

Diabetic Foot



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Objectives:

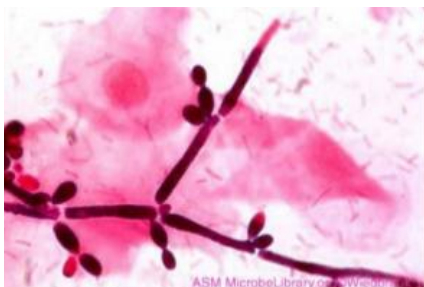
- Recall the reasons that diabetic patients are at increased risk to have infections
- Recall common infections in diabetic patients (with emphasis on diabetic foot infection)
- List the causative organisms and the pathogenesis of common infections in diabetic patients
- Recognize the clinical presentations of common infections
- Describe lab and radiological tests of common infections
- Recall the complications of diabetes mellitus (diabetic foot)
- Recall the management and antimicrobial therapy of common infections in diabetic patients

- Diabetic patients are predisposed to infections.
- Nearly half of all diabetic patients had at least one hospitalization or outpatient visit for infections compared to non-diabetic patients.
- Infections may increase the morbidity and mortality in diabetic patients.
- Why diabetic patients are at increased risk to have infections ?
Because of Host related factors & Organisms related factors

Organisms Specific Factors

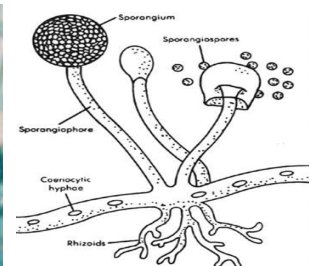
Candida Species

Glucose inducible proteins promote adhesion of *C. albicans* to buccal or **vaginal** epithelium (especially in pregnant) which in turn, impairs phagocytosis, giving the organism advantage over the host.



Rhizopus spp

Ketoacidosis allow Rhizopus spp. which cause Mucormycosis (Zygomycosis) to thrive in high glucose acidic conditions.



Host-Related Factors

Vascular Insufficiency

- Results in **local tissue ischemia** especially in small/medium sized blood vessels
- **enhances the growth of microaerophilic and anaerobic organisms.**
- **Depressing the O₂ dependent bactericidal functions of leukocytes^[1]**
- impairment of the local inflammatory response
- Affect **absorption of antibiotics**

Sensory Peripheral Neuropathy

Minor local trauma may result in **skin ulcers**, which leads to diabetic **foot infections**

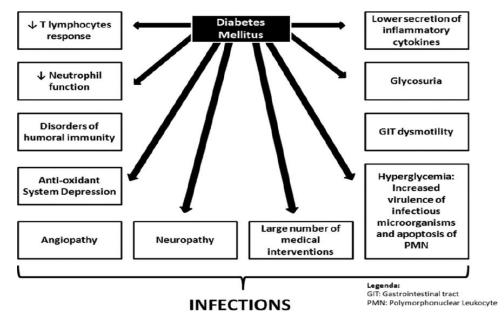
Autonomic Neuropathy

Diabetic patients may develop **urinary retention** and stasis that in turn, predisposes to develop **urinary tract infections**.

Immune Defects in diabetes^[2]

Such as :

- 1 - Depressed Neutrophil function
- 2 - Affected adherence to the endothelium.
- 3 - Compromised bactericidal activity.
- 4 - Affected chemotaxis and phagocytosis .
- 5 - Depressed cell mediated immunity



Increased Skin and Mucosal Colonization

- Diabetics on insulin have asymptomatic nasal and skin **colonization** with **S. aureus** particularly **MRSA**
- **Colonization** predisposes to skin infection and transient bacteremia which may result in distal sites infection such as damaged muscle.
- In type- 2 diabetes; Mucosal **colonization** with **C. albicans** is common. Vulvovaginitis caused by Non-albicans Candida spp. is common in patients with poor glycemic control

Surgical Site Infections

Associated with postoperative hyperglycemia which is related to deleterious effect on chemotaxis, phagocytosis and adherence of granulocytes

