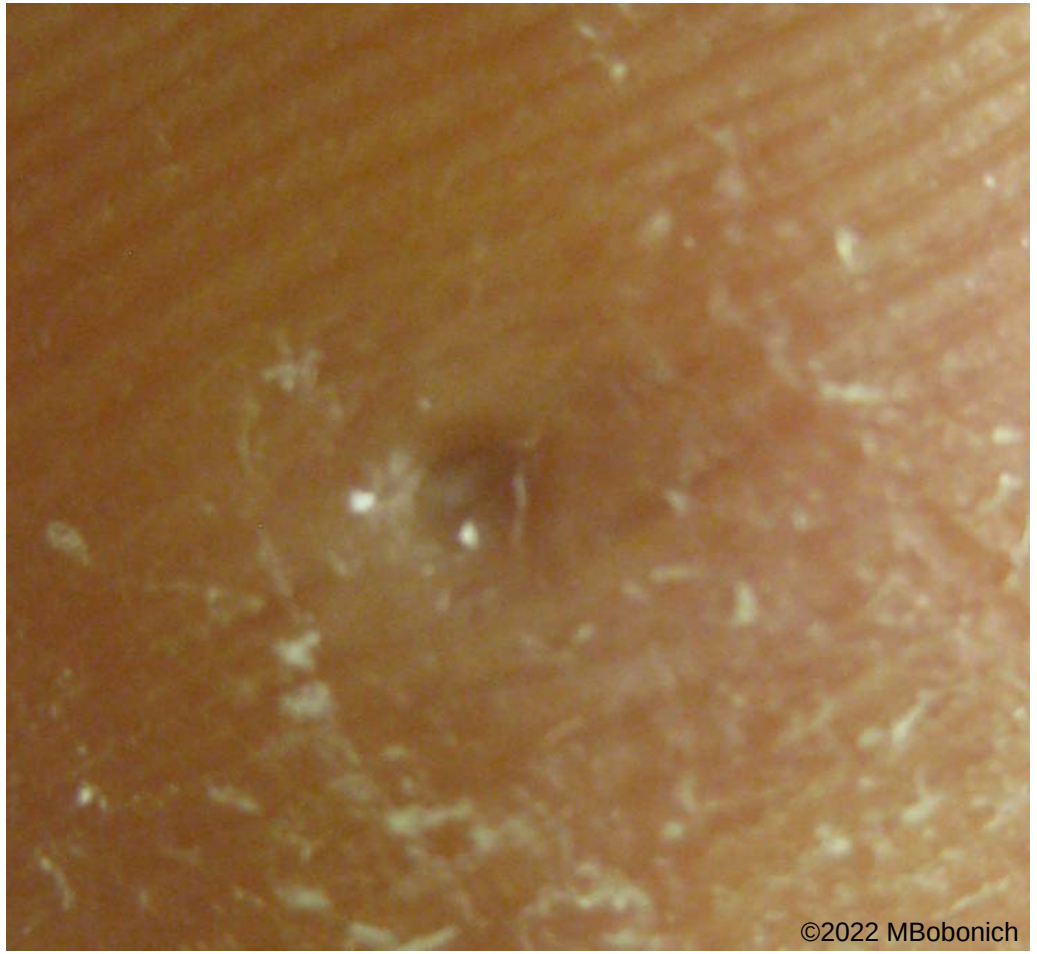


Photo courtesy of Veronica Richardson

Verruca vs Corn



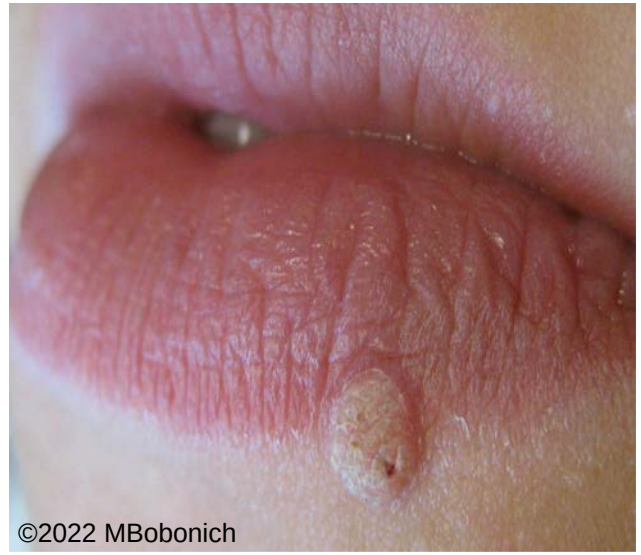
Wart with broken lines and black dots



Corn without black dots and has skin lines

Management of Verruca Vulgaris: Adults

- **First-line** for common warts
  - Cryotherapy
- **Second-line treatment**
  - IL bleomycin, 5FU, or cidofovir
  - Thermotherapy*
    (44°C [111°F] for 30 mins and repeat)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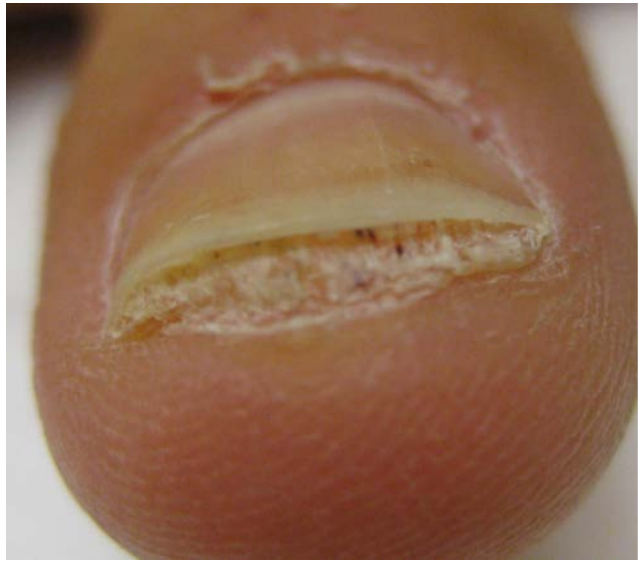
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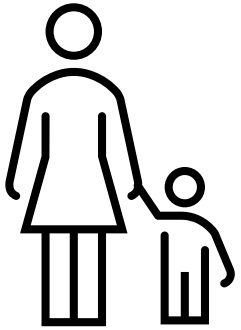
Source: Zhu, P., et al. (2022). Clinical guideline for the diagnosis and treatment of cutaneous warts (2022). *Journal of evidence-based medicine*, *15*(3), 284–301. https://doi.org/10.1111/jebm.12494

