Skin and soft tissue infections 2

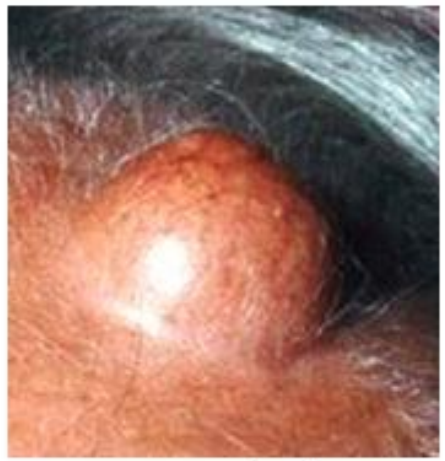
M Al Madadha

Sources :

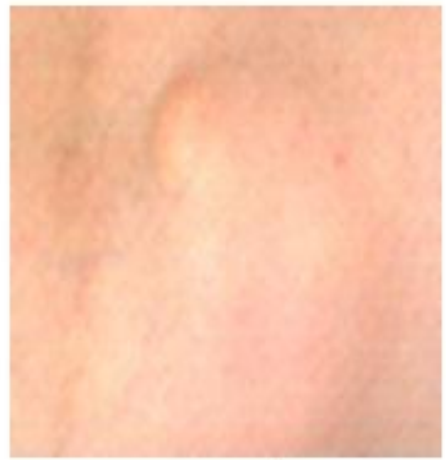
Harrisons infectious diseases 2nd edition, Oxford Handbook of Infectious Diseases and Microbiology 2nd edition

Definitions of infective skin lesions

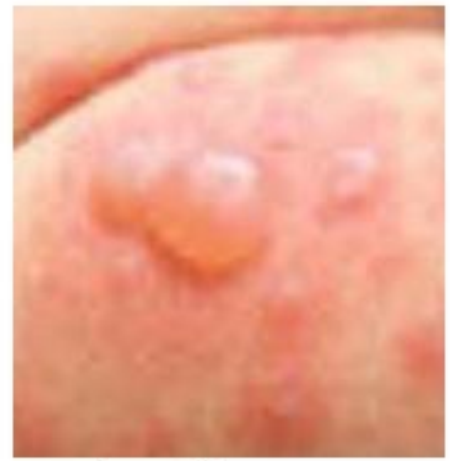
- Macules: are lesions that **have change in colour,** but not elevated or depressed from the rest of the skin surface They measure less than 10mm in diameter.
- Papules: are **elevated** lesions which are less than 10mm in diameter.
- Vesicles: are **small** fluid filled lesions, typically associated with viral infections.
- Bullae: are **large fluid** filled lesions.
- Crusted lesions : bullae that do not remain closed for long, fluid released crusts over/or lesion that crust during the course of infection.
- Ulcers: are a loss of the layers of the skin (or mucous membranes) which fails to heal.
- Petechiae : a small red or purple spot caused by bleeding into the skin.
- Purpura: a rash of purple spots on the skin caused by internal bleeding from small blood vessels (can think of it as a collection of petechiae).
- Eschar: a dry, dark scab or falling away of dead skin, typically caused by a burn, an insect bite, or infection with anthrax.



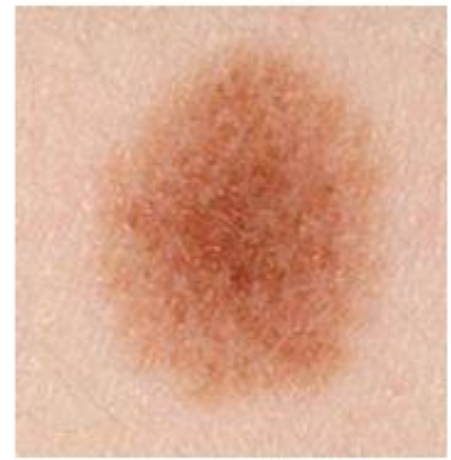
nodule



cyst

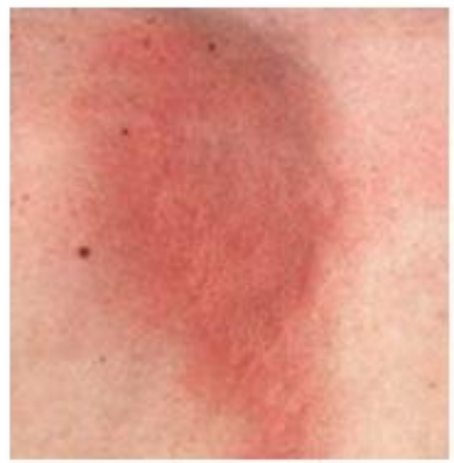


bullae

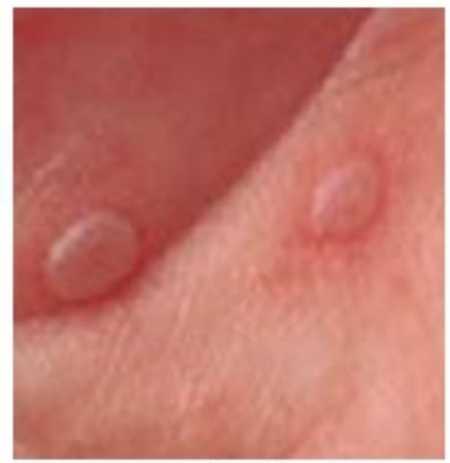


macule

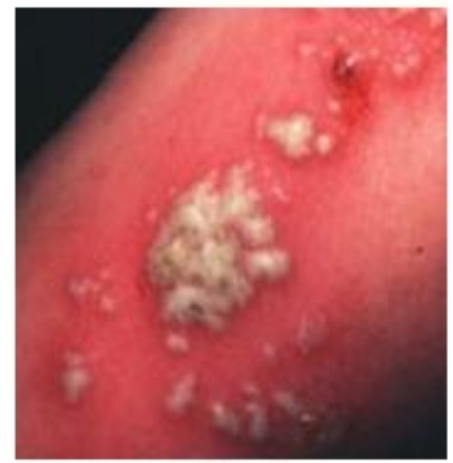
plaque



wheal



vesicle



pustule

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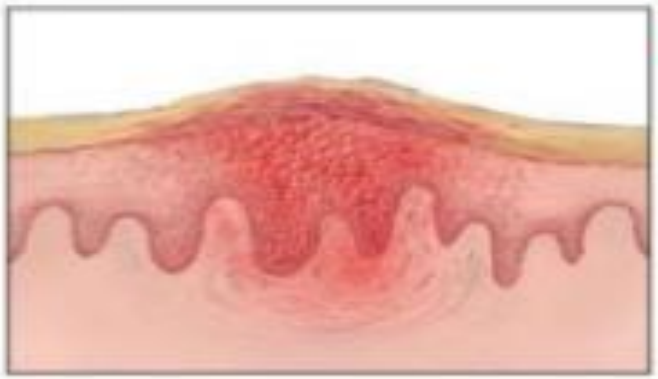
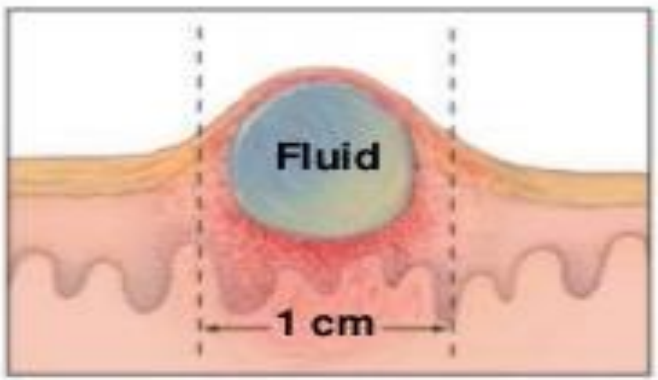
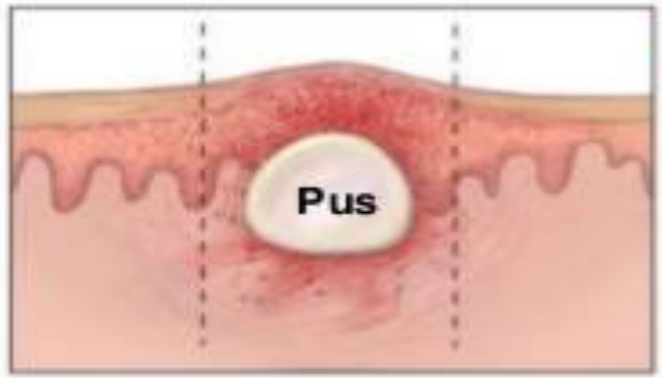
1 Macule



2 Papule

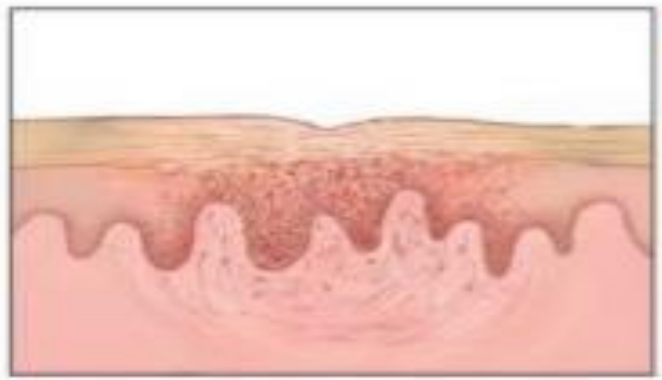


3 Vesicle



4 Pustule

5 Crust



6 Scar

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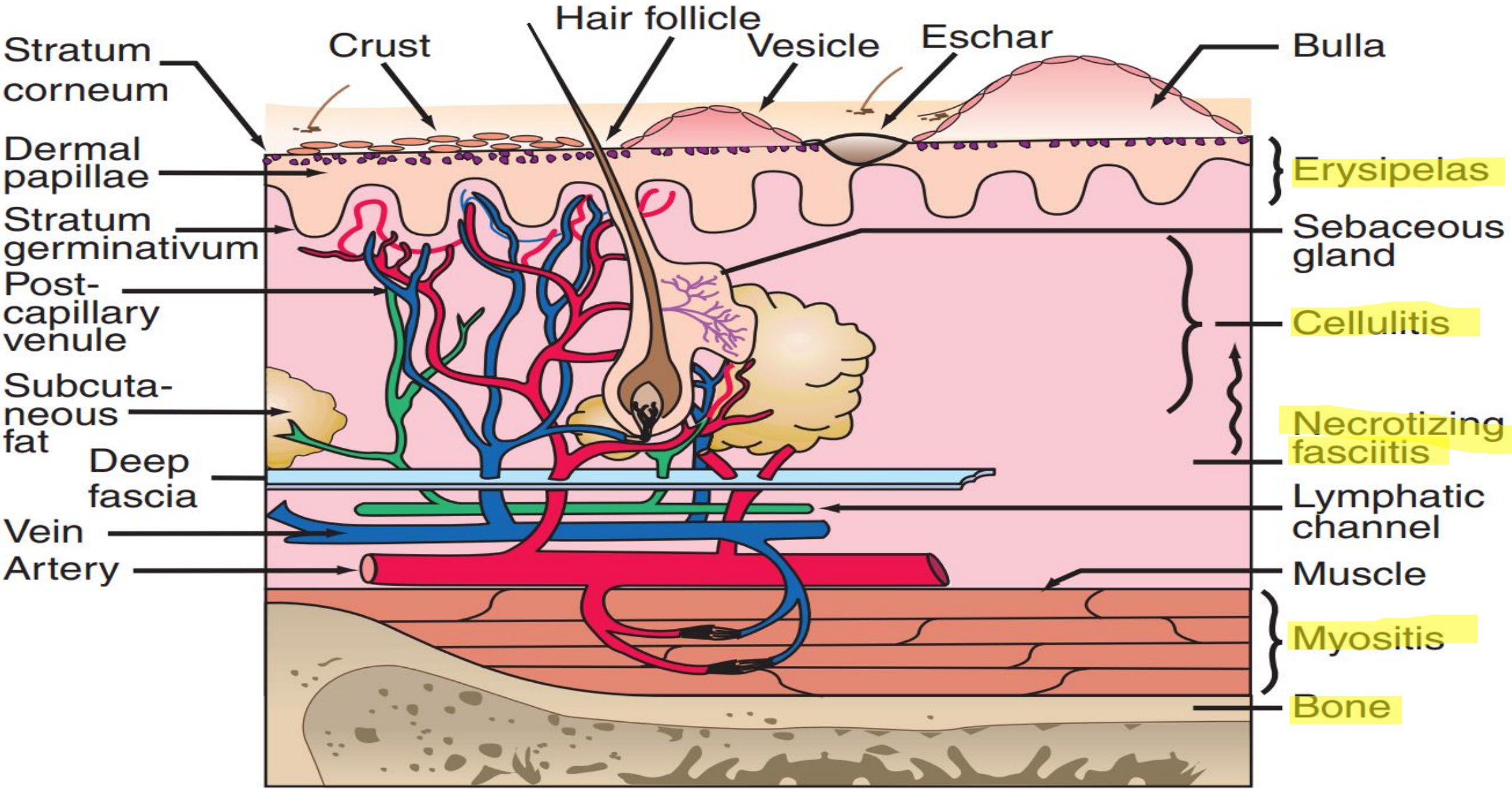

Stratum corneum
Crust
Hair follicle
Vesicle
Eschar
Bulla
Dermal papillae
Stratum germinativum
Post-capillary venule
Subcuta-neous fat
Deep fascia
Vein
Artery
Erysipelas
Sebaceous gland
Cellulitis
Necrotizing fasciitis
Lymphatic channel
Muscle
Myositis
Bone