Hyperglycemia

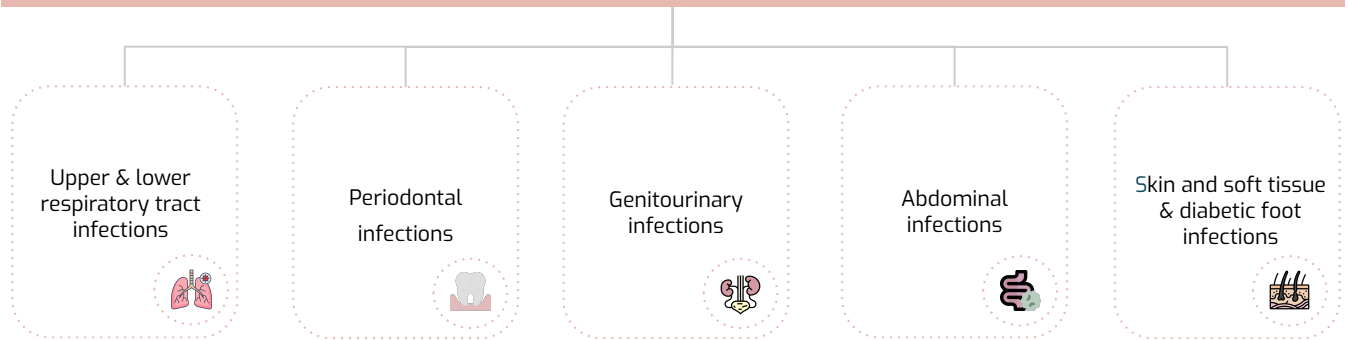
Metabolic derangements in diabetes may facilitate infection

^[1] in ischemic tissue, the environment becomes favorable to anaerobic/microaerophilic organisms. meanwhile, the leukocytes which need oxygen to function will not be able to clear the organisms. Net result will be impaired immune response and infection.

^[2] cells will not be able to phagocytose the bacteria nor will it be able to initiate chemotaxis of other cells.

Infections in diabetic patients

Common / **More severe** infections in diabetic patients



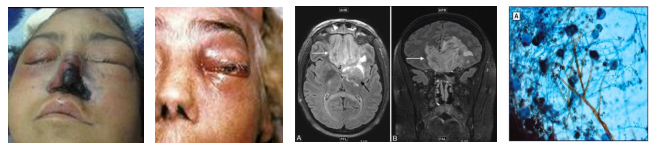
Upper respiratory tract infections

Invasive (malignant) **otitis externa**^[1]

- **General info** : uncommon but potentially life threatening
- **Cause** : Involves **Pseudomonas aeruginosa**
- **Pathogenesis** : After injury, it slowly invades from the external canal into adjacent soft tissues, mastoid and temporal bone and eventually spreads across the base of the skull.
- **Signs/Symptoms** : Patient presents with severe pain, otorrhoea, and hearing loss. Intense cellulitis and oedema of the ear canal.
- **Diagnosis** : CT scan and MRI studies to define the extent of bone destruction
- **Treatment** : Surgical debridement & IV anti-Pseudomonas antibiotics^[3] has to be both surgical and medical (you cannot treat it medically only)

Rhinocerebral Mucormycosis^[2]

- **General info.** : A life threatening fungal infection
- **Cause** : (Mucormycosis) Rhizopus mold (has non-septate hyphae) , Absidia and Mucor species
Mainly in: diabetic patients with ketoacidosis.
- **Signs and Symptoms** : sinus pain / sinusitis, facial or ocular pain and nasal stuffiness, generalized malaise and fever. May be intranasal black eschars or necrotic turbinate.
- **Diagnosis** : Biopsy of the necrotic tissue .
Direct smear examination for hyphae
- **Treatment** : Surgical debridement and prolonged IV therapy with Amphotericin B



Lower respiratory tract infections

Pneumonia and Influenza

- Diabetic patients are 4 times more likely to die from pneumonia or influenza than non-diabetic patients. **(it is way more severe in diabetic patients)**
- **Common organisms** :
 - Gram Positive: S.aureus , S. pneumoniae
 - Gram Negative: Enterobacteriaceae , Legionella
 - Others: Influenza virus , Mycobacterium tuberculosis
- **Routine pneumococcal and influenza^[4] vaccination recommended. (Can prevent it)**

^[1] In normal non-diabetic patients, infection of external auditory meatus is rarely seen. however, any ear injury (e.g. due to hearing aids/trauma) can result in otitis externa.

