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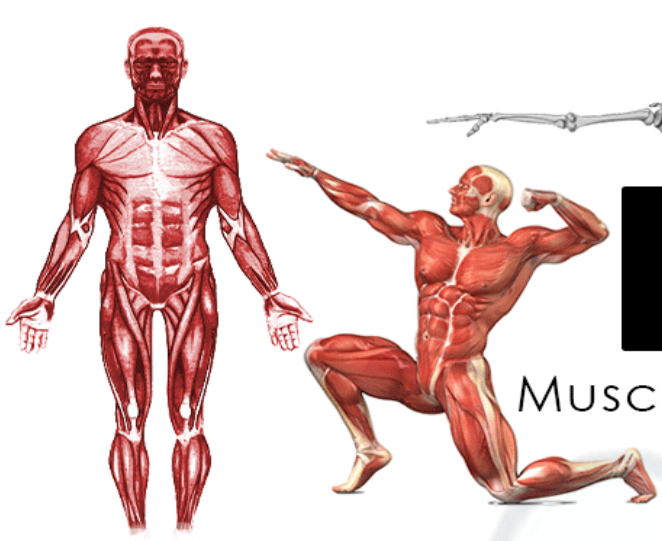

MSS

Musculoskeletal System

Microbiology

Doctor 2018 | Medicine | JU

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Contents of This Sheet

Erysipelas

- Erysipelas is due to **S. pyogenes** and is characterized by an abrupt onset of fiery red swelling of the face or extremities. The swelling happens very quickly and the infection spreads quickly through the lymph.
- The distinctive features of erysipelas are **well-defined** indurated margins, particularly along the nasolabial fold, rapid progression, and intense pain (inflammation, acute).
- Flaccid bullae may develop during the second or third day of illness, although it is rare. Extension to deeper soft tissues is also rare.
- **Treatment**: penicillin (flucloxacillin, clindamycin) is effective (so anti-staph and anti-strep)
- Swelling may progress despite appropriate treatment, **although fever, pain, and the intense red color diminish**. Any symptom that continues despite treatment indicates that a structure has been compromised and needs time to heal. In this case, the continued swelling is due to destroyed lymphatics.
- Desquamation of the involved skin occurs 5–10 days (about a week) into the illness.
- Infants and elderly adults are most commonly afflicted, and the severity of systemic toxicity varies.

> In general, in infections, the elderly are most susceptible and second to them are children, especially infants. In regard to the novel Corona virus, the mortality rate in China is very low (below 1%) for all age groups except for individuals over 60: 20%.

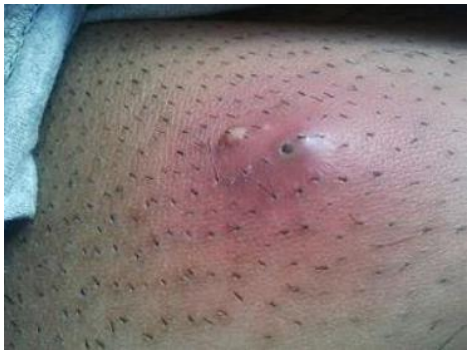
Cutaneous Abscesses

- They are collections of **pus** within the dermis and deeper skin structures.
- Usually polymicrobial containing skin/mucous membrane flora; S. aureus is the sole pathogen in 25% of cases.
- Clinical features—painful, tender, fluctuant nodules, usually with an overlying pustule and surrounded by a rim of erythematous swelling.

- Treatment is I&D (incision and drainage). Antibiotics are rarely necessary (except in extensive infection, systemic toxicity, or the immunocompromised).

Notice:

- The lesion is raised.
- It has a white head.
- The hair follicle might be the port of entry.



Diabetic Foot Infections

- A diabetic foot infection is defined as **any infection in a patient with DM** that is below the malleolus.
  - One important point of this definition is that it is an infection. Some people assume that if there is a diabetic ulcer, then this is the same as diabetic foot. But if the ulcer is not infected, then it is just a diabetic foot ulcer. If the ulcer is infected, then this is considered diabetic foot.
- The commonest of these lesions is an infected diabetic ulcer.
- However, as mentioned, it is a broad spectrum of infections ranging from: paronychia, cellulitis, myositis, abscess formation, necrotizing fasciitis, septic arthritis, tendonitis, and osteomyelitis (so there can be muscle and bone involvement as well).

Epidemiology

- Foot infections in DM are a common complication, they often carry a **high burden of morbidity** for the patient (lowered quality of life: they can't move, are in pain, and the infection is oozing and smells. They can't wear shoes or go to work properly). Diabetic foot is also notoriously difficult for doctors to manage (there are specialized DF surgeons and clinics!). It requires intense treatment, debridement, constant visits from the patient, and wound dressing.
- **Risk factors**: Recall the table from the last lecture for fasciitis, as the risk factors can be applied here. However, there are three main risk factors that apply for diabetics. For clarity, the risk factors from the slides will be bolded, while the professor's explanation will be placed below, it will not be bolded. But before we discuss the risk factors, let's look into what the situation is like for a diabetic:

Generally, the vascular supply of the lower limb, as it is farther away, will not have the same pressure as the upper limb. Also, the more distal you go in the lower limb, the less the vascular supply is. If a diabetic individual has a problem with his/her vascular supply, the main issue will be found in the most distal part of the lower limb: the foot. Diabetic foot can be thought of as a building that used to be occupied. The water and electricity were cut off, so all the residents left. Therefore, no matter what problem occurs, like animals entering the building, there's no one left to warn about or fix the problem. The issue of diabetic foot is not the animals (in this case, pathogens), but it's diabetes, the cause of the empty house.

1. **Neural: development of peripheral sensory, motor, and/or autonomic neuropathy** (neuropathy means dysfunction or damage of a nerve)**, and neuro-osteopathic deformity (e.g. Charcot joint).**

The blood supply to the nerves (and everywhere, really) is compromised due to atherosclerosis. The nerves start losing function. First, sensation is lost. Therefore, if trauma occurs to the foot, the person wouldn't feel it. Then the wound can become worse, and even not improve with dressing, until it becomes an infected ulcer. This is typically how diabetic foot occurs. Second is loss of autonomic neurons, so there is no feedback. Normally, the body should recognize that there is an ulcer and cells need to be recruited to heal said ulcer. In a diabetic foot, this feedback will not occur. Therefore, inflammatory cells will not be recruited and in the beginning the ulcer won't look inflamed. Additionally, if a pathogen enters the ulcer, the chance of response is low, so the likelihood of infection increases.

2. **Vascular: vascular insufficiency**

Atherosclerosis affects blood supply, so there aren't enough immune cells reaching the area. Chemotaxis is also impaired. Additionally, not enough oxygen is reaching the area, so anaerobes and facultative anaerobes can grow better than if they were in a well vascularized area.