Management of Warts: Pediatric Considerations



Treatment

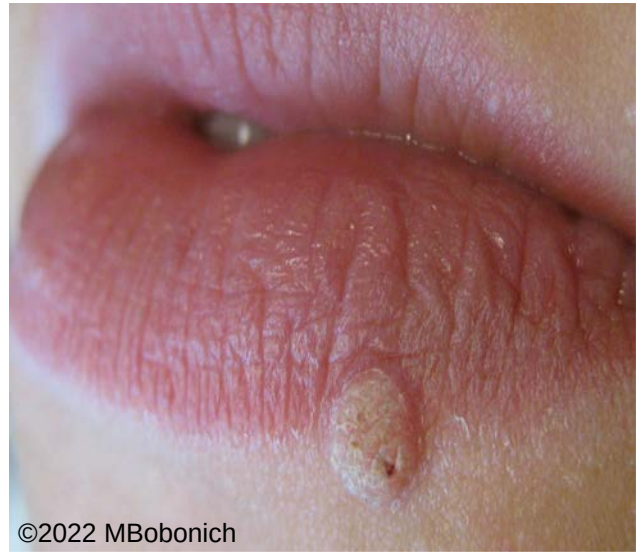
- 5% imiquimod cream **(Common Warts)**
- Monochloroacetic acid (MCA) **(Plantar Warts)**
- If injection tolerant: Intralesional *Candida* antigen immunotherapy for recalcitrant and multiple warts
- Combination 5-ALA -PDT with high-frequency electrocautery for children with (Condyloma Acuminata-CA)
- Children with recalcitrant CA around the anus could be treated with local thermotherapy.

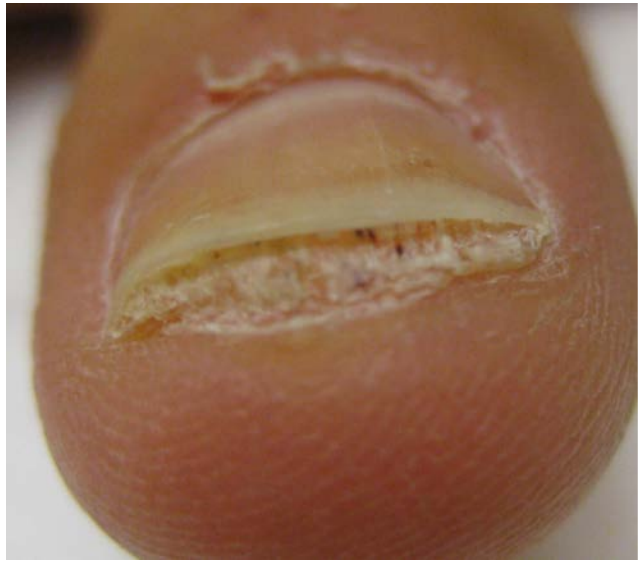
Source: Zhu, P., et al. (2022). Clinical guideline for the diagnosis and treatment of cutaneous warts (2022). *Journal of evidence-based medicine*, *15*(3), 284–301. https://doi.org/10.1111/jebm.12494

Wart Management Considerations: Reducing Risk

Additionally

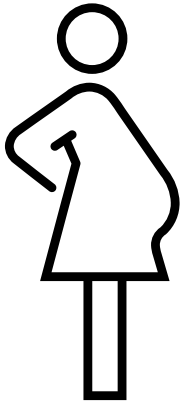
- Superimposed infections and inflammation should be controlled before treating CA lesions.
- Precaution to avoid contact with flowing particles should be taken during the evaporating surgical treatment of warts.





Source: Zhu, P., et al. (2022). Clinical guideline for the diagnosis and treatment of cutaneous warts (2022). *Journal of evidence-based medicine*, *15*(3), 284–301. https://doi.org/10.1111/jebm.12494

Management of Warts: Pregnancy Considerations



- Podophyllotoxin and imiquimod are not recommended for CA during pregnancy, but trichloroacetic acid can be used.
- CA during pregnancy could be treated by liquid nitrogen cryotherapy or surgery.
- Cesarean section is recommended when large warts may block the birth canal or cause massive bleeding.
- CA during pregnancy could be treated with local thermotherapy.
- Decision on the treatment of genital warts in pregnant women should be based on the size of warts and the impact on the fetus.

Source: Zhu, P., et al. (2022). Clinical guideline for the diagnosis and treatment of cutaneous warts (2022). *Journal of evidence-based medicine*, *15*(3), 284–301. https://doi.org/10.1111/jebm.12494

Genital Warts: Condyloma Acuminata (CA):

Recognizing Risk
Oncogenic types
• **Subtypes 16, 18, 31, 33, 45, 51, 52,56, 58, 59, 66, 68 have a propensity to have malignant transformation** • HPV types 16 & 18 account for ~70% of all cervical cancers: stay UTD on PAP • HPV types 6 & 11 (benign) account for ~90% genital warts • **HIV affected individuals** with anogenital warts at **greater risk for anal cancer and cervical cancer** • If high perianal burden- refer to GI/Colorectal for anoscopy

https://www.cancer.org/cancer/anal-cancer/causes-risks-prevention/risk-factors.html

Condyloma Acuminatum (CA) Treatments

Recommendation

- Combination 5% imiquimod **+** traditional physical therapy (lasers, cryotherapy) is recommended to treat CA.
- Topical treatment is recommended for genital warts with single lesion size less than 5 mm ***or*** confluent lesion size less than 10 mm, ***or*** a total number of warts less than 15.
- ALA-PDT alone is recommended to treat genital warts <5 mm in size.
- ALA-PDT combined with traditional physical therapy is recommended to reduce the rate of recurrence.
- Surgery is recommended for CA with pedicle or large volumes or recalcitrant.
- Destructive physical therapy followed by immunomodulators (imiquimod or recombinant human interferonα−2b) or photodynamic therapy is recommended.
- Topical 5% imiquimod or photodynamic therapy is considered for CA with underlying HIV infection.

HPV Vaccination: Reducing Risk

Gardasil 9 (9vHPV)	
Directed against HPV types: 6, 11, 16, 18, 31, 33, 45, 52, 58	
When:	ACIP* recommend vaccination be initiated at ages 11/12, but can be started as early as age 9
*Advisory Committee on Immunization Practices	
• Before 15th birthday: 2 dose schedule: 0, 6-12 months • On or after 15th birthday: 3 doses 0, 1-2, 6 months	
Who:	Children and adults aged 11-26 years (can start as early as 9)
	Clinical shared decision making for adults 27 through 46*
*MSM, transgender persons and persons with immunocompromising conditions.	