^[2] in normal patients, rhizopus does no harm, but in diabetic patients, it can lead affect blood vessels and lead to ischemia and necrosis etc..

^[3] Antipseudomonal antibiotics: **"CAMPFIRE"** (EXTRA)#438

Carbapenems, Aminoglycosides (e.g. gentamicin), Monobactams, Polymyxins (e.g. Polymyxin B, Colistin), Fluoroquinolones (e.g. Ciprofloxacin, levofloxacin), Third generation cephalosporins (e.g. Ceftazidime, cefepime), Extended-spectrum penicillins (e.g. Piperacillin, Ticarcillin)

^[4] because it can predispose patients to secondary bacterial infections

Infections in diabetic patients

Genitourinary infections (Boys' slide)

- Asymptomatic bacteriuria (> 100,000 /ml urine) is common.^[1]
- Symptoms/ Signs and time of onset similar to non-diabetics.
- Diabetes is not an indication for screening for treating^[2]
- Asymptomatic bacteriuria.

Cystitis (due to neuropathies)

- Same as non-diabetics, incomplete bladder emptying and high incidence of unsuspected upper UTI^[3]
- Bacteria: Gram negative rods (e.g. *E.coli*) or Group B Streptococcus (*S.agalactiae*)
- Fungi: *Candida albicans* may be involved. (not really albicans but other highly resistant types of candida)
- Symptoms: Pain above the pubic region

Bilateral Pyelonephritis

- Diabetes predisposes to a more severe infection of the upper urinary tract.
- Emphysematous Pyelonephritis exclusively an infection of diabetics (60%) and carries grave prognosis (30% fatal).
- Most common causative organism: **E.coli**
- **Diagnosis:**
 - flank mass & crepitus & High fever
 - CT scan shows gas in the renal tissues.
- **Management:** important to be quick to prevent pus formation
 - supportive & IV antibiotics, nephrectomy may be needed.

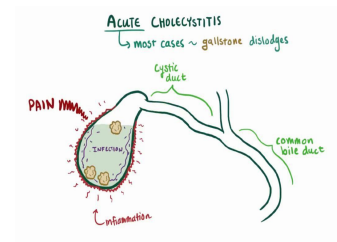
Vulvovaginitis

- As mentioned earlier.

Abdominal infections

Severe fulminating Cholecystitis

- **Common causes:**
 - Enteric Gram negative bacteria and **anaerobes**
 - Gall stone or peritonitis may be present.
 - **Gas gangrene** and perforation may occur.
- **Management:**
 - Cholecystectomy and broad spectrum antibiotics.



^[1] #Renal: we only treat it if the patient is pregnant or per-urological procedures

^[2] However, symptoms should be monitored and treated if there is any.

^[3] (it is more prevalent in diabetic patients because they have autonomic neuropathy which affects bladder emptying. Result will be residual urine which is welcoming place for ascending infection)

Infections in diabetic patients

★ Dr's Qs:

- What is the most severe soft tissue infection? Necrotizing fasciitis
- What is the most important cause of necrotizing fasciitis? Group A strept (S. pyogenes)

Skin and soft tissue infections

- **Risk factors in diabetic patients:**
 - Sensory neuropathy: no pain perception.
 - Atherosclerotic vascular disease
 - Hyperglycemia: >250 mg/ dl
 - History of cellulitis, peripheral vascular diseases, tinea infection, and dry skin.
- **Organisms**
 - Group A Streptococcus (S. pyogenes) and S. aureus
 - CA-MRSA (community acquired -MRSA) causes (77%) of skin and soft tissue infections

