Microbiology

Doctor 2017 | Medicine | JU

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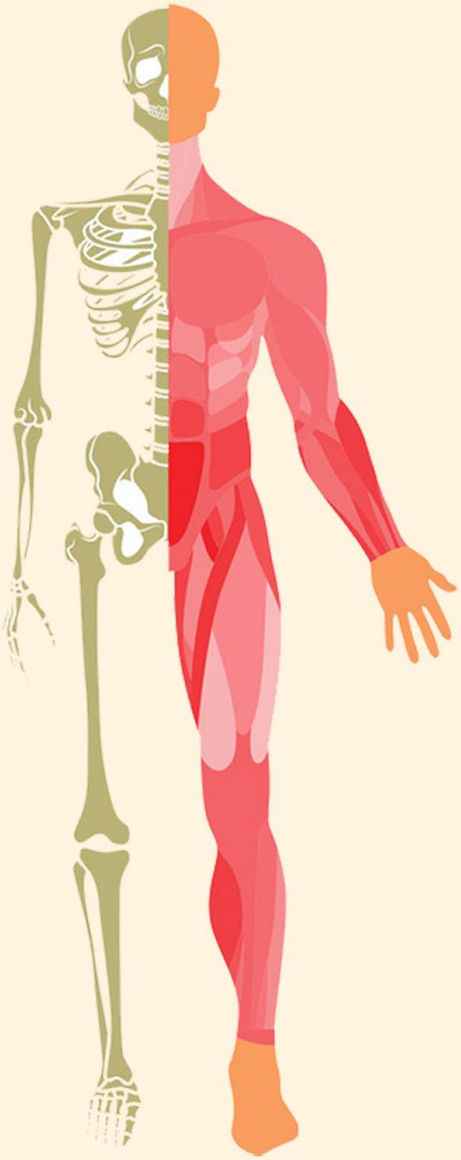
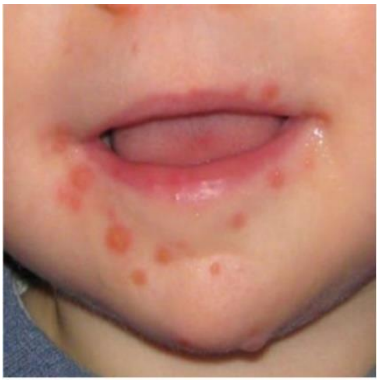


1st system - MSS

Hand foot and mouth disease

This disease shares a lot of similarities with HSV infections, but it also has some special characteristics that we can use to differentiate it from other diseases.



- It is a viral rash that occurs in ***outbreaks***, typically in schools (similar to HSV).
- Both typical and atypical disease are transmitted by ***fecal-oral route***, or direct close contact to rash.
- It occurs almost every year, and We had one outbreak a few months ago in November.
- Typically, an outbreak denotes presence of optimal conditions for growth and spread (children, schools, winters, large groups of people in small space = outbreak).
- In these kinds of outbreaks, people should try to limit their interactions, so if a child is infected, he is recommended to stay home rather than going to school because this disease might have serious complications.
- Usually, it is self-limited and only needs suppurative care.
- it is named this way to describe the rash distribution not the transmission of the disease, so rash appears on palms, soles and around the mouth.

Typical disease age groups and causative agents:

1) Children under 10 are mostly affected, more-so under 5.
2) The causative agents of HFMD are 2 enteric viruses:
   - ✓ Coxsackie virus A16.
   - ✓ Enterovirus 71 (***has been associated with encephalitis and myocarditis which is the real issue***).

> *Enteric viruses or bacteria:*
> *pathogens related to the intestines and they cause gastroenteritis.*
> *They are usually acquired by the fecal-oral route.*

you should tell the patient that he is in risk of encephalitis or myocarditis. and if you have noticed neurological symptoms (not seeing well, not hearing well, not walking or moving right, sleeping too much, etc..) you should start worrying about encephalitis.

- Children typically mount a less aggressive immunological response than adults, which may be beneficial since their immune system is naïve and being exposed for the first time for a large number of new pathogens.

- If adults are exposed to the infection for the first time, their immune response will be Exaggerated and may be more damaging and aggressive, so lucky for children their immune system is not will developed (because every thing they encounter will be for the first time).

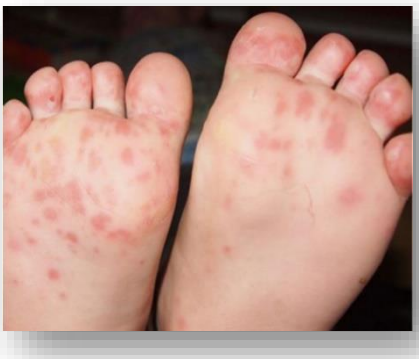
Atypical disease age groups and causative agents:

1) Higher age groups (adults and teenagers) ➔ immune system is more competent and mounts a more aggressive response so they can have severe presentation with fever, arthralgia and flu like symptoms with the rash as vesicles that affect (the nose, cheeks, extensor arms, elbows, thighs, buttocks, groin).
2) Caused by coxsackie A6.

Signs and symptoms of HFMD:

1) Upper respiratory track (URT) symptoms before the skin lesions occur, and this can easily be misdiagnosed with the normal flu especially because outbreaks are more common at the same time as the flu season.
2) Fever, malaise and pharyngitis.
3) Rash distribution: the patient will have vesicular rash in his mouth then a macular/ papular rash on his skin (typically on the soles and palms and buttocks).

➔ **SKIN: red papules that progress to gray vesicles on the soles, palms and buttocks.**
➔ **ORAL: football shaped (eye shaped) painful vesicles, involves the buccal mucosa and tongue. (spares posterior pharynx as opposed to herpangina that spares anterior pharynx).**



Treatment (Rx):

- ✓ Only symptomatic treatment (treat fever, pain)
- ✓ Must maintain hydration (fluids), this is essential as in all fevers.
- ✓ Tell the patient to come back if he noticed any of the red flags (in this case the red flags are encephalitis and myocarditis).
- ✓ Consider hospital admission in severe illness (enterovirus A71) which has high morbidity and mortality, as it carries risk of Encephalitis!