3. **Immune: hyperglycemia leading to poor immune function and wound healing.**
4. **Other factors: poor vision, limited mobility, previous amputations, and poor healthcare.**

Poor vision also makes it more likely for the individual to be injured. Poor vision is actually another complication of diabetes. When a pre-diabetic goes to the clinic, they scare him by telling him if he gets diabetes, he'll either lose his vision or his foot.

Etiology

Table 22.1 Aetiology of diabetic foot infections

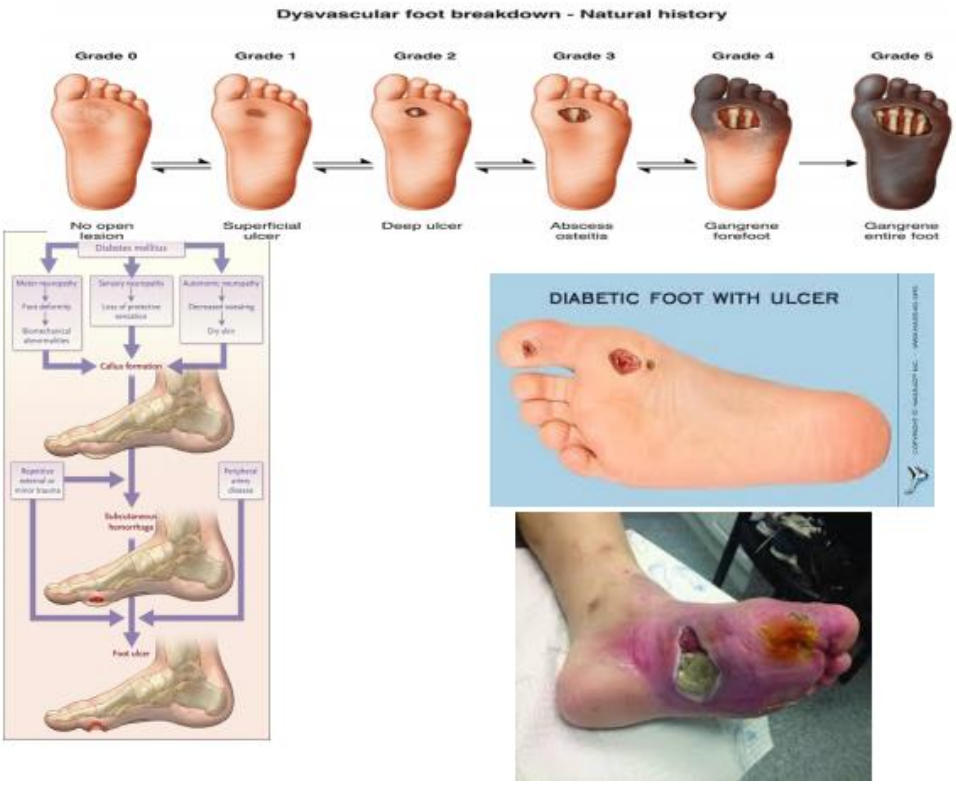
Foot infection syndrome	Pathogens
Cellulitis	β-haemolytic streptococci (groups A, B, C, and G), *S. aureus*
Infected ulcer, antibiotic-naïve	Often monomicrobial: *S. aureus* or β-haemolytic streptococci (groups A, B, C, and G)
Infected ulcer, chronic, previous antibiotic therapy	Usually polymicrobial: *S. aureus*, β-haemolytic streptococci (groups A, B, C, and G), *Enterobacteriaceae*
Macerated ulcer	*P. aeruginosa* ± other organisms as above
Long-standing, non-healing wound, prolonged antibiotic therapy	Usually polymicrobial with antibiotic-resistant organisms: aerobic Gram-positive cocci (*S. aureus*, CoNS, enterococci), diphtheroids, *Enterobacteriaceae*, *Pseudomonas* spp., non-fermentative GNRs, fungi
'Fetid foot': extensive necrosis or gangrene	Mixed aerobic Gram-positive cocci (*S. aureus*, CoNS, enterococci), *Enterobacteriaceae*, non-fermentative GNRs, obligate anaerobes

Notes on the table:

- **Cellulitis** in a diabetic foot will be similar to cellulitis in any other area. Infection includes gram positive streps and staphs.
- An **antibiotic naïve ulcer** has never been exposed to antibiotics. This ulcer is better than one that has been exposed to antibiotics. If an infection happens in a naïve ulcer, most likely the infective organism is part of skin flora: staph or strep.
- In a **non-naïve ulcer**, the flora has been compromised. The intention of giving antibiotics was to remove the normal flora that caused the naïve ulcer. However, if micro-organisms are removed from one niche, the area will never remain empty. The new species that will infect are exogenous (not from the normal flora) and are usually the gram negative Enterobacteriaceae. They tend to come from the environment, a hospital, and the patient himself. Additionally, at this point the infection is polymicrobial with gram negatives and positives.
- A **macerated ulcer** is an ulcer that has significant liquefication. This usually occurs if Pseudomonas is introduced, perhaps through water or from hospital staff.
- **Long-standing, non-healing wound, with prolonged antibiotic therapy**: Due to the risk factors mentioned above, in diabetics the healing time is longer than in non-diabetics. A non-diabetic ulcer would heal in a few days. A diabetic ulcer is more long-standing and does not heal easily (even a non-infected ulcer may take two weeks to heal). Antibiotics are continuously given for weeks, and the problem becomes more difficult to treat. Additionally, we now have antibiotic resistance

to face. Antibiotics, as drugs, reach the wound through the blood, which is compromised. So, the dose that is reaching the wound is not reaching optimal levels. Giving a suboptimal dose of an antibiotic opens the door for bacterial resistance. This is why resistance is very common in diabetes, so one of the treating mechanisms is by improving the blood supply.

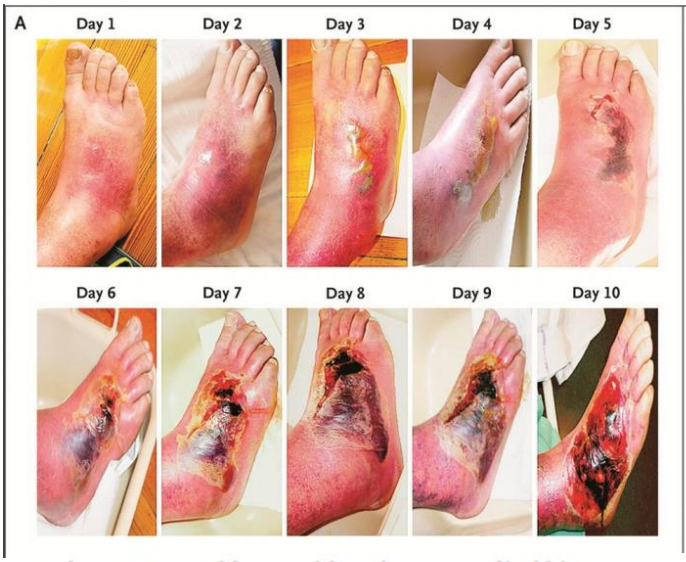
- **<u>Fetid foot</u>**: There is now necrosis, clostridia species may be involved with gangrene. Obligate anaerobes are now a part of the problem.



