

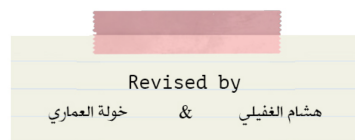
Microbiology

435's Teamwork

Endocrine Block

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Important **Males note** **Females note** **Team's note** **Organism**



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Resources:

2016-2017 Prof. Hanan Habib's Lecture

2016-2017 Dr. Ali Somily's Lecture

434's Teamwork

Sherris Medical Microbiology (CH. 59, 60, 63, 64)

Infections in Diabetic Patients

Learning Objectives:

By the end of this lecture, you should know the...

1. Definition
2. Epidemiology
3. Risk factors
4. Complications
5. Clinical presentation
6. Diagnostic approaches
7. Management and Prevention

Of infections in diabetic patients.

Introduction:

- ❖ Unlike healthy patients, diabetics are more susceptible to infections due to both **host-related** and **organism-specific** factors.
- ❖ Nearly half of all diabetics have visited the hospital (outpatient), or have been hospitalized (inpatient) due to infections.
- ❖ Infections can increase the morbidity and mortality in diabetic patients.
- ❖ The predisposing factors for diabetes are **genetic factors** and **environmental factors** (Viral infections that trigger the immune cells leading to autoimmune diabetes).
- ❖ Diabetes is common in Saudi Arabia. The lifestyle and diet in Saudi Arabia is a very high predisposition factor to diabetes.
- ❖ **Complications of diabetes:** Diabetic Nephropathy, Retinopathy, Neuropathy, Atherosclerosis, Endothelial abnormalities and Gangrene.
- ❖ Acute hyperglycemia and hyperinsulinemia enhance adrenergic vasoconstriction. When perfusion of peripheral blood vessels is decreased, ischemia and decreased oxygenation occur, leading to the growth of the anaerobic bacteria in return. Also, decreased perfusion leads to the decrease in the efficacy of phagocytosis as WBCs lack the required amount of blood needed for survival in the infected area.
- ❖ The relation between the affected peripheral nerve (neuropathy) with infection is that the patient does not feel any pain in their extremities. Ignoring the infection they have due to the painless wound will progress into infection, and because of the decreased blood perfusion to the injured area the infection will develop aggressively, which cause severe tissue necrosis, leading to amputation, or even death.

1. Organism-Specific Factors

Candida Species

Glucose inducible proteins promote the adhesion of *Candida Albicans* to the buccal (relating to the cheek) or vaginal epithelium which in turn, impairs phagocytosis, giving the organism advantage over the host. *Candida* is a normal flora in the mouth, GI and vagina. It is common in Diabetic patients, pregnant ladies, immunocompromised patients, children and patients with catheter.

Rhizopus Species

Rhizopus is a very serious fungi found in the environment as spores, and might be found in human noses, and it does not cause infection in healthy individuals. Ketone reductase allow *Rhizopus* species -which cause mucormycosis¹- to grow in high glucose acidic conditions. *Rhizopus* is the second most severe infection after Necrotising Fasciitis. It is acute, devastating and hard to treat.

¹ A fungal infection (most commonly of the sinuses, brain, or lungs) by fungi found normally in the soil or in decaying vegetation. It can also affect the gastrointestinal tract, skin, and kidneys.

2. Host-Related Factors

Vascular Insufficiency²

Result in local tissue ischemia that enhances the growth of microaerophilic and anaerobic organisms while depressing the O₂ 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 stasis³, hence, predisposes UTIs⁴.

Immune Defects⁵

- ❖ Depressed Neutrophil function.
- ❖ Affected adherence to the endothelium.
- ❖ **Decreased chemotaxis and phagocytosis.**
- ❖ Compromised intracellular bactericidal activity.
- ❖ Opsonization.
- ❖ **Depressed cell mediated immunity.**

Increased Skin and Mucosal Colonization

- ❖ Diabetics on insulin have asymptomatic nasal and skin colonization with *Staphylococcus Aureus*, particularly *MRSA* (Methicillin-Resistant Staphylococcus Aureus).⁶
- ❖ 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 *Candida Albicans* is common.
- ❖ Vulvovaginitis⁷ caused by *Non-Albicans Candida* species is common in patients with poor glycemic control.