MMWR - Human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices (cdc.gov)

Molluscum Contagiosum

- **Basics**
  - Poxvirus in epidermis
  - 6–8-week incubation
  - Duration: 6-12 months (up to 4 years)
- **Epidemiology:**
  - Immunocompetent Children (most common)
  - Immunocompetent adolescents/young adults (STD)
  - Immunosuppressed children and adults
- **Risk Factors:**
  - Impaired skin barrier
  - Immunosuppression

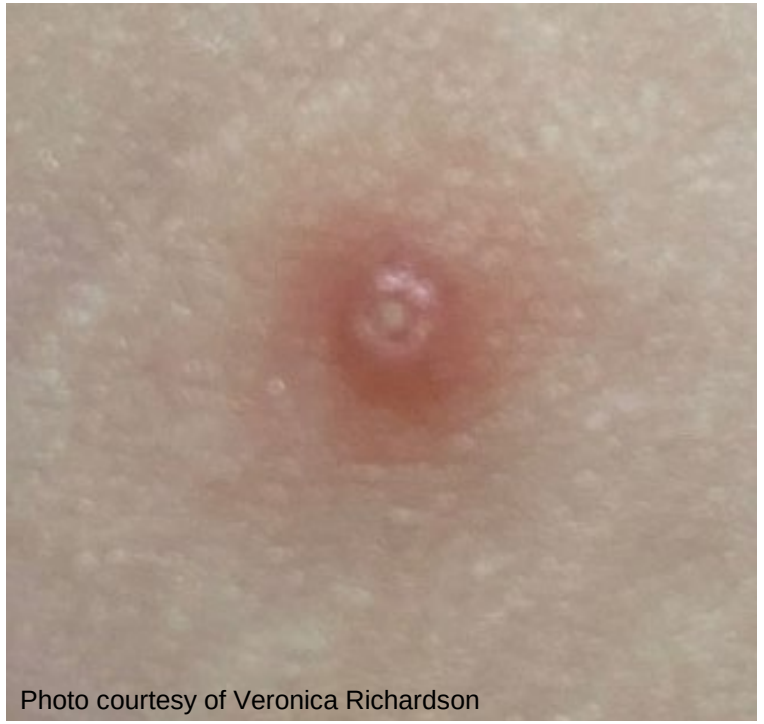
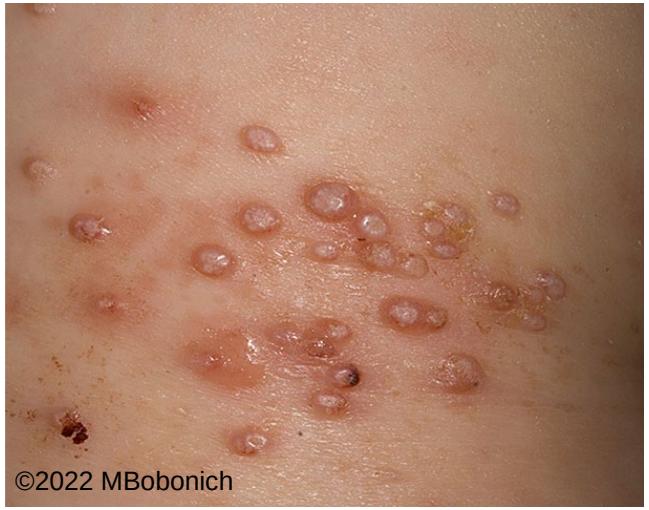


Photo courtesy of Veronica Richardson

Molluscum Contagiosum

Clinical Presentation
• **Umbilicated** papules and pustules • Occur anywhere • Dermoscopy: polylobular white-to-yellow amorphous structures, and peripheral crown vessels • “BOTE”” sign   • **B**eginning **o**f **t**he **E**nd; inflammatory phase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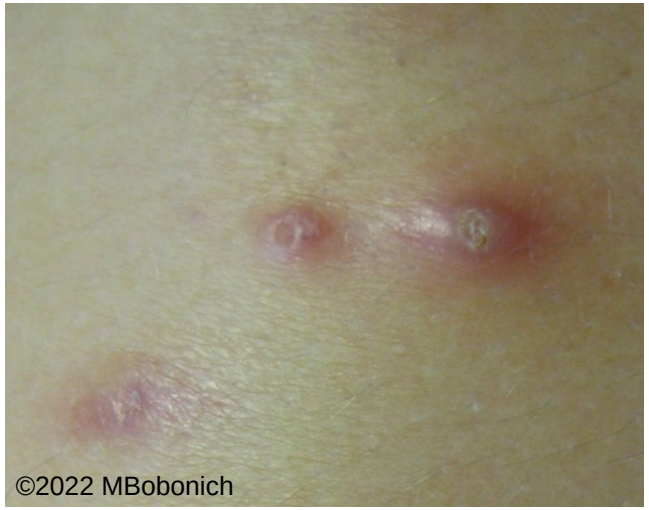
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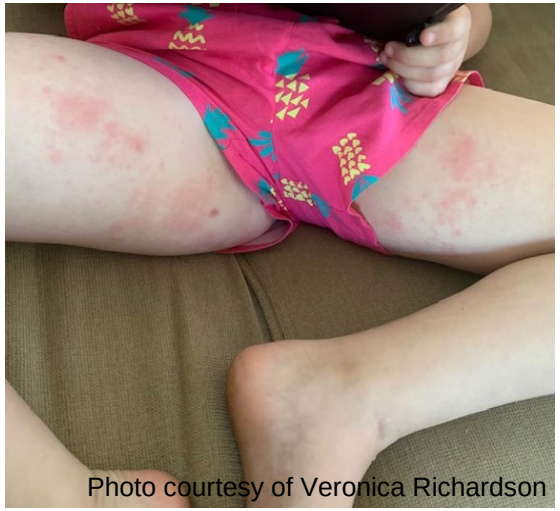


Photo courtesy of Veronica Richardson

Molluscum Contagiosum: Treatment

Active Observation

- Self-limited nature
- Lack of consensus on single-best therapy
- Special sites
  - Ocular: refer to optho
  - Perianal: must consider child abuse