At first, the diabetic foot may look infected or non-infected.

The more the necrosis and gangrene, the more the area that must be debrided. If the whole foot is gangrenous, then debridement of the entire foot would be an amputation.

Clinical Case



An obese 50-year-old man with no known medical history presented with a necrotizing infection of his right foot that had begun 10 days previously with lesions that he attributed to wearing new shoes. He was found to have diabetes (glycated hemoglobin level, 10.5%) with peripheral neuropathy; he was afebrile, without leukocytosis or radiographic evidence of bone involvement in his right foot. The patient had photographed the lesion twice daily, thinking it would heal spontaneously (Panel A). The preoperative photographs show erythema (day 1), blisters (day 3), a necrotizing abscess (day 6), and wound infection requiring surgery (day 10). The patient underwent operative débridement; tissue cultures grew *Enterobacter cloacae* and *Streptococcus agalactiae*. He was treated with antibiotic agents for 3 weeks. The infection resolved, with no recurrence or sequelae during 3 years of follow-up (Panel B); during this period, the infection-related swelling disappeared and the patient lost a considerable amount of weight. Diabetic foot infection may evolve rapidly, especially in patients with neuropathy.

This man didn't know he had diabetes, encountered trauma, and ended up with an ulcer. He photographed It every day. Day 1 it looks like the foot is inflamed. Day three it looks like cellulitis. By day 6 there is a necrotic abscess and by day 9 there is significant necrosis.

Panel B is the same patient after three years. We can conclude four things:

1. The wound was treatable.
2. There was no need for amputation, only a scar remains from debridement.
3. He **lost weight** and managed his blood sugar.
4. No more inflammation is present.

Having diabetic foot is a risk factor for another case of diabetic foot. But, since this patient managed his diabetes by improving his diet and blood sugar, exercising, and losing weight, after three years he has not had another issue of diabetic foot. This further proves the problem is not the invading micro-organisms, but diabetes itself.

Clinical Features

- Range from mild -> severe -> life-threatening
- Progresses as the following
  i. Foot ulcer with no signs of infection.
  ii. Foot ulcer with surrounding inflammation or cellulitis <2cm from edge of the wound.
  iii. Local complications – cellulitis >2cm from the edge of the wound. +lymphangitis, spread beneath the superficial fascia, deep tissue abscess, gas gangrene, and involvement of muscle, tendon, or bone.

iv. Systemic toxicity or metabolic instability—fever, chills, tachycardia, hypotension, confusion, vomiting, leukocytosis, acidosis, hyperglycemia, and uremia.

Diagnosis

1. Clinical features: must assess perfusion (peripheral pulses, less perfusion = more anaerobes), as well as sensation (using a mono filament).
    - You can assess different levels of the foot to determine where sensation and pulse is absent, and this informs you where the area of danger is.
2. Doppler ultrasound to determine ratio of ankle Vs brachial pressure index (aBPIs).
3. Imaging (MRI) may help determine the extent of infection (osteomyelitis, fasciitis). Basically, how much of the tissue is involved.
4. Deep tissue specimens (not superficial swabs) need to be sent to microbiology lab for microscopy and culture before Abx (antibiotic) treatment.

Management

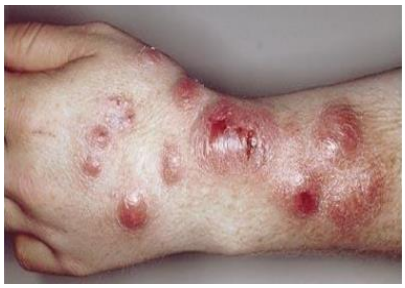
- Inpatient Vs outpatient management.
    - Inpatient: hospital
    - Outpatient: clinic
    - Outpatient management is preferred to prevent exposure to pathogens in hospitals, like pseudomonas aeruginosa.
- Inpatient Rx is based on correcting systemic instability.
- I- Medical treatment: Do not give Abx for non-infected ulcers (to ensure a future infected ulcer remains naïve). For infected ulcers, initial treatment is empiric therapy, oral for mild cases and IV broad spectrum for severe cases. Also work on fixing blood sugar levels.
- II- Surgery (Debridement)—For cases of severe infections in deeper tissues (necrotizing fasciitis, gas gangrene, extensive tissue loss, and critical limb ischemia). Debridement is both therapeutic and diagnostic, as samples of the removed tissues can be sent to the microbiology lab.
- Wound care plan following discharge.

Papular and Nodular Lesions

Papular and nodular lesions	
Fish-tank or swimming-pool granuloma	*Mycobacterium marinum*
Creeping eruption (cutaneous larva migrans)	*Ancylostoma braziliense*
Dracunculiasis	*Dracunculus medinensis*
Cercarial dermatitis	*Schistosoma mansoni*
Verruca vulgaris	Human papillomaviruses 1, 2, 4
Condylomata acuminata (anogenital warts)	Human papillomaviruses 6, 11, 16, 18
Onchocerciasis nodule	*Onchocerca volvulus*
Cutaneous myiasis	*Dermatobia hominis*
Verruca peruana	*Bartonella bacilliformis*
Cat-scratch disease	*Bartonella henselae*
Lepromatous leprosy	*Mycobacterium leprae*
Secondary syphilis (papulosquamous and nodular lesions, condylomata lata)	*Treponema pallidum*
Tertiary syphilis (nodular gummatous lesions)	*T. pallidum*

These lesions can be caused by viruses, bacteria, fungi and parasites.

1. Mycobacterium Marinum (refers to Marine life: fish)

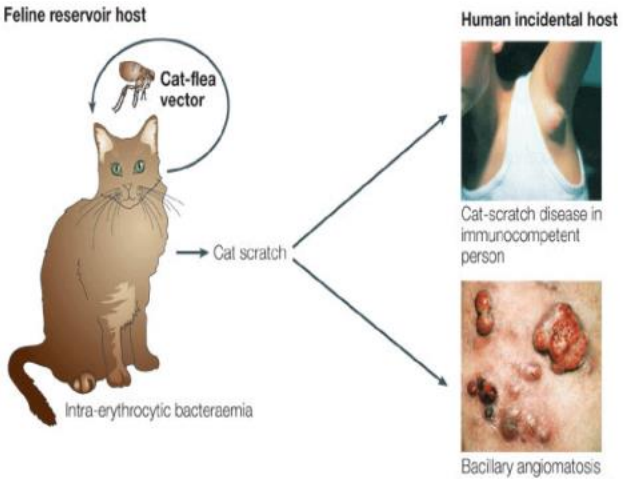


- Infections of the skin may present as cellulitis or as raised erythematous nodules (nodular cellulitis). This occurs when the pathogen enters the skin. As it is a mycobacterium, the body reacts by forming granulomas. The outcome of granulomas and cellulitis is large nodules. This nodular cellulitis differs in appearance from the form of cellulitis we studied previously. The nodules tend to be on the hands.
- The infection is an occupational hazard in jobs where there is contact with marine life, usually for aquarium cleaners, fishermen, and seafood handlers.
- Organism growth requires lower temperatures than 37C (24-32) and thus is limited only to skin.
- **Dx:** needle aspiration, then stain to see acid fact bacilli.
- **Rx:** rifampin+ethambutol for four months. Significant improvement may occur in the first month, but the nodules remain and longer treatment is needed for full resolution.

