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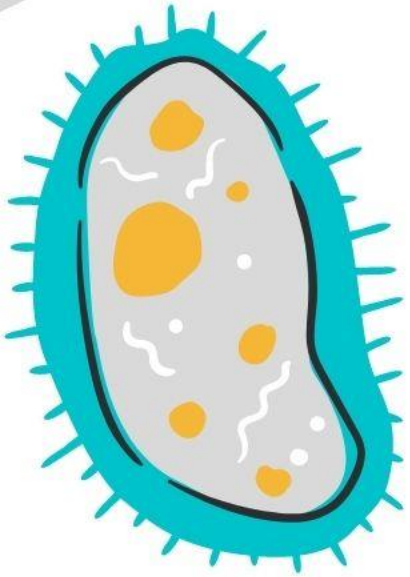
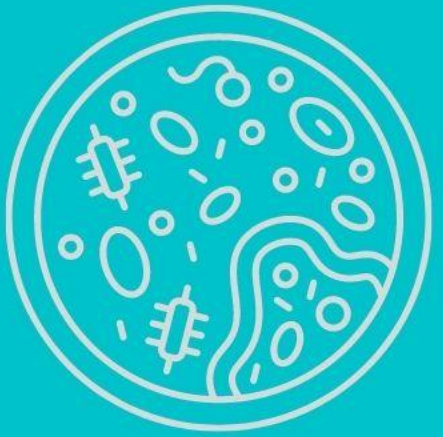


Microbiology

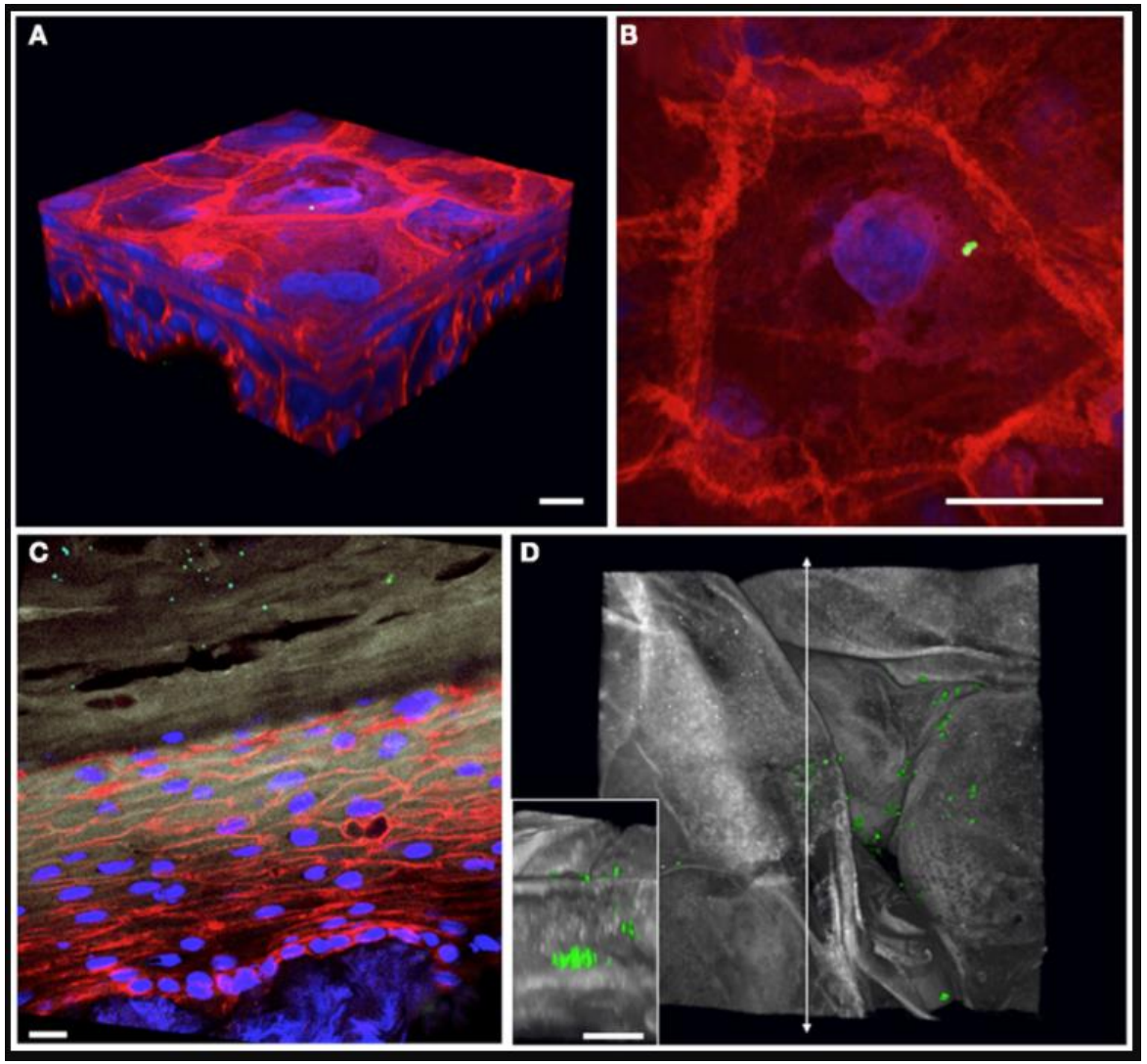
|Modified slides

Written by: Hala Masadeh
Correction: Roa’a Abuarab
Doctor: Anas Abu-Humaidan



Musculoskeletal System Microbiology

Anas Abu-Humaidan
M.D. Ph.D.



Necrotizing soft tissue infections

Overview

We will talk about infections of subcutaneous fat tissue, muscle fascia and muscles themselves.