Necrotizing fasciitis

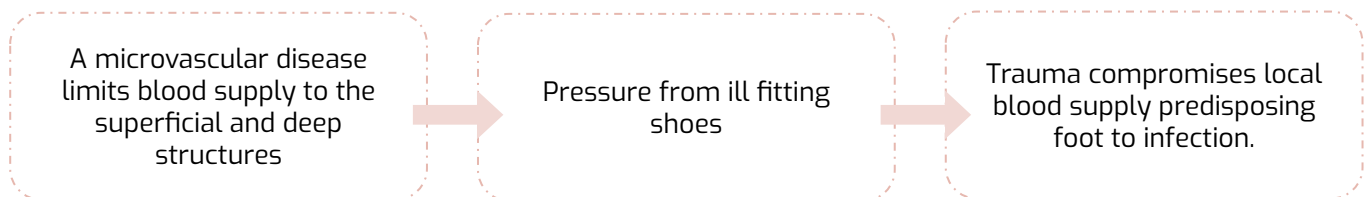
- A deep-seated ,life threatening infection of subcutaneous tissue with progressive destruction of fascia, fat and muscles.
- **Organisms:**
 - 10% associated with GAS ,with or without S.aureus, anaerobes may be involved.
- **Clinical features**
 - 1- Very **severe pain** of proportion of skin and anesthesia of overlying skin. *skin might not show severe redness (maybe mild edema and light redness only)*
 - 2- Violaceous discoloration of skin that evolves into vesicles and bullae.
 - 3- Crepitus.
 - 4- Soft tissue gas seen in radiograph or CT scan.
- **Management:**
 - Aggressive **surgical debridement & IV antibiotics**



Diabetic Foot Infections

- The most common and most important soft tissue infection in diabetic patient is diabetic foot infection, why ?
 - **because it is related to peripheral neuropathy and compromised microvascular circulation (↓blood supply) which limits the access of phagocytic cells (↓immunity) to the infected area and poor concentration of antibiotics (due to decreased blood supply) in the affected area.**
- Complicated by chronic osteomyelitis, gas gangrene, amputation and death.
- The spectrum of foot infection ranges from superficial cellulitis to chronic osteomyelitis.
- Combined infection involving bone and soft tissue may occur
- Infection may involve the skin, soft tissues, bone , or all.
- Diabetic neuropathy may lead to incidental trauma that goes unrecognized.
- Sinus tract may be present.

Pathophysiology



Organisms involved in diabetic foot infections

Cellulitis	Beta-hemolytic streptococci (group A,B Streptococcus), S. aureus , Enterobacteriaceae (E. coli, Klebsiella, Proteus spp.) in chronic ulcers.
Macerated ulcer or nail injury (sinus) (From object)	P. aeruginosa . because it is present in metal / wet object
Deep soft tissue infections (necrotizing fasciitis, or myositis).	GAS & gas producing gram positive bacilli(Clostridium perfringens).
Chronic osteomyelitis	GAS and Group B Streptococcus, S. aureus, Enterobacteriaceae (E.coli , Proteus mirabilis , K.pneumoniae.) & Bacteroides fragilis

Diabetic Foot Infections

Cellulitis

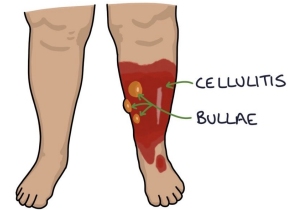
- **Tender, erythematous non-raised skin lesion** on the lower limb, may be accompanied with lymphangitis which suggests **GAS**.
- Bullae suggests *S.aureus* , occasionally GAS.



Erythematous non raised skin lesion



Bullous (raised) lesion



Deep skin and soft tissue infections

- Patient acutely ill, with painful induration of the limb especially the thigh.
- Foot may be involved.
- **Foul** wounds discharge suggest anaerobes.

Osteomyelitis

Acute osteomyelitis

Pain at the involved bone, fever and adenopathy (lymphadenopathy)

Chronic osteomyelitis

- Fever
- Foul discharge
- There may be pain
- No lymphangitis
- Deep penetrating ulcer and sinuses on the plantar surface of the foot

Factors that increases the development of Osteomyelitis

- Grossly visible bone or ability to probe to bone
- Ulcer size >2x2 cm
- Ulcer depth > 3mm
- Ulcer duration longer than 1-2 wks
- ESR >70 mm/hr.



Diabetic Foot Infections

Diagnosis



1:

Thorough **examination** to evaluate the patient's vascular and neurological status.



2:

Radiological examination including doppler ultrasonography, transcutaneous oximetry, MR angiography.



