Infections in Patients with Diabetes

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Introduction

- 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:

INFECTIONS

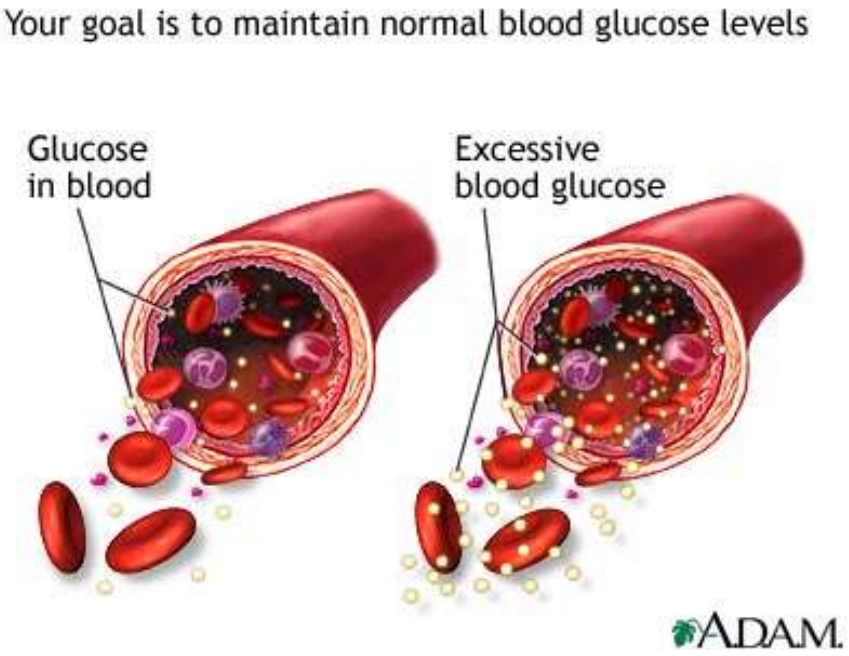
- Although not specifically an acute or a chronic complication, infections are a common concern of people with diabetes.
- Certain types of infections occur with increased frequency in people with diabetes:
  - Soft tissue infections of the extremities
  - Osteomyelitis
  - Urinary tract infections and pyelonephritis
  - Candidal infections of the skin and mucous surfaces
  - Dental caries and infections
  - Tuberculosis
- Suboptimal response to infection in a person with diabetes is caused by the presence of chronic complications, such as vascular disease and neuropathies, and by the presence of hyperglycemia and altered neutrophil function. Polymorphonuclear leukocyte function, particularly adherence, chemotaxis, and phagocytosis, are depressed in persons with diabetes, particularly those with poor glycemic control.
- Hyperglycemia and glycosuria may influence the growth of microorganisms and increase the severity of the infection.

Host Related Factors

- **Vascular insufficiency** 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 stasis that ,in turn, predisposes to develop UTIs.

Reasons for Increased Infections:

- Hyperglycemia
- Poor tissue perfusion from vascular disease



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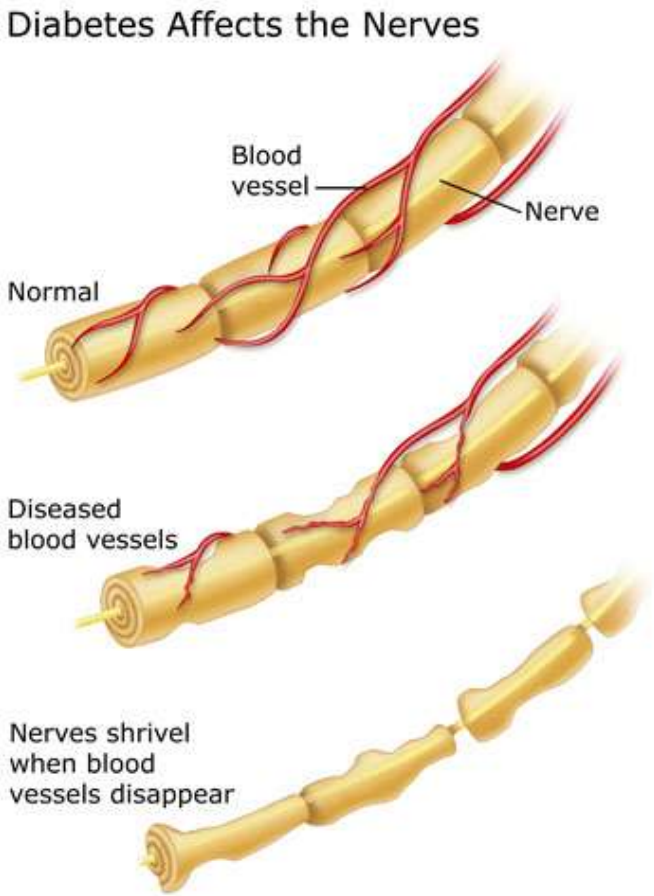
Reasons for Increased Infections:

- Sensory peripheral neuropathy
- Autonomic neuropathy



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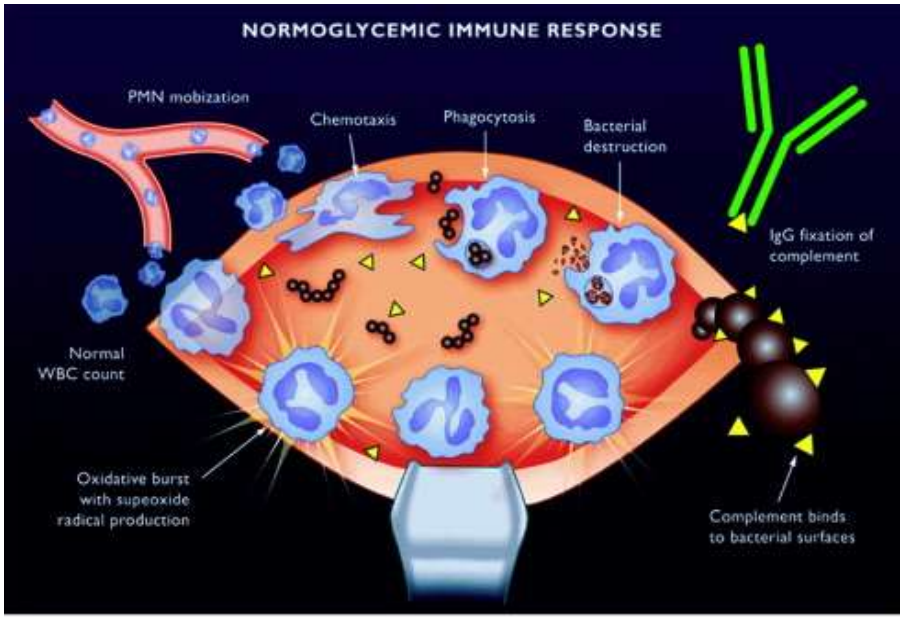
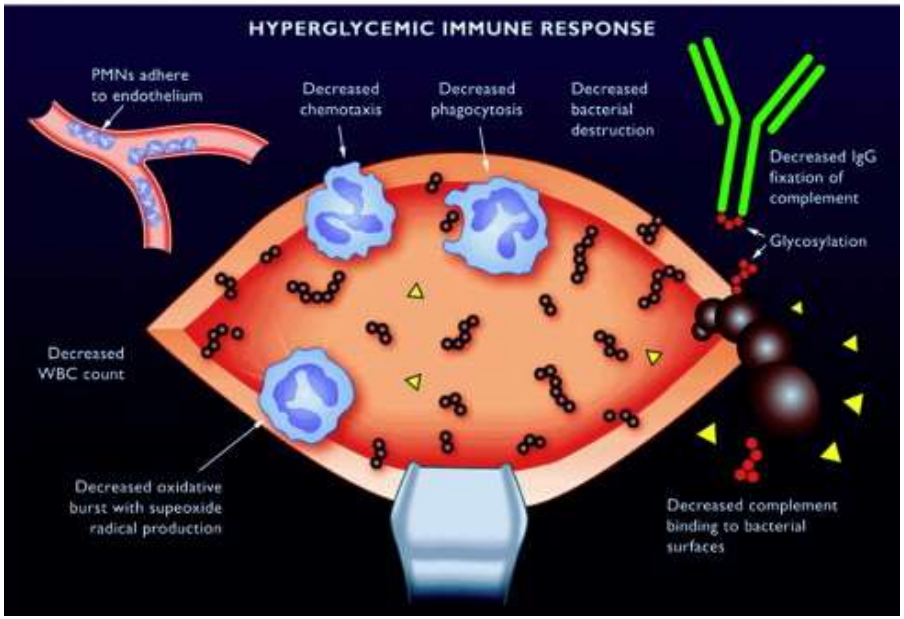
Normoglycemic vs. Hyperglycemic Immune Response





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Host Related Factors

- **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

Host Related Factors

- **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 bacteraemia which may result in distal sites infection such as damaged muscle.

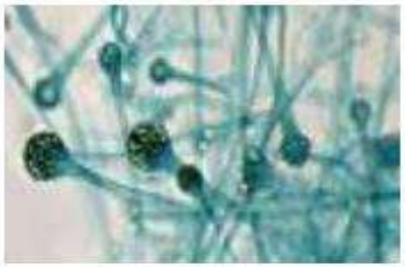
In type- 2 diabetes ;mucosal colonization with *C.albiacns* is common. **Vulvovaginitis** caused by non-albicans *Candida* spp. is common in patients with poor glycemic control.