In this lecture we will discuss:

- Necrotizing fasciitis .
- Clostridial myonecrosis
- Pyomyositis
- Diabetic foot infections

***Necrotizing soft tissue infection.**

Introduction

Necrotizing: Causing the death of tissues. (necrosis of the tissue).

- Necrotizing soft tissue infections (NSTIs) include necrotizing forms of **fasciitis**, **myositis**, and **cellulitis**. These infections are characterized clinically by **fulminant tissue destruction**, **systemic signs** of toxicity (because of the inflammatory mediators, PAMPs and DAMPs that are generated), **and high mortality**.

- NSTI can include involvement of **the epidermis, dermis, subcutaneous tissue, fascia, and muscle.**

- Necrotizing infection may be categorized based on microbiology (pathogen present: polymicrobial necrotizing fasciitis or monomicrobial necrotizing fasciitis) and the presence or absence of gas in the tissues.(For example, Clostridium perfingens form gas).

- Sometimes referred to in the press as flesh-eating bacteria (not a single bacteria, there are several pathogens that can cause this disease).

Necrotizing fasciitis

Caused by: Group A streptococcus (streptococcus pyogenes)

- Necrotizing fasciitis is an infection of the deep soft tissues that results in **progressive destruction of the muscle fascia and overlying subcutaneous fat**. muscle tissue is frequently spared because of its generous blood supply. You can't assess the damage that is happening in the deeper layers just by looking at the skin. (skin may appear with little erythema and swelling but the underneath fascia and muscles are destructed, and there will be systemic signs of inflammation).

- Initially, the overlying tissue **can appear unaffected**; therefore, necrotizing fasciitis is difficult to diagnose without **direct visualization of the fascia**.

- Necrotizing fasciitis may be divided into two microbiologic categories: **polymicrobial** (type I) and **monomicrobial** infection (type II).

Necrotizing fasciitis/ polymicrobial

- Typically, at least one anaerobic species (most commonly **Bacteroides** (part of the gut microflora, gram negative rods), **Clostridium** (gram positive rods), or **Peptostreptococcus** (gram positive, anaerobic)) is isolated in combination with **Enterobacteriaceae** (eg, Escherichia coli, Enterobacter, Klebsiella, Proteus) and one or more facultative anaerobic **streptococci** (other than group A Streptococcus [GAS]).

Polymicrobial infections happen somewhere near the perineal region.

- Necrotizing fasciitis of the perineum, known as **Fournier gangrene**(common disease), can occur as a result of a breach in the integrity of the gastrointestinal or urethral mucosa.

- **Fournier gangrene** is a form of **polymicrobial (type I) infection**. Fournier gangrene typically begins abruptly with severe pain and may spread rapidly to the anterior abdominal wall and the gluteal muscles. Men are more commonly affected than women. Involvement in men may include the scrotum and penis. (happens most commonly in diabetics or immunocompromised patients).

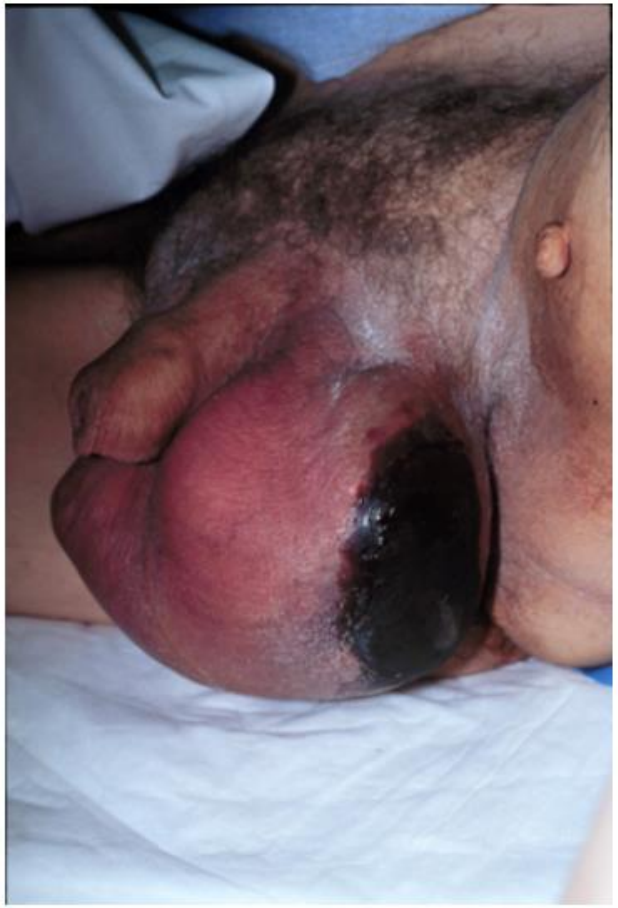
Necrotizing fasciitis/ polymicrobial

Necrotizing fasciitis involving the scrotum:

*There is swelling

Treatment: Open surgically and debride all the necrotic tissue + treat with antibiotics **(but without opening, the antibiotic will be useless)**

Fournier's gangrene in a patient with diabetes



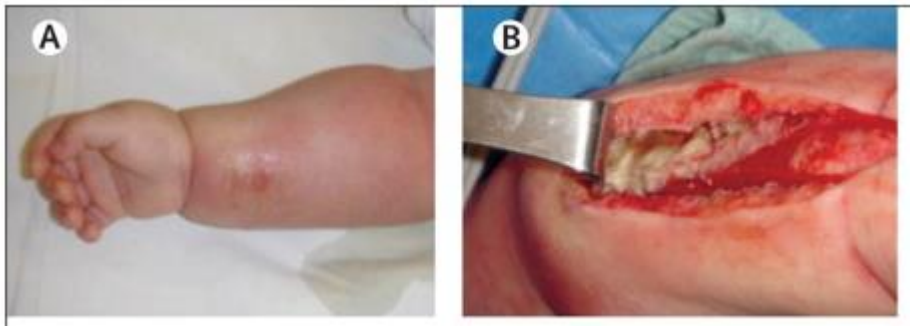
Necrotizing fasciitis of the perineum (Fournier's gangrene) can involve the scrotum. The infection can begin abruptly with severe pain and may spread rapidly.