2. Cat-Scratch Disease

- Caused by bartonella henselae, a gram-negative bacillus. It usually grows on Columbia agar supplemented with 5% sheep blood
- Transmission cycle is between cats and fleas (they can infect each other), then cats transmit to humans by a bite or scratch. The human is an incidental host. Predictably, the people most at risk are those who are continuously in contact with cats.
- Symptoms: myalgia, arthralgia, malaise, anorexia, maybe low-grade fever.

- Signs: Lesions (papule, pustule or large vesicles) developing at the primary site of inoculation of Bartonella henselae. In other words, a nodular lesion can be found at the site of the scratch. Then, in 85-90% of cases there is persistent painful regional IPSILATERAL (=same side) lymph adenopathy.
- In immune competent individuals, there is usually nothing to worry about. In immune compromised individuals, a fulminant, significant disease will occur with bacillary angiomatosis.



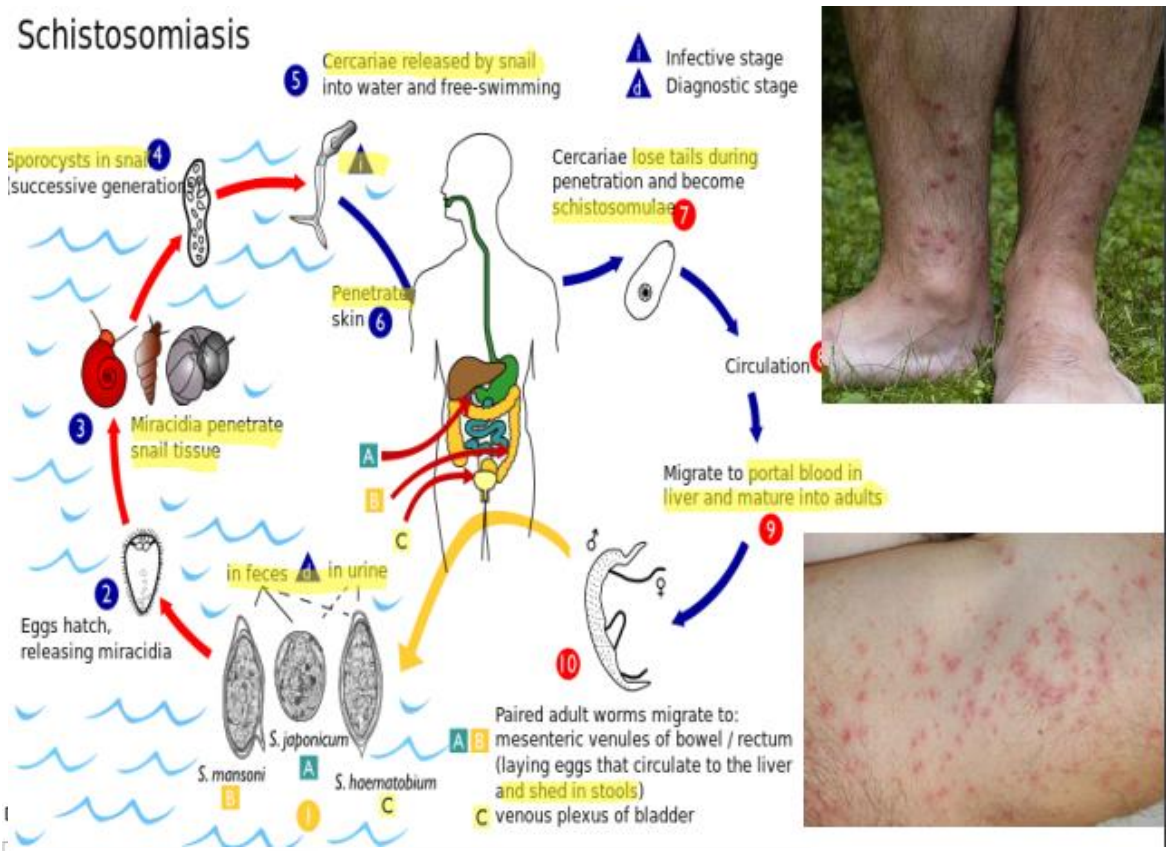
- **Dx:** Clinical but can verify with serology (IgM, or IgG titers) or biopsy of a lymph node.
- **Rx:** Self-limited in immunocompetent and resolves within 8 weeks. There is an increased risk of reaction if Abx are given in the first 48 hours.

3. Schistosomiasis

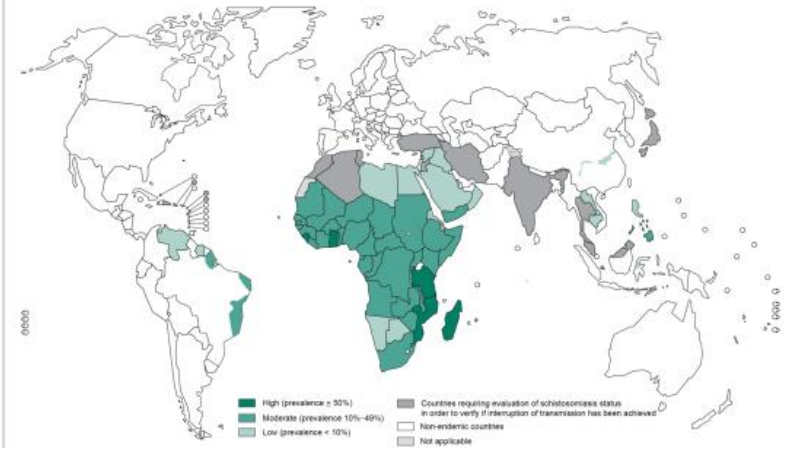
- Caused by Schistosoma; a parasitic blood fluke (trematodes, life cycle in two hosts).
- Multiple erythematous papules develop in schistosomiasis; each represents a cercarial invasion site (known as bilharzia).
- Acute phase (Katayama fever, whole body hypersensitivity-fever, malaise, etc.)
- **Dx:** stool and urine microscopy (shows the presence of eggs)
- **Rx:** single dose Praziquantel (antiparasitic)
- Skin signs: The skin manifestation is called **swimmer's itch** and it occurs due to an allergic reaction at the site of invasion by parasites. Especially by S. cercariae but other parasites as well.

Life Cycle

When someone is infected by Schistosoma, the eggs of the parasite will grow in their gut. They will migrate to the rectum and shed in the stool (and sometimes through the urine) into a water supply. The eggs will then hatch and must pass through a snail host. Therefore, the parasites will infect a snail, mature into sporocysts in the snail, and leave as mature parasites. When someone else comes and stands in this infected water, the parasites will invade the skin, and nodules will form where the parasites penetrated the skin. Bilharzia will occur and the parasite goes to the portal circulation and reaches the liver, spleen, and kidneys.