Surgical Site Infections

Associated with postoperative hyperglycemia which is related to deleterious⁸ effect on chemotaxis, adherence, and phagocytosis by granulocytes.

Hyperglycemia

Metabolic derangements in diabetes may facilitate infection, **especially candidiasis.**
It also plays a role in UTIs.

² In medium and small vessels.

³ In normal situation a person passes urine because of the tension and pressure in the bladder but a diabetic patient do not feel this pressure and when they feel it they go to the bathroom but do not fully empty their bladder and unfortunately most of them are elderlies and might also have benign prostatic hyperplasia as well (in males) leading to urine stasis in the bladder and stagnant water make the patient more susceptible to infections.

⁴ Hyperglycemia in diabetic patients also plays a role in the UTIs.

⁵ They're teaching you in details how the immune system cause diabetes, but they never mention what diabetes does to your immune system, and it is very important to know!

⁶ *Staph. Aureus* is the most common gram +ve cocci, and is divided into two classes (MSSA & MRSA) based on its sensitivity to methicillin. When we add methicillin, Staph. Aureus either respond (Sensitive) or resist (Resistant).

⁷ inflammation of the vulva and vagina.

⁸ Causing harm or damage.

Different Infections in Diabetic Patients

Upper Respiratory Tract Infections

Invasive (Malignant) Otitis Media Uncommon but potentially life-threatening		Rhinocerebral Mucormycosis A life-threatening fungal infection	
Cause	<i>Pseudomonas Aeruginosa</i>	Cause	<i>Rhizopus</i> , <i>Absidia</i> and <i>Mucor</i> species
MOA	Slowly invades from the external canal of the ear into adjacent soft tissues, mastoid and temporal bones, and eventually spreads across the base of the skull.	Risk Factor	Diabetic Ketoacidosis always accompany mucormycosis
Clinical	Severe pain, otorrhea, hearing loss, intense cellulitis and edema of the ear canal.	Clinical	Intranasal black eschars ⁹ or necrotic turbinate, facial or ocular pain, nasal stuffiness, generalized malaise, fever.
Diagnosis	CT or MRI to define the extent of bone destruction.	Diagnosis	Biopsy of the necrotic tissue + Direct smear examination for hyphae. ¹⁰
Treatment	<ol style="list-style-type: none"> Surgical debridement. IV anti-pseudomonals 3rd generation cephalosporins like Ceftriaxone.	Treatment	<ol style="list-style-type: none"> Surgical debridement. Prolonged IV 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

Cause	<ul style="list-style-type: none"> ❖ Gram positive bacteria: <i>Staphylococcus Aureus</i>¹¹ and <i>Streptococcus Pneumoniae</i>. ❖ Gram negative bacteria: <i>Enterobacteria</i> and <i>Legionella</i>¹². ❖ Other organisms: <i>Influenza Virus</i> and <i>Mycobacterium Tuberculosis</i>.
Prevention	Routine pneumococcal and influenza vaccination are recommended. ¹³

Abdominal Infections

Severe Fulminating Cholecystitis

Cause	<i>Enteric Gram Negative Bacteria</i> and <i>Anaerobes</i> . ¹⁴
Complications	<ul style="list-style-type: none"> ❖ Gall stone or Peritonitis may be present. ❖ Gas gangrene and perforation may occur.
Treatment	Cholecystectomy + Broad spectrum antibiotics.

⁹ A slough or piece of dead tissue that is cast off from the surface of the skin, particularly after a burn injury, but also seen in gangrene, ulcer, fungal infections, necrotizing spider bite wounds, spotted fevers and exposure to cutaneous anthrax.

¹⁰ If you collect a sample and see hyphae you have to suspect mucormycosis.

¹¹ Might lead to a secondary infection after Influenza is healed.

¹² Only common in hospitalized patients (Patients in the ICU).