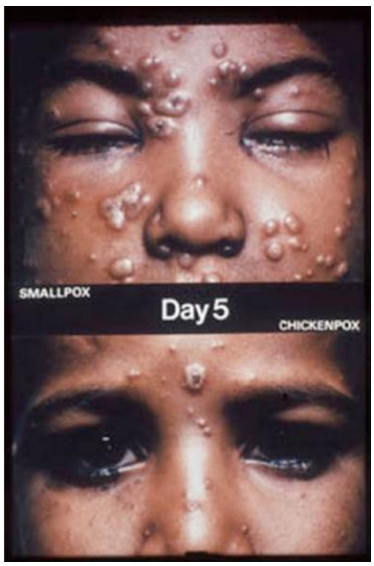
Smallpox

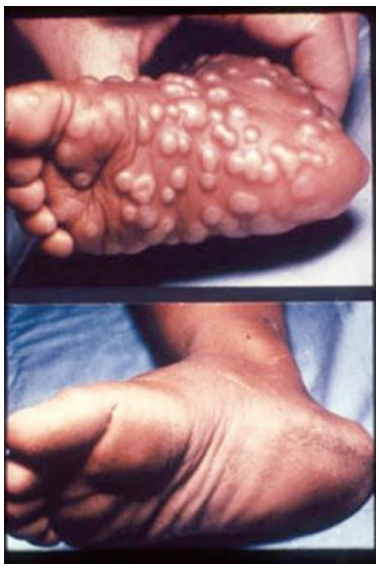
- Smallpox is caused by variola virus, and orthopoxvirus.
- Two strains of variola virus have been associated with smallpox:
  - ✓ ***variola major*** with high mortality rate (20–50%).
  - ✓ ***variola minor.***
- The last reported case was in Somalia in 1977, and the virus was declared eradicated by the WHO in 1980. do not confuse news outlets claims, which are chicken pox outbreaks or measles (common in anti-vaccination groups).
- Virus stocks exist in two laboratories, and there are concerns about its potential use as bioterrorism agent.

> *If a new virus antigen emerges and people were not immune against, the time it takes for the immune system to build up is slower than the destructive effects of the virus. That's what happened with Spanish flu in 1918, it spreads very fast between people and killed more people than the first world war did.*
>
> *And that is What's really scary about the presence of these viruses in laboratories because people nowadays are not immune or vaccinated against smallpox.*

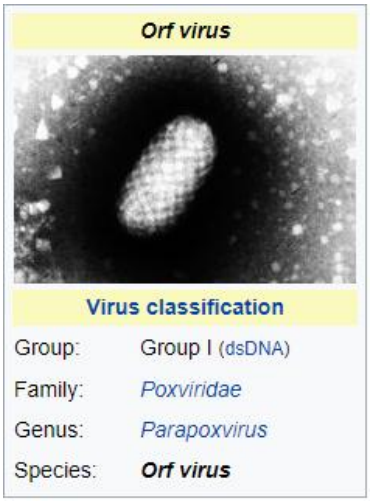
- The incubation period is 10–12 days and is followed by a prodromal period of 1–2 days.
- The centrifugal rash is initially maculopapular and progresses to vesicles, pustules, and scabs over 1–2 weeks, ***and it leaves scars (scar tissue remains after the disease).***
- Death may occur with fulminant (severe) disease.
- Diagnosis may be confirmed by EM or PCR (to differentiate it from other poxviruses).
- There is no specific treatment (supportive).

Notice the difference between chickenpox and smallpox in formation of scar tissue.

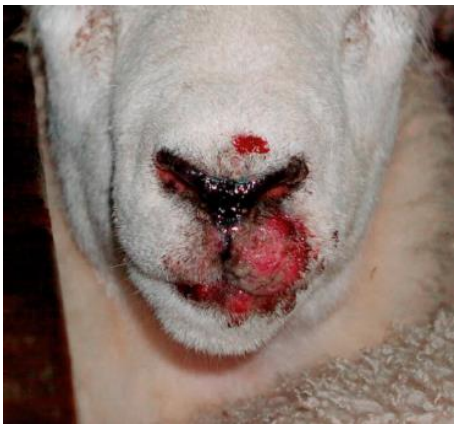




Orf



- Orf is caused by a DNA virus related to smallpox virus (parapoxvirus).
- Also called soremouth infection and infects the fingers of individuals who work around goats and sheep.
- Usually transmitted by coming into contact with infected animals (petting, milking, feedings, harnesses, bite), but can also transmit between people if the sore opens. ***(animal to human and human to human)***.
- People well not catch the disease by simply going to the zoo, because the infected animal is easily known (sores appear on the animal). And for the virus to reach the human there have to be a direct contact with the infected animal (not only by touching the area where the lesion is, any contact with the animal may transmit the virus).
- Can be infected multiple times throughout life (each time is less severe).

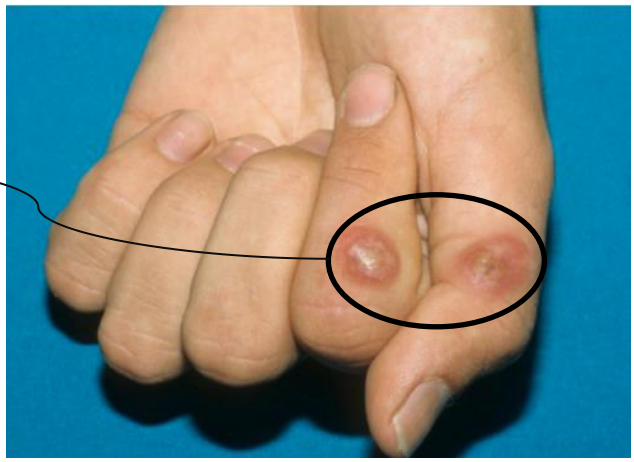


• There are Six stages of the disease: each last about a week.