The nodules indicate where the parasite entered.



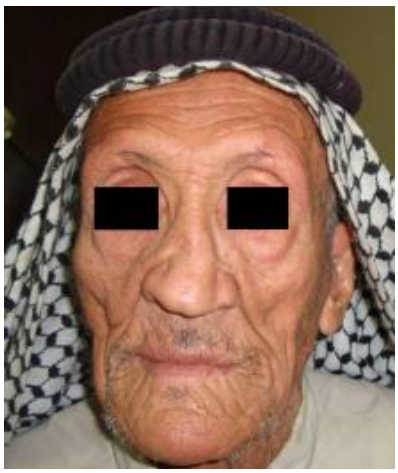
We are near an endemic area: Egypt (and the rest of Africa). Egypt has many cases of bilharzia, especially in older generations.

Prognosis

- <u>Early disease usually improves with treatment.</u>
- More advanced stages with hepatic and urinary disease improve following long-term therapy over months or years (even if fibrosis occurs). Hepatic disease usually improves due to the regeneration capacity of the liver.
- Renal and intestinal pathology also improves with treatment, as, usually, do brain lesions (depending on their location and size).
- Hepatosplenic schistosomiasis carries a relatively good prognosis because hepatic function is preserved until the end of the disease (unless variceal bleeding occurs).

4. Leprosy

- Leprosy is caused by **Mycobacterium leprae** (acid fast bacillus).
- It is a chronic infection of the skin that causes granulomas as the body aims to contain the slow-growing bacilli. (As seen earlier with Marinum).
- **Has two types:**
  - Tuberculoid: patient has intact immunity, usually nerve changes predominate.
  - Lepromatous: skin changes predominate (defect in cell immunity).
- Skin nodules as well as thickened subcutaneous tissue are prominent features of lepromatous leprosy.
- Long incubation (it could be 3 years and up to 20 years)
- Transmission is mostly by nasal secretion of untreated patients, however only low risk from casual contact is present. To infect another person, prolonged, intimate contact must occur with that person.
- **Skin changes:** bilateral symmetrical macules and papules, progresses to nodules and even plaques.
- Usually hypopigmented in dark skinned people and seen on the face, wrists, buttocks and knees, but spares groin and axilla (folded skin has higher temperature which doesn't favor its growth)
- **Dx:** Acid fast stain skin smears and biopsy (stain especially +ve in lepromatous leprosy).
- **Rx:** Anti mycobacterial drugs (Dapsone and Rifampin). Treatment at early stages is for 1-2 years and may be lifelong in late leprosy treatment. Treatment only halts the progression and prevents further complications and transmission. It does not remove the lesions.



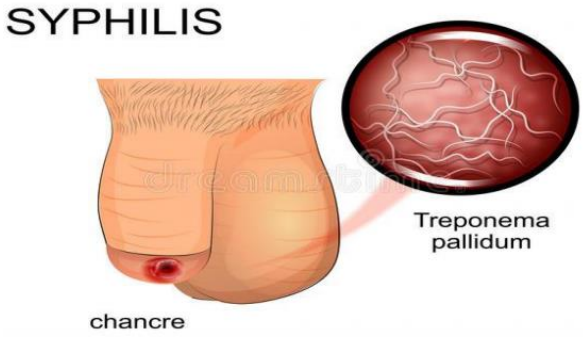
The man on the left has bilateral symmetrical lesions, so it looks like there's nothing wrong.

To the right is the classical appearance, where lesions appear around the mouth and eyes. Here, it looks "more like" leprosy.

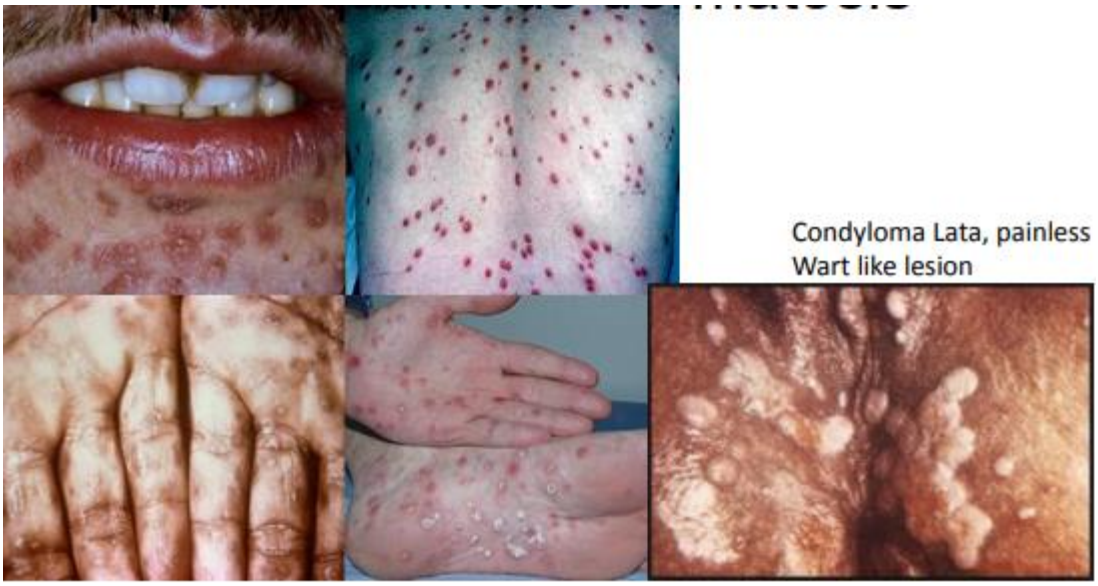
5. Syphilis

- Flat papulosquamous lesions are characteristic of <u>secondary syphilis</u>.
- Large nodules or gummas are features of <u>tertiary syphilis</u> (late untreated syphilis). Granulomas may form.

<u>Primary Chancre</u>



<u>Secondary Syphilis – Papulosquamous dermatosis</u>



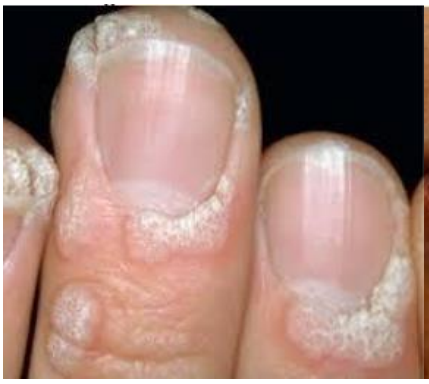
Condyloma Lata – Painless wart-like lesions around the anus.