Physical/Mechanical/Destructive

- Cryotherapy
- Curettage
- Pulse dye laser

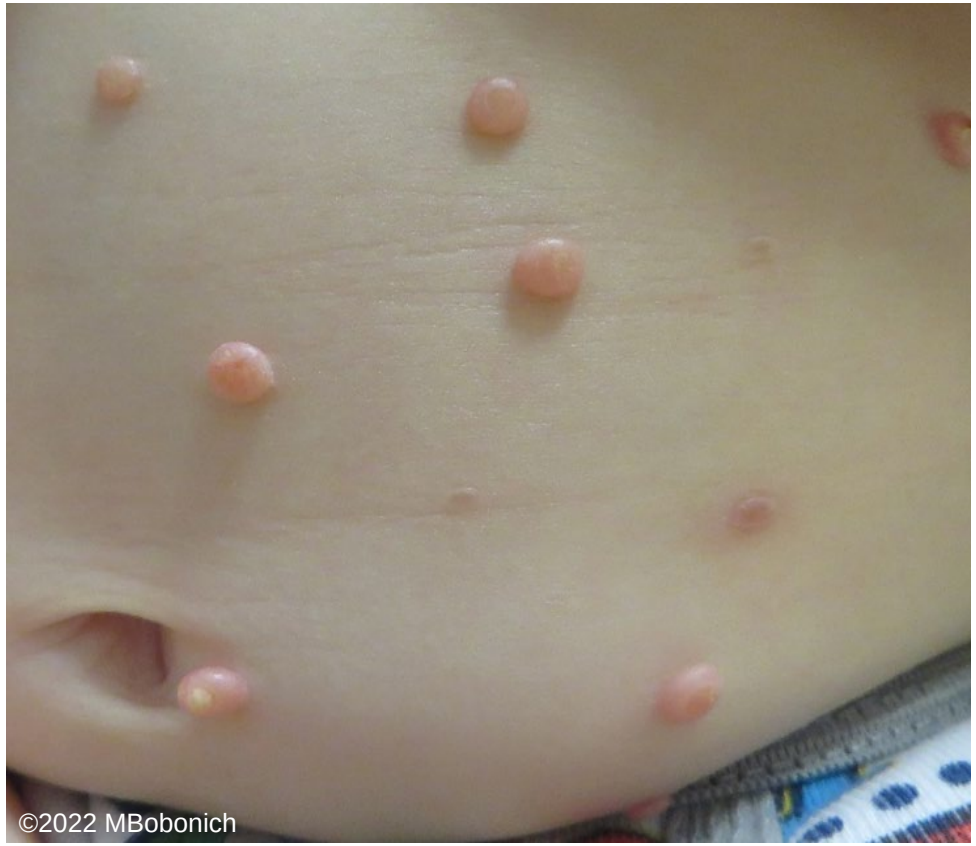
Topical

- **Cantharidin**
- **Ycanth (only FDA approved tx for MC, age 2+)**
- Podophyllotoxin
- Potassium Hydroxide
- Salicylic acid
- Tretinoin
- Trichloroacetic acid
- Cidofovir (immunosuppressed host)

van der Wouden, J.C., et al. *Cochrane Database of Systematic Reviews* 2017. Sterling, J. (2016). Current Opinion of Pediatrics. 28(4):490-499.

Molluscum Contagiosum: Patient Education

- **Highly contagious**
- **Don’t scratch/shave-autoinoculation**
- Gentle skin care, especially if AD
- Cover lesions
- Avoid baths with siblings
- Avoid sharing towel
- Safe-sex education



Herpes Simplex (HSV-1/HSV-2)

Primary Infection – many times asymptomatic
• Orolabial (HSV-1): Gingivostomatitis: Fever, bleeding gums, fatigue • Genital (HSV-2): Fever, myalgias, lymphadenopathy, urinary retention • Duration 2-6 weeks • Increased viral shedding
Recurrent Infection
• Prodromal symptoms (burning, tingling, pain) • Duration 4–10 days • Asymptomatic shedding
Triggers
• Ultraviolet radiation • Stress • Trauma • Immunosuppression

Herpes Simplex (HSV-1) Orolabial Herpes

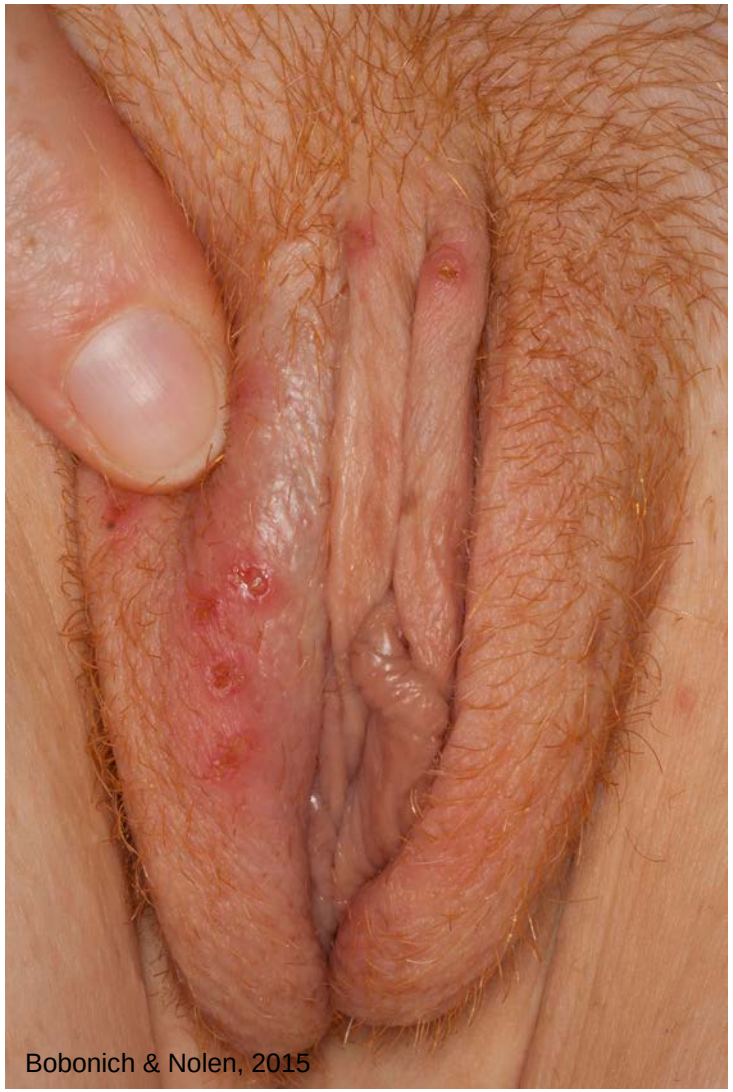
Clinical Presentation

- Erythematous papules rapidly develop into tiny vesicles become pustular & ulcerate
- Most common on vermilion border
- Key is intermittent recurrence of vesicles/pustule/ulceration in the **SAME LOCATION**


Photo courtesy of Veronica Richardson

HSV-2 Genital Herpes

- **Clinical Presentation**
  - Prodrome of burning/tingling
  - Punched out ulcerations on genitals, buttocks, perineum
  - Key is intermittent recurrence of vesicles/pustule/ulceration in the **SAME LOCATION**



Bobonich & Nolen, 2015

Herpes Simplex—PRIMARY INFECTION/FIRST EPISODE: GENITAL

Recommended Regimens*
• **Acyclovir**† 400 mg TID x 7–10 days • **Famciclovir** 250 mg orally TID x 7–10 days • **Valacyclovir** 1 gm BID x 7–10 days

* Treatment can be extended if healing is incomplete after 10 days of therapy.

† Acyclovir 200 mg orally five times/day is also effective but is not recommended because of the frequency of dosing.