• Small papule➔ nodules ➔ ulcerate and crust.

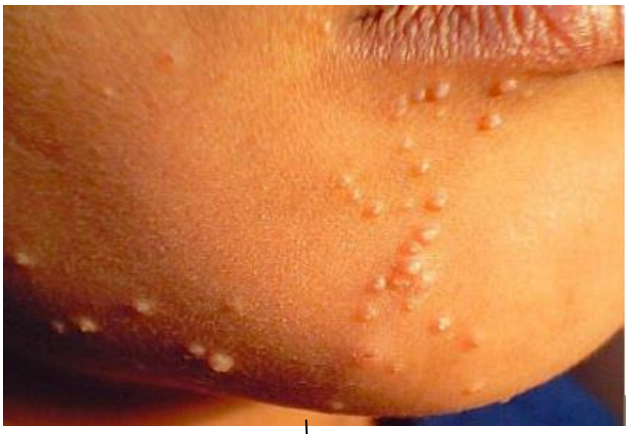
- There is no treatment, however, the papules may become infected by bacteria, ➔ treat with antibacterial drugs. And it also may become a problem in immune compromised patients.
- Clinically, it is seen in farmers, and usually they don't care about it, but you have to be familiar with it as it may become complicated, and you have to bandage the patient's lesion to prevent the transmission of the disease.

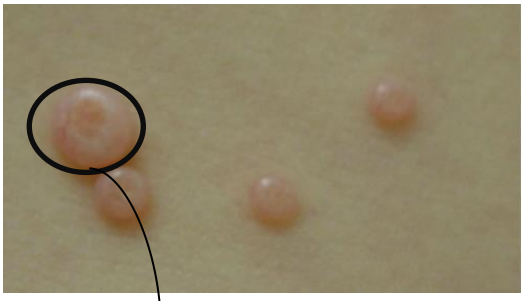
Just by looking to the lesion, you can easily tell it is not a typical bacterial infection.



Molluscum contagiosum

- Very common among people.
- Virus induces flaccid vesicles on the skin of healthy and immunocompromised individuals.
- Most commonly infect 2-11 years old children. And it is transmitted by direct contact.
- In adults it is a part of STD transmission by direct contact (e.g. kissing and touching).
- May look like vesicles, but not erythematous.
- Single or small clusters of vesicles (<30) raised papules with central umbilication (depression) for the large ones. One vesicle may branch to several ones.
- On face and trunk, pubis and rarely mucosa.
- Appear for several weeks (and may persist for years) then Resolve on their own.
- cryotherapy or other dermatologic treatments can be done to cut it off.
- It is associated with HIV because both of them are STDs and in this case it is severe.
- Complications are (Scarring especially if manipulated, bacterial infections, and conjunctivitis for those that are near the eyes).





Central umbilication

May be confused with HSV.

Differences:

1. ***HSV is associated with erythematous base unlike Molluscum contagiosum.***
2. ***HSV is more uniform while Molluscum contagiosum has different sizes.***
3. ***No prodromal signs with Molluscum contagiosum (fever, malaise, tingling, etc.…)***
4. ***Molluscum contagiosum persists for longer time.***

----------That is all about viral lesions----------

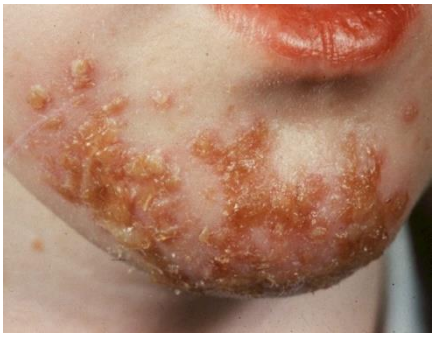
Infections Associated with Crusted Lesions

- Those lesions do not last for long, they will be opened and crusted releasing their fluid.
- Infections Associated with Crusted Lesions (most of them are either bacterial or fungal):

Crusted lesions	
Bullous impetigo/ecthyma	*S. aureus*
Impetigo contagiosa	*S. pyogenes*
Ringworm	Superficial dermatophyte fungi
Sporotrichosis	*Sporothrix schenckii*
Histoplasmosis	*Histoplasma capsulatum*
Coccidioidomycosis	*Coccidioides immitis*
Blastomycosis	*Blastomyces dermatitidis*
Cutaneous leishmaniasis	*Leishmania* spp.
Cutaneous tuberculosis	*Mycobacterium tuberculosis*
Nocardiosis	*Nocardia asteroides*

Impetigo

- Caused by ***Staphylococcus aureus and/or group A Streptococci (GAS).*** Both are G (+) species and both can be part of the normal skin flora.
- The most important defense mechanism against skin flora is the dead keratinized layer of the skin.
- local trauma allows colonizing bacteria to break through.
- Commonly affects children (2-5 years) in tropical/subtropical regions; also prevalent in temperate regions in summer months (warm weather >) [in contrast to winter when viruses are common].
- It is the most common bacterial skin infection in children.
- 70% are non-bullous and appear as crusted legions.



- It is highly contagious (scratching, towels, clothing, autoinfection and spread in daycares). You can see it spreads between children in the daycare which tells you that there is no proper hygiene there.

Clinical features:

- occurs on the face and extremities.
- Lesions start as small macule or papule ➔ small vesicles (with erythema) ➔ develop into flaccid bullae ➔ rupture, releasing a yellow discharge which forms thick crusts (sometimes called honey crusted lesions).
- Usually seen with regional lymphadenopathy.
- Can cause cellulitis (superficial infection can become deep).
- Can cause ***Poststreptococcal glomerulonephritis (PSGN).***

GAS colonizes the skin and the throat. some throat colonizing GAS strains share a surface protein that's similar to a protein on the interior of the heart, so, if someone made an antibody against that protein, that antibody will react with the heart causing ***rheumatic fever***. The longer the bacteria last the more antibodies the patient made (more sever rheumatic fever), that is why it is important to eliminate the bacteria and treat it to prevent rheumatic fever (similar to allergic reactions where we need to eliminate allergen).

