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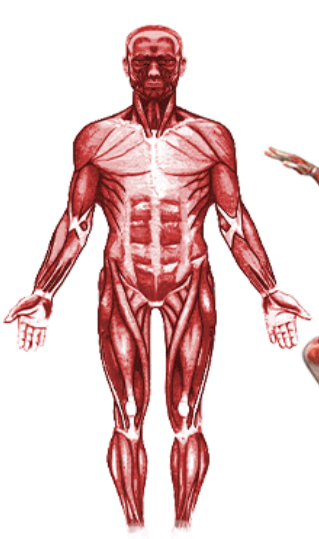

MSS

Musculoskeletal System

Microbiology

Doctor 2018 | Medicine | JU

Done by

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Hi everyone ☺

This is the first sheet from the FINAL EXAM material, which will continue our discussion about **infections associated with Bullae**

*Firstly, let us recall what is a bullous? It **is a fluid filled lesion**.

It is the **mark** that will restrict your diagnosis of your patient to certain infectious agents that are known to form these bullae at the infection site; mainly **G+ve** bacteria (cocci and rods) .

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*

We have already discussed SSSS, and now we will continue with other infections.

Necrotizing Fasciitis

It is **a RAPIDLY** progressing infection in the area between the fascia and deep subcutanous tissue. (Rapidly means two **important** things :

- ✓ Rapidly spreading through the tissue
- ✓ Once the symptoms start to appear (at first they are not there), they progress really quickly.)

- The only limiting factor for this rapid progression is the deep fascial bands, (remember how extremities are divided into compartments by fibrous tissue), once an infection occurs in a certain compartment, it will fill the entire compartment very rapidly. SO, **the more compartments there are, the less progressing will occur**, since they are separated by fibrous bands that will restrict infections from progressing. These bands are present in the head but not in the extremities (thus extremities are more susceptable).

->50% in extremities
- 20% in perineum or buttocks (especially in DM and alcoholics)
- 18% in trunk
- 9% head and neck

The order is according to the site of N.F

- ✓ **facultative anaerobes** are the first to invade the area to prime it for stronger and prepared soldiers (**obligate anaerobes**). Because of the difference in their oxygen requirements, facultative anaerobes will consume all the oxygen in the area for obligate anaerobic bacteria to survive and destruct the area (think of it in this way, but remember that these microorganisms are just looking for their survival requirements, there is no actual conspiracy between them to kill us ☹)

- ✓ **GAS (group A strep.)** are the facultative anaerobic bacteria associated with necrotizing fasciitis.

- ✓ In the US, the estimated incidence of invasive GAS infection is 3.5 cases per 100,000 persons - necrotizing infections account for 6% of these (so it is a rare condition).

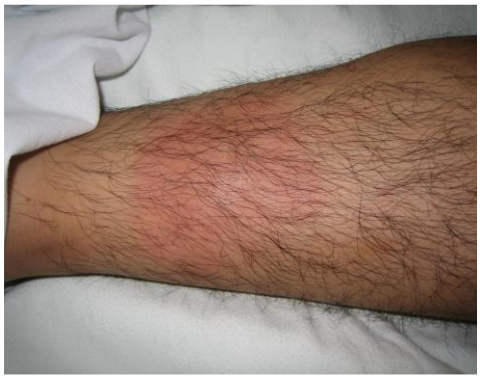
Risk factors associated with Necrotizing Fasciitis:

Chronic malnutrition: --*Hypoalbuminemia: immunity will decline because the body isn't synthesizing enough proteins. --* Alcoholism --*Cirrhosis  These will affect the production of acute phase proteins and others from the liver /reduced detoxification	**Patient conditions**: ->50 year olds: declined immunity - Obesity: can cause poor circulation (reduced blood perfusion)	**Poor blood supply**: - Heart disease -PVD (peripheral vascular disease) نقص التروية in limbs *remember that they are the most common sites for necrotizing fasciitis. - DM