Infections Associated with Vesicles

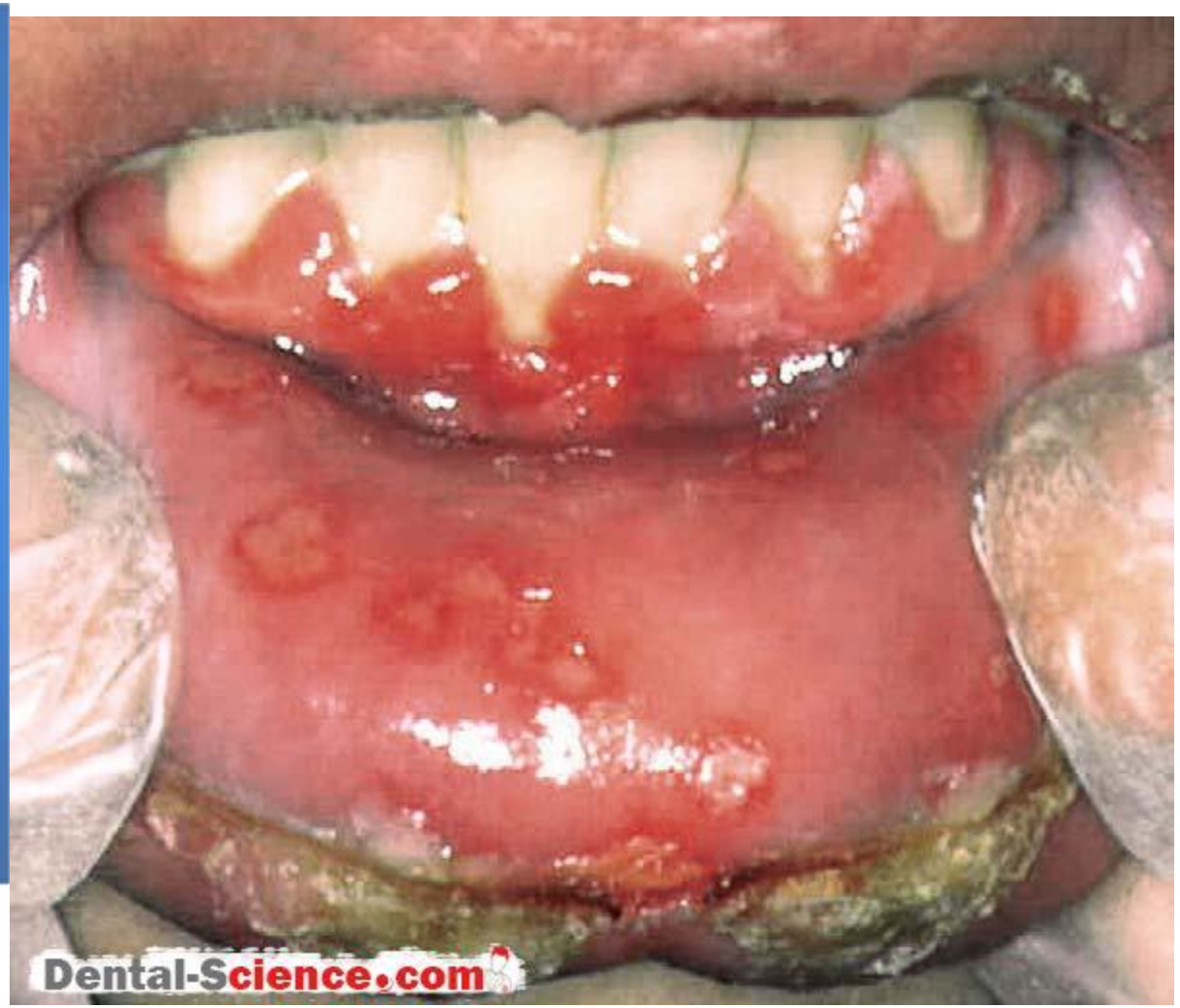
LESION, CLINICAL SYNDROME	INFECTIOUS AGENT
Vesicles	
Smallpox	Variola virus
Chickenpox	Varicella-zoster virus
Shingles (herpes zoster)	Varicella-zoster virus
Cold sores, herpetic whitlow, herpes gladiatorum	Herpes simplex virus
Hand-foot-and-mouth disease	Coxsackievirus A16
Orf	Parapoxvirus
Molluscum contagiosum	Pox-like virus
Rickettsialpox	*Rickettsia akari*
Blistering distal dactylitis	*Staphylococcus aureus* or *Streptococcus pyogenes*

Almost all (except rare ones) are viral agents

Viral skin infections

- Herpes simplex virus:
- → Cutaneous manifestations of HSV infection include:
- • pharyngitis/gingivostomatitis—this is the commonest presentation of primary HSV-1, generally seen in children and young adults.
- General features:
- *Fever, malaise, difficulty chewing, cervical lymphadenopathy*.
- Ulcers and exudative lesions are found on the posterior pharynx and sometimes the tongue, buccal mucosa, and gums.
- Patients with eczema may develop severe disease (eczema herpeticum), which may disseminate, requiring systemic therapy.
- HSV has been associated with up to 75% of cases of erythema multiforme;

HSV-1 Pharyngitis



Stomatitis

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http://www.dental-science.com/wp-content/uploads/2016/07/Herpes-stomatitis-2.jpg

Eczema herpeticum
A medical emergency

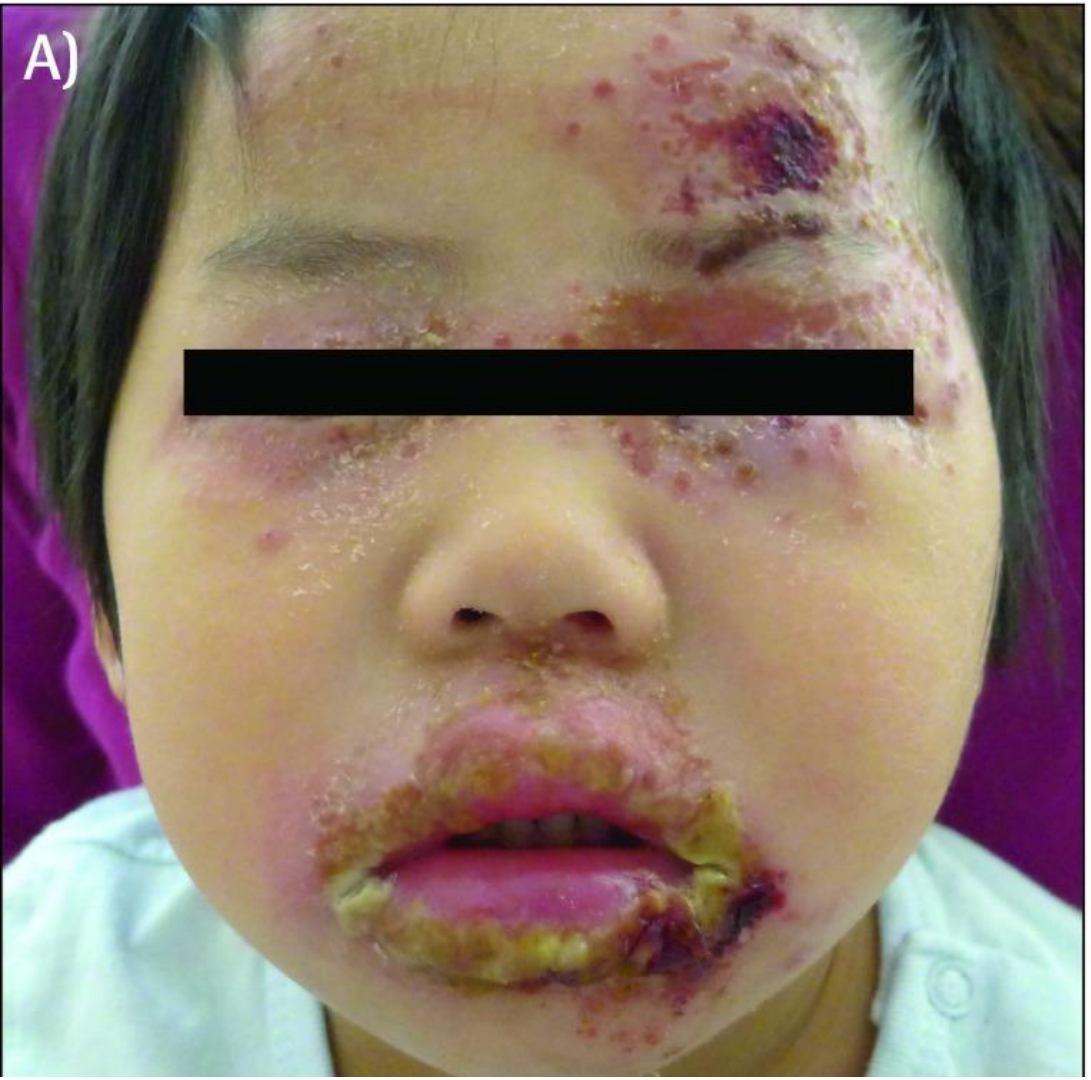
- Eczema herpeticum, also known as a form of Kaposi varicelliform eruption caused by viral infection, usually with the herpes simplex virus (HSV),
- It is an extensive cutaneous vesicular eruption that arises from pre-existing skin disease, usually atopic dermatitis (AD).
- Children with AD have a higher risk of developing eczema herpeticum, in which HSV type 1 (HSV-1) is the most common pathogen.
- Eczema herpeticum can be severe, *progressing to disseminated infection and death if untreated.*
- Bacterial superinfection and bacteremia are usually the complications that cause mortality.

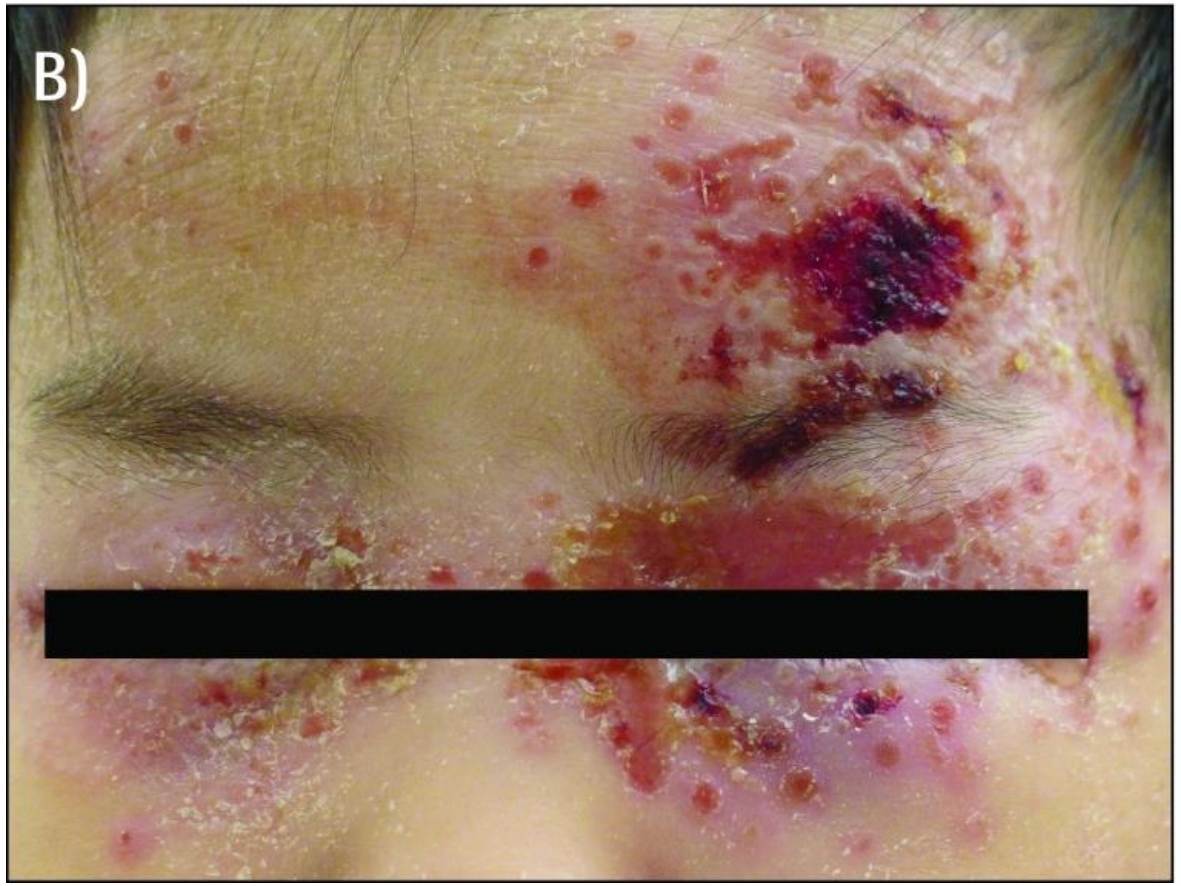
Next slide present a case in which eczema herpeticum was misdiagnosed as impetigo during a patient's initial treatment.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3520662/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3520662/

Figure 1. Multiple grouping punched-out ulcers with local dissemination over the frontal, periorbital and perioral areas and cheeks, with secondary impetiginization