In a similar process, some skin colonizing GAS strains share a similar surface protein to a protein found on the kidney, that's why one possible complication of skin infection is ***PSGN***, and it can happen in all patients (old or young patients).

So, you treat it regardless if you have known the causative agents or not and you give a systematic therapy if it persists for longer time.

Treatment:

- ✓ topical agents for most cases ➔ mupirocin is the best topical agent.
- ✓ Patients who have numerous lesions or who do not respond to topical treatment should receive oral antibiotics (flucloxacillin or cefalexin) because penicillins and cephalosporins are the best for skin infections.
- ✓ If MRSA is suspected/isolated, then treatment with doxycycline, clindamycin, or co-trimoxazole.

Organism	Type of Pathogenesis	Typical Disease	Predisposing Factor	Mode of Prevention
S. aureus	1. Toxigenic (superantigen)	Toxic shock syndrome	Vaginal or nasal tampons	Reduce time of tampon use
		Food poisoning	Improper food storage	Refrigerate food
	2. Pyogenic (abscess)			
	a. Local	Skin infection (e.g., impetigo, surgical-wound infections)	Poor skin hygiene; failure to follow aseptic procedures	Cleanliness; handwashing; reduce nasal carriage
	b. Disseminated	Sepsis, endocarditis[1]	IV drug use	Reduce IV drug use
S. epidermidis	Pyogenic	Infections of intravenous catheter sites and prosthetic devices	Failure to follow aseptic procedures or remove IV catheters promptly	Handwashing; remove IV catheters promptly
S. saprophyticus	Pyogenic	Urinary tract infection	Sexual activity	

IV = intravenous.

[1]For simplicity, many forms of disseminated diseases caused by *S. aureus* (e.g., osteomyelitis, arthritis) were not included in the table.

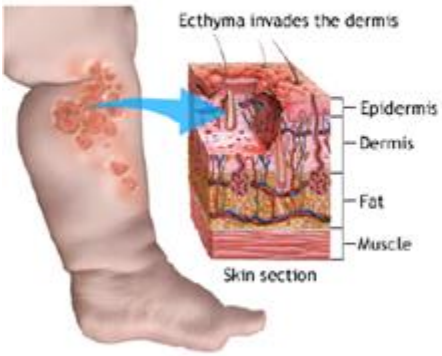
Organism	Type of Pathogenesis	Typical Disease	Flora (NF)
S. pyogenes (group A)	1. Pyogenic		
	a. Local	Impetigo, cellulitis	Skin (D)
		Pharyngitis	Throat (D)
	b. Disseminated	Sepsis	Bloodstream (D)
	2. Toxigenic	Scarlet fever	Skin (D)
		Toxic shock	Many organs (D)
	3. Immune-mediated (poststreptococcal, nonsuppurative)	Rheumatic fever	Heart, joints (D)
		Acute glomerulonephritis	Kidney (D)
S. agalactiae (group B)	Pyogenic	Neonatal sepsis and meningitis	Vagina (C)
E. faecalis (group D)	Pyogenic	Urinary tract infection, endocarditis	Colon (NF)
S. bovis (group D)	Pyogenic	Endocarditis	Colon (NF)
S. pneumoniae	Pyogenic	Pneumonia, otitis media, meningitis	Oropharynx (C)
Viridans streptococci	Pyogenic	Endocarditis	Oropharynx (NF)

The doctor only talked about s. aureus and s. pyogenes from the previous tables.

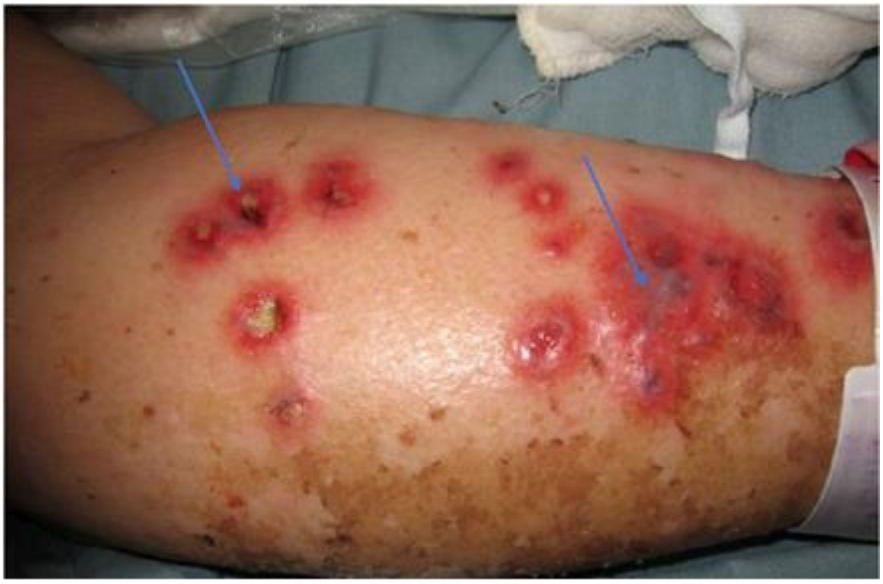
Ecthyma

- Ecthyma is a term that means Punched-out (instead of crusted-out) ulcers surrounded by raised deep red/violet margins and invades into the dermis and leaves highly inflamed regions on the sides.
- Caused by ***S. aureus or GAS,*** but it is more serious than impetigo.
- Other similar lesions ***(ecthyma gangrenosum***) may occur with Pseudomonas aeruginosa in neutropenic (reduced neutrophils in blood) patients.
- The difference between ecthyma and impetigo is that ecthyma is a deeper form of impetigo (can progress into or start as Ecthyma) and for some reason more localized. In ecthyma we are worried about deeper infections like cellulitis as it may cause loss of tissue or even loss of the limb.

Doctor talked about why ecthyma stays deep and localized rather than spreading as it depends on the individual, the bacteria and the presence of certain enzymes and collagenases, however, he didn't mention the details.