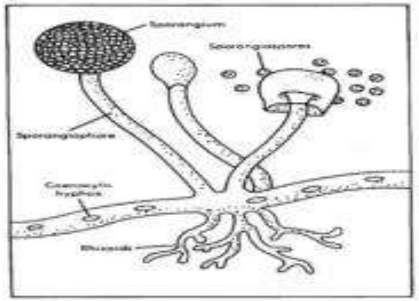
Host Related Factors

- **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

- Upper & lower respiratory tract infections
- Periodonatal infections
- Genitourinary infections
- Abdominal infections
- Skin and soft tissue infections & diabetic foot

Upper Respiratory Tract Infections

- Invasive (malignant) ottitis media, uncommon but potentially life threatening.
- Rhinocerebral mucormycosis

Invasive otitis media

Cause: *P.aeruginosa*. Slowly invades from the external canal into adjacent soft tissues, mastoid and temporal bone and eventually spreads across the base of the skull.

s/s :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.
- **Clinically**: facial or ocular pain and nasal stuffiness, generalized malaise and fever. May be intranasal black eschars or necrotic turbinates.
- **Diagnosis**: biopsy of necrotic tissue
- **Treatment:** surgical debridement and prolonged IV therapy with Amphotericin B .

Skin and soft tissue infections

- **Risk factors in diabetic patients :**

- Sensory neuropathy: no pain perception.
- Atherosclerotic vascular disease
- Hyperglycemia : >250 mg/ dl increased risk
- H/O of cellulitis, peripheral vascular diseases, *Tinea*, and dry skin.

- Organisms: *S.pyogenes* (GAS) and *S.aureus*

CA-MRSA (Community Acquired MRSA) is of concern, causes (77%) of skin and soft tissue infections .

Lower respiratory tract infections pneumonia and influenza

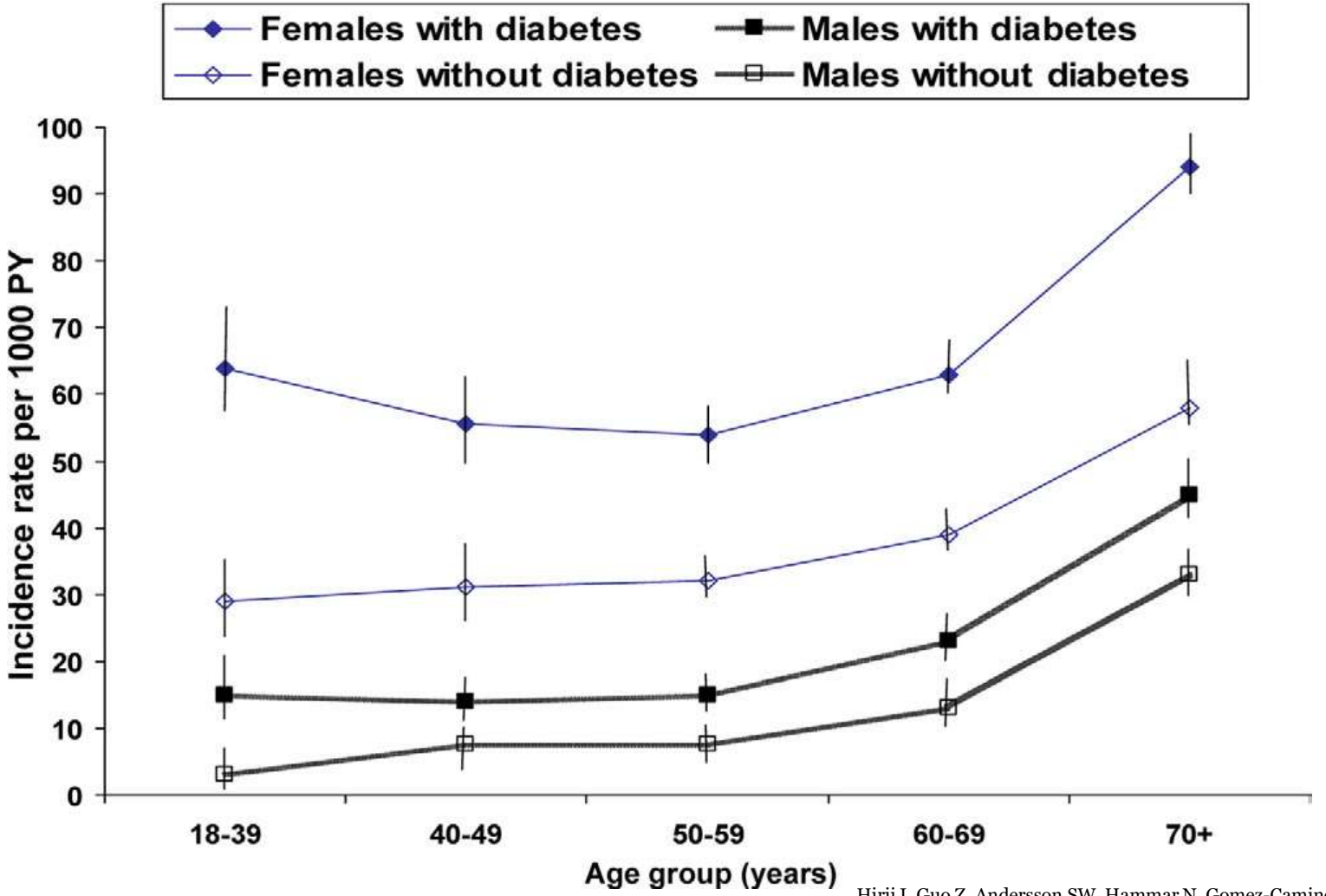
- Diabetic patients are 4 times more likely to die from pneumonia or influenza than non-diabetic patients.
- **Common organisms**: Gram positive bacteria :*S.aureus* , *S.pneumoniae*.