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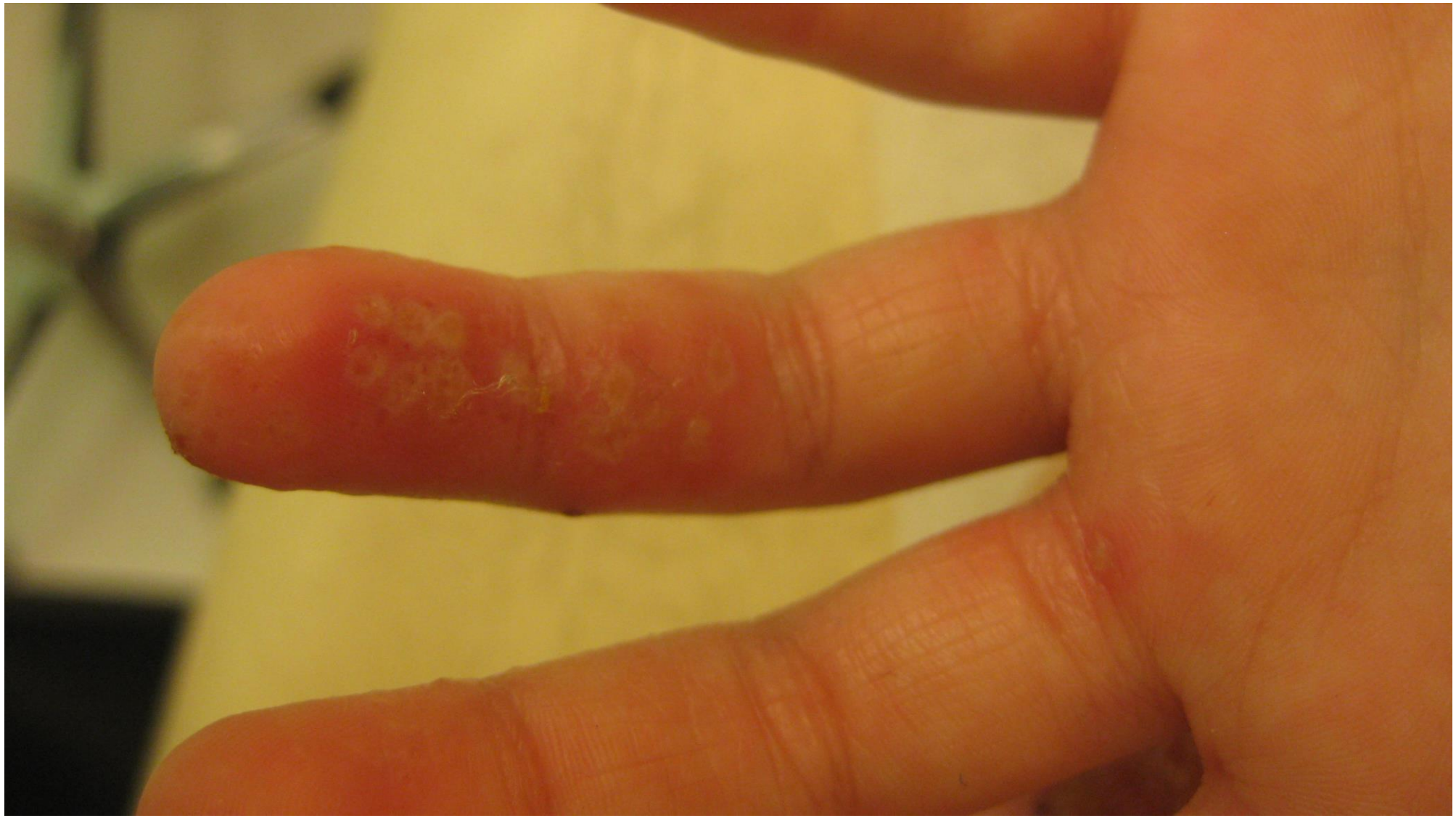
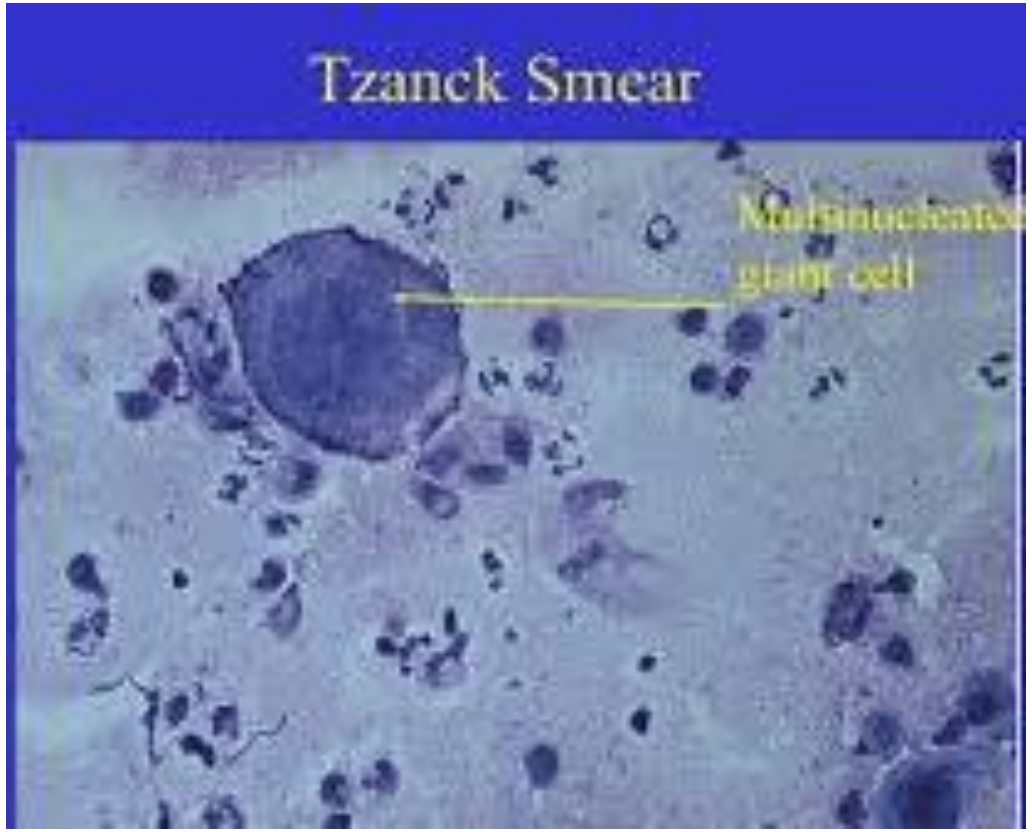
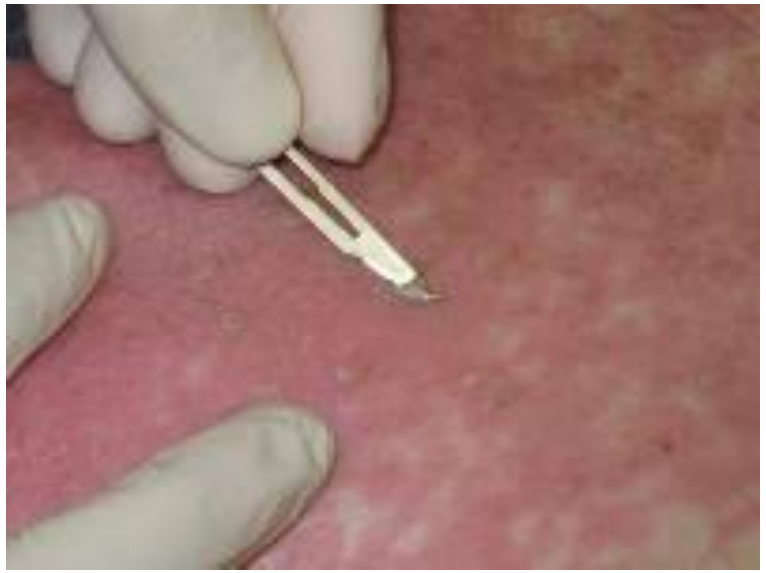


Dx

- Direct fluorescent antibody testing is accurate (distinguishes between HSV 1, HSV 2, and varicella) → it is also rapid (several hours)
- Viral culture is also diagnostic, results are accurate and reliable, and can distinguish between different viruses. However, results are slow (2 days).
- Tzanck smear requires **a skilled observer** to interpret, but results are immediate on examination of the smear.
- A Tzanck preparation: scrapings from the base of a blister or erosion on a glass slide → staining with Wright or Giemsa stain → examining under light microscopy for characteristic "Tzanck" cells (multinucleate keratinocytes).there cells can be seen in herpes, varicella, and CMV.
- PCR may be helpful in when the cutaneous lesions are old or atypical and viral particles are few in number.
- Pathology lab can also help in the diagnosis with characteristic viral cytopathic changes of the epidermis and follicular epithelium are present on hematoxylin and eosin (H & E)-stained tissue.
- IHC (immunohistochemistry, staining with antibodies) can also help





Giemsa stain

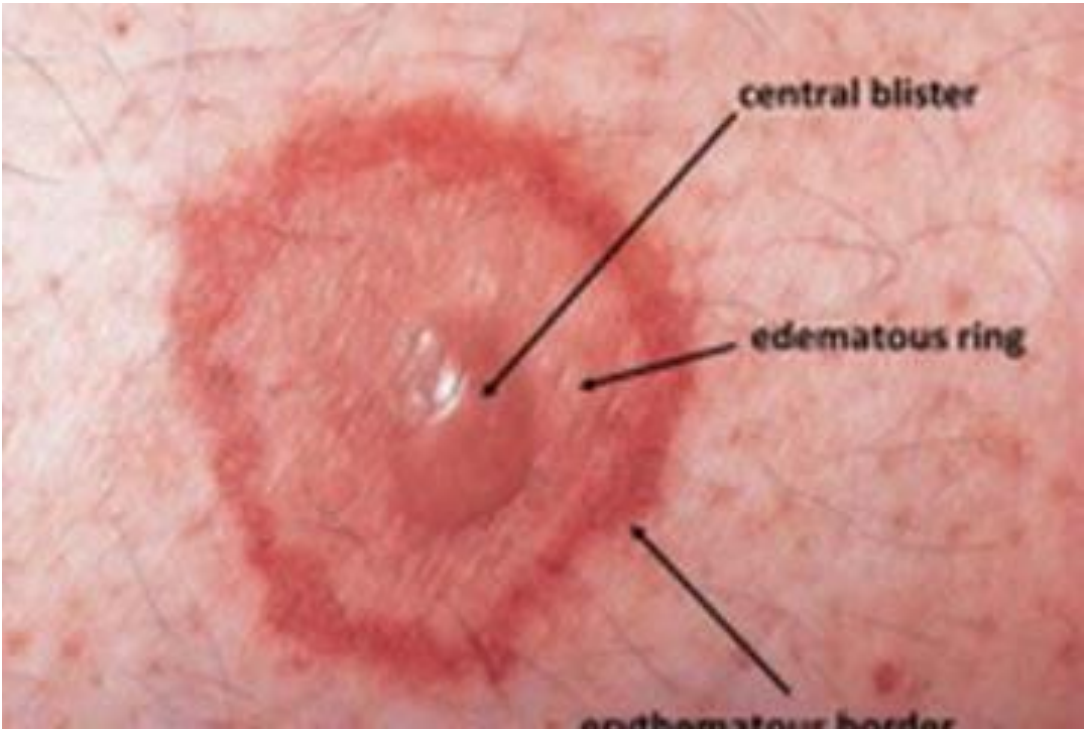
Rx

- Treatment with systemic antiviral agents should be initiated as soon as a diagnosis of Kaposi varicelliform eruption is suspected.
- (Oral) acyclovir is the preferred first-line treatment in otherwise healthy (immune competent) pediatric patients usually somewhat high dose, 5x/day for 7-10 days.
- (IV) acyclovir is for patients with systemic involvement or in patients who are immunocompromised.
- Foscarnet should be used in patients with acyclovir-resistant infection (*this is an antiviral medication, that works on herpes viruses, however it causes nephrotoxicity in 50%- question of mortality, you take morbidity >mortality*).
- Valacyclovir is efficacious and can be dosed only twice daily, an advantage over daily multiple dosing of acyclovir. However, it is cost-prohibitive for some patients.
- Two topical ophthalmic preparations, trifluridine and vidarabine, are available for use in patients with **ophthalmic involvement.** Immediate opthalmologic consultation is recommended for any patient with potential ocular infection.

Erythema multiforme

- Erythema multiforme is **an acute**, self limiting and at times **recurring** skin condition thought to occur **due to a hypersensitivity** reaction against certain infection(HSV-1)s and medications (antibiotics).
- Erythema multiforme is a term describing target lesions - circular lesions often with central blister with a symmetrical peripheral distribution, usually on limbs (Due to type 4 hyper sensitivity reaction).
- There are often mouth, genital and eye ulcers and fever - Stevens-Johnson syndrome.
- Spectrum of disease (now debated) goes from erythema multiforme minor → steven Jhonson's syndrome→ Toxic epidermolysis necrosis
- With its minimal mucous membrane association and <10% epidermal detachment, erythema multiforme is now considered to be a distinct condition from SJS and TEN. (10% is SJS, >30% emergency TEN)
- Frequently seen in adults between the ages of 20-40 years, with rash occurring 5-10 days **after the onset of viral illness**, happen over 3-5 days and persist for 1-2 weeks (urticaria is the major differential here which resolves in hours).

Lamoreux MR et al. Erythema Multiforme. AFP 2006;74(11)



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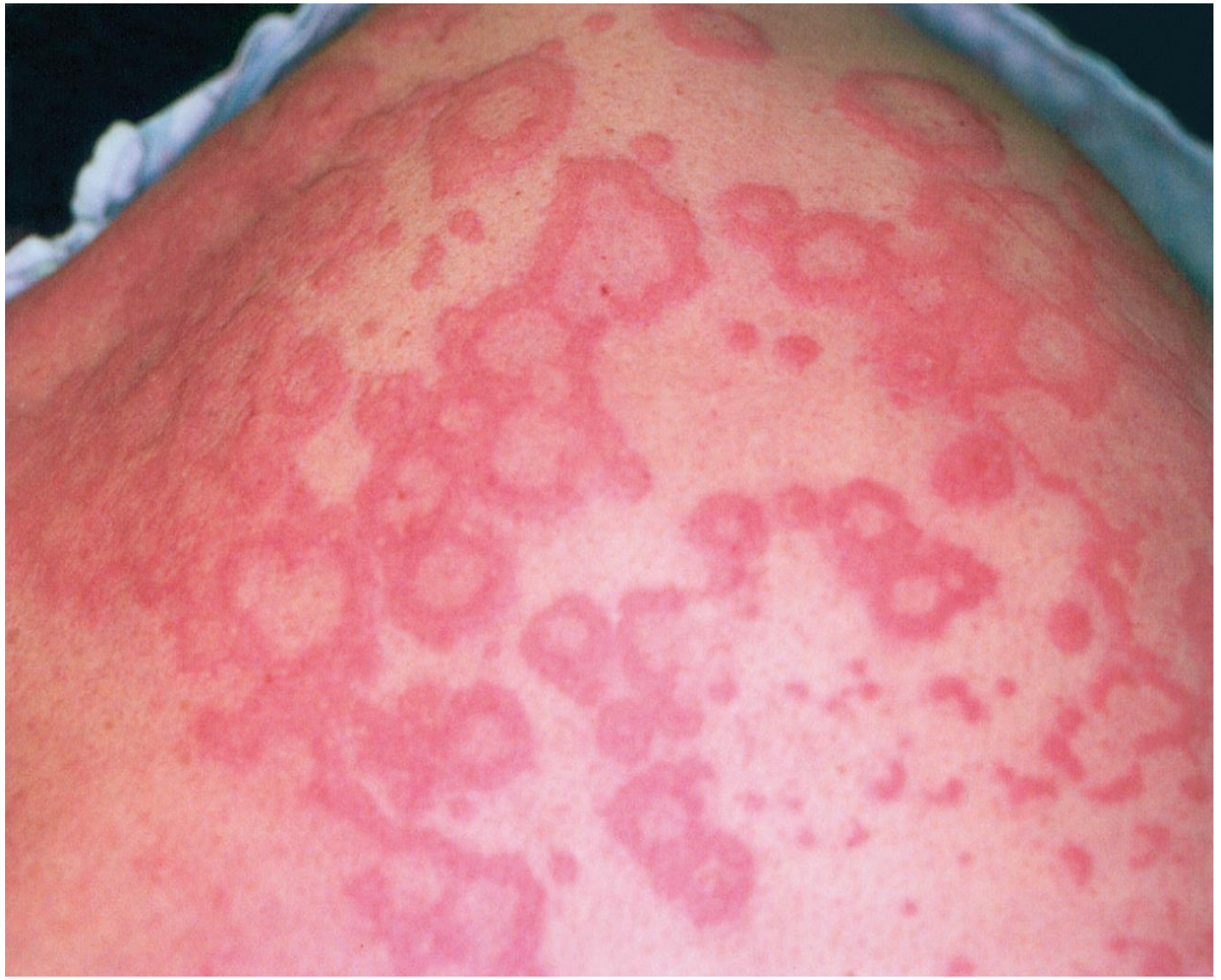

