Microbiology

Doctor 2017 | Medicine | JU

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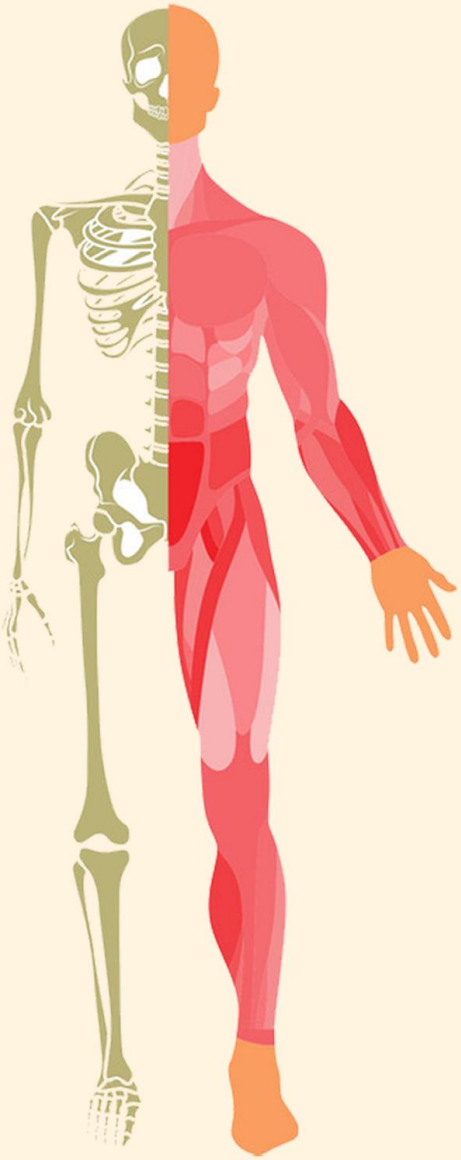


1st system - MSS

*We'll continue our discussion on **bullous forming skin infections**, remember we took the first type in the last lecture (SSSS → Staph. Scalded skin Syndrome).*

Necrotizing Fasciitis

- Where? In the area **between fascia and subcutaneous tissue**.
- Cause? All cases originate from ***deep*** **bacterial** infiltration, specifically two major types: skin flora or mixed aerobic and anaerobic bacteria, and these infiltrate from two major locations:
  - **Skin** ex. extremities, trunk, skull
  - **Lumen** ex. trunk, perineal area, around the mouth

  This point will be discussed further below.

Necrotizing fasciitis	
Streptococcal gangrene	*S. pyogenes*
Fournier's gangrene	Mixed aerobic and anaerobic bacteria
Staphylococcal necrotizing fasciitis	Methicillin-resistant *S. aureus*

- Differentiating features? **3** main features:
  - **Rapidly Progressing**
  - **Masked** initial symptoms
  - **High mortality rate**
- Note: **Fibrous bands** in the area between fascia and subcutaneous tissue **prevents** spread of infection (these bands are present in the head but not in the extremities, thus extremities are more susceptible)
  - **>50% in extremities**
  - 20% in perineum or buttocks (especially in diabetics and alcoholics)
  - 18% in trunk
  - **9% head and neck**

  In general, subcutaneous spread of infections is faster and more common in the extremities than other body areas.

- Note: In the USA, the estimated incidence of invasive GAS infection is 3.5 cases per 100,000 persons—necrotizing infections account for 6% of these.

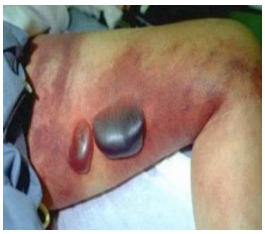
- Risk factors:
  - **Breaks in the mucosa** of GI/GU tracts: like tears in the anus/urethra that help infectious bacteria infiltrate into deep layers of skin.
  - **Low perfusion**: this results in
    - Less O_2 → anaerobes flourish.
    - Less drainage → more nutrients for infectious bacteria.
    - Necrosis.
    - Less leukocyte infiltration → **reduced immunity**.
  - **Reduced immunity**: caused by low perfusion but can also be caused by **Diabetes Mellitus** and **age (>50)**.
  - **Obesity** causes skin in the trunk to be further away from the heart, which leads to: Low Perfusion.
  - **Skin trauma** in the last **3 months** (not later).
  - **Malnutrition** can lead to hypoalbuminemia → less immunoglobins/collagen synthesis.