Reproduced with permission from Lawrence B Stack, MD.

Necrotizing fasciitis/ monomicrobial

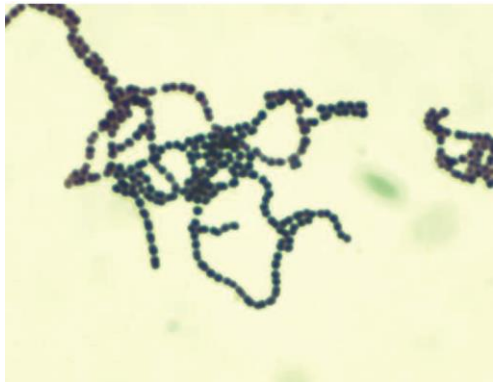
- Monomicrobial (type II) necrotizing infection is usually caused by **GAS or other beta-hemolytic streptococci**. Infection may also occur as a result of **Staphylococcus**. Infection with no clear portal of entry occurs in about half of cases; in such circumstances, the pathogenesis of infection likely consists of **hematogenous translocation of GAS** from the throat (asymptomatic or symptomatic pharyngitis) to a site of blunt trauma or muscle strain.

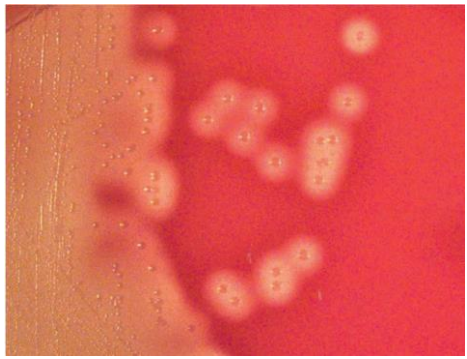
- **M protein** is an important virulence determinant of **GAS**. Necrotizing infection caused by GAS strains with M types 1 and 3 is associated with streptococcal toxic shock syndrome in about 50 percent of cases.



A) The skin doesn't look like that affected it's just a little bit swollen.

B) After opening there is a lot of tissue disruption, and the infection has reached the fascia and probably the muscle.