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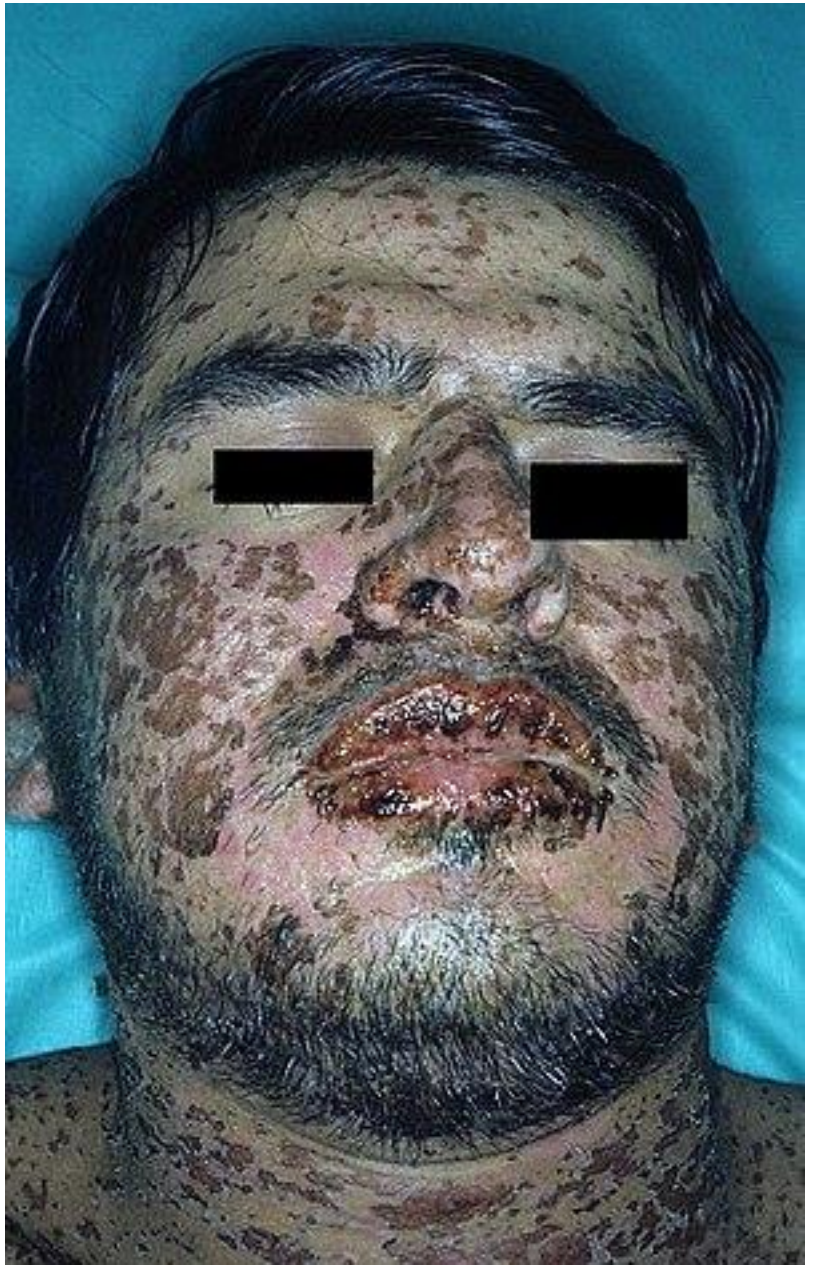
- **Causes**
- Idiopathic (50%)
- HSV (>50%)
  - Occurs 10 days after acute eruption
  - HSV may be cause even without active lesions
- Other infections : (*Mycoplasma pneumoniae*, VZV, HCV, CMV, HIV)
- Drugs: *antibiotics and antiepileptic drugs are mostly implicated (SJS as well), sulfa drugs, penicillin and ciprofloxacin. However other medications may cause it*
- Rx (?): 1)remove the precipitating factor (HSV, mycoplasma) or medication 2) supportive care (pain meds, antihistamines, wound dressing) 3) antiviral therapy for HSV causes - oral acyclovir
- 4) must tell patient if bullae erupt, or systemic symptoms recur, must return (SJS or TEN emergency!)

SJS→ TEN



ACUTE – LIFE THREATNING

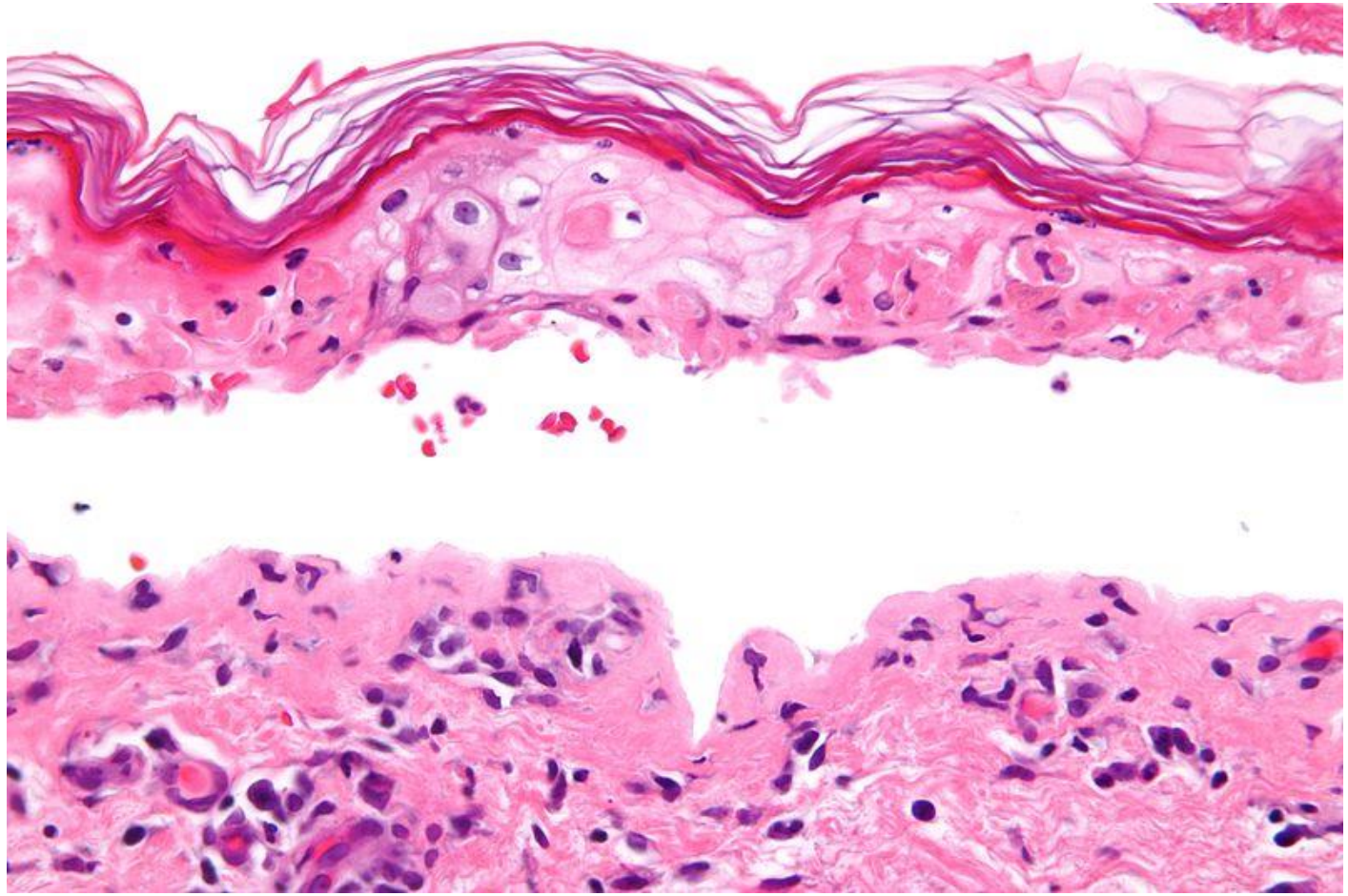
Begin with prodromal symptoms, then progress to skin ulcerations
That begin in trunk and face and typically involve the mouth and eyes (with genital sores as well)

- Clinically linked to one of the causes below
- Toxic looking patient
- Positive nikolsky sign (bullous disease)

Dx: clinical, biopsy confirms

Rx: supportive- ICU admission (or burn unit) some immune based therpay shows promise.

SJS mortality 3%
TEN mortality 30%! (upto 50%)



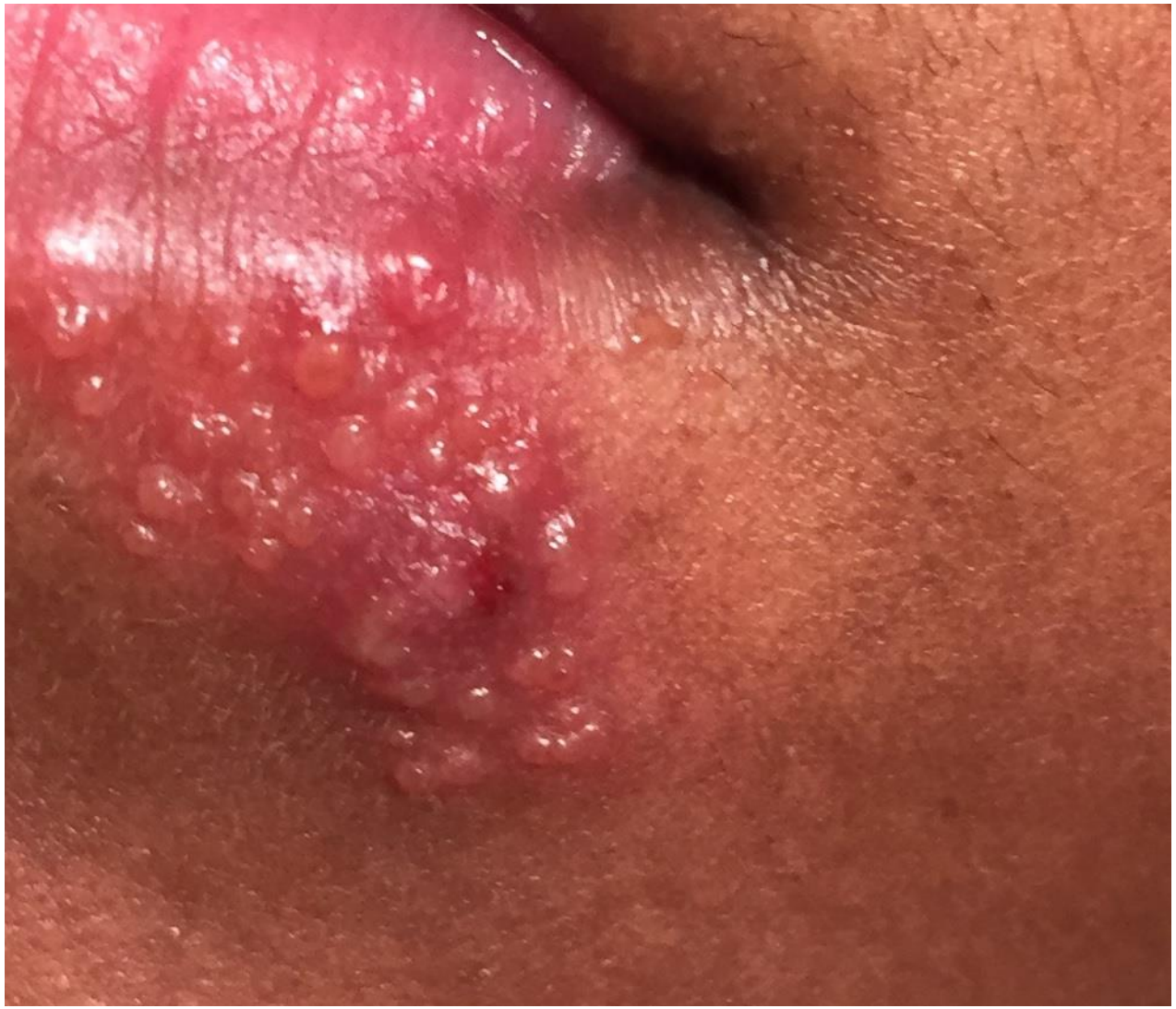
1. Drug-Induced Skin Reaction (50% of Stevens Johnson and 90% of Toxic Epidermal Necrolysis)
    1. Highest risk with higher doses and rapid drug introduction
    2. Antibiotics
        1. Trimethoprim-Sulfamethoxazole (Bactrim) - most common
        2. Other antibiotics have also been implicated (Cephalosporins, Penicillins, Quinolones)
    3. Anticonvulsants
        1. Carbamazepine
        2. Phenytoin
        3. Phenobarbital
        4. Valproic Acid
    4. Acetaminophen
    5. Allopurinol
    6. NSAIDs
    7. Corticosteroids
    8. Vaccinations
2. Infectious disease
    1. HIV Infection
    2. Herpes Simplex Virus
    3. Mycoplasma
    4. Hepatitis A
3. Other causes
    1. Connective tissue disease (e.g. Systemic Lupus Erythematosus)
    2. Pregnancy
    3. Radiotherapy
    4. Vasculitis

