

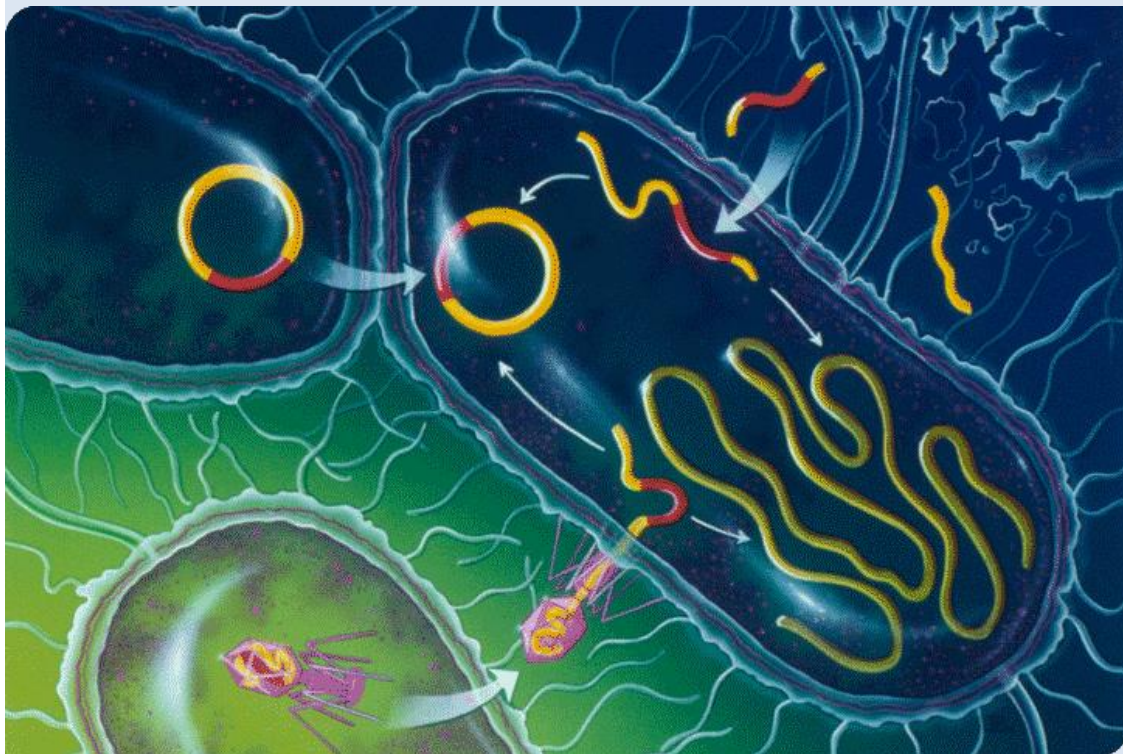
# 431

## *Microbiology Team*

### Common Infections in Diabetes Mellitus

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- ❖ Diabetic patients are predisposed to infections.
- ❖ **Why diabetic patients are at increased risk to have infections?**

Because of Host related factors & Organisms related factors.

### Host Related Factors

- **Vascular insufficiency:** result in local **tissue ischemia** that enhances the growth of **microaerophilic and anaerobic organisms** while depressing the O<sub>2</sub> dependent bactericidal functions of leukocytes. There may be also **impairment of the local inflammatory response** and 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 UTIs**.
- **Hyperglycemia and metabolic derangements** in diabetes may facilitate infection.
- **Immune defects** in diabetes such as:
  - Depressed Neutrophil function.
  - Affected adherence to the endothelium.
  - Affected chemotaxis and phagocytosis.
  - Compromised bactericidal activity.
  - Depressed cell mediated immunity
- **Increased skin and mucosal colonization**
  - **Diabetics on insulin have asymptomatic nasal and skin colonization** with [***S.aureus***] particularly **MRSA** (Methicillin-resistant Staphylococcus aureus). **[IMP!!!]**
  - Colonization predisposes to skin infection and transient bacteraemia 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.

## Organism Specific Factors

- **Candida albicans:** glucose inducible proteins promote adhesion of C.albicans to buccal or vaginal epithelium 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.



## Common infections in diabetic patients:

### 1- Upper Respiratory Tract Infections

- Invasive (malignant) otitis media (it's written media in the slide but the doctor kept saying otitis externa, and when we searched we found that it is known as externa NOT media) so uncommon but potentially life threatening.
- Rhinocerebral mucormycosis "These two infections are almost exclusively seen in Diabetic patients only."

#### ✚ Invasive otitis Externa

**Cause:** [*P.aeruginosa*]

**Pathogenesis:** 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 present with severe pain, otorrhea, and hearing loss, intense cellulitis and oedema of the ear canal.