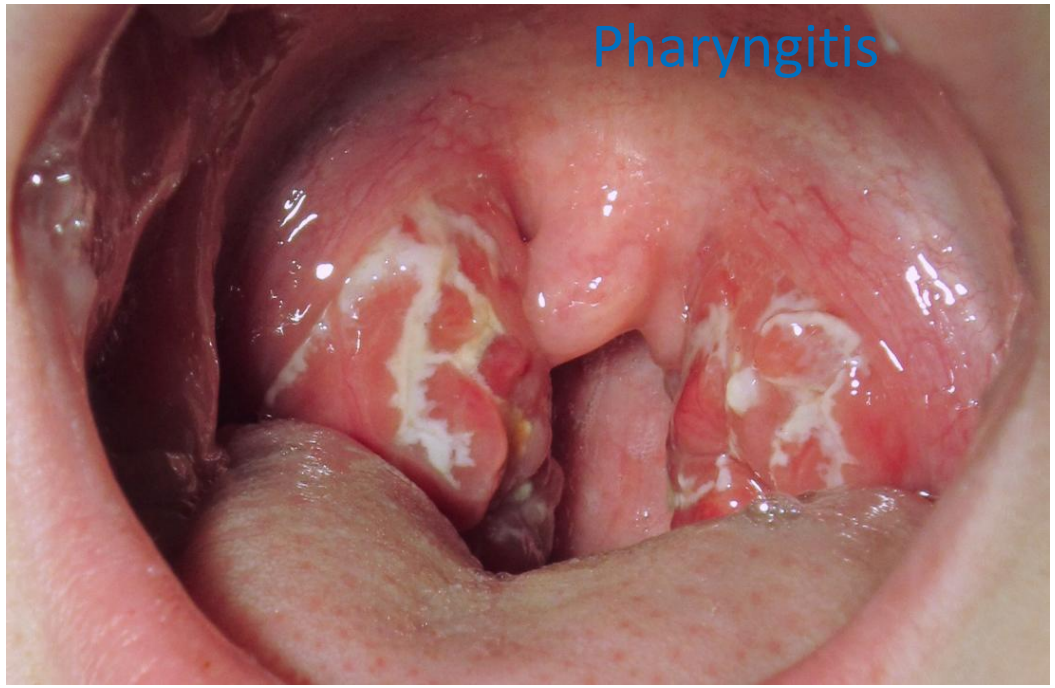




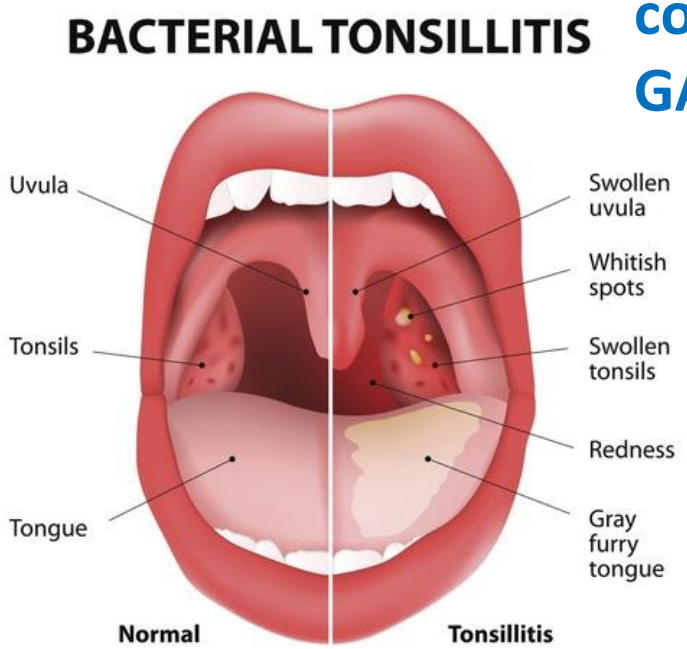
Streptococcus pyogenes

Sore throat

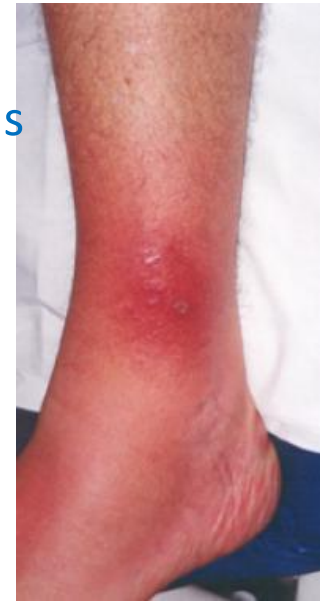
Pharyngitis



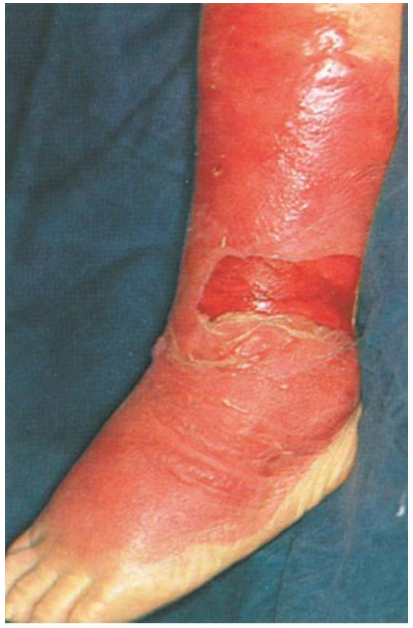
Suppurative complications of GAS infections



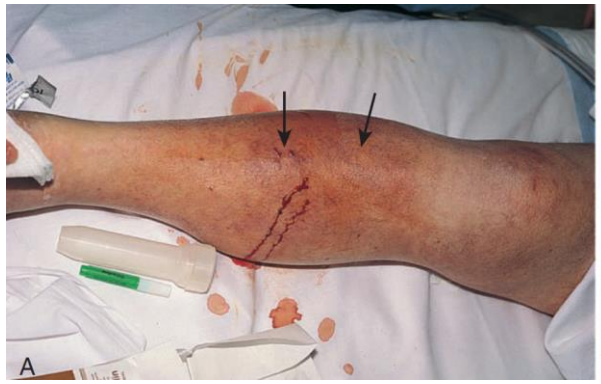
Erysipelas

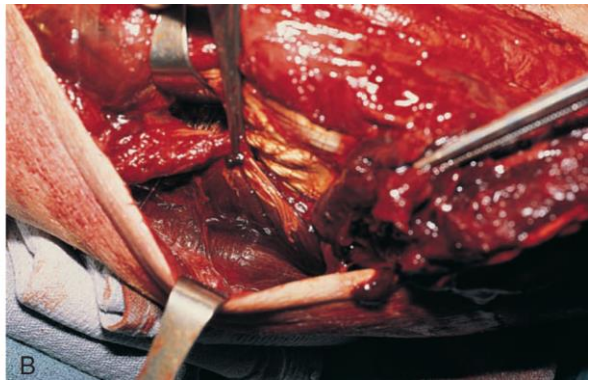


Cellulitis



Necrotizing fasciitis





Necrotizing fasciitis/ risk factors

- Necrotizing infection can occur among healthy individuals with no past medical history or clear portal of entry in any age group (but it's very rare).

Risk factors for NSTI include:

- Penetrating trauma.

- **Recent surgery** (including colonic, urologic, and gynecologic procedures as well as neonatal circumcision) and **Mucosal breach** (hemorrhoids, rectal fissures, episiotomy).

****Any breach of the epithelial layer.**

- Immunosuppression (**diabetes**, cirrhosis, **neutropenia**, **HIV infection**, malignancy)

Diabetes is a particularly important risk factor for necrotizing infection involving the lower extremities, perineum (Fournier gangrene), and head and neck region.

Necrotizing fasciitis/ CLINICAL MANIFESTATIONS

- Necrotizing infection most commonly involves the **extremities** (lower extremity more commonly than upper extremity), particularly in patients with diabetes and/or peripheral vascular disease. Necrotizing infection usually presents **acutely** (over hours); rarely, it may present subacutely (over days). **Rapid progression** to extensive destruction can occur, leading to **systemic toxicity**, limb loss, and/or death.