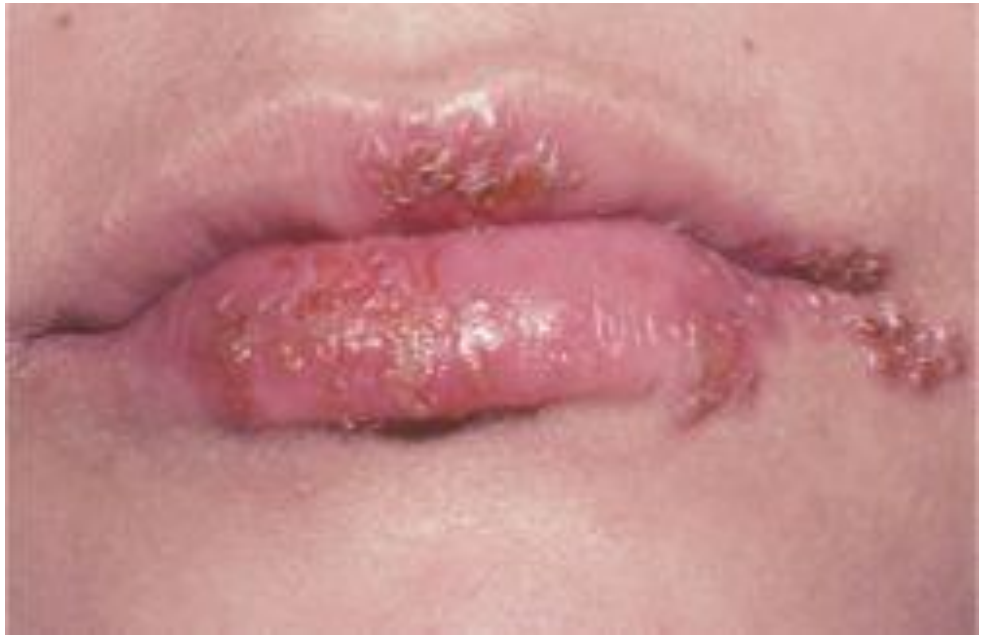
• Recurrent herpes labialis *HSV-2

- —the most frequent manifestation of HSV-2 reactivation.
- More common in college students (AB positive 37% at y1 college and 46% at year 4 in US)
- May be asymptomatic or present with symptoms that are milder and of shorter duration than primary infection(*cold sores in about ¼ of college students).*
- Mild prodromal tingling is followed by the development of lesions within 48h and usually resolve within 5 days.
- Immunosuppressed patients may experience severe mucositis, with spread to skin surrounding the mouth;

pathophysiology

- HSV-1 > HSV-2
- Transmission via mucous membranes (kissing), direct contact with open skin or sharing of formites (towels, utensils..etc)
- After contact 2-20 days may get the symptoms, however SHEDDING is the first 2-4 days max.
- After the episode , the virus remains dormant in trigeminal ganglion and triggers again (recurrence) due to stressors such as:
- *Fever, stress, sun exposure, trauma, immune suppression, hormonal changes-menses- , fatigue (travel)*





Grouped vesicles on erythematous base
Form on vermillion border edge
Lips-gingiva-palate-tonge +-LAP

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https://img.tfd.com/mosby/thumbs/500105-fx8.jpg

- First episode usually severe (fever , LAP, mouth or gingival ulcers)
- Secondary episode , after recurrence, lesions *(itch, burn, tingling first 12-36 hours, then visicles erupt…heal in 7-14 days*

- Rx: (only reduces symptom DURATION, does not remove virus completely)
- First episode can give acyclovir, reduces the lesion time to 4 days Vs 10 and shedding to 1 vs 5 days(less shedding = less spread).
- Recurrence:
- Oral : Acyclovir (reduce eruption healing time by 2 days) famciclovir or valacyclovir
- Topical (reduces healing time by less than 1 day)

Genital herpes

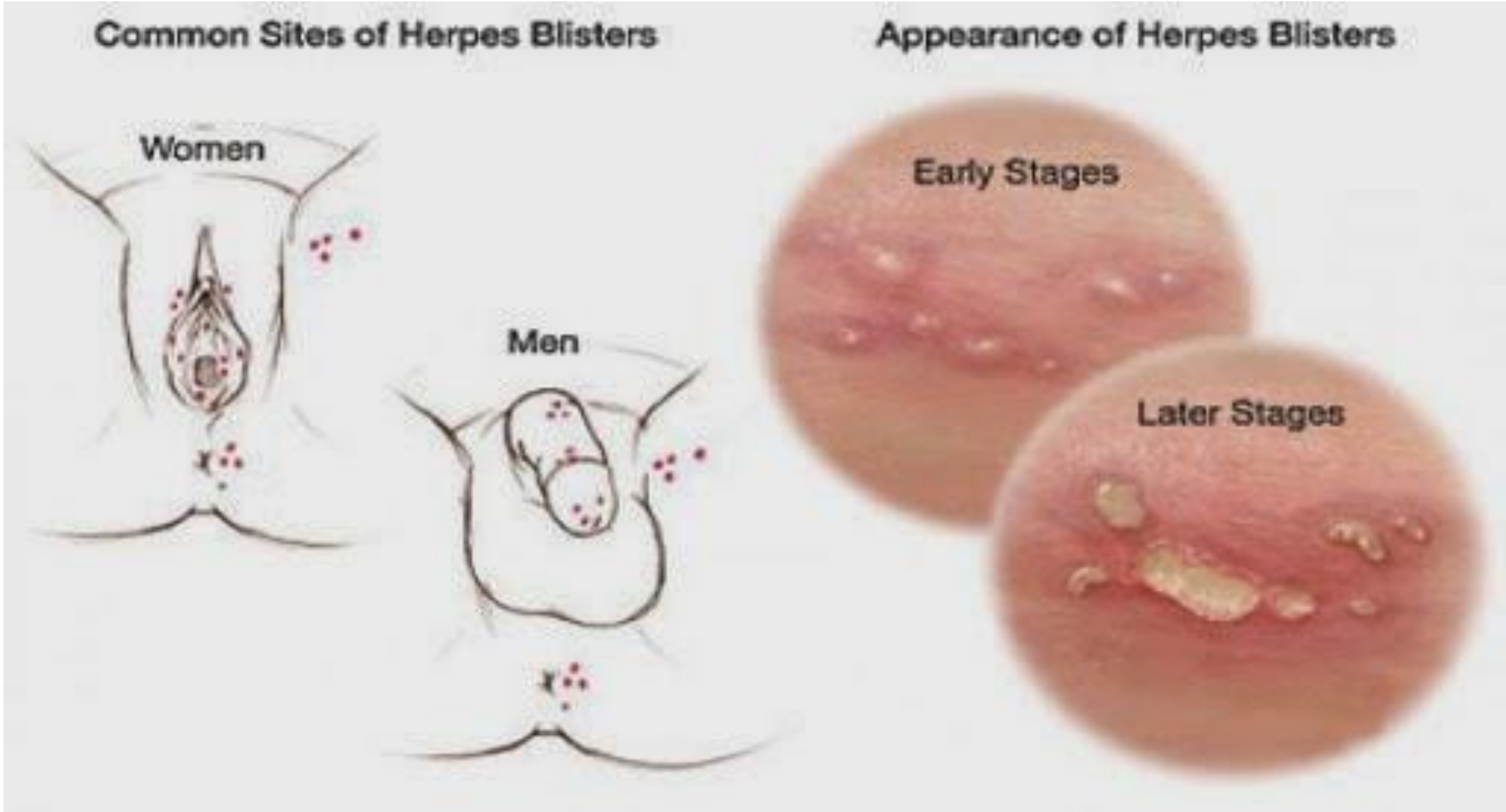
- MCC of genital ulcers (60-70% of STD ulcers)
- High prevalence in western countries (12% roughly) or 10-30% of sexually active people.
- 300k cases a year in US alone!
- Caused by HSV-2 (90%) HSV-1 (although now HSV-1 on the rise!)
- Asymptomatic in majority of patients (>2/3)→ helps spread
- Virus SHEDS ASYMPTOMATICALLY (so without outbreak the virus can be shedding in 10-20% OF DAYS!)

Primary infection

- (Primary Genital Herpes) may be associated with fever, malaise and adenopathy
- HSV DNA migrates up the infected axon to the affected spinal cord sensory Ganglion (similar story in the herpes viruses)
- HSV persists in the sensory Ganglion **life long**, dormant until next outbreak
- On periodic reactivation, HSV DNA migrates down axon and erupts again
- **First infection is worst,** then subsequent outbreaks are typically less severe

Vesicular eruption:

- Similar to oral herpes, preceded by tingling, itch and burning
- Lesions occur in the distribution shown below
- Primary vesicles remain upto to 2 weeks, reactivation 6-12 days
- Hsv-1 genital herpes is milder and fewer outbreaks than hsv-2



http://www.herpesland.com/wp-content/uploads/2015/01/genital-herpes.jpg

Dx :

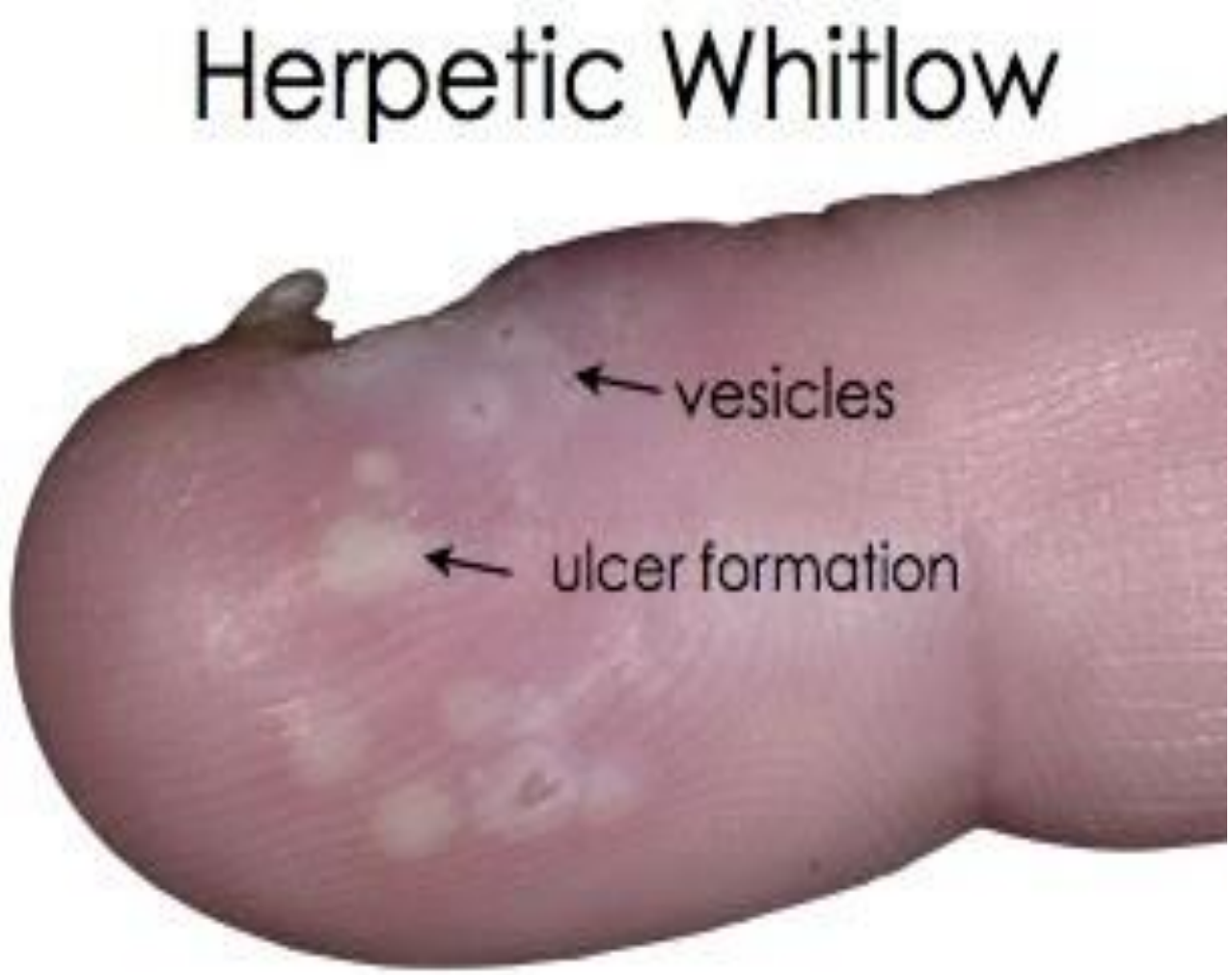
- Clinical picture is diagnostic
- (HSV test PCR)

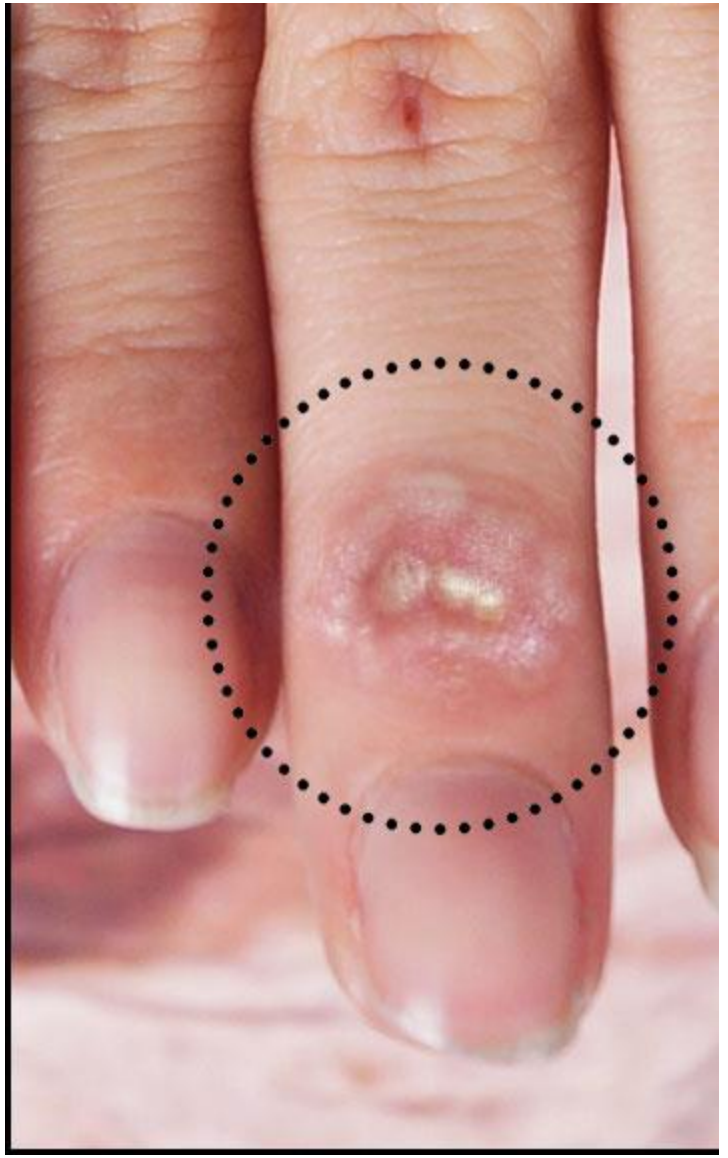
Rx :