¹³ To prevent Influenza and to prevent the pneumococcal infection that might come after Influenza as a secondary infection.

¹⁴ Any bacteria from the GI tract.

Genitourinary Infections

Asymptomatic Bacteriuria ¹⁵ > 10 ⁵ bacteria/ml urine (common)		Cystitis Bladder infection		Pyelonephritis Kidney infection	
Clinical	Symptoms, Signs, and duration of onset are similar to non-diabetics.	Clinical	Same as non-diabetics.. Incomplete bladder emptying and high incidence of unsuspected upper UTI.	Types	❖ Bilateral: Diabetes predisposes to a more severe infection of the upper urinary tract.
Prevention	Screening is indicated for diabetic patients to treat asymptomatic bacteriuria.	Cause	❖ Gram positive: <i>Group B Streptococcus (Streptococcus Agalactiae).</i> ❖ Gram negative: <i>Escherichia Coli.</i> ❖ Fungal: <i>Candida Albicans.</i>		❖ Emphysematous:¹⁶ Exclusively present in diabetics (60%). Carries grave prognosis (30% fatal).
Diagnosis	Flank mass, crepitus ¹⁷ , and CT scan shows gas in the renal tissues.				
Treatment	Supportive + IV antibiotics + Nephrectomy if needed.				

Skin and Soft Tissue Infections

Necrotizing Fasciitis¹⁸ and Myositis

Deep life threatening infection of subcutaneous tissue with progressive destruction of fascia, fat, muscles, and bones

Risk Factors	<ul style="list-style-type: none"> ❖ Sensory neuropathy with no pain perception. ❖ Atherosclerotic vascular disease. ❖ Hyperglycemia: >250 mg/dl. ❖ History of cellulitis, peripheral vascular diseases, tinea infection, and dry skin.
Causes	<ul style="list-style-type: none"> ❖ <i>Streptococcus Pyogenes (Group A Streptococcus)</i> - 10% of Necrotizing Fasciitis. ❖ <i>Staphylococcus Aureus.</i> ❖ <i>CA-MRSA (Community Acquired MRSA)</i> - 77% of skin and soft tissue infections. ❖ <i>Clostridium Fragilis</i> (Gas producing gram positive bacilli) - Especially in Myositis. ❖ <i>Anaerobes</i> - Requires wound discharge.
Clinically	<ul style="list-style-type: none"> ❖ Very sever pain of proportion of skin and anesthesia of overlying skin. ❖ Violaceous discoloration of skin that evolves into vesicles and bullae. ❖ Acute illness with painful induration of the limb especially the thigh, foot may be involved. ❖ Crepitus. ❖ Soft tissue gas seen in radiograph or CT scan.
Treatment	Aggressive surgical debridement with wound discharge + IV antibiotics.

¹⁵ Mostly all the infected patients are elderly and will develop asymptomatic bacteriuria and sometime they will present with urosepsis and complication of shock (septic shock) because of the UTI.

¹⁶ 55 year old male - diabetic - not feeling well came to clinic complaining of Fever. They gave him antibiotic then the other day they found him dead (sudden death) they took him to find out the cause of death, they found microabscess in the kidney. This means the patient had bacteremia that caused sepsis then the abscess developed to kidney. So we have to be careful in case of diabetes for kidney because diabetic patient are already susceptible to nephropathy so any compression to kidney vessels will cause renal failure, and some will develop severe pyelonephritis.

¹⁷ Grating sound or sensation produced by friction between bone and cartilage or the fractured parts of a bone.

¹⁸ There are two types (type 1 & type 2). Type 1 is caused by multiple organism flora and type 2 is one organism only which is Group A Streptococcus.

Skin and Soft Tissue Infections (Cont...)