Immune compromised: - cancer - steroid therapy	**Skin trauma in last 3 months**: - burns - penetrating trauma -IV drugs -surgery	**Breaks in the mucosa of the GI or GU tracts (anaerobs)**: - colon cancer (can cause ulcer) - diverticulae -hemorrhoids of fissues -Urethral tears

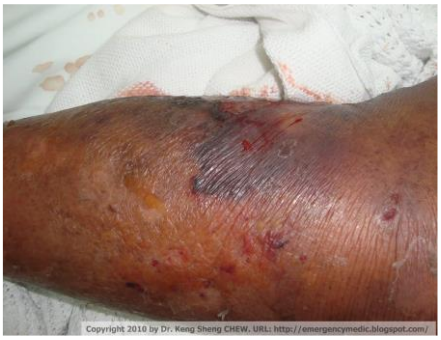
SIGNS &SYMPTOMS (occur in order) :

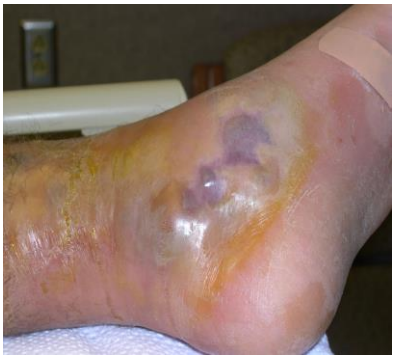
- **Pain and tenderness (Good sign; the condition is still early on)**



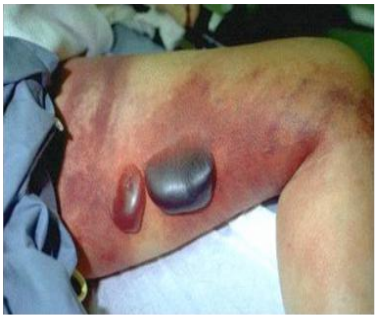
Look! There is nothing that tells you that you should be worried, many things will come to mind, such as target legions, allergy due to histamine release and many more.
The patient will come to your clinic with a pain in his/her leg for example, early on you can't see an obvious mark for necrotizing fasciitis , so try to take the full history from your patient, you might catch one of the previously mentioned risk factors . Since it is a rare condition, you will not think of it as your first intention.

- **Unexplained fever**
  Early Diagnosis maybe difficult when pain or unexplained fever is the only presented manifestation, remember that the infection is deep; might not present with pain yet).
- Later on: **swelling** (infection at this point is severe, it has taken its time and appears on the surface, we are late ☹)
- **Dark red induration** (indicates hemorrhage and early necrosis); part of the compartment syndrome. Insufficient blood supply reaches the infected compartment, making it a favorable site for anaerobes growth where they release gases.
- **BULLAE**, filled with blueish or purple fluid, which is basically all the dead cells and the debris that is coming out of the deep fascia.
- **Thrombosis** of dermal blood vessels (The affected area becomes anesthetic as a result of small vessel thrombosis and destruction of superficial nerves)
- Extension to deep fascia with rapid spread.





Swelling & Dark red induration → Progressing to → Bullae & thrombosis



Last stage

- Necrotizing fasciitis has the components of gas gangrene in it, if there is an involvement of anaerobes > gas gangrene will develop.
- Keep in your mind that gas gangrene can develop as a separate pathologic condition without passing through necrotizing fasciitis.

Microbiology causes:

A) Polymicrobial (**Type I necrotizing fasciitis** involves at least one anaerobic species (Bacteroides or Peptostreptococcus spp. which are part of Normal flora in the GI tract), as well as one or more facultative anaerobic species (e.g. non-GAS, E.coli, Enterobacter, Klebsiella, Proteus spp.).