Notice that this is different from condyloma acuminata, caused by HPV infection (seen next)

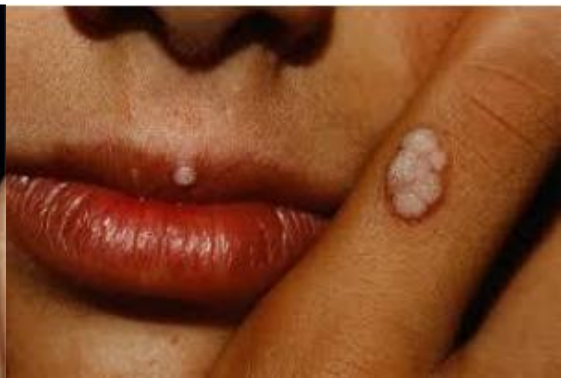
6. Human Papilloma Virus

- Human papillomavirus may cause singular warts (verruca vulgaris) or multiple warts in the anogenital area (condylomata acuminata), which is a major problem in HIV patients).
- Verruca vulgaris: HPV 1,2,4, 7, common in children and young adults
- Transmitted by skin contact, sharing certain tools/cloth, or as an STD in the case of condyloma acuminata.
- Usually on the hands and nail edges, can auto inoculate face
- Management: Dermatologists
- HPV is an STD, and can cause cervical cancer (HPV strains 16, 18, 31,33).
- HPV on the fingers is similar to herpetic whitlow, but the lesions are larger/more pronounced.

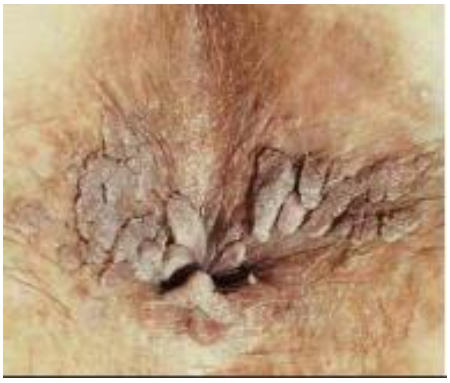
Digits



Digits + Autoinoculation



Condyloma Acuminata



Diagnosis of Skin Infections

With HPV being the last skin infection to be discussed in this course, we will now look into a general framework to work upon if you ever come in contact with a skin infection.

As discussed, so far diagnosis of skin infections depends on three main clinical observations:

1. Appearance of lesion – how it looks (macule, papule, vesicle…etc.)
2. Location within the layers of soft tissues – how deep it is (stratum corneum, epidermis, dermis…etc.)
3. Location relative to the body – where it is on the body (trunk, face, extremities…etc.)

Knowing these helps eliminate what infections don't apply and allows you to have a clearer idea on what the possible diagnosis could be.

In regard to depth, we can order different infections from the most superficial to the deepest.

- Impetigo (Most Superficial)
- Ecthyma
- Erysipelas
- Lymphangitis
- Cellulitis
- Fasciitis
- Myositis
- Osteomyelitis (Deepest)

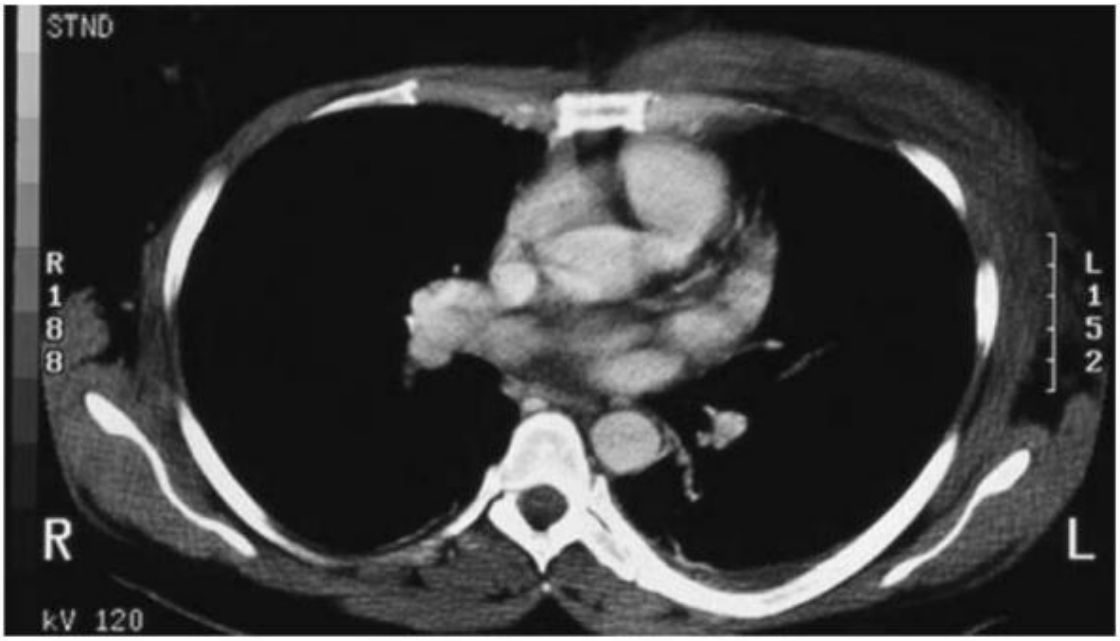
Other information that helps fine tune the pathogenesis of the infective agent:

- The temporal progression of the lesions (e.g. appear in crops or appear acutely…etc.). For example, the pictures showed the temporal progression of diabetic foot, from cellulitis, to a necrotic abscess, and then further necrosis. Another example is Orf, which starts as a scratch, then a vesicle, then a nodule.
- The patient's travel history (for exogenous or exotic sources of pathogens)
- Animal exposure or bite history
- Age of the patient
- Previous surgery – Indicates a surgical site infection
- Underlying disease status – Cancer, diabetes, cirrhosis, and taking medication may indicate if this person is in a condition prone to have a certain kind of infection, as a healthy individual might not be.
- Lifestyle – Including occupation

However, even the most experienced clinician will find it difficult to diagnose all infections of the skin and soft tissue by history and inspection alone. Thus, aiding diagnostic tests can help:

1. Soft tissue radiography, CT (next figure), and MRI may be used to help determine the depth of infection.
   - They help in assessing deeper infections and its extent.
   - You might recall that serious infections like fasciitis are rapidly progressing.
   - May provide evidence of a systemic inflammatory response syndrome (to find a local infection that may be releasing toxins).

- Another value for these tests is for defining <u>a localized abscess or detecting gas</u> in tissue (air pockets) where anaerobes are present (not GAS infection, which may only show swelling as shown in next figure).



This scan shows left anterior chest wall fasciitis. You can see swelling, edema, and inflammation of the left chest wall. It looks larger than that of the right.

FIGURE 22-2
Computed tomography showing edema and inflammation of the left chest wall in a patient with necrotizing fasciitis and myonecrosis caused by group A *Streptococcus*.