Diabetic Foot

The most common and most important soft tissue in diabetic patients

Significance	<ul style="list-style-type: none"> ❖ Peripheral neuropathy may lead to incidental trauma that goes unrecognized. ❖ Compromised microvascular circulation¹⁹ which limits the access of phagocytic cells to the site of infection. ❖ Poor concentration of antibiotics in the affected area. ❖ Can lead to amputation and death.
Complicated By	<ul style="list-style-type: none"> ❖ Chronic Osteomyelitis. ❖ Gas Gangrene²⁰ (due to <i>Clostridium Perfringens</i>)²¹
Spectrum	<ul style="list-style-type: none"> ❖ Ranges from superficial cellulitis to chronic osteomyelitis. ❖ Infection may be involving bone or soft tissue or both. ❖ Sinus tract may be present.
Pathogenesis	<p>Compromised local blood supply predisposing foot to infection, that is due to:</p> <ul style="list-style-type: none"> ❖ Microvascular disease. ❖ Pressure from ill-fitting shoes. ❖ Trauma. ❖ Compromises local blood supply predisposing foot to infection.
Diagnosis	<ul style="list-style-type: none"> ❖ Vascular and neurological state examination. ❖ Radiology: <ul style="list-style-type: none"> - Doppler ultrasonography. - Transcutaneous oximetry²². - MR angiography. ❖ CT, MRI, or Gallium scan²³ for soft tissue and bone. ❖ Exploration of ulcer to determine its depth and the presence of sinus tract. ❖ Deep specimens (tissues) for culture and susceptibility testing.
Treatment	<ul style="list-style-type: none"> ❖ Control blood sugar and hydration. ❖ Continuous evaluation of neuropathy and vasculopathy. ❖ Mild case: Debridement of necrotic tissue + Antibiotic according to the causative bacteria e.g. Cloxacillin, Cephadrine, Clindamycin, TMP-SMX (for CA-MRSA), Aminoglycosides, Quinolones. ❖ Moderate to sever case: Hospitalization + IV antibiotics + Possible surgery (amputation).
Prevention	<ul style="list-style-type: none"> ❖ 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.

¹⁹ It is the **circulation** of the blood in the smallest blood vessels, present in the vasculature embedded within organ tissues.

²⁰ Rapidly spreading gangrene occurring in dirty wounds infected by bacteria that give off a foul-smelling gas.

²¹ This organism perfuse fast because they have phospholipase and they degrade the tissue and produce gas. This gas is really important because it is an easy way to diagnose by X-ray because you can see the gas.

²² **Transcutaneous** oxygen measurement (TCOM or TcPO₂) is a non-invasive method of measuring the oxygen level of the tissue below the skin. Since oxygen is carried by the blood, TCOM can be used as an indirect measure of blood flow to the tissue.

²³ Gallium scan is a test to look for swelling (inflammation), infection, or cancer in the body. It uses a radioactive material called **gallium** and is a type of nuclear medicine exam.

Skin and Soft Tissue Infections (cont...)

Cellulitis

Causes	<ul style="list-style-type: none"> ❖ <i>Beta-hemolytic streptococci (Group A or B).</i> ❖ <i>Staphylococcus Aureus.</i> ❖ <i>Enterobacteriaceae (E.coli, Klebsiella, and Proteus)</i> - in chronic ulcers.
Clinically	<ul style="list-style-type: none"> ❖ Tender, erythematous, non-raised skin lesion on the lower limb, may be accompanied with lymphangitis (which suggests <i>Group A Streptococcus</i>). ❖ Bullae Suggests <i>Staphylococcus Aureus</i> and occasionally <i>Group A Streptococcus</i>.