- **Erythema** (without sharp margins; 72 percent)

Results of a study on necrotizing fasciitis

- **Edema** that extends beyond the visible erythema (75 percent)

- Severe **pain** (out of proportion to exam findings in some cases; 72 percent)

- **Fever** (60 percent)

- **Crepitus** (50 percent) (mostly in clostridial myonecrosis, we will talk about it)

- **Skin bullae, necrosis, or ecchymosis** (38 percent)

Necrotizing fasciitis/ Diagnosis

- NSTI should be suspected in patients with **soft tissue infection** (erythema, edema, warmth) and **signs of systemic illness (**fever, hemodynamic instability) in association with crepitus, **rapid progression** of clinical manifestations, and/or severe pain (out of proportion to skin findings in some cases). Early recognition of necrotizing infection is critical.

- **Surgical exploration** is the only way to establish the diagnosis of necrotizing infection. (during it you can try to take a specimen from the deep tissue for culture and know the causing pathogens).

- Intraoperative specimens should be sent for Gram stain and culture

- **Radiographic imaging** studies can be useful. The most useful finding is **presence of gas in soft tissues,** which is seen most frequently in the setting of clostridial infection or polymicrobial (type I) necrotizing fasciitis.

Necrotizing fasciitis/ Treatment and outcome

- Treatment of necrotizing infection consists of **early and aggressive surgical exploration and debridement** of necrotic tissue, together with **broad-spectrum empiric antibiotic therapy** and **hemodynamic support (because there is a high risk that the patient will have spsis)**. Administration of antibiotic therapy in the absence of debridement is associated with a mortality rate approaching 100 percent.

- In general, empiric treatment of necrotizing infection should consist of **broad-spectrum antimicrobial therapy**, including activity against gram-positive, gram-negative, and anaerobic organism. (e.g. **carbapenem broad spectrum plus vancomycin for MRSA** plus Clindamycin for the antitoxin activity).

- Necrotizing infection **is associated with considerable mortality**, even with optimal therapy.

Clostridial myonecrosis/ INTRODUCTION

Very similar to necrotizing fasciitis, the difference here that it always forms gas.

- **Clostridial myonecrosis** (**gas gangrene**) is a life-threatening muscle infection that develops either contiguously from an area of **trauma** or **hematogenously** from the gastrointestinal tract with muscle seeding. Early recognition and aggressive treatment are essential.

- **Clostridium species** (especially clostridium perfingens) are widespread in nature due to their ability to form **endospores**. They are commonly found in soil and marine sediments as well as human and animal intestinal tracts (ubiquitous), can also enter the human's body by injections.

- Myonecrosis (clostridial gas gangrene) is characterized by **rapidly progressive invasion** and **destruction of healthy muscle** and other soft tissues. Traumatic gas gangrene is most commonly caused by C. perfringens; spontaneous gangrene is most commonly caused by the more aerotolerant C. septicum.

  It has high mortality.

- **Traumatic wounds with vascular compromise** (particularly deep penetrating injuries such as knife wounds, gunshot wounds, and crush injuries) create an **anaerobic environment** that is ideal for **proliferation of clostridia**. Traumatic injury accounts for about 70 percent of gas gangrene cases, and about 80 percent of these are caused by **C. perfringens**.

- Gas gangrene was a common infection in the Civil War, World War I, and World War II due to delayed treatment of injuries.

- Many extracellular toxins are produced by C. perfringens; of these, **alpha and theta toxins** have been implicated in pathogenesis.

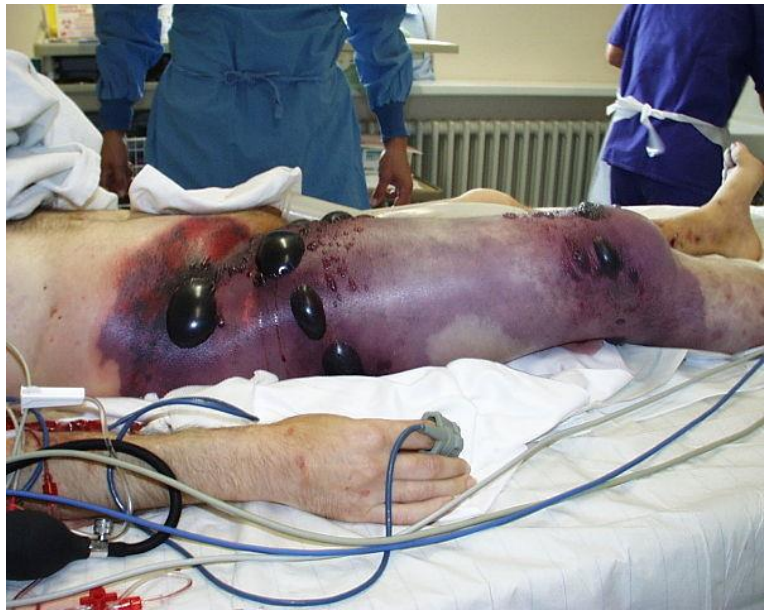
- **Shock** associated with gas gangrene may be attributable to both direct and indirect effects of alpha and theta toxins. (sepsis and septic shock)

Clostridium perfringens

- *C. perfringens* is responsible for a range of soft-tissue infections including **cellulitis,** fasciitis or suppurative **myositis,** and **myonecrosis** with gas formation (caused by the metabolic activity of the rapidly dividing bacteria) in the soft tissue (**gas gangrene**). The toxin involved in gas gangrene is known as **α-toxin**, which inserts into the plasma membrane of cells, producing gaps in the membrane that disrupt normal cellular function

- **Clostridial food poisoning,** an **intoxication** characterized by (1) a short incubation period (8 to 12 hours), (2) a clinical presentation that includes abdominal cramps. (3) a clinical course lasting less than 24 hours.

- *C. perfringens* produces **enterotoxin**, The enterotoxin is produced during the phase transition from vegetative cells to spores and is released in the alkaline environment of the small intestine when the cells undergo the terminal stages of spore formation **(sporulation).**



Treatment is usually **debridement and excision**, with amputation necessary in many cases. Water-soluble antibiotics (such as penicillin) alone are not effective because they **do not penetrate ischaemic muscles** sufficiently to be effective.