CDC Sexually Transmitted Infections Treatment Guidlelines, 2021.
https://www.cdc.gov/std/treatment-guidelines/herpes.htm

Herpes Simplex—Episodic for Recurrence ORAL

Recurrent, Episodic Dosing
Acyclovir • Oral: 400mg TID x 5 days **Topical/local** • Topical: Penciclovir 1% cream q2h x 4 days • Topical: Acyclovir 5% ointment 5x/day x 4 days • Acyclovir 50mg buccal tab x 1 (upper gum) **Valacyclovir** • Oral: 2gm bid x 1d **Famciclovir** • Oral: 1500mg x 1 dose

Photo courtesy of Veronica Richardson

Herpes Simplex—Episodic for Recurrence GENITAL

Recommended PO Regimens*	
Acyclovir 400mg TID x 5 days	OR
Acyclovir 800 mg BID x 5 days	OR
Acyclovir 800 mg TID x 2 days	OR
Famciclovir 1 gm BID x 1 day	OR
Famciclovir 500 mg once, followed by 250 mg BID for 2 days	OR
Famciclovir 125 mg BID x 5 days	OR
Valacyclovir 500 mg BID X 3 days	OR
Valacyclovir 1 gm QD x 5 days	

*Acyclovir, famciclovir, and valacyclovir appear equally effective for episodic treatment of HSV

CDC Sexually Transmitted Infections Treatment Guidlelines, 2021. https://www.cdc.gov/std/treatment-guidelines/herpes.htm

Treatment for Herpes Simplex

Oral & Genital Regimens for Chronic Suppression
Uncomplicated, Immunocompetent

Chronic Suppression
Acyclovir • 400mg BID • 400mg orally TID starting at 36 weeks if pregnant** **Valacyclovir** • 500mg daily (<10 episodes/yr) • 1000mg daily (>10 episodes/yr)* **Famciclovir** • 250mg bid

Albrecht, M. (2022). Treatment of genital HSV. www.uptodate.
CDC (2021). Genital Herpes-CC Fact Sheet www.cdc.gov.

Treatment for Herpes Simplex

Oral & Genital Regimens for Chronic Suppression Uncomplicated, Immunocompetent

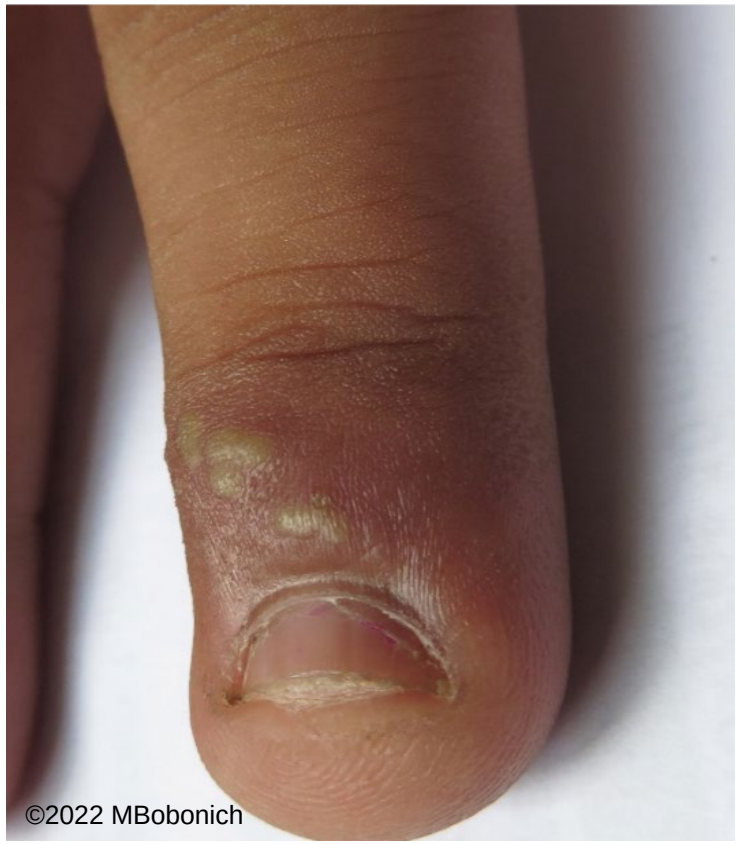
* **Valacyclovir 500 mg once a day might be less effective than other valacyclovir or acyclovir dosing regimens for persons who have frequent recurrences (i.e., ≥10 episodes/year).**
Famciclovir appears somewhat less effective for suppression of viral shedding.
Heterosexual couples with h/o HSV-2 should consider suppressive antiviral therapy as part of a strategy for preventing transmission, in addition to consistent condom use and avoidance of sexual activity during recurrences.
**Acyclovir is preferred agent in pregnancy

Albrecht, M. (2022). Treatment of genital HSV. www.uptodate.
CDC (2021). Genital Herpes-CC Fact Sheet www.cdc.gov.

Herpes Whitlow

- HSV infection usually distal digit
- Children-primary oral infection due to autoinoculation from lips
- Common among dental workers

- **Clinical Presentation**
  - Recurrence vesicles/erosions perionychium
  - Typically resolve over 2–3 weeks
  - **Often misdiagnosed as ACUTE PARONYCHIA**
  - Supportive care and antiviral prn



Betz, D., Fane, K. Herpetic whitlow. StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK482379/.

Case Study

Mr. Lopez is a 68-year-old male with psoriasis on adalimumab who presents for an urgent visit for evaluation of painful rash on his left abdomen. It started about 7 days ago. You perform a complete exam and note erythematous patches studded with fluid filled vesicles in a dermatomal distribution. He reports having had the Zostavax vaccination 6 years ago. You diagnose him with herpes zoster. What is your next step in management.

A. Initiate Gabapentin given his high risk of post herpetic neuralgia
B. Inform patient that since he is out of the 72-hour window, and his vaccination status, antivirals would be ineffective
C. Initiate treatment with Valacyclovir
D. Refer patient to ER for admission and IV Acyclovir

Case Study

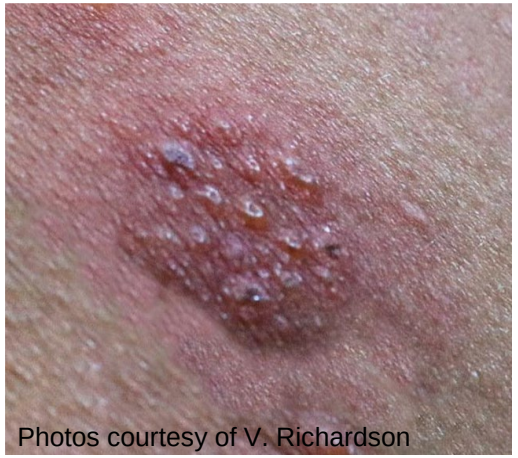
Mr. Lopez is a 68 yo male with psoriasis on adalimumab who presents for an urgent visit for evaluation of painful rash on his left abdomen. It started about 7 days ago. You perform a complete exam and note erythematous patches studded with fluid filled vesicles in a dermatomal distribution. He reports having had the Zostavax vaccination 6 years ago. You diagnose him with herpes zoster. What is your next step in management.

