Skin and soft tissue infections 2

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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.
## Infections Associated with Vesicles

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

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3520662/figure/f1-0581358/
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). These 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
• **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 ophthalmologic 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 infections (HSV-1s) 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 hypersensitivity 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. AJP 2006;74(11)
• 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 therapy 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 year 1 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 vermilion border edge
Lips-gingiva-palate-tongue + -LAP
• 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
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 disseminated 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)
Herpetic Whitlow

- vesicles
- ulcer formation
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.medcapestatic.com/pi/meds/ckb/19/28819kn.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 (transplacental)
• 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
Three Phases of Chicken Pox Rash

Red or Pinkish Bumps
Fluid-filled Blisters/Vesicles
Crusts & Scabbed Lesions

Hard Crust
Blister
Red Spot
• 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 households that are large and in immunocompromised 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 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, ophthalmic)

• Pain management NSAID → opioids → 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
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

Associated with herpes zoster ophthalmicus
• 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 ophthalmology 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

The tip of the nose (and of the penis) is a typical location for KS
• 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