2. <u>Lab Diagnostics</u>
   - **Aspiration** (without saline is better as there is less dilution) or **punch biopsy with frozen section** might help if imaging is positive. However, there is a large false negative rate (~80%) because there is a lot of inflammation, which might dilute the area and make it less likely for the aspirate to contain the microorganism.
     - When do you use saline? If you try to aspirate but no fluid is coming out, then you can inject some saline and take it back out in an attempt to retrieve the microorganism.
   - Frozen sections are especially useful in <u>distinguishing SSSS from TEN</u> and is also quite valuable in cases of <u>necrotizing fasciitis</u> (determining depth and level of involvement).
   - **Open surgical inspection (+debridement)** is the <u>optimal way</u> to determine the extent and severity of infection. It also is the <u>superior method to obtain specimen for culture and Gram stain</u>.

- Although the surgical approach may be an aggressive approach, it is an important step and may be lifesaving in the course of fulminant infections where there is evidence of systemic toxicity.

An Overview of Treatment

- Furuncles, carbuncles, and abscesses caused by MRSA and MSSA are commonly encountered
- Rx here depends on the size of the lesion.
    - Furuncles < 2.5 cm in diameter -> treated with moist heat.
    - Furuncles > 4.5 cm of erythema + induration -> surgical drainage
    - larger lesions + fever, chills, or leukocytosis -> drainage and antibiotic treatment.
- A study in children showed that surgical drainage of abscesses (mean diameter, 3.8 cm) was as effective when used alone as when combined with trimethoprim-sulfamethoxazole treatment. However, recurrence was less in groups that added Abx with I&D

For the tables below, the professor wants us to know the primary and alternative treatment for each.

TABLE 22-2

TREATMENT OF COMMON INFECTIONS OF THE SKIN

DIAGNOSIS/CONDITION	PRIMARY TREATMENT	ALTERNATIVE TREATMENT	SEE ALSO CHAP(S).
Animal bite (prophylaxis or early infection)[a]	Amoxicillin/clavulanate, 875/22 mg PO bid	Doxycycline, 100 mg PO bid	35
Animal bite[a] (established infection)	Ampicillin/sulbactam, 1.5–3 g IV q6h	Clindamycin, 600–900 mg IV q8h, *plus* Ciprofloxacin, 400 mg IV q12h, *or* Cefoxitin, 2 g IV q6h	35
Bacillary angiomatosis	Erythromycin, 500 mg PO qid	Doxycycline, 100 mg PO bid	65
Herpes simplex (primary genital)	Acyclovir, 400 mg PO tid for 10 days	Famciclovir, 250 mg PO tid for 5–10 days, *or* Valacyclovir, 1000 mg PO bid for 10 days	84
Herpes zoster (immuno-competent host >50 years of age)	Acyclovir, 800 mg PO 5 times daily for 7–10 days	Famciclovir, 500 mg PO tid for 7–10 days, *or* Valacyclovir, 1000 mg PO tid for 7 days	85

Cellulitis (staphylococcal or streptococcal[b,c])	Nafcillin or oxacillin, 2 g IV q4–6h	Cefazolin, 1–2 g q8h, *or* Ampicillin/sulbactam, 1.5–3 g IV q6h, *or* Erythromycin, 0.5–1 g IV q6h, *or* Clindamycin, 600–900 mg IV q8h	38, 39
MRSA skin infection[d]	Vancomycin, 1 g IV q12h	Linezolid, 600 mg IV q12h	38
Necrotizing fasciitis (group A streptococcal[b])	Clindamycin, 600–900 mg IV q6–8h, *plus* Penicillin G, 4 million units IV q4h	Clindamycin, 600–900 mg IV q6–8h, *plus* Cephalosporin (first- or second-generation)	39
Necrotizing fasciitis (mixed aerobes and anaerobes)	Ampicillin, 2 g IV q4h, *plus* Clindamycin, 600–900 mg IV q6–8h, *plus* Ciprofloxacin, 400 mg IV q6–8h	Vancomycin, 1 g IV q6h, *plus* Metronidazole, 500 mg IV q6h, *plus* Ciprofloxacin, 400 mg IV q6–8h	69
Gas gangrene	Clindamycin, 600–900 mg IV q6–8h, *plus* Penicillin G, 4 million units IV q4–6h	Clindamycin, 600–900 mg IV q6–8h, *plus* Cefoxitin, 2 g IV q6h	46

Myositis and Myonecrosis

Myositis and myonecrosis	
Pyomyositis	*S. aureus*
Streptococcal necrotizing myositis	*S. pyogenes*
Gas gangrene	*Clostridium* spp.
Nonclostridial (crepitant) myositis	Mixed aerobic and anaerobic bacteria
Synergistic nonclostridial anaerobic myonecrosis	Mixed aerobic and anaerobic bacteria

- Muscle involvement (inflammation or infection) can occur with:
  - viral infection (systemic infections such as influenza, dengue, or coxsackievirus B infection).
  - Parasitic invasion (trichinellosis, cysticercosis, or toxoplasmosis).
- **Myalgia** (muscle pain) can occur in most of these infections. Severe muscle pain is the hallmark of pleurodynia (coxsackievirus B), trichinellosis, and bacterial infection.
- Usually, it is not the virus itself invading the muscle tissue and causing myalgia. The cause of pain is the systematic inflammatory response to an intracellular pathogen.

Why systemic? Because muscles are well perfused tissues, so viremia is likely to cause inflammation at the muscle and therefore pain. Most individuals complain of muscle pain at their thighs or back.

- The same applies to systemic intracellular bacterial infections
- Myalgia differs from **myositis**, which is a localized infection to the muscle.
- **Acute rhabdomyolysis** (breakdown of damaged muscle) predictably occurs with clostridial and streptococcal myositis, as both these organisms have enzymes that breakdown muscle.
- Rhabdomyolysis is less so associated with influenza virus, echovirus, coxsackievirus, Epstein Barr virus, and Legionella infections.

Necrotizing Myositis

- S. pyogenes (GAS) may induce primary myositis (referred to as streptococcal necrotizing myositis) in association with severe systemic toxicity
  - this is basically necrotizing fasciitis (Type2) that involves the muscle tissue.
- Myonecrosis occurs in about 50% of cases in typical necrotizing fasciitis without muscle involvement being the primary tissue infected! In other words, there may be fasciitis that may cause necrosis in the muscle without the bacteria actually infecting the muscle. This happens when the bacteria in the fascia is causing significant necrosis that spreads to surrounding tissues, including muscles.
- As can be seen, myonecrosis has two forms:
  - From necrotizing fasciitis that progresses into the muscle.
  - Necrotizing Myositis

Pyomyositis

- Pyomyositis, a pus forming (purulent) infection of skeletal muscle tissue, is usually due to **S. aureus** (remember it is the typical pus former in skin), especially those that have PVL toxin.
- Abscess formation is the usual consequence when these pyogenic bacteria reach the muscle tissue.
- Pyomyositis is common in tropical areas, and generally has no known portal of entry (in contrast to necrotizing fasciitis).
- Cases of pyomyositis caused by MRSA producing the PVL toxin have been described among children in the United States.
- Muscle infection begins at the exact site of blunt trauma or muscle strain.