Note: these risk factors can also apply to diabetic foot and cellulitis.

Risk factors associated with necrotizing fasciitis

Malnutrition	*Patient conditions*	*Immune compromised*	*Poor blood supply*	*Skin trauma in last 3 months*	*Breaks in mucosa of GI or GU tracts (anaerobes)*
-Hypo-albuminemia -Alcoholism -Cirrhosis	- >50 Year olds -Obesity	-Cancer -Steroid therapy	-Heart disease -PVD -DM	-Burns -penetrating trauma -IV drugs -surgery	-colon cancer -diverticulae hemorrhoids or fissues -urethral tears

- Signs and Symptoms: **occur in order**, but first, please note that one major symptom of skin infections in general is absent; there is **NO RASH** or any other skin manifestations in the early stages (because the infection is deep and not superficial), which can make its diagnosis especially hard.
  1) **Pain/tenderness**, but this does not help much in Dx because pain can be caused by maaaaany causes such as trauma, allergy, immunologic conditions etc., plus the patient may not remember if or when a deep skin breach happened in that area, because as we said, the breach needs to have happened 3 months before or earlier.
  2) **Unexplained fever**: again, early diagnosis may be difficult when pain or unexplained fever is the only presenting manifestation (remember the infection is deep and might not present with pain yet).
  3) **Swelling**: infection at this point is severe (this happens after pain/fever).
  4) **Dark red induration** indicates hemorrhage and early necrosis.
  5) **BULLAE** formation: filled with blueish or purple fluid, does not happen in all cases, but if the infection includes bacteria that is <u>anaerobic</u> (lumen), bullae will form. →



  6) **Thrombosis** of dermal blood vessels: the affected area becomes anesthetic as a result of small vessel thromboses and destruction of superficial nerves.
  7) **<u>Extension to deep fascia with rapid spread.</u>**
  8) Most progressed symptoms: **toxicity, shock, and multi organ failures** (when infection has progressed beyond local infection site).

- Microbial Causes: there are two main types of necrotizing fasciitis (NF):

1. **Type I NF: Polymicrobial**

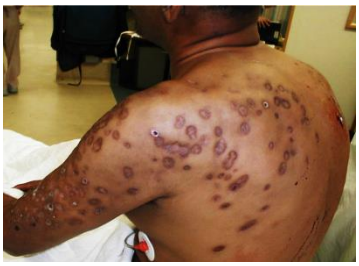
   21% mortality rate with **<u>optimal</u>** treatment!

   Usually a **<u>mix</u>** <u>of aerobic and anaerobic bacteria</u> **<u>from the gut lumen</u>**:
   a) At least one obligate anaerobic species besides **Clostridium** perfringens (Bacteroides fragilis or Peptostreptococcus), as well as
   b) one or more facultative anaerobic species (→ **aerobic**): non-GAS, **E. coli**, Enterobacter, Klebsiella, Proteus.

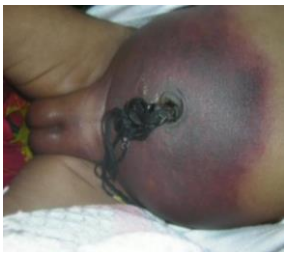
   <u>Pathophysiology</u>: Facultative anaerobes like E. coli and Klebsiella start destroying the surrounding tissue → perfusion starts to drop → less O_2 → anaerobes thrive.
   This process applies wherever anaerobic infection takes place ex. dental caries (tooth decay)

2. **Type II NF: GAS** (sometimes with other **skin flora** like Staph)
   Up to **50% mortality** rate even with optimal treatment!
   Usually caused by **GAS** (Group A Strep) alone or in combination with other species like S. aureus. Strains of **MRSA** that produce the Panton Valentine Leukocidin (PVL) toxin have been reported to cause necrotizing fasciitis (also necrotizing pneumonia). Pathophysiology:
   1) When the skin is penetrated, GAS enters but so does staph, and just like in polymicrobial NF where one type of bacteria helps set the stage for another, a deep staph infection helps the GAS infection take hold.
   2) Fasciitis progresses to skin contusions due to seeding by transient bacteria.
   3) Gas production if mixed infections occur!! (gas gangrene from anaerobes).
   4) Severe toxicity and renal impairments → shock
      Myositis (destruction of muscle tissue markedly increases creatine phosphokinase (CPK))

   Skin popping: IV drug abusers keep injecting themselves ignoring aseptic techniques → introduce skin flora into deep subQ tissue.