**Diagnosis:** CT and MRI studies to define the extent of bone destruction.

**Treatment:** surgical debridement & IV anti-pseudomonas antibiotics.

#### ✚ Rhinocerebral Mucormycosis

A life threatening fungal infection

**Cause:** (Mucormycosis) *Rhizopus*, *Absidia* and *Mucor* species. Usually it's seen in DKA patients. It goes to the Blood in DKA patients because it likes acidic pH. This will block the blood supply and cause necrosis.

**Clinically:** facial or ocular pain and nasal stuffiness, generalized malaise and fever, may be intranasal black eschars نديبات or necrotic turbinates.

**Diagnosis:** biopsy of necrotic tissue.

**Treatment:** surgical debridement & prolonged IV therapy with Amphotericin B.

## 2- Lower respiratory tract infections (pneumonia and influenza)

- Diabetic patients are 4 times more likely to die from pneumonia or influenza than non-diabetic patients.
- **Common organisms:** Gram positive bacteria: *S.aureus* it is fatal especially if it comes after influenza, *S.pneumoniae*.  
Gram negative bacteria: **Enterobacteria:** eg. *E.colli* & *Legionella*. [IMP!!!]  
Other organisms: *Influenza virus* & *Mycobacterium tuberculosis*.
- Routine pneumococcal vaccination and influenza recommended.

## 3- Genitourinary infection

- Asymptomatic bacteriuria ( > 10<sup>5</sup> /ml urine) is common.
- Symptoms/ signs & time of onset similar to non-diabetics.
- Diabetes is an indication for screening for treating asymptomatic bacteriuria.
- **Cystitis:** same as non-diabetics, incomplete bladder emptying and high incidence of unsuspected upper UTI.
- **Bacteria** (Gram negative rods or **group B streptococci very common**) or fungi (**Candida albicans**) may be involved.
- **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).

**Diagnosis:** flank mass & crepitus , CT show gas in the renal tissues.

**Management:** supportive & IV antibiotics , nephrectomy may be needed. **serious condition**

- **Vulvovaginitis:** as mentioned earlier.

## 4- 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.

## 5- Skin and soft tissue infections

- Risk factors in diabetic patients :
  - Sensory neuropathy: no pain perception.
  - Atherosclerotic vascular disease
  - Hyperglycemia : blood glucose >250 mg/ dl increased risk
  - history of cellulitis, peripheral vascular diseases, Tinea, and dry skin.
  - Organisms: **S.pyogenes** (GAS) and **S.aureus**. GAS = Group A streptococcus or S.pyogenes

**CA-MRSA (Community Acquired MRSA)** is of concern 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 & muscle.

**Causes:** 10% associated with **GAS [IMP!!!]**, with or without S.aureus, anaerobes may be involved.

**Clinically:** pain of proportion of skin, anaesthesia of overlying skin. Violaceous discoloration of skin that evolves into vesicles and bullae, crepitus, soft tissue gas seen in radiograph or CT.

**Management:** aggressive surgical debridement & IV antibiotics.

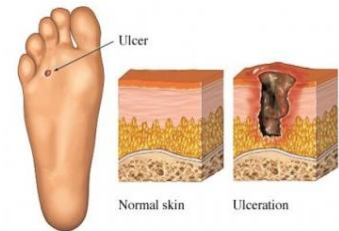
## 6- Diabetic foot infection [IMP!!!]

- **the most common and most important soft tissue infection in diabetic patients, why ?**  
because it is related to peripheral neuropathy and compromised microvascular circulation which limits the access of phagocytic cells to the infected area and poor concentration of antibiotics in the affected area.
- Complicated by: chronic Osteomyelitis, gas gangrene, amputation & death.
- The spectrum of foot infection ranges from superficial cellulitis to chronic Osteomyelitis.
- Combined infection involving bone and soft tissue may occur.
- **Pathophysiology:** microvascular disease limits blood supply to the superficial and deep structures. Pressure from ill fitting shoes, trauma and compromised local blood supply predisposing foot to infection.
- 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.

## Organisms involved in diabetic foot infections

<b>Cellulitis</b>	beta-hemolytic streptococcus ( group A,B streptococi ), <i>S.aureus</i> , <i>Enterobacteriaceae</i> ( <i>E.coli</i> , <i>Klebsiella</i> , <i>Proteus spp.</i> ) in chronic ulcers.
<b>Macerated ulcer or <u>nail</u> injury (sinus)</b>	<b><u><i>P.aeruginosa</i></u></b> .
<b>Deep soft tissue infections (necrotizing fasciitis or myositis)</b>	<u>GAS &amp; gas producing gram positive bacilli (<i>Clostridium</i>)</u> .
<b>Chronic Osteomyelitis</b>	GAS and Group B <i>Streptococcus</i> , <i>S.aureus</i> , <i>Enterobacteriaceae</i> ( <i>E.coli</i> , <i>Proteus mirabilis</i> , <i>K.pneumoniae</i> .) & <i>Bacteroides fragilis</i>

Factors that increases the development of Osteomyelitis: grossly visible bone or the ability to probe to bone, ulcer size >2x2 cm, ulcer depth > 3mm, ulcer duration longer than 1-2 weeks, ESR >70 mm/hr.