Notice that all of them are enteric bacteria

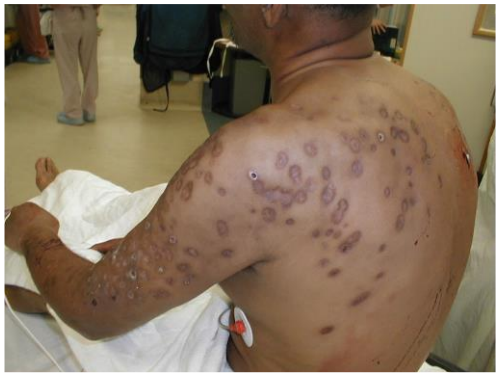
- Usually a mix of aerobic and anaerobic bacteria (clostridium perfringens)
- Break in Gastrointestinal or Genitourinary mucosa, typically on trunk and extremities (bacteria ascend up to the deep fascia)
- Mixed infection usually have comorbid states (DM, PVD, immunocompromised)

**21% mortality rate with optimal treatment, while in type II the mortality rate with optimal treatment is 50% (worse).

B) **Type II necrotizing fasciitis** is usually caused by **GAS alone** or in combination with other species (e.g. S.aureus). Group A, Beta hemolytic strep (GAS), S. pyogenes +- S. aureus (the connection here is that these are skin representatives, so the bacteria in this type descend down to the deep fascia).

- Strains of MRSA that produce the **Panton Valentine leucocidin (PVL)** toxin have been reported to cause necrotizing fasciitis (also necrotizing pneumonia).

- ✓ Usually following trauma in otherwise healthy individual or IV **drug abusers** (skin popping), they keep injecting themselves on the same area over and over until it becomes indurated (common case), not like the previous picture of a co-morbid patient with gastric, genitourinary tract disruption.
- ✓ Fasciitis progresses to skin contusions due to seeding by transient bacteremia
- ✓ Gas production if mixed infections occurs >> (you need anaerobes), the patient will not have gas production in type II unless it progressed to anaerobic infection.
- ✓ Severe toxicity and renal impairments →shock (caused by lipoteichoic acid)
- ✓ Myositis (destruction of muscle tissue markedly increases CPK)
- ✓ Mortality is high (up to 50% even with optimal treatment!!)



As drug abuse is becoming a common case, you should be familiar with this skin popping

Necrotizing fasciitis caused by mixed aerobic-anaerobic bacteria **begins with a breach in the integrity of a mucous membrane barrier, such as the mucosa of the gastrointestinal or genitourinary tract.

* The portal can be a malignancy, a diverticulum, a hemorrhoid, an anal fissure, or a urethral tear.

*Other predisposing factors include peripheral vascular disease, diabetes mellitus, surgery, and penetrating injury to the abdomen (these risk factors were mentioned in a previous table).

>>Leakage into the **perineal area** results in a syndrome called **Fournier's gangrene**; a form of necrotizing fasciitis that affects the male genitals and is usually polymicrobial

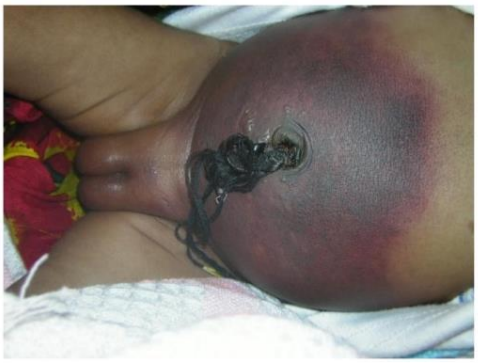
(Part of GIT), characterized by massive swelling of the scrotum and penis with extension into the perineum or the abdominal wall and legs.

Other forms:

-- **Craniofacial necrotizing fasciitis** is usually associated with trauma and caused by GAS (skin).

-- **Cervical necrotizing fasciitis** is usually associated with dental or pharyngeal infections and is Polymicrobial (part of GI tract).

--In newborns, necrotizing fasciitis may complicate omphalitis and spread to involve the abdominal wall, flanks, and chest wall.



The problem in this case is with aseptic techniques after delivery, when the umbilicus becomes colonized with many different types of bacteria. A study shows that using chlorhexidine as a topical antiseptic will reduce neonatal mortality and omphalitis even greater.