3. Other forms: it's still the same NF but different names are assigned to different locations or conditions.
   a) **Omphalitis**: In the newborn, infection of the umbilical cords is called omphalitis, necrotizing fasciitis may complicate omphalitis and spread to involve the abdominal wall, flanks, and chest wall, and is one of the causes of early infant mortality.



   b) **Fournier's gangrene** is a form of necrotizing fasciitis that affects the perineal area due to urethral tears/surgery/other and that the perineal area normally has low perfusion rate. Fournier's is usually polymicrobial (lumen).
   c) **Craniofacial** NF: usually associated with trauma and caused by GAS (skin).
   d) **Cervical** NF: usually associated with dental (ex. due to careless dentist) or pharyngeal infections and is polymicrobial (part of GI tract).

REMEMBER! 1. Gas production is by anaerobes.

2. Anaerobes present = Type 1 NF = mixed infection.

- Dx:

a) **Clinical findings** are suggestive (do not really isolate NF)
    - Soft tissue infection signs (redness/swelling/pain) in 70-80% of cases.
    - Bullae show an advanced stage, usually not reached before clinical exam.
    - Tenderness outside the red erythematous borders.
    - Fever in less than 50% of the cases! (meaning that systemic signs do not show in most cases).
    - Low BP in 21%
    - Crepitation (feeling of air pockets under skin upon examination) in 20%
b) Altered mental status (systemic involvement)
c) **Surgical exploration/sample**: this is the best way.

- Rx:

a) **Empiric**: means we treat from experience not from diagnosis, we keep the drugs that work and change those which don't. In the case of NF, we aim our treatment at G – 's, G+'s, and anaerobic bacteria, basically everything. Why? Because we don't know which type (I or II) we're dealing with without surgery, consequently, we don't know what bacteria are deep inside the skin. Therefore, we either use a drug or two with a broad target, or several drugs with a specific target for each. Let's specify more:
   We can administer a 3-drug combo, 2-drug combo or only 1 drug, each with an additional obligatory MRSA coverage:
    - 3-drug combo:
        1. Anaerobic (and inhibits ribosomal production of toxins): Clindamycin
        2. G +ve: Ampicillin
        3. G-ve: Ciprofloxacin
    - 2-drug combo:
        1. Anaerobic: Metronidazole or Clindamycin
        2. G+ and G -: Cefotaxime
    - 1-drug: Carbapenem
    - MRSA coverage: Vancomycin
b) Surgical debridement, is the mainstay of NF therapy, used to:
    1. Confirm the diagnosis.
    2. Reduce compartment pressure in extremities.
c) Prophylaxis for exposed house hold members: Penicillin

**Note: the Dr mentions a ton of different abX in both empiric Rx and prophylaxis, but I think 98% of us are incapable of memorizing them for 1 mark only (we all know who the 2% includes, god help u ppl), so I included the first example of each only. ☺*

Gas Gangrene (Clostridium infection)

Gas production due to **G + anaerobic** bacteria, specifically **Clostridium Perfringens** (80–95% of cases). It occurs by contamination of deep tissue plus O_2 supply reduction, usually due to trauma (like from a car accident) along with spore infiltration from the environment like soil. Trauma + low O_2 → perfect environment for anaerobes.

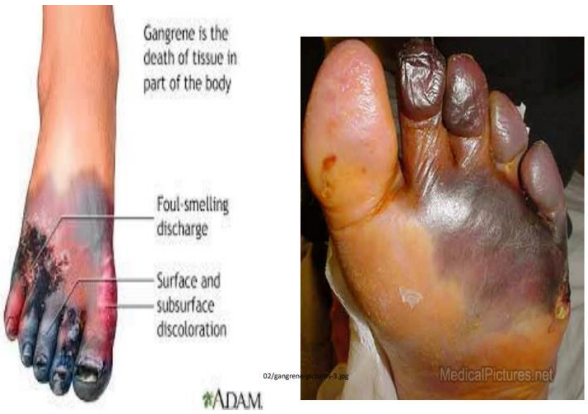
Also progresses similarly to other types of infection: fasciitis → toxemia → organ failure.