- Antivirals for primary and recurrence, do not cure but shorten span of illness
- DURING PREGNANCY, might transmit vertically and cause neonatal HSV infection (*can cause encephalitis or dissiminated HSV infection in new borns, or cause congenital HSV infection which may lead to microcephalus or hydrocephalus or chorioretinitis*)
- In pregnancy abstinence, vaccine (experimental) + antivirals
- C/S in patients with active lesions
- As for measures for active lesions : loose clothing, ice pack or baking soda compression
- Topical antivirals and low dose anasthetics can be given

Herpetic whitlow

- *HSV infection of the finger which may result from auto-inoculation (existing oral or genital infection)* or by direct inoculation from some other environmental source.
- Presents with vesicles ± regional lymphadenopathy;
- Differentiate from acute paronychia (bacterial)
- Rx: Prevent transmission (bandage)
- Antiviral incase of recurrent infection or immunocompromised
- Tzanck smear can be done
- • Herpes gladiatorum—mucocutaneous infection of surfaces such as chest, ears, face, and hands seen in rugby players and wrestlers.(long intimate contact)





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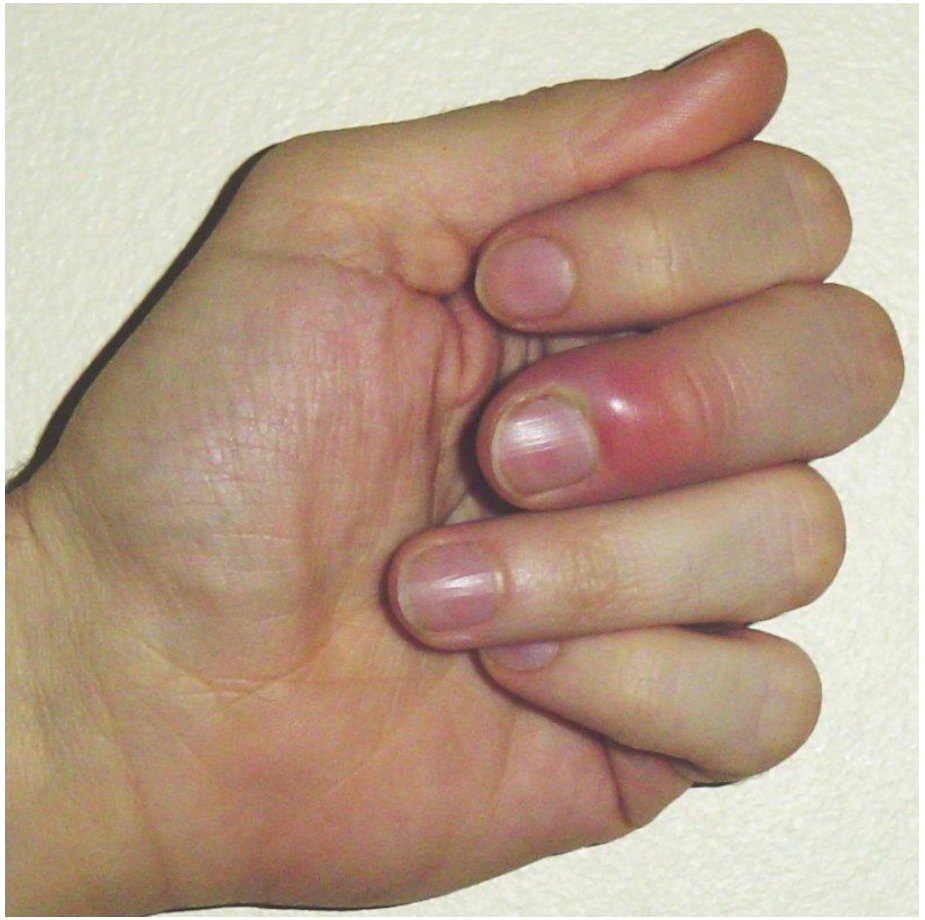
https://www.epainassist.com/images/herpetic-whitlow-preview.jpg

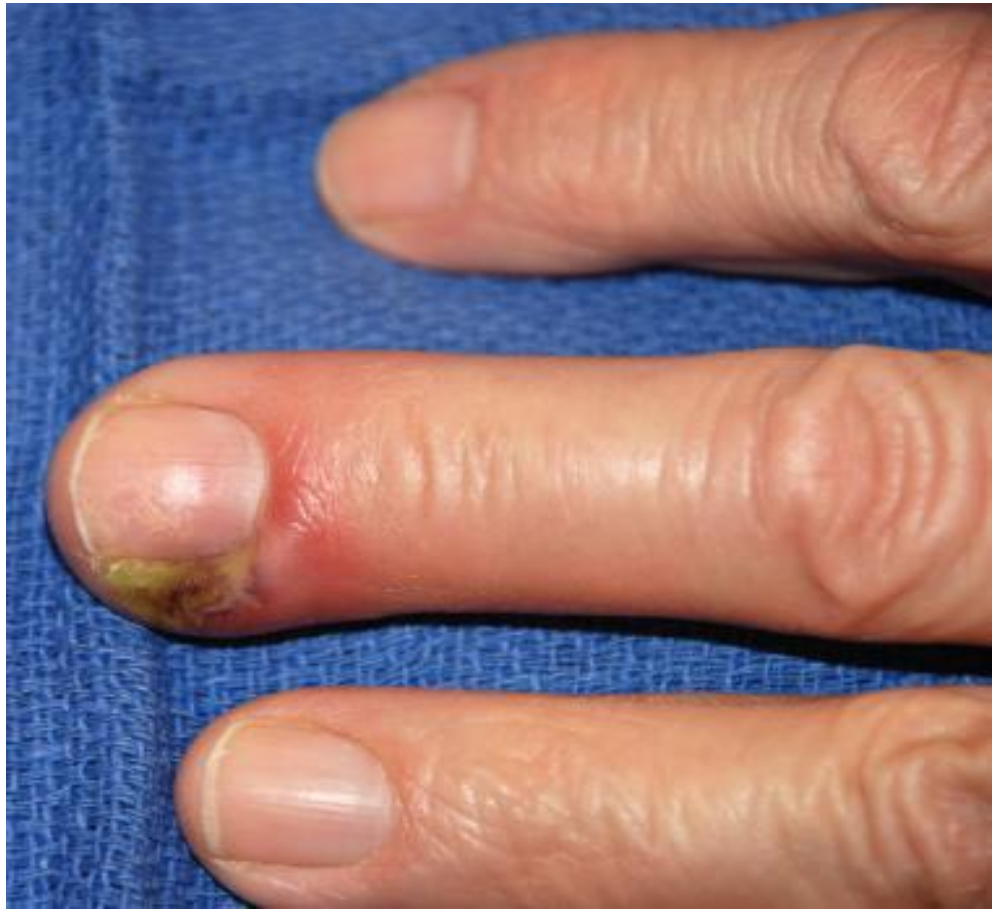
Paronychia

- Paronychia usually more in females
- Due to penetrating trauma (finger biting, manicure ..etc)
- Bacteria from skin (*Staph aureus*) or from mouth (*Streptococcus pyogenes*, maybe *bacteroides*) enter the tissue → infection
- Infection 2-5 days after trauma, with pain at site and local inflammation signs (red, hot, painful/tender)
- Can progress to abscess formation and nail bed infection (serious)
- Most differentiating feature from whitlow?
- Rx: soak for 15 minutes in warm water or acetic acid soak (1:1)
- I & D (if abscess)

Acute paronychia



https://upload.wikimedia.org/wikipedia/commons/c/c5/Paronychia.jpg



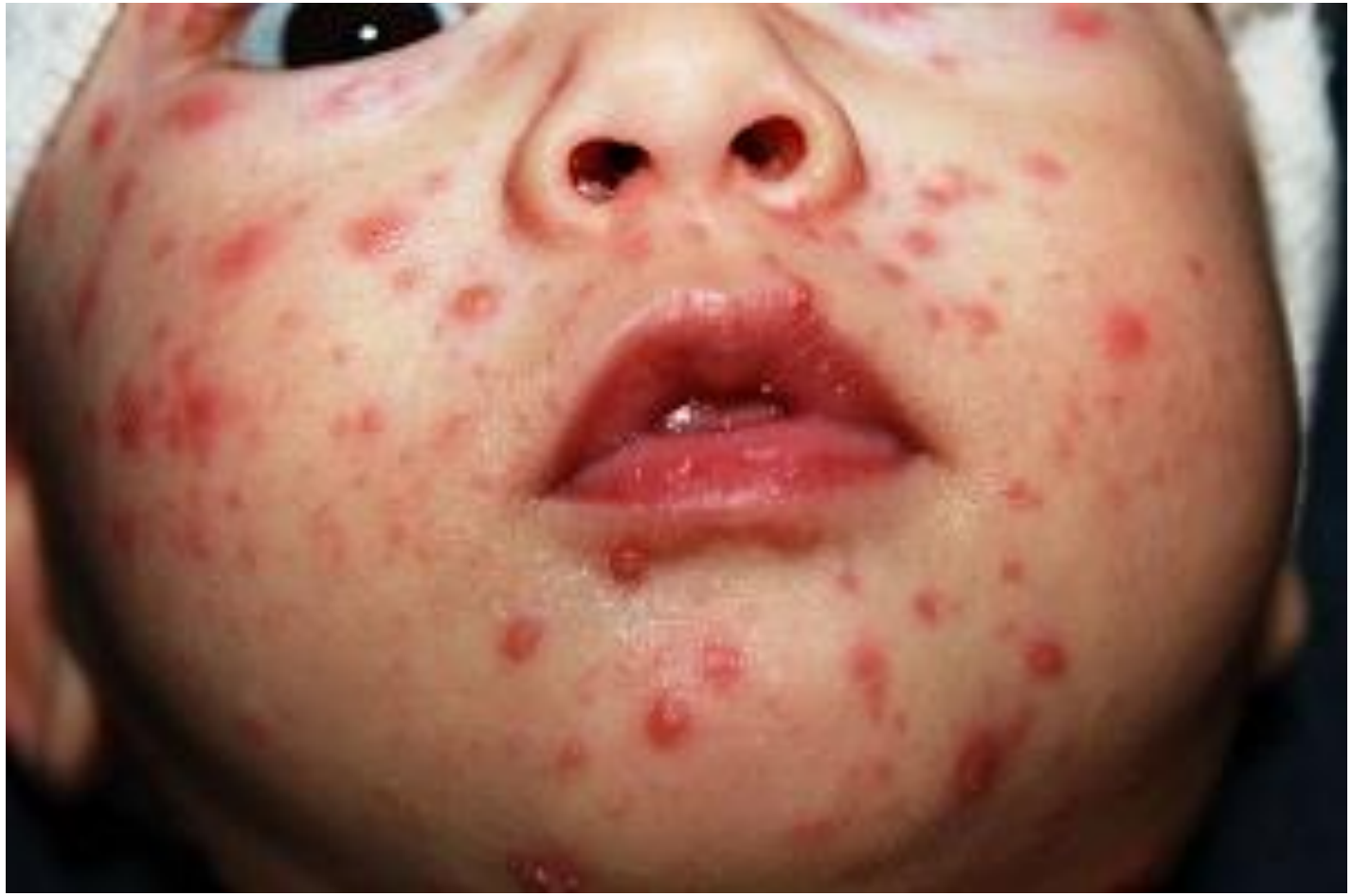
https://img.medscapestatic.com/pi/meds/ckb/19/28819tn.jpg

Rx for paronychia

- Topical antibiotic (mild cases) topical Bacitracin, gentamicin, fluoroquinolone
- Can add topical steroid as well to reduce inflammation (quicker healing)
- Prolonged case : Systemic antibiotics (suspect cellulitis or ingrown nail), must do I and D and then give Cephalexin or Dicloxacillin as first line therapy
- Second line therapy : TMP-SFX or doxycycline-especially if you suspect MRSA
- Remember MRSA colonizes nose , so biting can bring it easily to nail bed!

Varicella-zoster virus (Human herpes 3)

- • Causes Chickenpox جدري الماء:
- 90% of cases occur in children under 13 years of age.
- Peak onset ages 5 to 9 years old (this is in what age you suspect it most-SCHOOL)
- Peak outbreak time (January to May- cold season-fall)
- Incubation is 10–14 days .
- Transmission : respiratory droplets or through direct contact
  - Can also be vertical (translplacental)
- Following incubation patient may have a 1- to 2-day febrile prodrome before the onset of constitutional symptoms (malaise, itch, anorexia) and then papulo vesicular rash (<5mm across) which is **itchy!** Pruritic red papules and vesicles