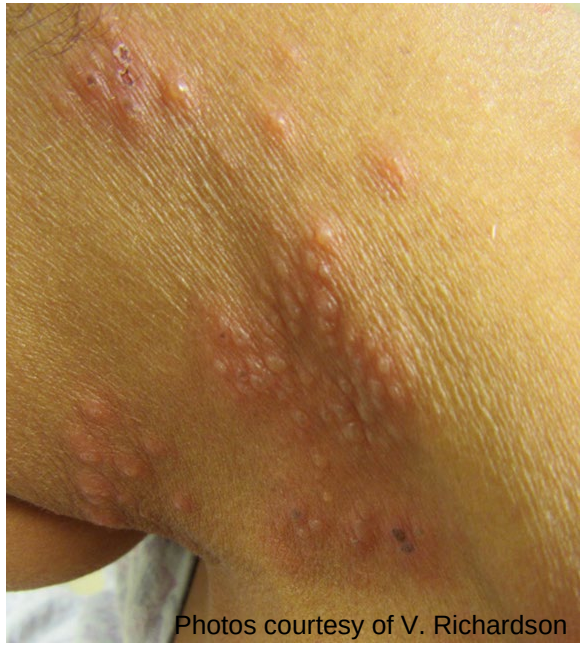
C. Initiate treatment with Valacyclovir

Even if beyond 72-hour window if patient is over the age of 50 and still has vesicles, or they are immunosuppressed, they should be treated.

Herpes Zoster (Shingles)

- Cutaneous viral infection
- Lies dormant in dorsal root ganglia
- Caused by reactivation of **varicella zoster virus (VZV)**
- Incidence increases with age
  - 75% of cases occurring in pts over 50-years old
  - 1/3 of Americans will develop shingles in their lifetime
- Can be early clinical sign of HIV
  - Young adults, recurrent cases, or involves more than one dermatome


Photos courtesy of V. Richardson


Photos courtesy of V. Richardson

Herpes Zoster

Prodrome	
Eruptive hyperesthesia pain, itching, or burning often begins 4–5 days before the eruption	
Clinical presentation	
Rash	Dermatomal, unilateral
	Vesicles arise in clusters from the reddened base
	“Dew drops on a rose petal”
Resolution	Form crusts/scabs which fall off in 2–3 weeks
	Usually resolves over 2 weeks
Risk	Secondary bacterial infection

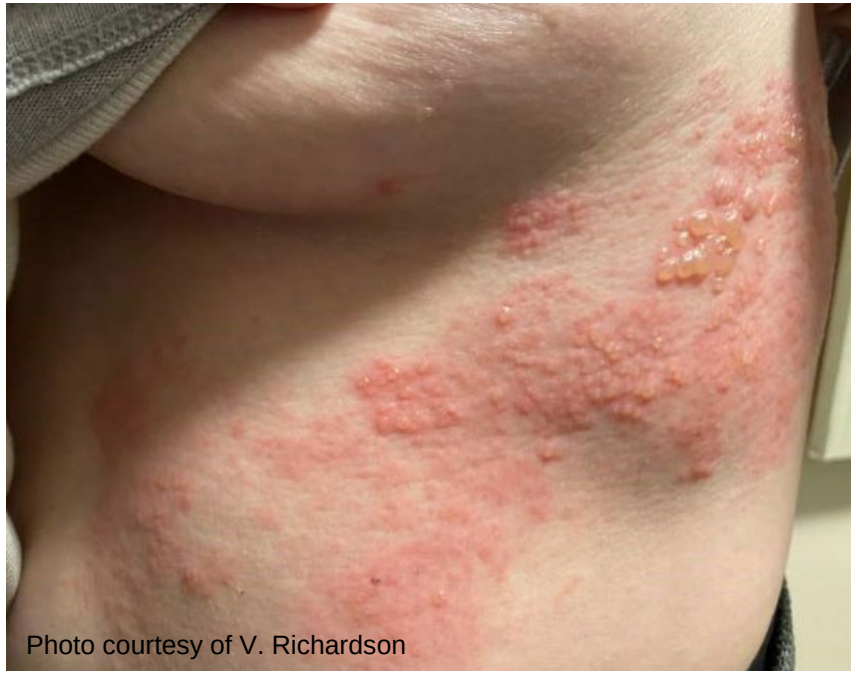
Herpes Zoster

Management	
First-line: systemic therapies	
• for outbreak less than 72 hours	*Or*
• still getting new lesions, patients 50+	*Or*
• immunosuppressed	
Treatment Goals	
• Reduce/lessen severity of pain • Prevention of new lesions • Decrease viral shedding • Reduce risk of PHN	

Oral therapy options for Zoster
• Acyclovir 800 mg 5x/day x 7-10 days • Valacyclovir 1g TID X 7-10 days* • Famciclovir 500mg TID x 7 days *Most effective at reducing risk of PHN

Nam, K.H., et al. (2021). *J Am Acad Dermatol,* 85(4):1010-1011.
Nair P.A., et al. (2022). Herpes Zoster. In: StatPearls [Internet].

Herpes Zoster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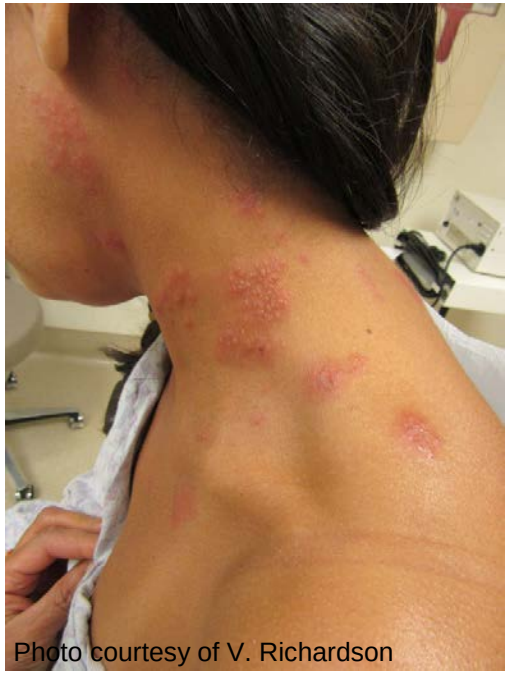
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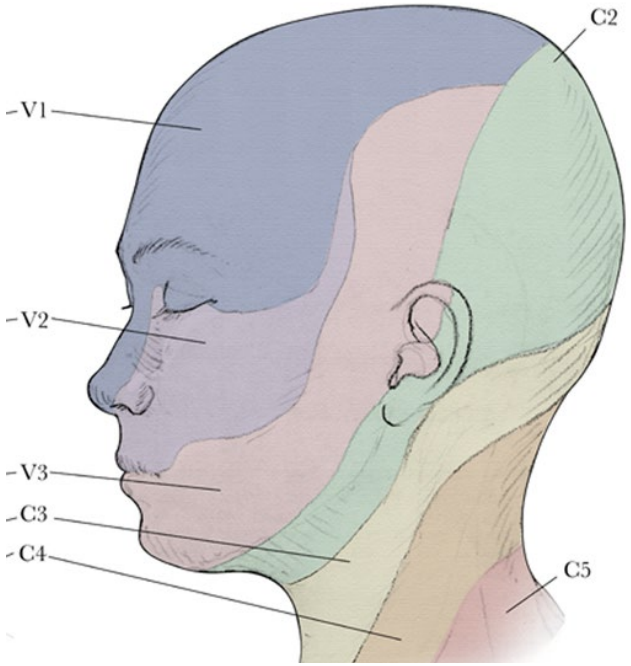
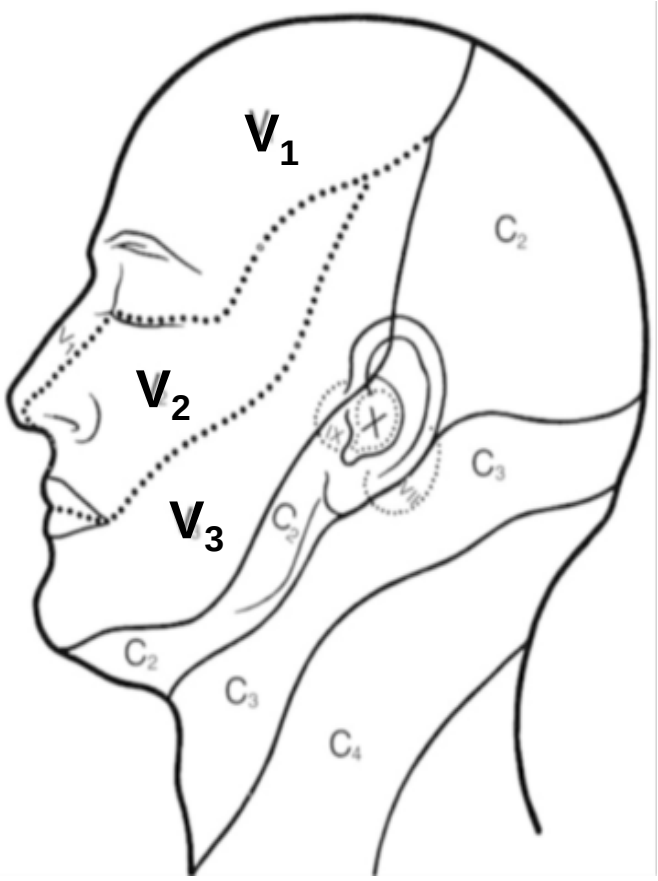