Alpha toxin

C. perfringens pathological effects are mediated by α and λ toxins. α toxin is a phospholipase C (PLC) with sphingomyelinase and lectinase activity and likes to target small blood vessels → **intravascular hemolysis**, platelet aggregation, and capillary damage → loss of blood supply → **loss of oxygen supply + less leukocytes** → favorable for the proliferation of C. perfringens.

***NON-traumatic** gas gangrene may also occur, it is associated with Clostridia other than Perfringens and intestinal abnormalities.

Clinical features



- **2-3 days incubation period**. (Remember in NF it was about 3 months)
- 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 (check for an open wound).
- Herniation of muscle, foul smelling discharge, crepitus, skin discoloration, and **EARLY skin necrosis** (unlike NF). Progression is rapid, and death may occur within hours.

Diagnosis

- **Clinical**
- Confirmed by Gram stain of the wound or aspirate.
- Plain radiographs may show gas in the affected tissue.

Management

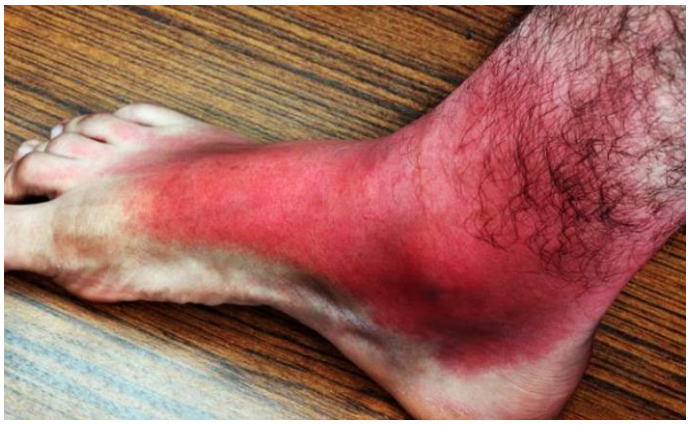
- Emergency **surgical debridement**.
- Empirical **antibiotic** therapy with Piperacillin plus Vancomycin (if risk of MRSA)
  Remember: **G+ ANAEROBES are the target!**
- *Hyperbaric oxygen therapy is not recommended, as it has unproven benefits, may also delay resuscitation/surgery treatment.

Cellulitis

Cellulitis is an **acute strong inflammation** of the skin that occurs within days only and it is the 2nd most common form of infection after impetigo. Pathogenesis is by the penetration of a **foreign body** through the skin, this can either introduce **skin flora** like Staph/Strep into the skin, or other bacteria from the **environment** like Pseudomonas.

*Note: Strep spreads via lymph.

Dx: Clinical: easy to identify, characterized by a rapidly spreading, erythematous, hot, tender lesion. Cultures are rarely positive (only 20%), this suggests **bacterial numbers are low** and local to tissue and that the **inflammatory effect is exaggerated** due to toxins.



Rx: NO TOPICAL Rx! Must be systemic, Abx are administered like Penicillins in addition to Vancomycin for MRSA. Sometimes Pseudomonas coverage is recommended too.

Pseudomonas

A very **drug-resistant** (due to **biofilm** and 1ry resistance), **obligate aerobe**, **G-** bacterium that is commonly seen in hospital settings due to its love for **moisture and oxygen** (ventilators).

Causes 3 types of infections in MSS:

1. **Ecthyma** gangrenosum in neutropenic patients (1st lec.)
2. **Cellulitis** following penetrating injury (this lec.)
3. Hot-tub **folliculitis** (self-reading: read below)

Rx:

- Surgical inspection and drainage/debridement (recall biofilm of pseudomonas)
- **Empirical treatment**:
    a) Aminoglycoside
    b) A 3rd-generation Cephalosporin
    c) Semisynthetic penicillin (Piperacillin)
    d) Fluoroquinolone (not in pediatric patient)

    Pseudomonas is notoriously hard to treat.

*The Dr mentioned that the rest of the slides were self-reading material. The slides cover folliculitis, M. furfur, cutaneous abscesses, furuncles, carbuncles, Erysipelas, and swimmer's itch in about 15 slides, don't worry about 7 of them are picture slides. Stay Strong! ☺