Bone Infections

Chronic Osteomyelitis

Acute Osteomyelitis

Risk Factors	<ul style="list-style-type: none"> ❖ Grossly visible bone or ability to probe to bone. ❖ ESR > 70 mm/h. ❖ Size > 2x2 cm. ❖ Depth > 3mm. ❖ Duration > 1-2 weeks. 		
Cause	<ul style="list-style-type: none"> ❖ <i>Group A and B Streptococcus.</i> ❖ <i>Staphylococcus Aureus.</i> ❖ <i>Enterobacteriaceae.</i> <ul style="list-style-type: none"> - <i>Escherichia Coli</i> - <i>Proteus Mirabilis</i> - <i>Klebsiella Pneumoniae</i> ❖ <i>Bacteroides Fragilis.</i> 	Clinical	<ul style="list-style-type: none"> ❖ Pain at the involved bone. ❖ Fever. ❖ Adenopathy.
Clinically	<ul style="list-style-type: none"> ❖ Fever. ❖ Foul discharge. ❖ Pain (possible). ❖ No lymphangitis. ❖ Deep penetrating ulcers²⁴ and sinuses on the plantar surface of the foot. 		
Treatment	<ul style="list-style-type: none"> ❖ Control blood sugar and hydration. ❖ Continuous evaluation of neuropathy and vasculopathy. ❖ Mild case: Debridement of necrotic tissue + Antibiotic according to the causative bacteria. ❖ Moderate to sever case: Hospitalization + IV antibiotics + Possible surgery (amputation). 		
Prevention	<ul style="list-style-type: none"> ❖ 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. 		

²⁴ When you get in MCQ a question saying Patients is diabetic presented with ulcer WHAT IS THE BEST SAMPLE TO COLLECT? **TISSUE SAMPLE** IS THE BEST SAMPLE TO COLLECT.

Integrated MCQs and SAQs

A 56-year-old woman is brought to the emergency department with a 5-day history of fever, facial pain, and headache and a 1-day history of epistaxis, visual disturbances, and increasing lethargy. Physical examination reveals a toxic appearing woman with proptosis (forward bulging) of the left eye. Erosive lesions of the sinus and orbit are seen on CT of the head. Culture of material from a sinus aspirate grew the organism *Candida Albicans*.

Q1: What underlying condition most likely predisposed the woman to this infection?

- (A) **Diabetes**
- (B) Graves disease
- (C) HIV infection
- (D) Hypothyroidism
- (E) Osteoporosis

Q2: Which of the following is the most likely diagnosis in the above case?

- (A) Chromoblastomycosis
- (B) Invasive Aspergillosis
- (C) Sporotrichosis
- (D) **Rhinocerebral zygomycosis**

Q3: Which one of the following is most likely the causative organism in the disease?

- (A) *Candida albicans*
- (B) *Aspergillus*
- (C) ***Rhizopus***
- (D) *Cryptococcus*

Q4: List the most common causes of Rhinocerebral zygomycosis:

Rhizopus, *Absidia* and *Mucor* species.

Q5: Explain how *Rhizopus* spp. causing the group of infections referred to as zygomycosis:

These opportunistic fungi readily invade blood vessels, entering tissues and producing necrotic lesions.

Q6: The most common predisposing factor for this infection is:

Diabetic ketoacidosis.

Q7: What is your step to diagnose this case?

Biopsy of the necrotic tissue + Direct smear examination for hyphae.

Q8: What is the initial step in the management of such a case?

Surgical debridement and prolonged IV therapy with Amphotericin B.

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. Sensations to vibrations and light touch are also markedly diminished.

Q1: The development of polyneuropathy in this patient correlates best with which of the following conditions?

- (A) Anti-insulin antibody titer
- (B) **Hyperglycemia**
- (C) Insulin deficiency
- (D) Intermittent hypoglycemia
- (E) Ketoacidosis

Q2: List “Host Related factors” other than hyperglycemia:

- Vascular insufficiency
- Sensory peripheral neuropathy
- Autonomic neuropathy
- Immune defects
- Increased skin and mucosal colonization
- Surgical site infections

Q3: In the above case, which of the following is the most common infection in diabetic patients related to peripheral neuropathy?

- (A) Necrotizing fasciitis
- (B) Vulvovaginitis
- (C) **Diabetic foot**
- (D) Pyelonephritis

Q4: 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.

Q5: Which of the following is life-threatening infection related to diabetic foot infection:

- (A) **Necrotizing fasciitis**
- (B) Vulvovaginitis
- (C) Cellulitis
- (D) Pyelonephritis

Q6: What is the best specimen to collect in such case?

Deep tissue specimen.

Q7: Explain the management and treatment of “moderate to severe” cases:

Places the foot at risk of amputation. Needs hospitalization with IV antibiotics and surgical intervention if needed.