Dx of necrotizing fasciitis

--Clinical findings are suggestive + surgical exploration/sample:

a) Altered mental status (systemic involvement)

b) Soft tissue infection signs (redness/swelling/pain) **70-80% of cases**

- Bullae Pain is typically exaggerated out of exam

- Tenderness is outside the red erythematous borders (indicates further progress)

-- are only seen in ¼ of cases

a) Fever in less than 50% of the cases!
b) Low BP in 21% of cases (releasing bacterial protein into the blood stream is the cause of decreased blood pressure)
c) Crepitation (feeling of air pockets under skin upon examination) in 20% of cases

Rx - EMPIRIC

- You have to cover G+ves + G-ves ± MRSA .

**3 drug combo/ 2 drug combo/ 1 drug (each +MRSA coverage)

- ✓ **3 drug combo**:

1-**anaerobic coverage** (and inhibits ribosomal production of toxins) = **Clindamycin**

2-**G +ve coverage** (**Ampicillin-sulbactam**) or (**Piperacillin-tazobactam** →antipseudomonal)

3-**G-vecoverage** (**Ciprofloxacin**)

- ✓ **2 drug combo**>> (**Cefotaxime covers** G+ and G- bacteria) + (anaerobic coverage by **metronidazole or clindamycin).**
- ✓ **1 drug combo** (**Carbapenem/Imipenem, meropenem, ertapenem)**
- ✓ The MRSA coverage to be added to any chosen empiric regimen includes **Vancomycin or Linezolid**.
- ✓ Hemorrhagic bullae may indicate presence of vibrio vulnificus, in this case **doxycycline** is used.

Rx.

Surgical debridement and treatment in hospital ER, surgical exploration and debridement>> removing the fatalized tissue that anaerobes use to cause necrosis which might improve systemic drug delivery as well as the immune system.

1-confirm the diagnosis (send a sample to a microbiology lab to do the sensitivity profile for definite treatment) 2-mainstay of therapy 3-Reducing compartment pressure in extremities

- ✓ Prophylaxis for exposed house hold members (**penicillin, rifampin, clindamycin or azirthromycin**)

Gas gangrene (Clostridium infection)

- ✓ Gas production due to anaerobic bacteria
- ✓ G+ve rods = toxin formation (few exceptions)
- ✓ Typically due to contaminated DEEP wounds -no oxygen- (surgery, car crash..etc) to introduce spores of G+ve clostridia into the wound (from environment), these spores will then germinate.
- ✓ Also progresses similarly to other types: fasciitis →toxemia →organ failure (it skips all the phases of necrotizing fasciitis to reach the last phase).

- ✓ Gangrene usually occurs following muscle injury and contamination of the wound by soil or foreign material containing clostridial spores. (**typical scenario**)
- ✓ C.perfringens is the predominant cause (anaerobic G+ve spore forming rods) (80–95%), and its pathological effects are mediated by **α and λ toxins.**

Alpha toxin

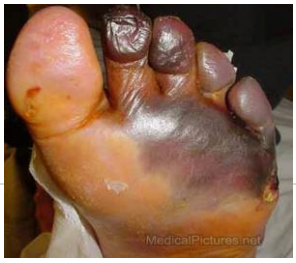
- Alpha toxins are zinc-dependent, phospholipase C (PLC) with sphingomyelinase and lectinase activity (break down the fascia) and approximately 42.528 kDa.
- Alpha toxins are responsible for intravascular hemolysis, platelet aggregation, and capillary damage →loss of blood supply = loss of oxygen.
- These factors stop leukocytes and oxygen from getting to the site of infection → favorable for the proliferation of C. perfringens.
- Alpha toxins help in immune evasion by interfering with neutrophil migration to the infected tissue, minimizing the number of mature cells in the bone marrow, and causing the accumulation of neutrophils in adjacent vessels.