Notice how the ulceration affects the epidermis and the dermis.

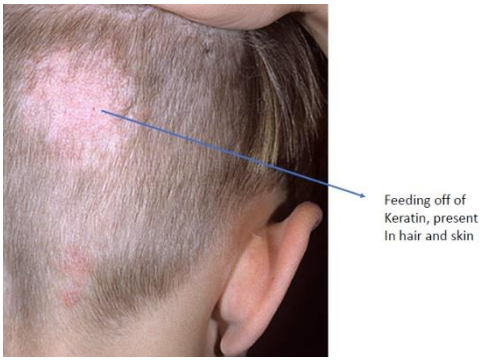


Treatment:

- ✓ Only systematic Treatment because the infection is deep.
- ✓ Empiric treatment is with flucloxacillin or cephalexin (unless cultures yield streptococci alone, in which case penicillin is appropriate).
- ✓ Antipseudomonal agents, e.g. piperacillin-tazobactam, should be given for P. aeruginosa infections.

Dermatophytes

- A large group of fungi (more than one), the connection between them is that they are capable ***of invading and feeding off of the dead keratin*** of skin, hair, and nails (require keratin for their growth).
- They have mechanisms to invade the keratin layer and persist on the skin, otherwise they will be slipped off with the keratin layer.

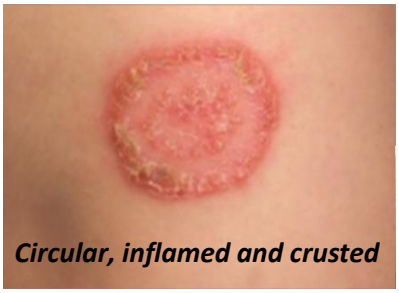


Tinea capitis (القَعلبة)

- They are spread by direct contact with patients (human to human), animals or soil (environment which is the most common).
- Commonly known as ringworm, corporis and Circinata.

Clinical classification is by age group:

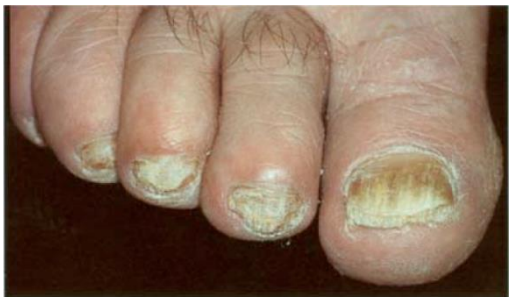
Children:



Circular, inflamed and crusted

- ✓ tinea capitis (scalp hair) and it is the most common among children.
- ✓ tinea corporis (trunk and limbs).
- ✓ tinea faciale (face).

Adolescents:

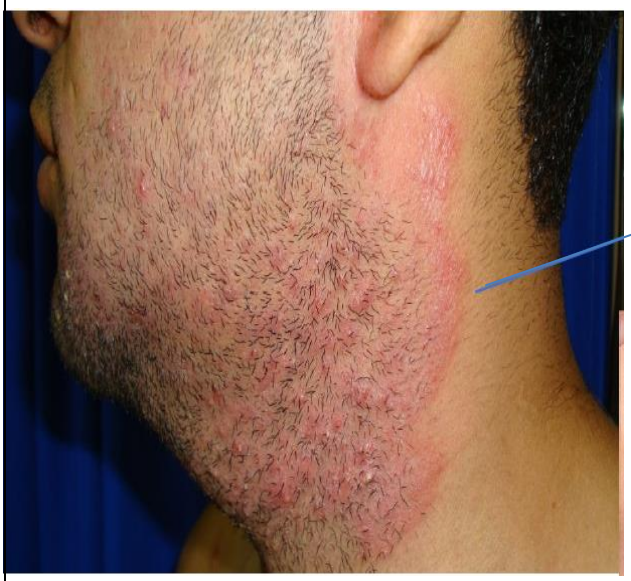


- ✓ tinea manuum and pedis (palms and soles -athletes foot-, and it is the most common overall worldwide).
- ✓ tinea unguium (nail—also known as onychomycosis).

Adults:

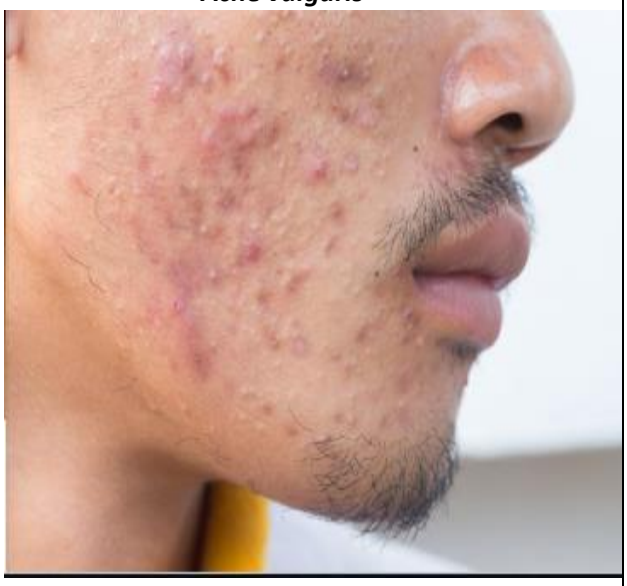
- ✓ tinea cruris (groin) AKA jock itch.
- ✓ tinea barbae (beard area and neck).
- ✓ Tinea corporis Gladiatorum (wrestlers).