3:

CT scan ,MRI and gallium scan for soft tissue and bone evaluation.



4:

Exploration of ulcer to determine its depth and the presence of sinus tract.



5:

Deep specimens (bone tissues) for culture and susceptibility testing.

Management & Treatment

- Control blood sugar and hydration
- Evaluation of neuropathy and vasculopathy

Mild cases

Surgical debridement (first) of necrotic tissues and use of antibiotics according to the causative bacteria

eg. **Cloxacillin** (staph), Cephalexin, **Clindamycin** ,
TMP-SMX (for CA-MRSA), Quinolones,
Amoxicillin-clavulanic acid, **Aminoglycosides**.

For staph: Cloxacillin, Clindamycin

For MRSA: TMP-SMX, vancomycin

For strept: Cephalexin, Clindamycin

For pseudomonas: Carbapenems, aminoglycosides

Moderate to severe cases

- Places the foot at risk of amputation.
- Needs hospitalization, IV antibiotics and surgical intervention as needed

Prevention

- Is the cornerstone of diabetic foot care.
- It is a multidisciplinary including family physician, social worker, home care nurse and specialist.
- Patient education about the control and complication of diabetes.
- Blood sugar should be controlled promptly (shift to insulin if oral hypoglycemic agents were not effective) , weight reduction , a diet low in fat and cholesterol.
- Proper foot care, using protective footwear and pressure reduction.
- Self and family member examination of foot.

Extra but helpful in SAQ

Gram +ve	
S.aureus	<ul style="list-style-type: none"> -Cocci in clusters -Catalase: + -Coagulase : + -Yellow colonies on blood agar -DNase +ve
Strept. pyogenes (group A)	<ul style="list-style-type: none"> -Cocci in chains -Catalase: - -Coagulase : - -β hemolytic - Bacitracin sensitive
Strept. agalactiae (group B)	<ul style="list-style-type: none"> -Cocci in chains -Catalase: - -Coagulase : - -β hemolytic - Bacitracin resistant
Strept. pneumoniae	<ul style="list-style-type: none"> -Diplococci -Catalase: - -Coagulase : - -α hemolytic -Bile soluble -Optochin sensitive
Clostridium perfringens	<ul style="list-style-type: none"> -Spore forming rods -Double zone of hemolysis -Transmission: foodborne and traumatic implantation
Gram -ve	
Enterobacteriaceae	<ul style="list-style-type: none"> -Oxidase : - -Catalase : + -Ferment glucose
Legionella	<ul style="list-style-type: none"> -Gram stains poorly, use silver stain -Grow on charcoal yeast extract medium -Transmission: aerosols from environmental water source habitat (air conditioning systems) , no person-to-person transmission
Pseudo. aeruginosa	<ul style="list-style-type: none"> - Bacilli - Non-lactose fermenter - Oxidase: +
Bacteroides fragilis	<ul style="list-style-type: none"> -Reservoir: predominant anaerobe in the human colon -Transmission: endogenous from bowel defect