Etiology and pathogenesis

-- Spontaneous or non-traumatic gas gangrene may occur in the absence of an obvious wound. This form is usually caused by **C.septicum** and is associated with intestinal abnormalities, e.g. colonic cancer, diverticulitis, bowel infarction, necrotizing enterocolitis (if it travels through the blood, it can seed to the deep fascia causing gas gangrene without trauma).

Clinical features

- The incubation period is **usually 2–3days but may be shorter.**
- Patients present with acute onset of excruciating pain and signs of shock (fever, tachycardia, hypotension, jaundice, renal failure).
- Local edema and tenderness may be the only early signs, or there may be an open wound, herniation of muscle, a serosanguinous and foul smelling discharge, crepitus, skin discoloration, and necrosis.
- Progression is rapid, and death may occur within hours.



Diagnosis

- The diagnosis is usually **clinical** but may be confirmed by Gram stain of the wound or aspirate.
- Liquid anaerobic cultures may be positive within 6hrs.
- Plain radiographs may show gas in the affected tissues.

Management

- Emergency surgical exploration and debridement of the affected area should be performed.
- Empirical antibiotic therapy with **piperacillin–tazobactam plus vancomycin** (if risk of MRSA) is appropriate, pending cultures.
- Definitive treatment for clostridial myonecrosis is with **penicillin and clindamycin**.
- Hyperbaric oxygen therapy is not recommended, as it has unproven benefits and may also delay resuscitation/surgery treatment.

Cellulitis: (NOT BULLOUS FORMING)

Cellulitis	*Staphylococcus* spp., *Streptococcus* spp., various other bacteria

Usually caused by indigenous flora colonizing the skin (s. *aureus* and s. *pyogenes*) mainly, or by a variety of non-colonizing exogenous bacteria.

Examples of exogenous bacteria: Enterobacteriaceae, L. pneumophila, A. hydrophila, V. vulnificus, and C. neoformans.

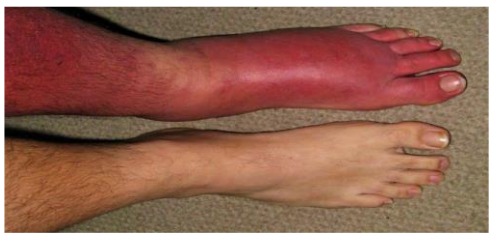
These organisms are introduced to the dermis, and since we have nerves and blood vessels there, the main symptoms are pain, erythema and swelling (inflammation signs). So the keyword for cellulitis is **ACUTE INFLAMMATORY CONDITION.**

To detect the source of the exogenous bacteria involved in cellulitis, a thorough history (+ epidemiologic data) is needed, as these bacteria occupy small niches in nature.

- Supporting data which gives clues to other exogenous causes include:

• Physical activities - trauma - water contact - animal, insect, or human bites - immunosuppression.

Notice that cellulitis is a spreading, erythematous, hot & tender lesion; very painful!



Clinical features:

• → Spreading, erythematous, hot and tender lesion.

• → Usually accompanied by systemic symptoms.

• The Dx is usually clinical, as cultures are rarely positive*(explanation below) (only 20%) - this suggests bacterial numbers are low and local to tissue but the inflammatory effect is exaggerated due to toxins.

• Can produce cultures if there is drainage or a site of entry is seen.

Remember, acute, spreading and inflammation is the major mode of pathology here.

• Treatment—empiric treatment:

• IV flucloxacillin or clindamycin.

• Vancomycin, teicoplanin, linezolid, or daptomycin are for MRSA cellulitis.

• Gram-negative and anaerobic cover may be required for cellulitis in the context of diabetic ulcers (ulcer + cellulitis is the common case).

• The affected limb should be immobilized and elevated.

---

*the cultures are rarely positive since the infection happens in the dermis so we need to access it, and even if we did , the area is so swollen and diluted to the point where the bacteria won't appear.

Remember: bioburden is how much we can tolerate a certain organism. When the skin is disrupted, our bioburden becomes lower so we will be infected easily. Also, when a foreign body is inserted in the body, fewer organisms are required to cause the infection.