Clostridial myonecrosis/ Diagnosis, treatment, and outcome

- **Pain** at a site of traumatic injury together with signs **of systemic toxicity** and **gas in the soft tissue** support the diagnosis of gas gangrene. Physical evidence of **crepitus** in the soft tissue is the most sensitive and specific finding on clinical examination.

- Radiographic studies can help. Blood cultures should be obtained.

- Treatment of traumatic gas gangrene consists of **surgical debridement**, **antibiotic therapy**, and **supportive measures**. Patients with trauma who have not received **tetanus immunization** for 5 years should receive a booster vaccine against tetanus. Use of **hyperbaric oxygen** (HBO) ? (Hyperbaric oxygen: oxygen in high pressure, probably used because clostridium is anerobic, still not sure if it's useful)

- Antibiotic agents with excellent in vitro activity against C. perfringens include **penicillin**, **clindamycin**, tetracycline, chloramphenicol, metronidazole.
- Patients with associated bacteremia and intravascular hemolysis have the greatest likelihood of progressing to shock and death. Mortality is highest for patients in shock at the time of diagnosis.

Clostridial myonecrosis

1:36 Notice the bubbles rising when he apply pressure → that means there is gas.

3:57
a radiograph shows that there is a gas in the soft tissue.

https://www.youtube.com/watch?v=53FgitG2jl4

Muscle infection

- **Pyomyositis** is a **purulent** infection of skeletal muscle that arises from **hematogenous** spread, usually with **abscess** formation (within the muscle). It is classically an infection of the tropics, although it has been recognized in temperate climates with increasing frequency.

- Risk factors for pyomyositis include **immunodeficiency** (particularly HIV infection), **trauma**, **injection drug use**, concurrent infection, and **malnutrition.**

- **Staphylococcus aureus** is the most common cause of pyomyositis; it causes up to 90 percent of tropical cases and up to 75 percent of temperate cases.

- **Pyomyositis** presents with **fever and pain** with **cramping localized to a single muscle group**. It develops most often in the lower extremity. (Erythema is less common)

Pyomyositis

Pyomyositis can be divided into three clinical stages:

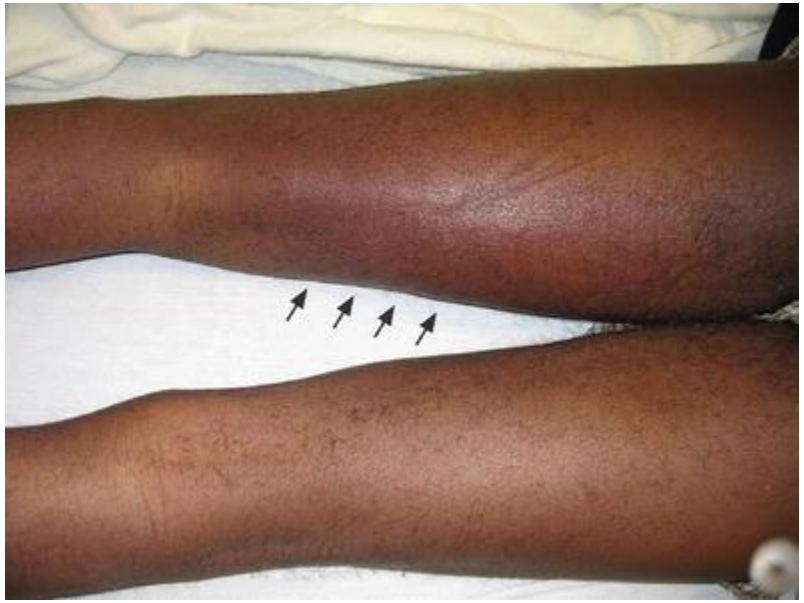
- Stage 1 is characterized by crampy local muscle pain, swelling, and low-grade fever.
- Stage 2 occurs 10 to 21 days after the initial onset of symptoms and is characterized by fever, exquisite muscle tenderness, and edema. (systemic signs, not just localized pain)
- Stage 3 is characterized by systemic toxicity. (the muscle is probably all destroyed) The affected muscle is fluctuant. Complications of S. aureus bacteremia such as septic shock, endocarditis, septic emboli, pneumonia, pericarditis, septic arthritis, brain abscess, and acute renal failure can occur

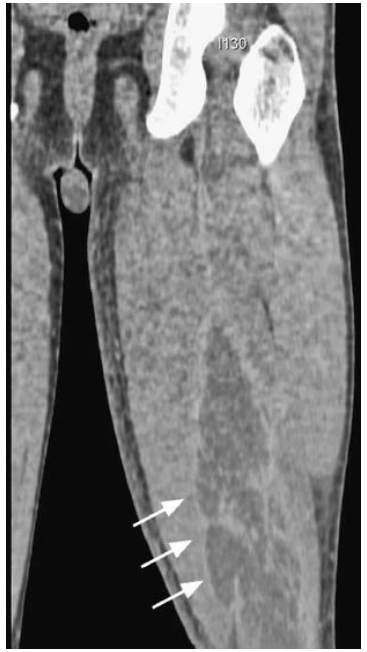
Pyomyositis

- **Radiographic imaging** with magnetic resonance imaging is **the most useful tool** for diagnosing pyomyositis, defining the site(s) of infection, and for ruling out other entities. Bacteriologic diagnosis can be made by cultures of drainage specimens and/or blood.