Tinea barbae



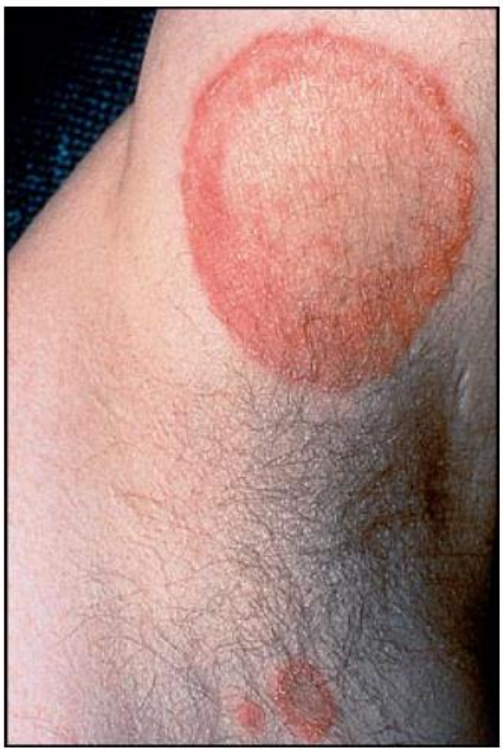
Demarcation line

Acne vulgaris

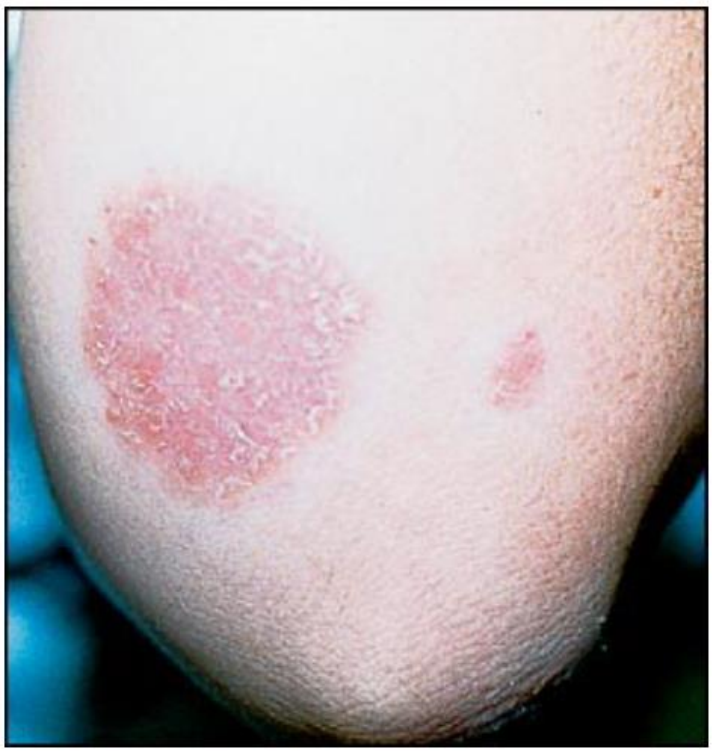


Demarcation line hints a possible dermatophyte Infection, rather than acne vulgaris

The main thing to differentiate tinea corporis from psoriasis is that the psoriasis lesions are silvery scaly.



Tinea corporis



psoriasis

Diagnosis (Dx):

- ✓ The goal is to distinguish dermatophytosis from other causes of skin inflammation (such as psoriasis) because Infections caused by bacteria, other fungi, and non-infectious disorders (psoriasis, contact dermatitis) may have similar features.
- ✓ ***KOH*** mounts of skin scrapings and infected hairs demonstrate ***hyphae***. (e.g. you can't see hyphae in case of acne).
- ✓ Some species ***fluoresce*** by a U.V. lamp
- ✓ Culture is used when KOH preparations are negative.

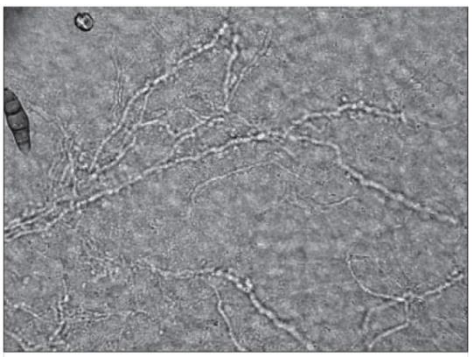
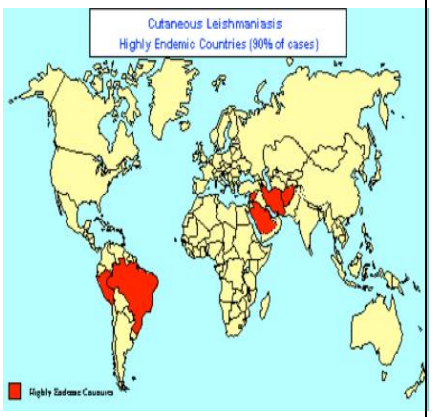


Figure 1: Skin scraping and KOH mount showing branching fungal hyphae in dermatophyte infection

Treatment and prevention:

- ✓ Many local skin infections resolve spontaneously without chemotherapy.
- ✓ but fungal infections do not resolve within hours or days, it usually takes week, so treatment may be needed and even the topical treatment may not work so systematic treatment may be needed as well.
- ✓ topical use of tolnaftate, allylamines, or azoles (antifungals) is usually sufficient**.**
- ✓ Nail bed and more extensive skin infections (like athletic foot) require systemic therapy with **griseofulvin** or itraconazole and terbinafine + combined with topical therapy.
- ✓ Therapy must be continued over weeks to months, and relapses may occur.
- ✓ No specific preventive measures such as vaccines exist.