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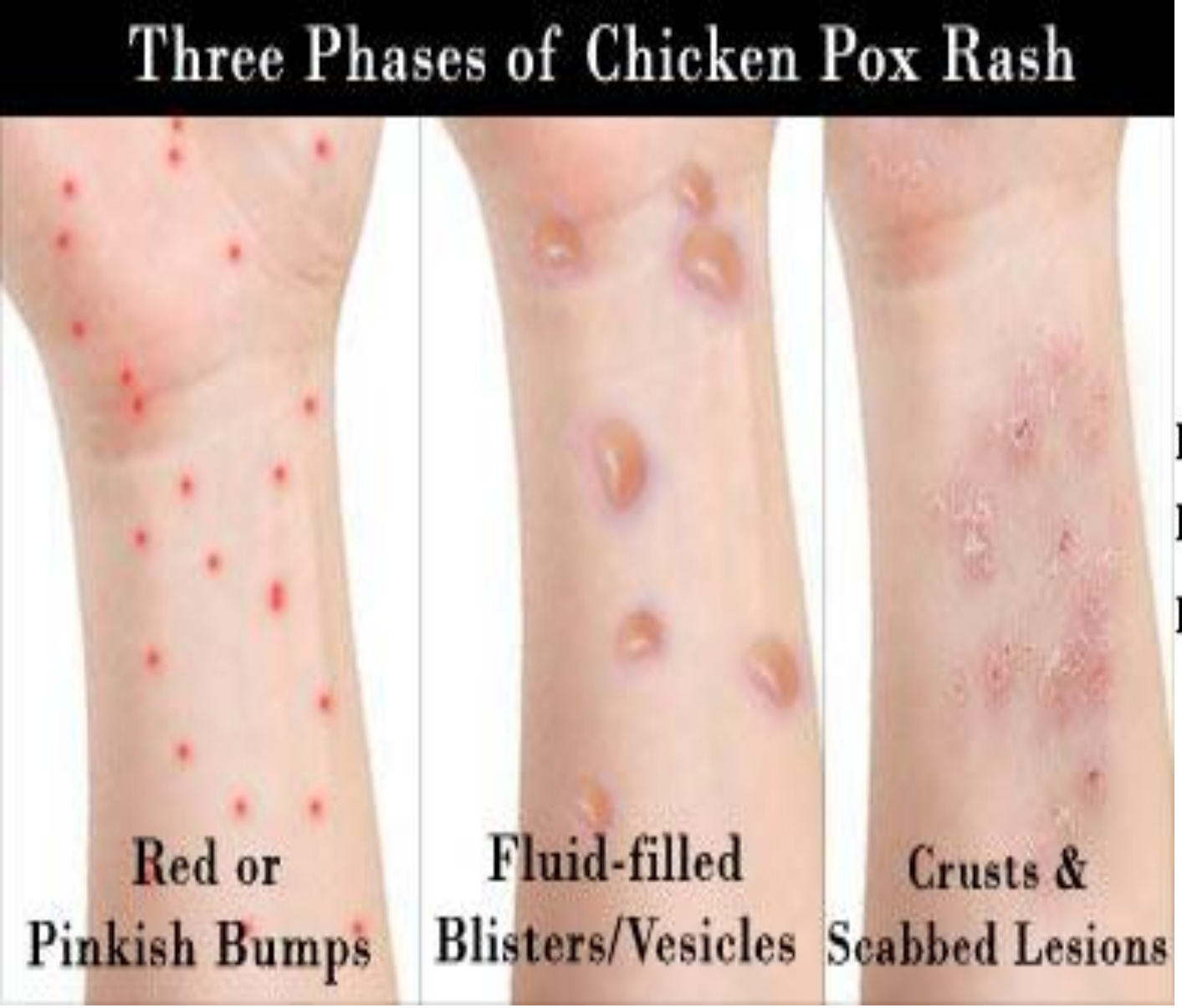
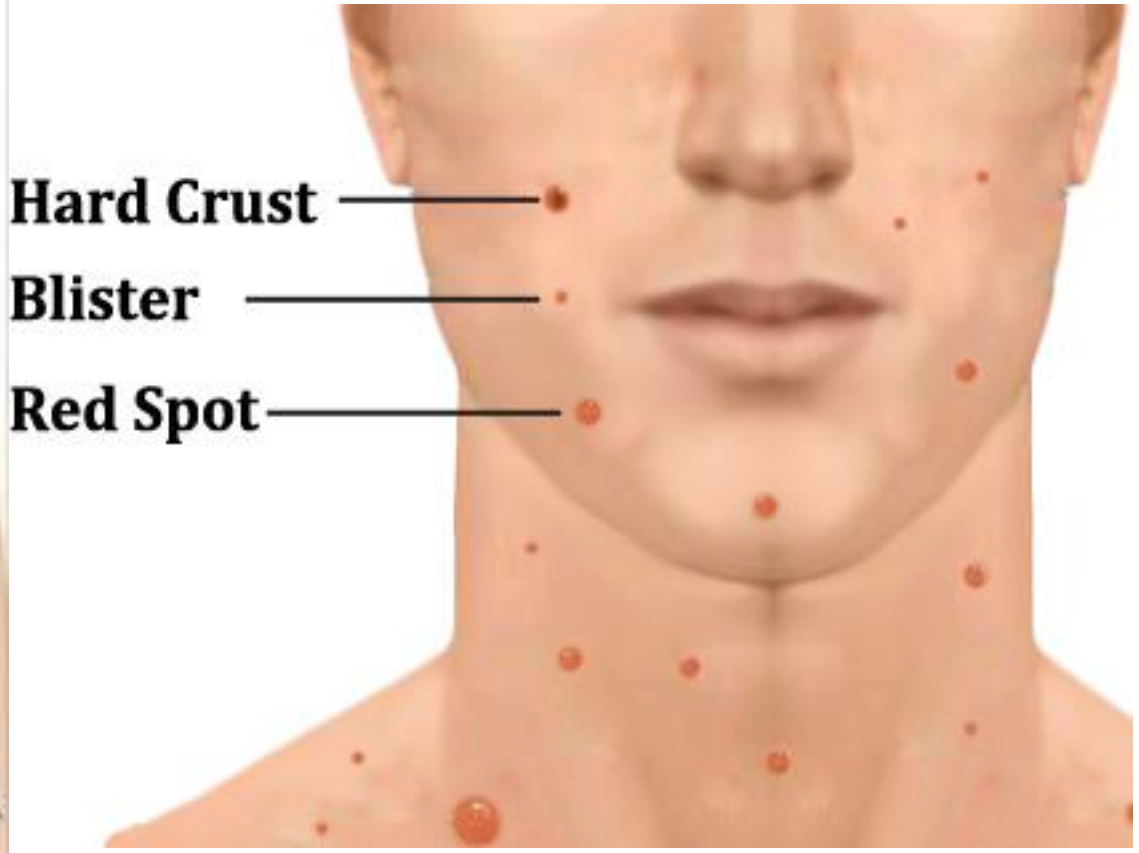


http://www.medindia.net/symptoms/images/three-phases-of-chicken-pox.jpg



http://chickenpox.me/wp-content/uploads/2018/01/Chickenpox-Symptoms.jpg

- 90% transmitted by direct contact in house hold (pox parties!)
- Generalized LAP (lymphadenopathy) is common.
- Should be differentiated from shingles (dermatomal distribution – very painful)/herpes zoster
- progressing to vesicles which quickly pustulate and form scabs which fall off 1–2 weeks after infection.
- They appear in successive crops over 2–4 days, starting on the trunk and face and spreading centripetally → *this means the patient will have different stages of vesicles all over and not uniformly shaped vesicles.*

Complications of chicken pox

- May rarely involve the mucosa of the oropharynx and vagina.
- Other complications include: secondary bacterial infection, pneumonitis, and encephalitis.
- Disease may be severe in pregnancy (congenital varicella or pneumonia for the mother) and the immunocompromised.
- Rx → usually no antivirals (some guidelines depict oral antivirals in house holds that are large and in immunecompromised patients)
- just reduce itch (calamine lotion, oatmeal bath) give antihistamine at bed time.
- Give bacitracin for bacterial superinfection (impetigo) especially crusted open lesions.

Shingles

- Herpes zoster—localized recurrence of varicella virus
- Causes a unilateral vesicular eruption in a dermatomal distribution.
- Called in Arabic (حزام ناري), in older medicine, flame snake (if the head of the snake eats the tail the patient dies)
- Most commonly thoracic and lumbar dermatomes along the cutaneous spinal nerve distribution.
- This is typically and often preceded by 2–3 days of pain in the affected area.

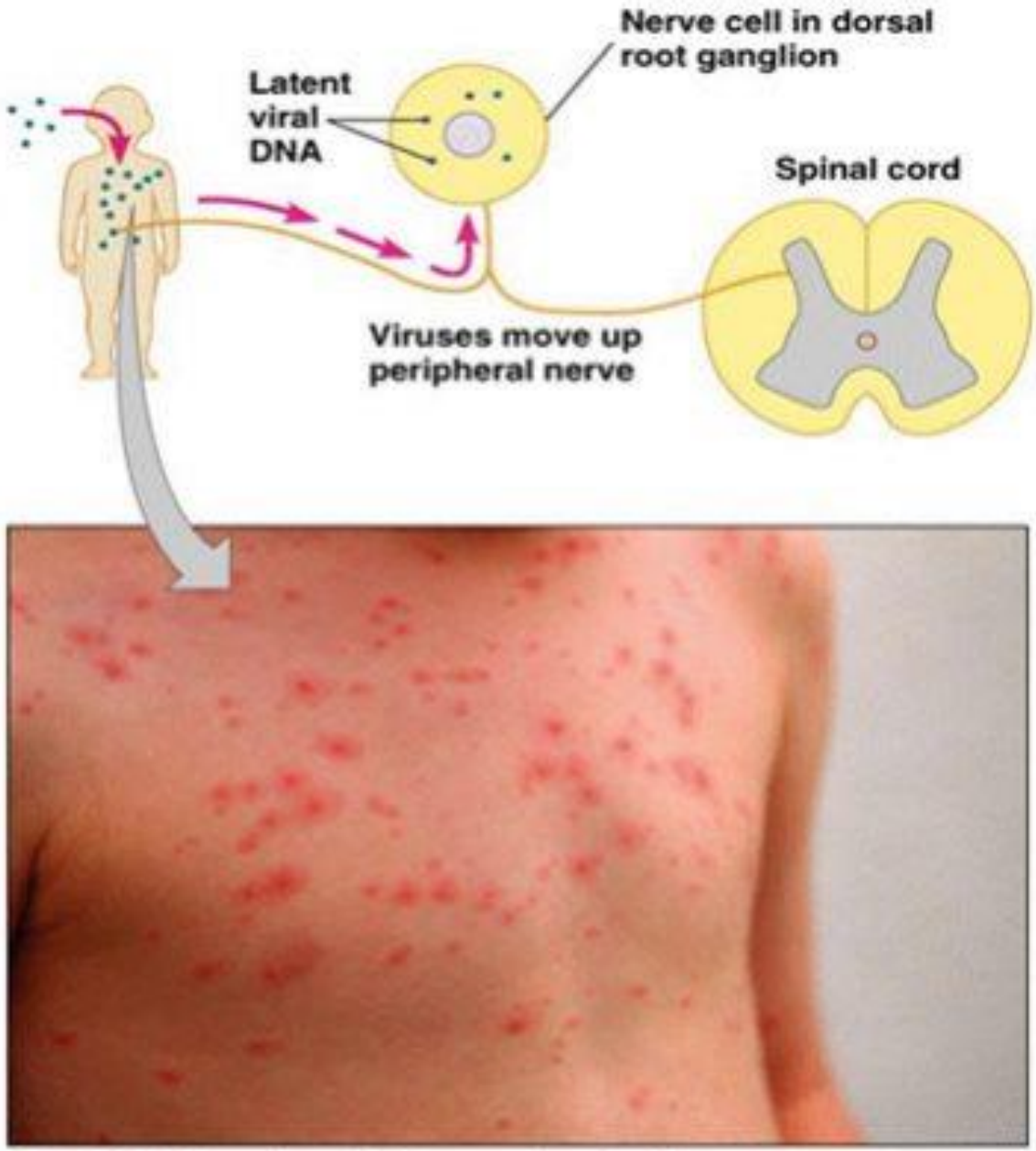
- In us (300 million population) has a 1 million case incidence yearly
- Peak age is in older patients (50-80) why?
- 60% females.(also why?) menopause

Pathophysiology:

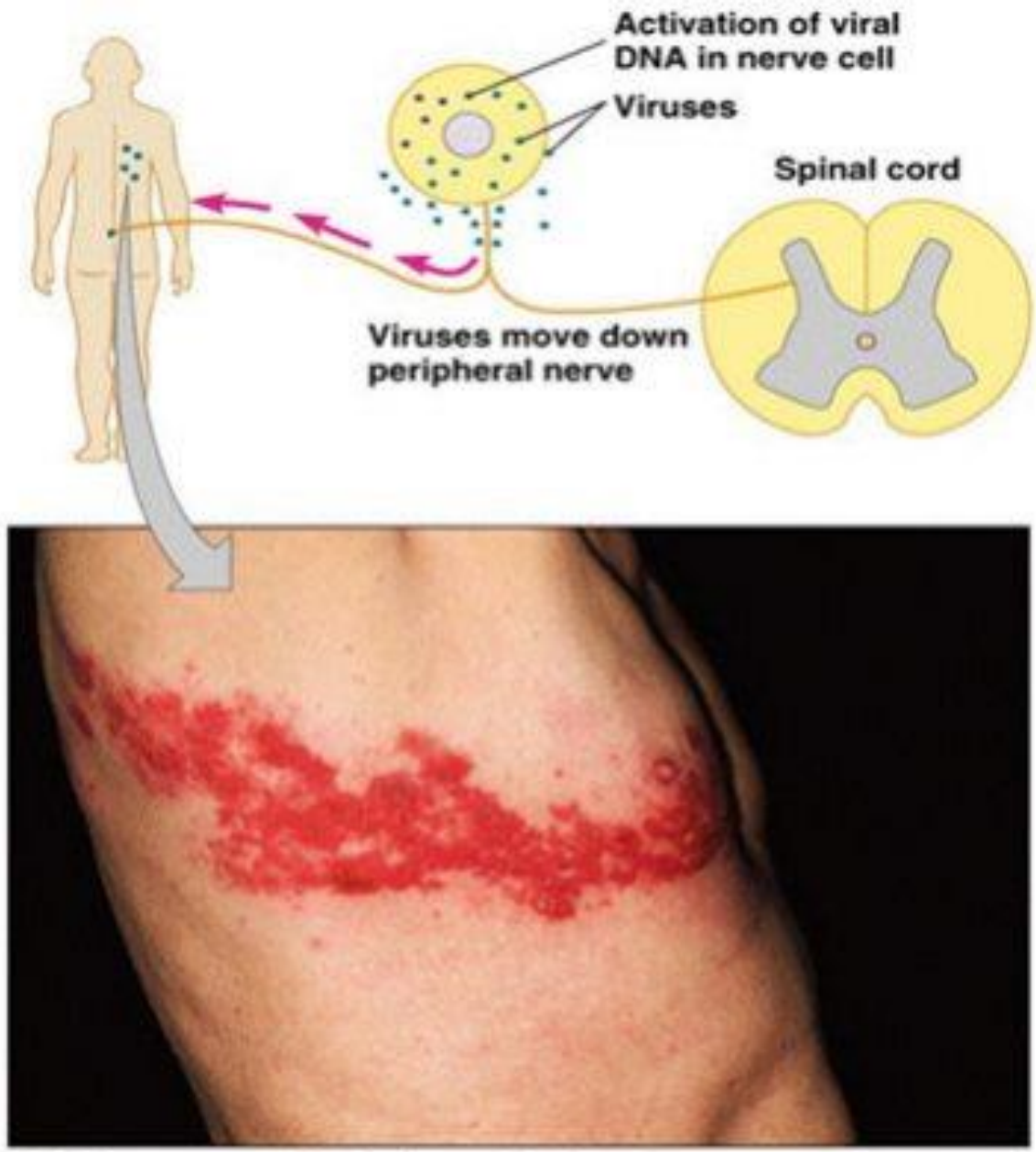
- *The virus infects dorsal root ganglionic cells and remains dormant, typically following a Varicella zoster infection (chicken pox)*
- Reactivation of the dormant virus causes shingles.
- Reactivation occurs in states of reduced cell immunity (older age, immunosuppression, sometimes stress- all what applied for reactivation of HSV1,2)
- It is contagious! Must avoid contact until rash heals (days to few weeks!)