Pathogenesis

• Cellulitis caused by S. aureus spreads from a central localized infection (abscess, folliculitis, or an infected foreign body (see the box above) such as a splinter, a prosthetic device, or an IV catheter).

• MRSA is rapidly replacing methicillin-sensitive S. aureus (MSSA) as a cause of cellulitis in both inpatient and outpatient settings.

• Recurrence is seen in patients with eosinophilia.

• Cellulitis due to S. pyogenes is more rapidly spreading; diffuse process that is frequently associated with lymphangitis and fever. (streptococci use the lymphatic system in their spread).

• Recurrent streptococcal cellulitis of the lower extremities may be caused by organisms of group A, C, or G in association with chronic venous stasis or with saphenous venectomy for coronary artery bypass surgery. (In a bypass surgery we take a vain from the lower limb, which can lead to venous congestion and lymphatic congestion; perfect area for streptococci)

(Anything related to lymph should lead us to think of GAS).

• Also, recurrent streptococcal cellulitis is seen among patients with chronic lymphedema resulting from elephantiasis, lymph node dissection, or Milroy's disease; in both cases is due to poor drainage of limb.

• This is all due to the fact that streptococci use the lymphatic system in their spread.

Slide 35, 36, 37 and 46 : the doctor said we can read them alone; so refer to them.

P. aeruginosa

• Causes 3 types of infections in MSS • 1→ Ecthyma gangrenosum in neutropenic patients • 2→ Hot-tub folliculitis (discussed below) • 3→ Cellulitis following penetrating injury (usually stepping on a nail or surgery) **(wound + air+ water = aeruginosa)**

• Commonly seen in hospital setting/immune compromised patients.

• Rx: surgical inspection and drainage/debridement (recall biofilm of pseudomonas).

• Empirical treatment: * -Aminoglycoside - a third-generation cephalosporin (ceftazidime, cefoperazone, or cefotaxime),* -semisynthetic penicillin (ticarcillin, mezlocillin, or piperacillin), *or a fluoroquinolone (not in pediatric patient); pseudomonas is notoriously hard to treat.

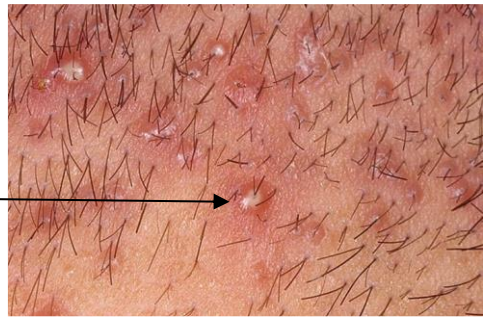
Folliculitis:

Folliculitis	
Furunculosis	*S. aureus*
Hot-tub folliculitis	*Pseudomonas aeruginosa*
Swimmer's itch	*Schistosoma* spp.
Acne vulgaris	*Propionibacterium acnes*

• **A superficial infection of the hair follicles and apocrine structures**.

• Causative organisms**: S. aureus (commonest)**, **P. aeruginosa** ('hot tub' folliculitis), Enterobacteriaceae (complication of acne), Candida spp., and M. furfur (in patients taking corticosteroids).

• Eosinophilic pustular folliculitis occurs in AIDS patients.



• Clinically: lesions consist of small, erythematous, pruritic papules, often with a central pustule.