- In ischemic areas, the environment becomes favorable to anaerobic/microaerophilic organisms. Meanwhile, the leukocytes which need oxygen to function will not be able to clear the organisms. Net result will be impaired immune response and infection. Decreased antibiotics bioavailability due to many reasons e.g. ischemia, delay in gastric motility, or any other problem will lead to faster progression of the infection too.
- **To sum up, why are infections more prevalent and risky in diabetic patients?**
 1. **Vascular insufficiency** and ischemia in small/medium sized blood vessels.
 2. **Neuropathies / absence of pain perception** (sensory: foot infection) and (autonomic:UTI)
 3. **Impaired immunity (impairment in:** adherence, neutrophils function, phagocytosis, chemotaxis, CMI, bactericidal activity)
 4. **Increased colonization** of skin by different organisms such as MRSA and c.albicans.
 5. **Hyperglycemia** (uncontrolled diabetes or post-surgical hyperglycemia)
- Prevalence of MRSA used to be 10% but now it is increasing up to 50-70%, and it also used to be in the hospitals only, but now it can be community acquired too.
- In normal non-diabetic patients, infection of external auditory meatus is rarely seen. however, any ear injury (e.g. due to hearing aids/trauma) can result in otitis externa.
- Inflammation of external ear or extremities can be severely painful because the space for inflammation to occur is limited.
- Rhinocerebral Mucormycosis starts as secretions coming from the nose, reach the orbit, and finally ischemia/ necrosis might develop as well. The infection can reach the brain within several hours.
- Cystitis is more prevalent in diabetic patients **because they have autonomic nephropathy** which affects bladder emptying. Result will be residual urine which is welcoming place for ascending infection.
- **Dr's Qs:**
 1. What is the most severe soft tissue infection? Necrotizing fasciitis
 2. What is the most important cause of necrotizing fasciitis? Group A strept (*S. pyogenes*)
- Diabetic foot is a spectrum of diseases, and it is often related to socioeconomic factors and age. For a patient to develop diabetic foot, he has to have uncontrolled diabetes for at least 10-15 years.
- Diabetic foot usually starts as a minor injury from an object. Later on, it will ulcerate and reach to the muscle tissue, and it will finally reach the bone causing osteomyelitis.
- The best sample in case of diabetic foot is bone tissue after surgical debridement (because the superficial area of the ulcer will most likely have staph aureus only). Microbiological examination must include anaerobic sampling technique as well.
- **Management is: (1) Surgical debridement (2) Antibiotics.** Due to the difficulty of determining the causative pathogen for most diabetic foot cases, clinicians may select antibiotics that cover both *Staphylococcus aureus* and group A strep.

Quiz

MCQ

Q1: Which one of the following is the most common infection in diabetic patients related to peripheral neuropathy ?

- A- Necrotizing fasciitis
- B- Diabetic foot
- C- Pyelonephritis
- D- Cystitis

Q2: Which one of the following antibiotics is recommended in treatment of diabetic foot caused by MRSA ?

- A- TMP-SMX
- B- Erythromycin
- C- Penicillin
- D- Tetracycline

Q3: Which of the following vaccines are recommended to give to diabetic patients ?

- A- Hepatitis A & B
- B- Mumps & Rubella
- C- Pneumonia & Influenza
- D- Measles

Q4: A 76 year old patient came to the clinic because of pain in his feet on examination there is a tenderness on erythematous area the lesion is not raised there is a swelling on lymph nodes (lymphangitis), there is no sign for fluid-filled sac under his skin. What is the diagnosis ?

- A- Osteomyelitis
- B- Necrotizing fasciitis
- C- Pneumonia
- D- Cellulitis

Q5: Which one of the following factors increase the development of osteomyelitis ?

- A- Ulcer size < 2x2 cm
- B- Ulcer depth > 3mm
- C- Ulcer duration shorter than 1-2 weeks
- D- ESR < 70 mm/hr

Q6: Which one of the following is life-threatening infection related to diabetic foot infection ?

- A- Necrotizing fasciitis
- B- Cellulitis
- C- Pyelonephritis
- D- Cystitis

Answers: Q1:B | Q2:A | Q3:C | Q4:D | Q5:B | Q6:A

SAQ

Case: A 60 year old man with diabetes mellitus complains of deep burning pain and sensitivity to touch over his hands and fingers. Nerve conduction studies show slow transmission of impulses and diminished muscle stretch reflexes in the ankles and knees. Sensation to vibrations and light touch are also markedly diminished.

Q1: In the above case, what is the most common infection in diabetic patients related to peripheral neuropathy ?

Diabetic Foot

Q2: Explain the pathophysiology of diabetic foot infection

Microvascular disease limits blood supply to the superficial and deep structures pressure from ill fitting shoes, trauma compromises local blood supply predisposing foot to infection

Q3: What is the life-threatening infection related to diabetic foot infection ?

Necrotizing fasciitis

Q4: What is the most important cause of necrotizing fasciitis ?

Group A strep (S.pyogenes)

Q5: What is the best specimen to collect in such case ?

Deep tissue specimen

Q6: Explain the management and treatment of mild cases ?

Surgical debridement (first) of necrotic tissues and use of antibiotics according to the causative bacteria eg. **Cloxacillin** (staph), Cephalexin, **Clindamycin**, TMP-SMX (for CA-MRSA), Quinolones, Amoxicillin-clavulanic acid, Aminoglycosides.

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