Thoracic: most common dermatome affected

Herpes Zoster Clinical Pearls!

You must:

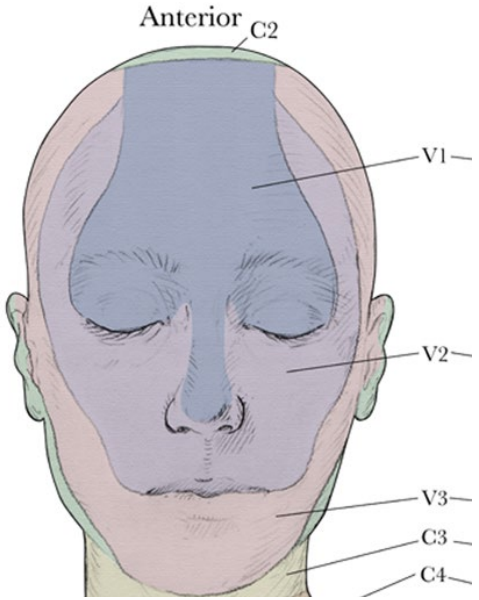
- Rule out **dissemination**
  - **More than 20 lesions outside neighboring dermatomes**
  - **More common in HIV/AIDS, immunosuppressed**
  - **Require IV Acyclovir**
  - **Can spread to liver, lungs, CNS**
- Identify if high-risk dermatomes involved
  - **V1 (Ophthalmologic), trigeminal nerve**
  - **STAT Ophthalmology consult**
- Isolate patient from neonates, pregnant women, people who never had chicken pox, & immunosuppressed people
- Educate
  - Active lesions are potentially infectious
  - Avoid contact with high-risk individuals until lesions crusted over
  - Still should get vaccinated once recovered.

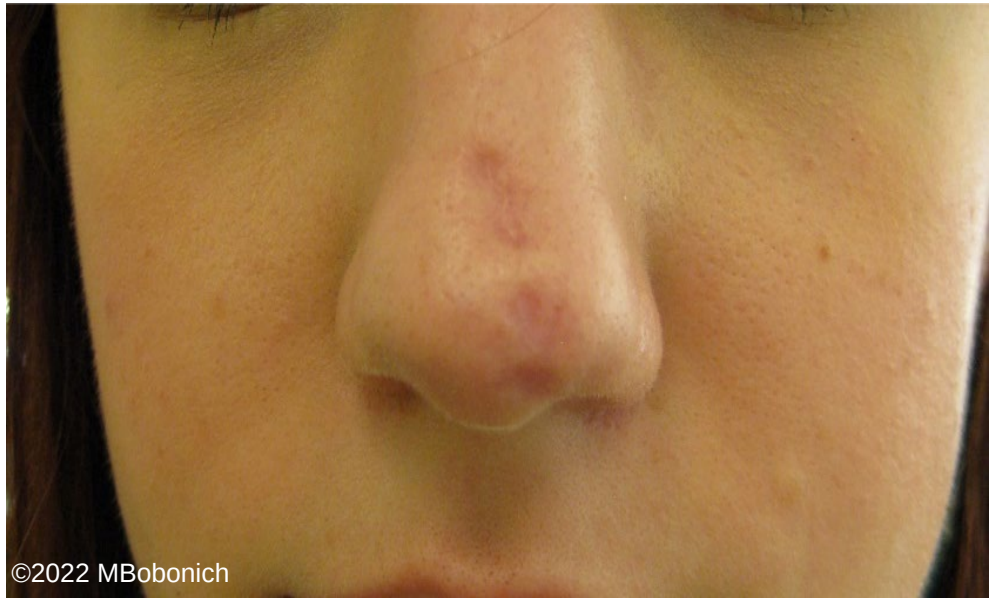


Clinical Pearls for Herpes Zoster

+ Hutchinson Sign

Involvement on the tip of the nose should increase suspicion for ophthalmic nerve involvement





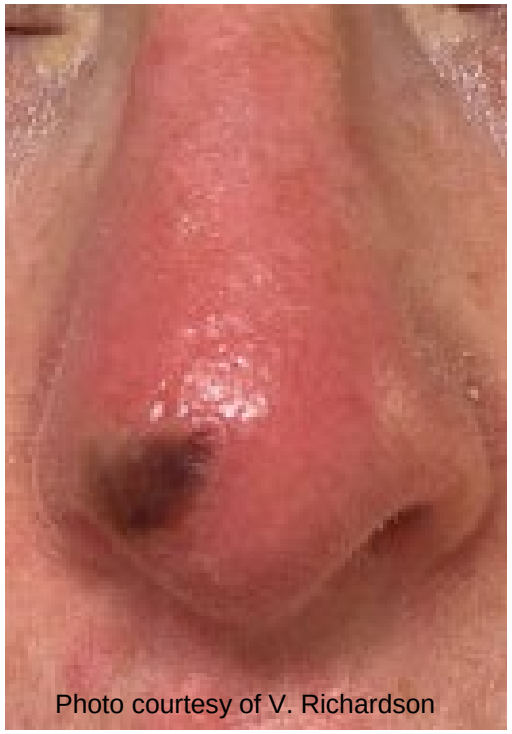


Photo courtesy of V. Richardson

Case Study Continued

Mr. Lopez returns 1 month later for his regularly scheduled skin check and psoriasis follow up. His rash has cleared but he notes continued pain and discoloration in the area where his prior eruption occurred. Your counseling includes all of the following except:

A. He can proceed with getting the Shingrix vaccination
B. Post herpetic neuralgia is more common in individuals over the age of 50
C. He will have to wait at least another 8 weeks before he can receive the Shingrix vaccination
D. The persistent discoloration may persist for up to 6-9 months

Case Study Continued

Mr. Lopez returns 1 month later for his regularly scheduled skin check and psoriasis follow up. His rash has cleared but he notes continued pain and discoloration in the area where his prior eruption occurred. Your counseling includes all of the following except:

C. He will have to wait at least another 8 weeks before he can receive the Shingrix vaccination

There is no specific length of time that you need to wait after having shingles before you can receive Shingrix, but generally the shingles rash should be resolved (CDC.GOV).