- Most commonly preceding the rash fever, headache, numbing along the nerve root is reported.

- The rash starts erythematous, maculopapular, later clear distinct vesicles erupt.
- Vesicles turn cloudy after 3-5 days and crust by 10 days, may leave residual scar.
- Resolution may take 2–4 weeks.
- LAP with tenderness is also a common finding



(a) Initial infection: chickenpox (varicella)



(b) Recurrence of infection: shingles (herpes zoster)

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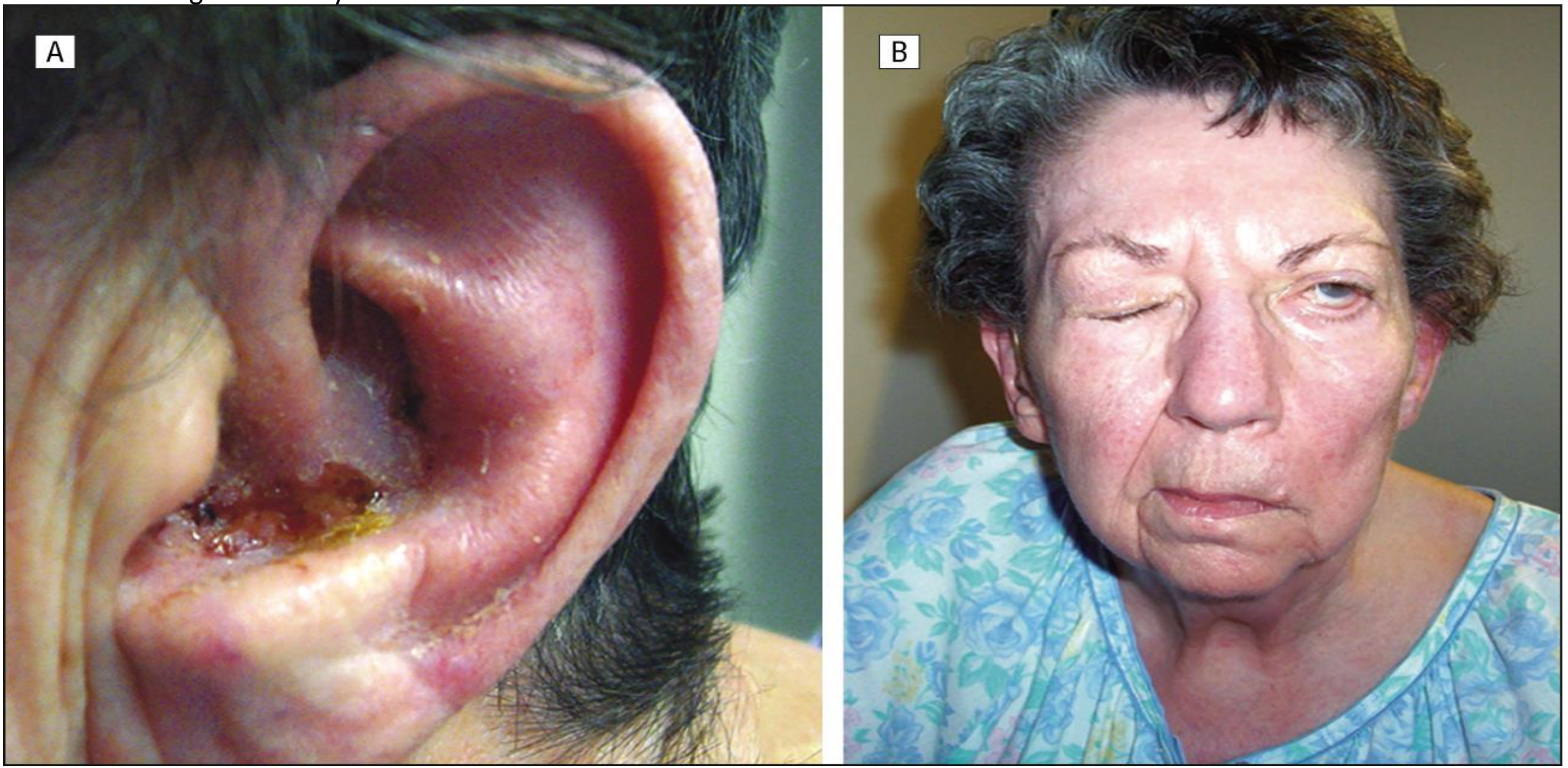
Dx and Rx

- Dx: rash develop 2-3 days of of first symptoms and last for 2-4 weeks
  - Follow a dermatomal distribution, proximal then distal to the dermatome
  - Most common sites: Back T1, T2
  - And face (see later)
- Rash is described as erythematous maculopapular with clear vesicles that crust after a week or so.
- PCR is the most sensitive and specific test to be done.
- Rx: antivirals (within 3 days of onset is best) (why?) 50> y/o and more than 50 lesions or complication (facial, opthalmic)
- Pain management NSAID→ opiods→ refractory pain amitriptline or gabapentin
- + Steroids
- Can give B vitamins to promote healing

Variants of shingles

- Zoster Sine Herpete (zoster without a rash) = Zoster without rash, this is uncommon, the pain, prodrome and fever are all present, with no (or little) rash seen. (rare, but on the rise).
- Ramsay hunt syndrome (VZV of facial nerve)
  - Rapid onset with facial pain
  - Tinnitus and vertigo if cranial nerve 8 is involved
- Seen as unilateral herpetic rash of ear pinna, hearing loss may occur.
- Peripheral facial paralysis
- Management (similar to bell's palsy = facial nerve paralysis due to VZV reactivation) : antivirals+corticosteroids+pain killers

Some doctors might brush this off, and think of this older patient as an old stroke patient and send them home,,
looking at the ear you can see the rash



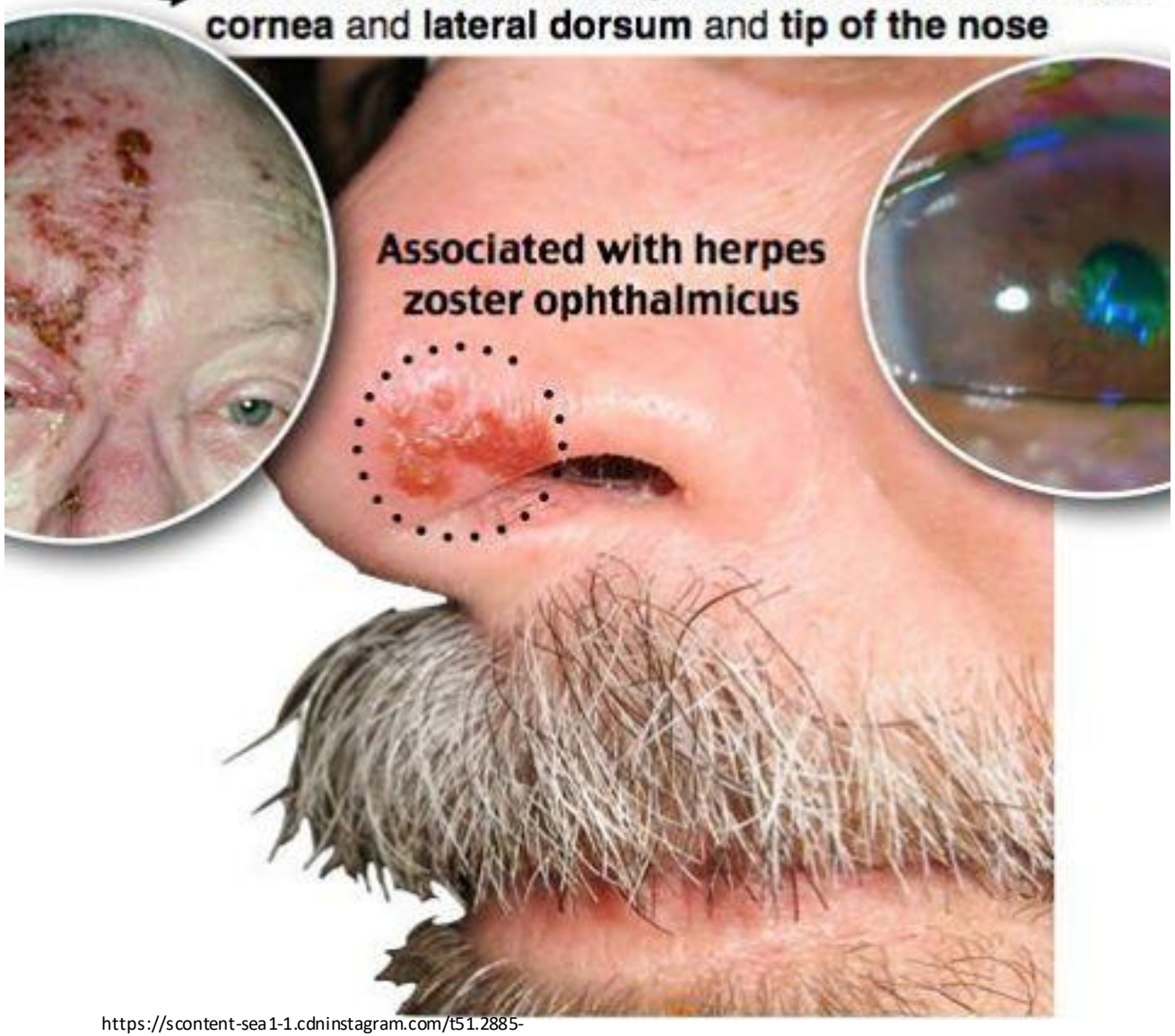
https://jamanetwork.com/data/Journals/NEUR/12051/nim40064f1.png

Herpes Ophthalmicus:

- When the virus is dormant in the trigeminal nerve ganglion
- Reactivates more in advanced age and immunocompromised patients (HIV, cancer, chemo or radio therapy)
- May also reactivate in systemic illness, or stress (much like typical shingles)
- Huntchinson's sign is typical (has a two fold risk of ocular involvement)
- Can cause eye complications (keratitis, iritis, episcleritis) VISUAL LOSS

Hutchinson's sign

Nasociliary branch of trigeminal nerve innervates the **cornea** and **lateral dorsum** and **tip of the nose**



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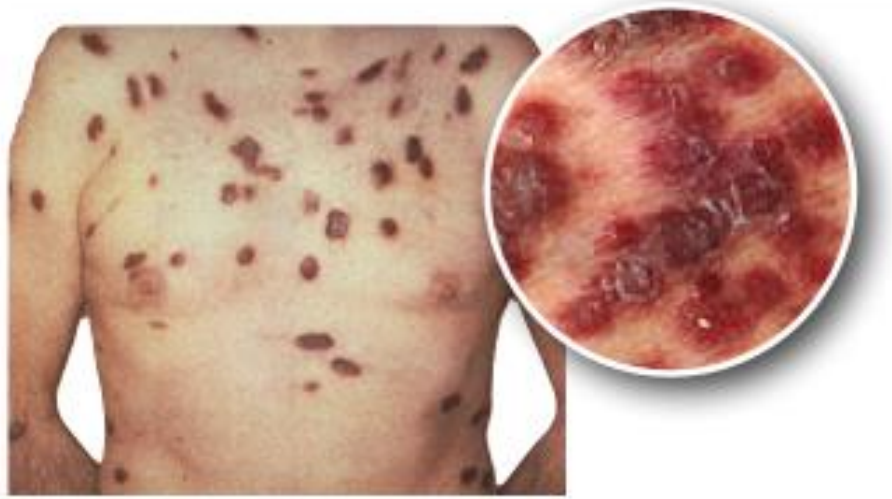
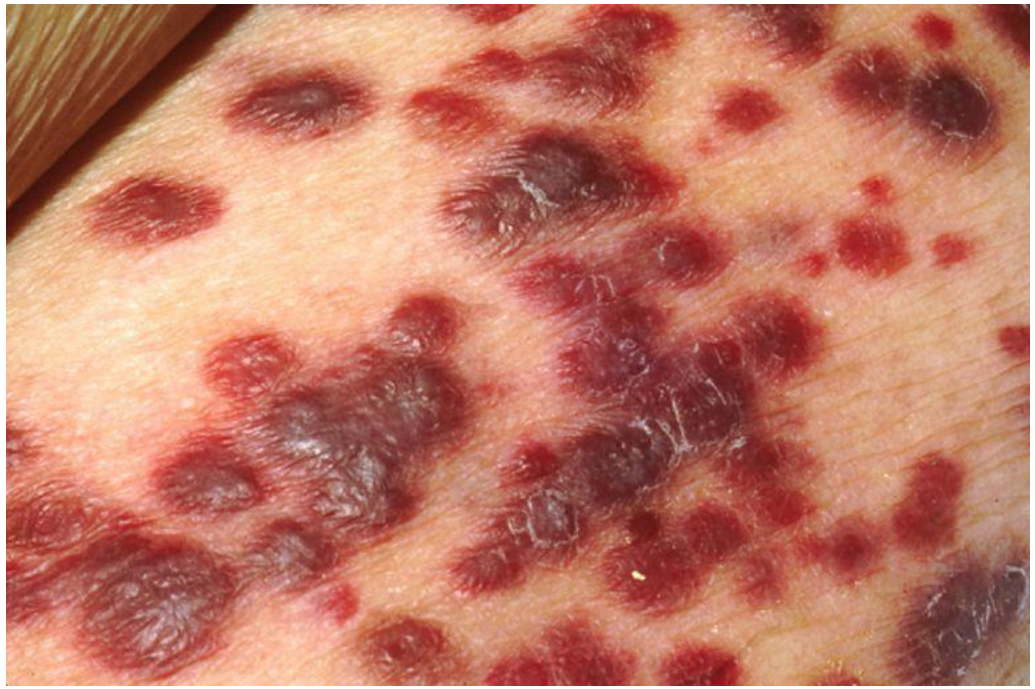
- Rx: consult the ophthalmologist
- Antivirals (acyclovir 800 mg PO five times a day for 7-10 days), also can use Valacyclovir (1000mg 3 times a day for 1-2 weeks), famciclovir (500 mg 3 times a day for 7 days).
- Antistaph antibiotics
- Corticosteroids (only under the opthlamology consultation- has a risk of corneal perforation).

Kaposi Sarcoma

Kaposi sarcoma-associated herpesvirus (KSHV)
↳ **aka Human herpesvirus 8 (HHV-8)**





Clinical

- Purplish, reddish blue or dark brown/black macules, plaques, and nodules
- Nodular lesions may ulcerate and bleed

- Form of Cancer, due to HHV8
- NOT IN A DERMATOMAL distribution
- If seen must suspect immunocompromised state, (e.g HIV..)
- Management is aimed at the cause of the immunocompromised state