## Clinical presentations of 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**.
- **Deep skin and soft tissue infections:** patient acutely ill, with painful induration of the limb especially the thigh . Foot may be involved. Wound discharge suggest anaerobes.
- **Acute Osteomyelitis:** pain at the involved bone, fever, adenopathy.
- **Chronic Osteomyelitis:** fever, foul discharge, may be pain, no lymphangitis, **deep penetrating ulcer**, and sinuses on the planter surface of the foot. **Diagnosis: Probing the ulcer, if rattling is heard, it's probably Osteomyelitis (take deep biopsy from bone).**

## Diagnosis of foot infections

- Thorough examination to evaluate the patient's vascular and neurological status.
- Radiological examination including doppler ultrasonography, transcutaneous oxymetry, MR angiography.
- CT scan, MRI and gallium -67 scan for soft tissue and bone evaluation.
- Exploration of ulcer to determine its depth and presence of sinus tract.
- Deep specimens (tissues) for culture and susceptibility testing.

## Management & Treatment

- Control blood sugar and hydration
- Evaluation of neuropathy and vasculopathy.
- **Mild cases:** debridement of necrotic tissues and use of antibiotics according to the causative bacteria eg. Cloxacillin, Cephadrine, Clindamycin, TMP-SMX (for CA-MRSA), Aminoglycosides, Quinolones.
- **Moderate to severe cases:** places the foot at risk of amputation. Needs hospitalization, IV antibiotics and surgical intervention if needed.

## Prevention

- Is the cornerstone of diabetic foot care.
- It is 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.

## Summary

- Diabetic Patients are more susceptible to infections due to various host factors and organism related factors.
  - Impaired immune function, Vascular Insufficiency, Neuropathy are the most important Host factors.
  - Organism Specific Factors include Glucose inducible adhesion proteins for Candida, Acidic pH as in "DKA" for Rhizopus.
- Malignant Otitis externa [Pseudomonas] and Rhinocerebral mucormycosis [Rhizopus] are exclusively seen in Diabetic patients.
- Mortality increases from Pneumonia in diabetic patients, the most common organisms are S. Pneumoniae and Staphylococcus aureus (unusual in non-diabetics).
- UTI is very common in diabetics and if it is present, it has to be treated as Upper UTI. Group B streptococci is very common. Vulvovaginitis is not uncommon, and it is caused by non-albicans Candida species especially in patients with poor Glycemic Control.
- Skin and soft tissue infections are mostly caused by Gram positive cocci, specifically Group A Streptococci and Staphylococcus Aureus. Necrotizing Fasciitis is usually associated with Group A Streptococci.
- Diabetic foot is the most common and most important soft tissue infection in diabetic patients.
  - In cellulitis cases it's most probably Beta Hemolytic Streptococci.
  - In nail injuries: almost always Pseudomonas aeruginosa.
  - Deep soft tissue infection: Group A Streptococci or gas producing Gram positive organism (clostridium).
  - Chronic Osteomyelitis: Group A/B Streptococci, S.aureus, Enterobacteriaceae.

## Questions:

1. 67 year-old diabetic came to the ENT department because of severe pain in his left ear. He told the doctor that he cannot sleep at night because of the severity of the pain. Which of the following is the most probable etiology:
  - a. Haemophilus influenzae causing otitis media.
  - b. Rhizopus causing Mucormycosis.
  - c. Pseudomonas aeruginosa Causing Invasive Otitis externa.
  - d. Beta Hemolytic Streptococci causing cellulitis.
2. Which of the following organisms is most of the time associated with Necrotizing Fasciitis:
  - a. Group A Streptococci.
  - b. E coli.
  - c. Staphylococcus Epidermedis.
  - d. Pseudomonas aeruginosa.
3. 55 Year-old Diabetic was walking to his local mosque when suddenly a nail perforated his shoe and injured his foot. By time the ulcer inflamed, he went to see his Family practitioner. During examination, the doctor noticed sinus formation with no rattling sound while probing. Which of the following is the most probable etiology:
  - a. Group A Streptococci.
  - b. Staphylococcus aureus.
  - c. Pseudomonas aeruginosa.
  - d. Rhizopus.
4. 62 year old diabetic developed osteomyelitis. Deep biopsy was taken from bone and sent to microbiology lab to check for bacterial invasion. Gram Stain showed gram positive cocci in clusters, Which of the following organisms is the etiology:
  - a. Pseudomonas aeruginosa.
  - b. Staphylococcus aureus.
  - c. Group A Streptococci.
  - d. Clostridium Perfringens.

Answers: C – A – C – B