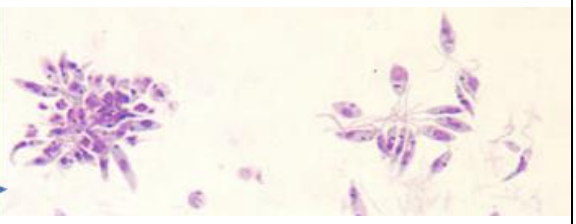
Cutaneous leishmaniasis



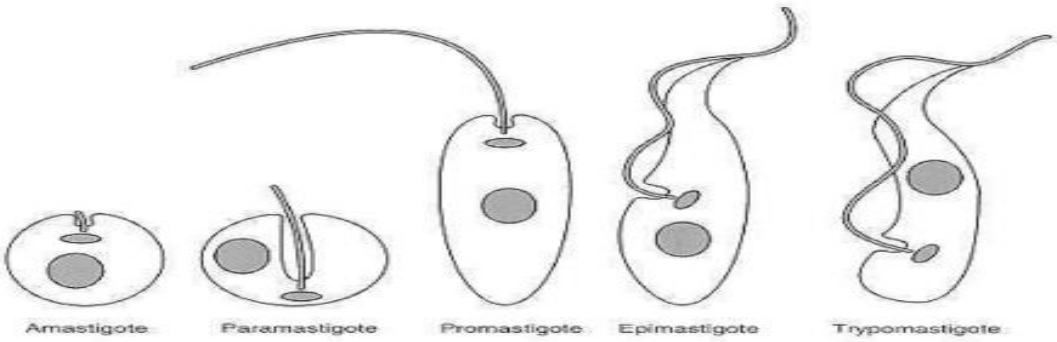
- An endemic disease in our areas. And used to be called "حبة بغداد" because most the people of Baghdad had the disease as they were sleeping on roofs and getting bitten by the flies.
- It is related to the standards of living (the lower the standard the more prevalence the disease is and vice versa).
- That is why Cutaneous leishmaniasis spikes between refugees.
- L. major and L. tropics are the most common.
- Resolve over months, round depressed scars remain.
- May resemble other skin lesions (nodular lymphangitis) caused by waterborne pathogens (such as Sporothrix schenckii, Nocardia brasiliensis, Mycobacterium marinum, Leishmania (Viannia).
- Nodular lymphangitis- granulomatous reaction to these pathogens on the path of lymphatics (only happens over the lymph distribution if the fly bits there).
- 700 000 to 1 million new cases and 20 000 to 30 000 deaths occur annually.

Vector and parasite:

Sandflies ***Trypanosome***



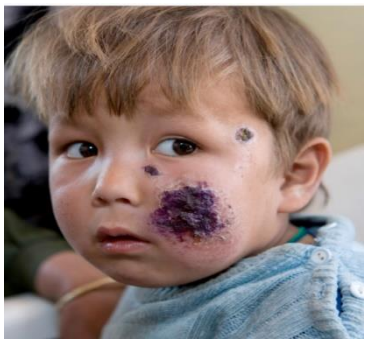
- Transmitted by sandflies or Trypanosome (single flagella).
- Parasite (trypanosome) Has two forms: disease causing (resistant) form and infectious motile form
- Those are the forms of trypanosomes (some forms are more resistant):



- Deemed as a neglected tropical illness (causes mortality with small effort to battle it) ➔ Disease of the poor

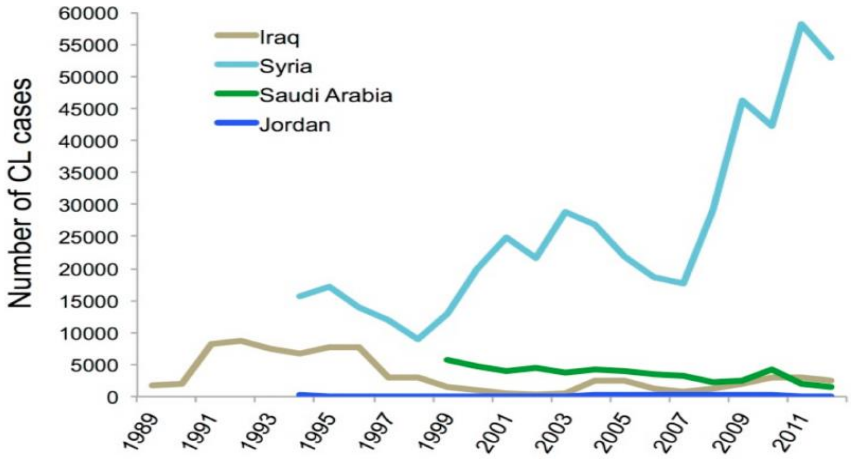
Leishmania comes in 3 forms ***Visceral (or Kala Azar- serious form), mucocutaneous and cutaneous***. *We will discuss the cutaneous forms.*

- The cutaneous forms Has many types:
  1. Old world in Asia, Africa and Europe which has a long incubation time (MONTHS 2-24): Skin lesion(s) on the face or leg (exposed area s where the patient gets bitten): papules become necrotic and then pigmented scars. (papule at site of bite ➔ small nodules ➔ painless ulcer ➔ crust (pigmented) ➔ leave ugly scars after healing (social stigma and is).
     In 2015 over two thirds of new CL cases occurred in 6 countries: Afghanistan, Algeria, Brazil, Colombia, Iran and the Syrian Arab Republic.
  2. Mucocutaneous: leads to partial or total destruction of mucous membranes of the nose, mouth and throat. Over 90% of mucocutaneous leishmaniasis cases occur in Bolivia (the Plurinational State of), Brazil, Ethiopia and Peru.



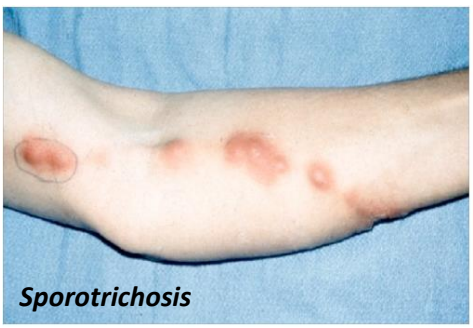
- This picture shows an infected child.
- Actually, each lesion represents a sand fly bite that has developed into these scars over an extended period of time.
- Notice the discoloration which is typical for leishmaniasis.

Becoming an increasing problem in surrounding countries (Syria and Iraq) with poor sanitation and reduced living standards. *Cutaneous leishmaniasis new cases show that Jordan is doing very well however after 2011 there was a spike because of the region's issue.*



Dx of CL:

- ✓ Sporotrichosis, one of many differentials.
- ✓ Remove crusts and take skin scrape for microbiology.
- ✓ Biopsy (punch or needle aspirate) to retrieve organism and detect under microscope.
- ✓ On CBC shows reduced cell count (red, white or all).
- ✓ Diagnosis by culture.