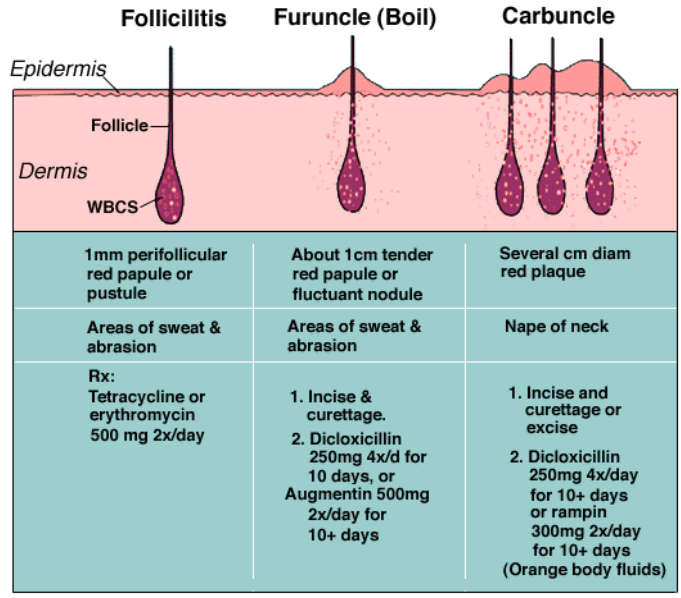
• Treatment—empiric treatment is with oral flucloxacillin.

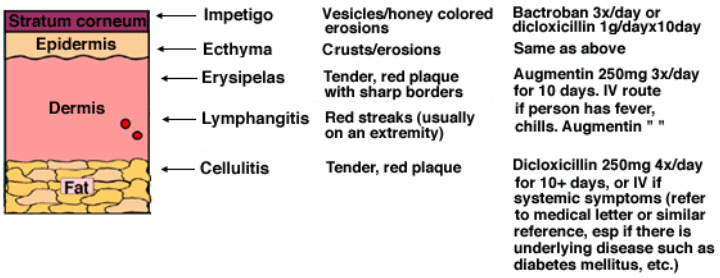
• If the clinical response is slow → consider other pathogens.

• Chronic folliculitis is uncommon except in acne vulgaris, where constituents of the normal flora (e.g., Propionibacterium acnes) may play a role.

• Sebaceous glands that empty into the hair follicle maybe blocked and cause swelling that is similar to an abscess (sebaceous cyst).

Bacterial Infections





Development of folliculitis

Folliculitis: 1mm of perifolicular red papule or pustule, small that can be treated with just antimicrobials.

Furuncle: more than one folliculitis joined together, also called boil.

Carbuncle: several furuncles.

Both Furuncle and Carbuncle need drainage and then antimicrobials.

The doctor only said what's in the box about the development of folliculitis, but I will put what's in the slides.

Furuncles and Carbuncles

• A furuncle (boil) is a deep inflammatory nodule that usually develops from preceding folliculitis. • Occur in areas of the hairy skin, e.g. face, neck, axillae, and buttocks. • A carbuncle is a larger, deeper lesion made of multiple abscesses extending into the subcutaneous fat. • Usually occur at the nape of the neck, on the back, or on the thighs. • Patients may be systemically unwell. • Outbreaks of furunculosis caused by MSSA and MRSA have been described in groups of individuals with close contact, e.g. families, prisons, and sports teams.

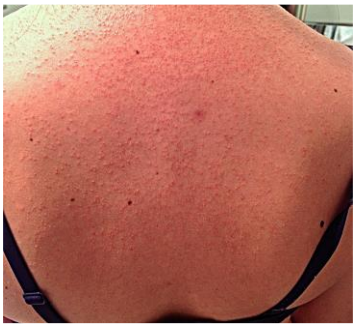
Rx for Furuncles

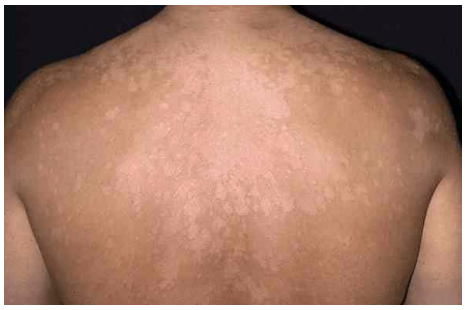
• Application of moist heat promotes localization and spontaneous drainage. • Large lesions require surgical drainage. • Systemic antibiotics are indicated→ 1- fever; 2-cellulitis 3-lesions are located near the nose or lip. • Outbreaks control with chlorhexidine soaps, stopping the sharing of clothing articles or towels, and decolonization of staph.