- Pyomyositis infection usually remains localized, and shock does not develop unless organisms produce
  i. Toxic shock syndrome toxin 1 - acts as a super antigen that causes exaggerated immune response that is many folds the normal response -> shock.
  ii. Enterotoxins (exotoxins produced by S. aureus).
- If the patient lacks antibodies to the toxins above, then they are prone to developing toxic shock when these toxins are produced.
- Pyomyositis usually arises from <u>hematogenous spread</u> (deeper infections, muscle and bone, are typically more related with hematogenous spread rather direct inoculation).

<u>Epidemiology of Pyomyositis</u>

- There are two main scenarios:
  1. <u>In tropical climates:</u>
     - Occurs more in males than females, and in two main age groups with no significant medical history:
       - children (aged 2–5 years)
       - adults (aged 20–45 years)
     - There is direct inoculation from the blood into the muscle.
     - Somehow this happens with high temperature and humidity, but we don't know why.
  2. <u>In temperate climates:</u>
     - Pyomyositis typically affects adults or the elderly (not children).
     - Patients usually have predisposing conditions such as HIV infection, DM, malignancy, cirrhosis, renal insufficiency, organ transplantation (reduced cell immunity), and immunosuppressive therapy.
     - Other risk factors include trauma, IDU (Injection drug use), and concurrent infections (toxocariasis caused by roundworms, VZV)
     - Typically, patients have past medical history, which allows bacteria to reach the blood. With trauma, some muscle necrosis may occur. Together, this will allow the bacteria to seed into the muscle. Then, three phases will occur (as discussed below in the "Clinical Stages" section).

<u>Microbiology</u>

- <u>S. aureus 90% of tropical cases 75% of temperate cases</u>.
- GAS account for 1–5% of cases all around.

- E. coli ST131 is an emerging cause in patients with hematological malignancy.
- Uncommon causes are B, C, and G streptococci, S. pneumoniae, and S. anginosus.
- Rare causes include Enterobacteriaceae, Y. enterocolitica, N. gonorrhoeae, H. influenzae, A. hydrophila, anaerobes, B. mallei, B. pseudomallei, A. fumigatus, Candida spp., MTB, and MAC.

Clinical Features

- In between 20% and 50% of cases patients have had recent blunt trauma or vigorous exercise of the affected area –myolysis-
- The muscle area is damaged and becomes susceptible for infections.
- Seen more in the lower extremity (thigh, calf, gluteal muscles), but it is not limited to that area and can affect any muscle group.
- Multifocal infection occurs in up to 20% of cases! (multifocal = more than one location)
- Since it is usually from a hematologic cause, the patient must be assessed for complications of bacteremia (endocarditis).

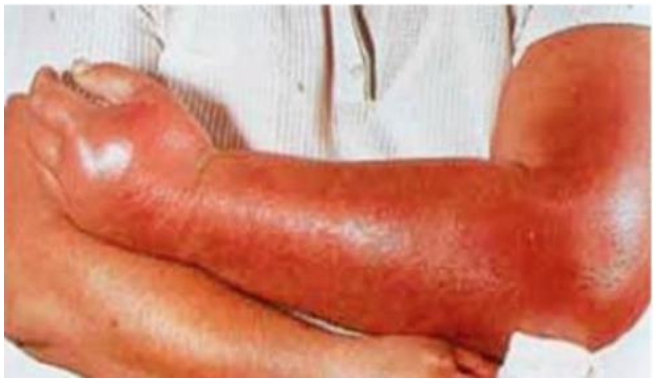
Clinical Stages

- Stage 1 (early invasive stage)
  - crampy local muscle pain, swelling, and low-grade fever. Induration (hardening) of the affected muscle + leukocytosis may be present.
  - The bacteria is everywhere in the area of trauma, and therefore causes non-specific symptoms.
- Stage 2 (suppurative stage)
  - at 10–21 days after onset of symptoms (most patients present at this stage). Fever, very sharp muscle tenderness and swelling. An abscess may be clinically apparent, aspiration of which yields pus. There is marked leukocytosis.
  - After 10 days, the abscess starts to form, and at the same spot, the patient complains of pain. There is also significant inflammation in the area. Since we are discussing skeletal muscle, this occurs in the upper or lower limb.
  - If phase 2 progresses into the system, it reaches phases 3.
- Stage 3 (systemic stage)
  - The affected muscle is fluctuant. Patients may present with complications of S. aureus bacteremia, e.g. septic shock, endocarditis, septic emboli, pneumonia,

pericarditis, septic arthritis, brain abscess, and ARF (acute renal failure). Rhabdomyolysis may occur

Diagnosis

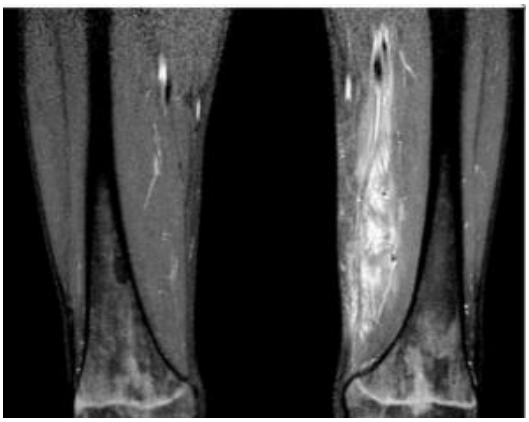
- Early pyomyositis is difficult to distinguish from other possible diagnoses (thrombophlebitis, muscle hematoma, muscle rupture, fever of unknown origin osteomyelitis).
- Iliacus pyomyositis may mimic septic arthritis of the hip, and iliopsoas pyomyositis may mimic appendicitis.
- Imaging:
  - MRI is the gold standard technique (may show muscle enhancement and intramuscular abscesses- see next).
  - CT (may detect muscle swelling and well-defined abscesses).
  - Ultrasound can be helpful for Dx and Rx
- Microbiology:
  - diagnostic aspirates before starting Abx to get a specific culture
  - Blood cultures are only positive in 10% of tropical cases and 35% of temperate cases!



Seeing this, you might assume the patient has cellulitis or some other infection, as it is still in the early stage. This is where an MRI is useful.

Pyomyositis in the inner thigh in a young patient with severe aplastic anemia (E. coli)

The white area is where all of the bacteria has been sequestered. The abscess spans along the side of this skeletal muscle.



Management

- Antibiotics— Stage 1 use antibiotics alone
- HOWEVER, most patients present with stage 2 or 3 of the disease and require antibiotics and drainage.
- Empiric therapy for these stages:
  - Directed against S. aureus and streptococci (flucloxacillin or vancomycin if MRSA is suspected or there is a risk of MRSA).
  - Immunocompromised patients -> broader Abx such as piperacillin– tazobactam ± vancomycin.
- Once culture is out -> Tailored Abx for 3-4 weeks
- Drainage—percutaneous drainage Dx and Rx (drainage and send drain sample for Micro). The drainage may be CT-guided or ultrasound-guided.