Sporotrichosis

Treatment:

- ✓ Local heat to area for 2-3 hours a day.
- ✓ The drug of choice for CL is ***Pentavalent antimonials.***
- ✓ Others include: (Liposomal amphotericin B, Oral miltefosine, Pentamidine).
- ✓ Given for a minimum of 20 days!

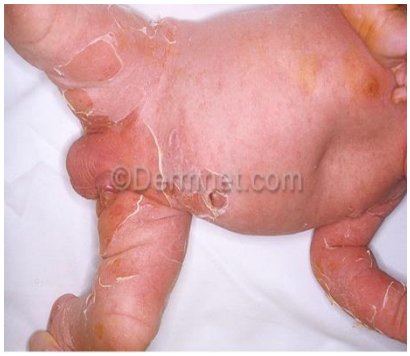
Infections Associated with Bullae

we mentioned that SJS and TEN are associated with bullae also.

Bullae	
Staphylococcal scalded-skin syndrome	*S. aureus*
Necrotizing fasciitis	*S. pyogenes, Clostridium* spp., mixed aerobes and anaerobes
Gas gangrene	*Clostridium* spp.
Halophilic vibrio	*Vibrio vulnificus*

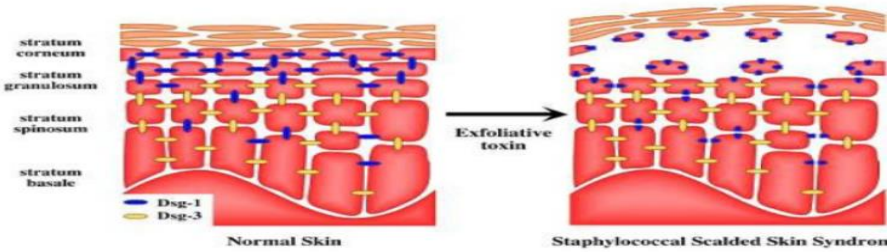
So, the same organism like S. aureus with the same mechanism of pathophysiology (local invasion) can cause different types of skin lesions (impetigo, ecthyma, cellulites, etc.).

Staphylococcal scalded-skin syndrome (SSSS)



- Staphylococcal scalded-skin syndrome (SSSS) in neonates is caused by a toxin (exfoliatin) from phage group II (bacteria that is infected by this phage, acquires the gene to produce the toxin and it can pass it to other bacteria).
- The normal microbiome is defensive against SSSS, that is why it happens in neonates because they are delivered sterile (they acquire their microbiome from the mother later when they breastfeed, touches the mother……etc.)
- Not all strains of Staph aureus carry exfoliative toxins A and B (only about 5% of all S. aureus strains do carry these toxins).
- Due to hematologic (not local) spread of staphylococcal exotoxin. That means there is a point of infection somewhere else in the body like Otitis media or Respiratory tract infection and the bacteria has access to the blood. So, if you see a baby with SSSS you need to look for a point of infection.
- The toxin Breaks down desmoglein-1 resulting in Acantholysis (breakage of cell to cell adhesions) in the stratum corneum of the epidermis, this causes the upper part of the epidermis to be detached from the lower part but, the epidermis will still be attached to the dermis so it is a bullae formation within the epidermis, and it will collect fluids.

PATHOPHYSIOLOGY

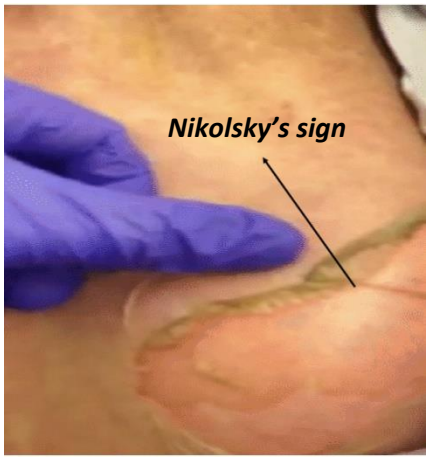


- S. aureus. SSSS must be distinguished from toxic epidermal necrolysis (TEN), which occurs primarily in adults, is drug-induced, and is associated with a higher mortality rate.
- Punch biopsy with frozen section is useful in making this distinction since the cleavage plane is the stratum corneum in SSSS and the stratum germinatum in TEN.
- In children, SSSS is more likely than SJS or TEN, because drugs are major causes of SJS or TEN and obviously the child is not on drugs yet.

Symptoms:

- ✓ Preceded by a prodromal illness (URTI) or Otitis Media, Pharyngitis, Conjunctivitis.
- ✓ Then the acute phase hits: fever! + malaise (loss of fluids) and red painful skin with bullae formation.

Signs:



- ✓ Paper thin (peeling) skin.
- ✓ Large flaccid BLISTERS, more in the flexor creases.
- ✓ Mucous membranes are ***spared.***
- ✓ Positive Nikolsky's sign (detects acantholysis). You can make the bullae spread further by rubbing the side from affected skin to non-affected skin and this tells you this is a bulla and all the skin is involved.

SSSS Dx:

- ✓ blood cultures are often positive (remember hematologic spread of toxin – bacteremia).
- ✓ Skin biopsy will show typical acantholysis.
- ✓ In lab we can do exotoxin assay.

SSSS Rx:

- ✓ ***Must admit the child (burn or ICU unit) because this is a serious condition.***
- ✓ Systemic IV antibiotics are given (anti MRSA or anti S. aureus)+ Systemic steroids (only if patient ***doesn't look*** toxic otherwise it is not used).
- ✓ In severe cases removal and replacement of plasma to get rid of the toxins (IV Immunoglobulins and plasmapheresis).

As for TEN:

- ✓ TEN is primarily seen in adults and is potentially fatal.
- ✓ Intravenous γ-globulin is a promising treatment for TEN.

GOOD LUCK