Hot tub folliculitis

Notice:* All follicles are affected, *Patient is young,* Usually self-limited, and happens in waters that are not sufficiently chlorinated and maintained at 37 Celsius.

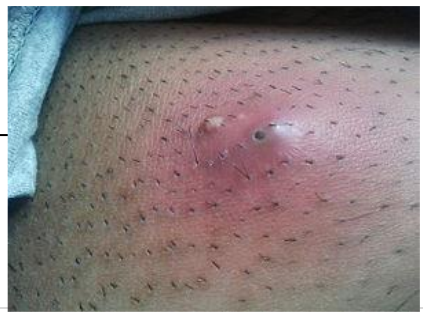
Remember: p.*aeruginosa*





This is not folliculitis, its Tinea veriscolor –M. furfur (fungal infection)

Cutaneous abscesses

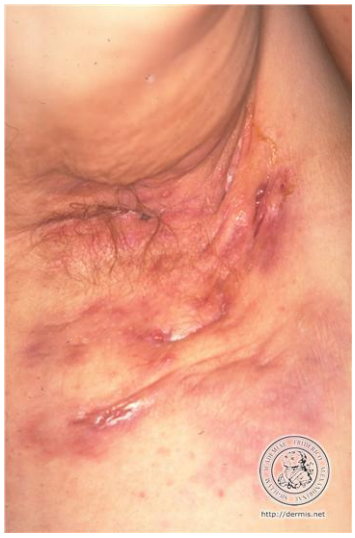


Notice: raised lesion, white head Hair follicle might be port of entry, the pus is pushed to the outside rather than to the inside because of pressure

Hidradenitis Suppurativa

- **Infection of sweat glands (hidradenitis suppurativa) can also mimic infection of hair follicles, particularly in the axillae.**

Usually in sweaty areas where skin folds (axilla, Buttocks, breasts, inner thighs)



ANTIBACTERIAL AGENTS

Table 5.1 Principal types of antibacterial agent (other than agents used exclusively in mycobacterial infection)

Agent	Usual activity[a] against: Site of action	Staphylococci	Streptococci	Enterobacteria	*Pseudomonas aeruginosa*	*Mycobacterium tuberculosis*	Anaerobes
Penicillins	Cell wall	+R	+	V	V	–	+[b]
Cephalosporins	Cell wall	+	+	+	V	–	+[b]
Other β-lactam agents	Cell wall	V	V	+	V	–	V
Glycopeptides	Cell wall	+	+	–	–	–	+[c]
Tetracyclines	Ribosome	+R	+R	+R	–	–	+R
Chloramphenicol	Ribosome	+	+	+	–	–	–
Aminoglycosides	Ribosome	+	–	+	V	V	–
Macrolides	Ribosome	+	+	–	–	–	+
Lincosamides	Ribosome	+	+	–	–	–	+
Fusidic acid	Ribosome	+	+	–	–	+	+
Oxazolidinones	Ribosome	+	+	–	–	–	–
Streptogramins	Ribosome	+	+[d]	–	–	–	
Rifamycins	RNA synthesis	+	+	+	–	+	+
Sulphonamides	Folate metabolism	+R	+R	+R	–	–	–
Diaminopyrimidines	Folate metabolism	+	+	+R	–	–	–
Quinolones	DNA synthesis	V	V	+	V	V	–
Nitrofurans	DNA synthesis	–	–	+	–	–	+
Nitroimidazoles	DNA synthesis	–	–	–	–	–	+

[a]Usual spectrum of intrinsic activity
[b]Poor activity against anaerobes of the *Bacteroides fragilis* group.
[c]Poor activity against most Gram-negative anaerobes.
[d]Poor activity against *Enterococcus faecalis*.
+, active; –, inactive; V, variable activity among different agents of the group. +R indicates that acquired resistance is very common.

The doctor said that this table will help us to memorize antibacterial agents.

GOOD LUCK ☺

Refer to the last 3 slides ☹ ,