- Although stage 1 pyomyositis **can be treated with antibiotics alone** (but it's better to explore and remove any necrotic tissue), most patients present with stage 2 or 3 disease and therefore require both antibiotics and drainage for definitive management.

https://intjem.biomedcentral.com/articles/10.1007/s12245-008-0067-6





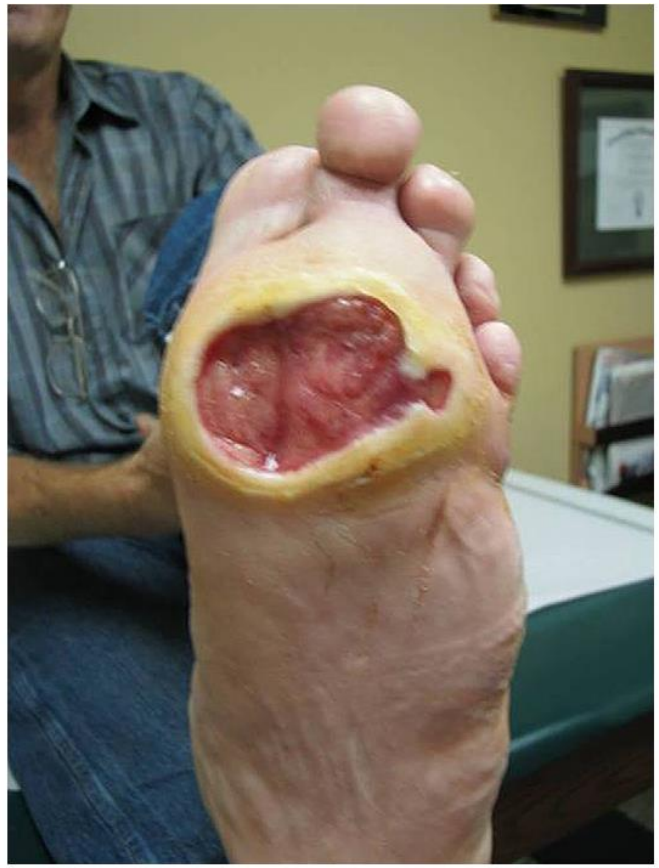
Diabetic foot infections/ introduction

- Diabetic foot infections are associated with substantial morbidity and mortality.

- Important risk factors for development of diabetic foot infections include neuropathy, peripheral vascular disease, and poor glycemic control.

- In the setting of sensory neuropathy, there is **diminished perception of pain** and temperature; thus, many patients are slow to recognize the presence of an injury to their feet. Autonomic neuropathy can cause **diminished sweat secretion resulting in dry, cracked skin** (becomes less resistant to bacterial infections) that facilitates the entry of microorganisms to the deeper skin structures. In addition, motor neuropathy can lead to **foot deformities**, which lead to pressure-induced soft tissue damage.
- **Peripheral artery disease can impair blood flow necessary for healing** of ulcers and infections.
- **Hyperglycemia impairs neutrophil function and reduces host defenses**. Trauma in patients with one or more of these risk factors precipitates development of wounds that can be slow to heal and predispose to secondary infection.

Diabetic foot infections



- Fig. 1. Large forefoot ulcer in patient with diabetes. (Courtesy of William DeCarbo, D.P.M., Columbus, OH.)

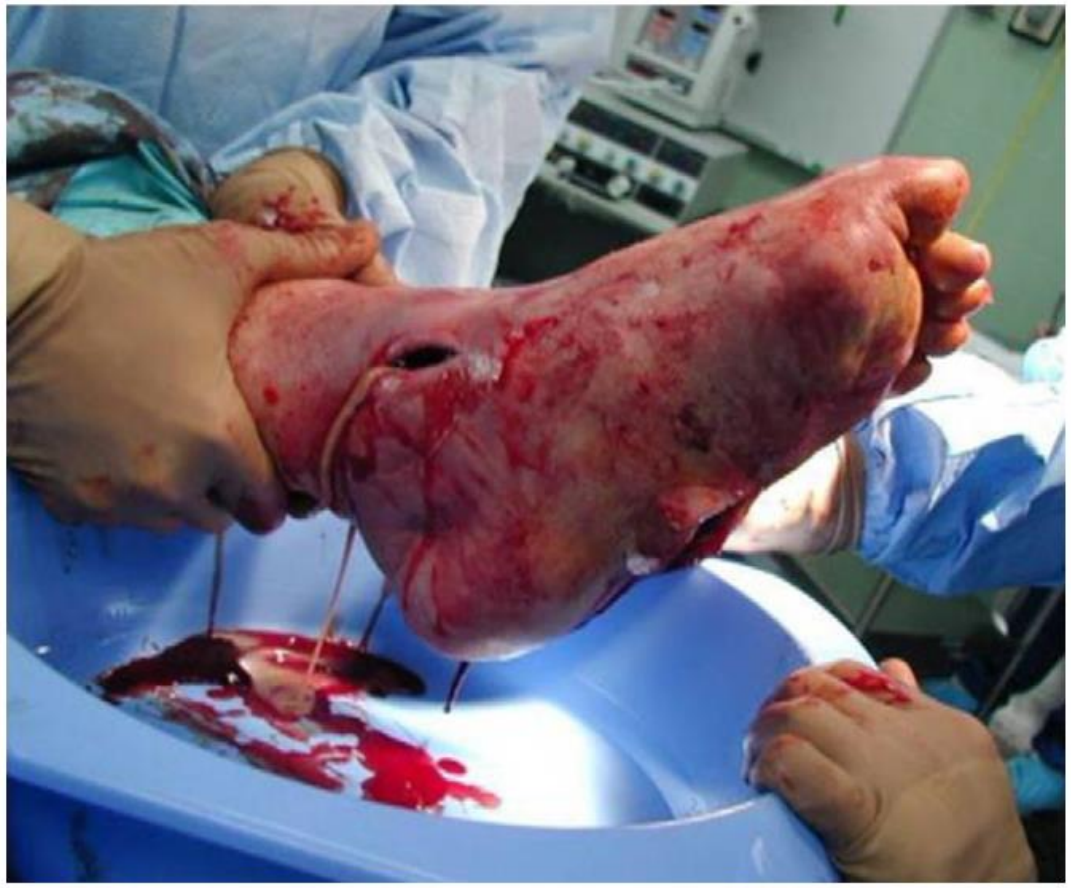


Fig. 3. Diabetic foot with abscess undergoing surgical irrigation and debridement. (Courtesy of William DeCarbo, D.P.M., Columbus, OH.)