Herpes Zoster Vaccination (Shingrix)

- Who should get it:
  - Immunocompetent adults ages 50 and up
  - Immunosuppressed (due to disease or therapy) adults ages 19 and up
- **When**: NOT during an acute episode of herpes zoster
  - Avoid during pregnancy
  - 2 doses: 2nd dose 2–6 months after 1st
  - Immunosuppressed can have accelerated 2nd dose (1–2 months after 1st)
  - Previously received Zostavax: wait at least 8 weeks before giving Shingrix

Post-Herpetic Neuralgia (PHN)

Definitions vary:

- Persistent pain lasting at least 30 days past initial outbreak

Older patients at greatest risk

- 50% of persons over 60 years of age
- 75% of persons over 70 years of age

Treatment:

- Challenging due to sedating SEs of drugs used
  - Gabapentin
  - TCAs—Amitriptyline 25mg q.h.s.
  - Lidoderm patch
  - Referral to pain clinic

Post-Herpetic Neuralgia (PHN)

Risk of PHN or severity of PHN may be reduced if:

- Antiviral initiated within 72 hours of symptom onset
  - Oral antiviral agents recommended in all patients over 50 years of age with pain who still have blisters
- Patients are vaccinated with Shingrix vaccine

Syphilis

STD caused by spirochete *Treponema pallidum*

Chronic/intermittent clinical course

Primary (3–90 days after exposure)

- Painless ulcer Chancre (round, pink, raised border)
- Consider ddx for ALL ulceration on genitals
- Resolves spontaneously after 3–6 weeks without scar

Secondary (3–12 weeks after primary) THE GREAT IMITATOR

- **Localized or diffuse mucocutaneous lesions** (90-97%)
  - Asymptomatic or pruritic
  - Diffuse copper or “ham colored” scaly macules or papules on trunk/extremities
  - **Palmar/Plantar lesions: pink, red-brown macules or papules**
- **Generalized symptoms possible**
  - Generalized Lymphadenopathy (50-85%)
  - Malaise, myalgias, sore throat, low grade temps
- Resolves spontaneously

Syphilis Differentials: Primary

PRIMARY

- HSV
- Bacterial (*S.aureus*)
- Granuloma inguinale
- Trauma
- Neoplasm (SCC)
- Fixed Drug
- Zoon balanitis
- Behçet's disease

CDC Sexually Transmitted Infections Treatment Guidelines, 2021. https://www.cdc.gov/std/treatment-guidelines/p-and-s-syphilis.htm

Syphilis Differentials: Secondary

SECONDARY

- **Truncal**
  - Acute HIV
  - Viral exanthem
  - Pityriasis Rosea Drug eruption
  - Psoriasis
- **Palmar/Plantar**
  - Erythema Multiforme
  - Hand/foot/mouth
  - Rocky Mountain Spotted Fever

CDC Sexually Transmitted Infections Treatment Guidelines, 2021. https://www.cdc.gov/std/treatment-guidelines/p-and-s-syphilis.htm

Syphilis

<table>
<tr><td colspan="2">Screening Tests</td></tr>
<tr><td colspan="2">• Nontreponemal test—measure tissue damage cause by syphilis antibodies
  • RPR (rapid plasma reagin)
  • VDRL (venereal disease research laboratory
  • ONLY IF POSITIVE, MOVE TO TREPONEMAL/CONFIRMATION TESTING</td></tr>
<tr><td colspan="2">Confirmation Testing</td></tr>
<tr><td rowspan="3">Treponemal specific test</td><td>TPPA (treponema pallidum particle agglutination assay)
FTA-ABS (fluorescent treponemal antibody absorbed)</td></tr>
<tr><td>EIA (enzyme immunoassay)</td></tr>
<tr><td>CLIA (chemiluminescence assay)</td></tr>
<tr><td colspan="2">Serologic treatment response testing: (baseline, 6 mos, 12 mos, 24 mos)</td></tr>
<tr><td colspan="2">A fourfold decline in the nontreponemal titer</td></tr>
<tr><td colspan="2">Successful treatment results in seroconversion</td></tr>
<tr><td colspan="2">HIV infected individuals monitored more frequently</td></tr>
</table>

CDC Sexually Transmitted Infections Treatment Guidelines, 2021.
https://www.cdc.gov/std/treatment-guidelines/p-and-s-syphilis.htm

Syphilis: Treatment CDC Guidelines*

- ALL patients should be screened for HIV
- ALL patients screened for STDs
- All infants born to +women should be examined
- Treatment should be initiated to sexual partners (90 days)
- Reportable in EVERY state to the CDC

Primary and Secondary
Benzathine PCN G (Bicillin L-A) 2.4 million units IM x1

Tertiary/Late
Benzathine PCN G 7.2 million units (2.4m IM weekly x3)
Refer neurosyphilis, ocular, otic, and cardiovascular syphilis to I.D.

If PCN allergy:

Doxycycline 100mg bid x 14 d
OR
Ceftriaxone 1gm IM daily x 10-14d

Pregnant & PCN Allergy

Must be desensitized and then treated with PCN G

CDC Sexually Transmitted Infections Treatment Guidelines, 2021. https://www.cdc.gov/std/treatment-guidelines/p-and-s-syphilis.htm

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Abbreviations

- 4vHPV, 4-valent human papillomavirus vaccine
- 9vHPV, 9-valent human papillomavirus vaccine
- AD, atopic dermatitis
- CA, Condyloma Acuminata
- CLIA, chemiluminescence assay
- ED&C, electrodesiccation and curettage
- EIA, enzyme immunoassay
- FTA-ABS, fluorescent treponemal antibody absorption
- HPV, human papillomavirus
- HSV, herpes simplex
- HZV, herpes zoster virus
- MSM, men who have sex with men
- PHN, post-herpetic neuralgia
- RPR, rapid plasma regain
- STD, sexually transmitted disease
- TCA, tricyclic antidepressant
- TPPA, treponema pallidum particle agglutination assay
- VDRL, venereal disease research laboratory
- VZV, varicella-zoster virus

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