Diabetic foot infections/ Microbiology

- Most diabetic foot infections are **polymicrobial**, with up to five to seven different specific organisms often involved. The microbiology of diabetic foot wounds is variable depending on the extent of involvement.

- **Superficial diabetic foot** infections (including cellulitis and infected ulcers in antibiotic-naïve individuals) are likely due to aerobic **gram-positive cocci** (including Staphylococcus aureus, Streptococcus agalactiae, Streptococcus pyogenes, and coagulase-negative staphylococci).

- **Ulcers that are deep**, chronically infected, and/or previously treated with antibiotics are more likely to be **polymicrobial**. Such wounds may involve the above organisms in addition to enterococci, Enterobacteriaceae, Pseudomonas aeruginosa (it's common in many of diabetic foot infections associated with deep ulcers, because it's resistant to many antibiotics), and anaerobes.

- **Wounds with extensive local inflammation**, **necrosis**, **malodorous drainage**, or gangrene with signs of systemic toxicity **should be presumed to have anaerobic organisms** in addition to the above pathogens. Potential pathogens include anaerobic streptococci, **Bacteroides** species, and **Clostridium** species

Diabetic foot infections/ clinical manifestation

- Diabetic foot infections can develop as a result of **neuropathic or ischemic ulcers, traumatic wounds, skin cracks or fissures**, or other defects in the skin of the foot or nail beds (paronychia).

- Thus, infection can present as localized **superficial skin involvement** at the site of a preexisting lesion or as infection of the skin or deeper skin structures that has spread beyond the site of local trauma. Such infections can subsequently extend to **joints, bones, and the systemic circulation**.

- Diabetic foot infections are often accompanied by the cardinal manifestations of inflammation (**erythema, warmth, swelling, and tenderness**) and/or **the presence of pus** in an ulcer or sinus tract.

- **Osteomyelitis** can occur in the setting of a diabetic foot wound with or without evidence of local soft tissue infection.

Diabetic foot infections/ management

- The evaluation of a patient with a suspected diabetic foot infection involves three key steps: 1) **determining the extent and severity of infection**, 2) **identifying underlying factors** that predispose to and promote infection, and 3) assessing the **microbial etiology**.

- Clinical examination should note the location of the lesions, extent of infection (eg, involving skin, subcutaneous tissue, muscles, tendons and/or bone) and whether bone is grossly visible or palpable by probing. Although osteomyelitis is highly likely if bone is visible, it may be present in the absence of such findings.

- Clinical examination should also include a neurologic evaluation that documents the extent of sensory loss as well as a vascular evaluation.

Diabetic foot infections/ management

Clinical classification of a diabetic foot infection

Infection severity	Clinical manifestations of infection
Uninfected	Wound lacking purulence or any manifestations of inflammation.
Mild	Presence of ≥2 manifestations of inflammation (purulence, or erythema, pain, tenderness, warmth, or induration), but any cellulitis/erythema extends ≤2 cm around the ulcer, and infection is limited to the skin or superficial subcutaneous tissues; no other local complications or systemic illness.
Moderate	Infection (as above) in a patient who is systemically well and metabolically stable but which has ≥1 of the following characteristics: cellulitis extending >2 cm, lymphangitic streaking, spread beneath the superficial fascia, deep-tissue abscess, gangrene, and involvement of muscle, tendon, joint or bone.
Severe	Infection in a patient with systemic toxicity or metabolic instability (eg, fever, chills, tachycardia, hypotension, confusion, vomiting, leukocytosis, acidosis, severe hyperglycemia, or azotemia).

Foot ischemia may increase the severity of any infection, and the presence of critical ischemia often makes the infection severe.

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Graphic 55551 Version 1.0

Diabetic foot infections/ management

- **Wound management** — Local wound care for diabetic foot infections typically includes debridement of callus and necrotic tissue, wound cleansing, and relief of pressure on the ulcer.

- **Obtaining samples for culture** — Because microorganisms often colonize lower extremity wounds regardless of the presence of a true infection, cultures should be performed only in selected patients. If the clinical suspicion for infection is low, samples from the wound should not be submitted for culture. The preferred clinical specimens for reliable culture include **aspirate from an abscess or curettage from the ulcer base**.

- **Surgery** — Consultation with a surgeon with experience in diabetic foot infections is important for cases of severe infections and in most cases of moderate infections.

- **Antimicrobial therapy** — Empiric antibiotic therapy should be selected based on the severity of infection and the likelihood of involvement of resistant organisms

Further reading:

- Necrotizing soft tissue infections
  https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?topicRef=3993&source=see_link#H3846414689

- *Clostridial myonecrosis*

https://www.uptodate.com/contents/clostridial-myonecrosis?topicRef=7662&source=see_link

- Pyomyositis

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- *Diabetic foot infections*

https://ezlibrary.ju.edu.jo:2119/contents/clinical-manifestations-diagnosis-and-management-of-diabetic-infections-of-the-lower-