Gram negative bacteria: Enterobacteria and *Legionella*.

Other organisms: Influenza virus & *Mycobacterium tuberculosis* .

- Routine pneumococcal vaccination and influenza recommended.

Incidence: Urinary Tract Infections



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Genitourinary infections

- **Asymptomatic bacteriuria** (> 10 5 /ml urine) is common.

Symptoms/ signs and 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) 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.

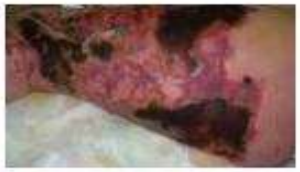
- **Vulvovaginitis :** as mentioned earlier.

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



- **Necrotizing fasciitis** :a deep –seated ,life threatening infection of subcutaneous tissue with progressive destruction of fascia, fat and muscle.

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

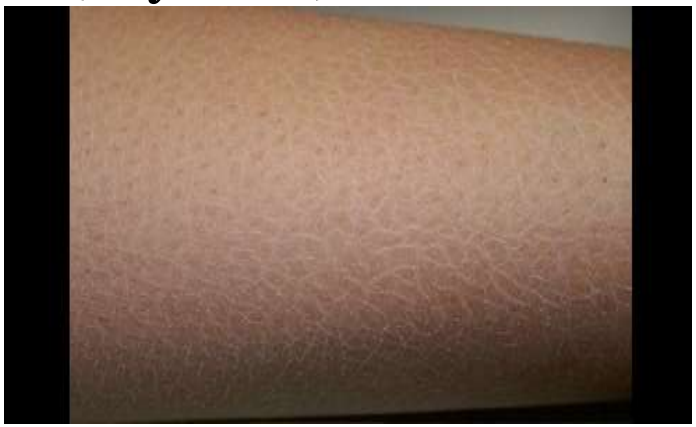
Clinically: pain of proportion of skin, anaesthesia of overlying skin. *Violaceous discoloration* of skin that evolves into vesicles and bullae, crepitus ,soft tissue gas seen in radiograph or CT.

Management :aggressive surgical debridement & IV antibiotics.

- 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.

Incidence: Cutaneous Infections

- One case control study assessed prevalence of skin infections in adolescents with and without type 1 diabetes:
  - 142 (68%) of type 1 patients with diabetes had at least one cutaneous infection vs. 52 (26.5%) of control subjects ($p < 0.01$)
  - The most common skin condition was xerosis (dry skin)



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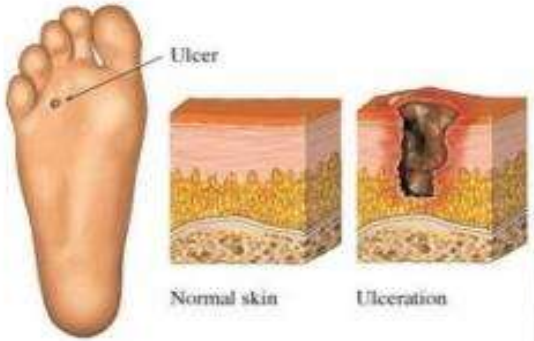
- Infection may involve the skin, soft tissues, bone ,or all.
- Diabetic neuropathy may lead to incidental trauma that goes unrecognized.
- Sinus tract may be present.

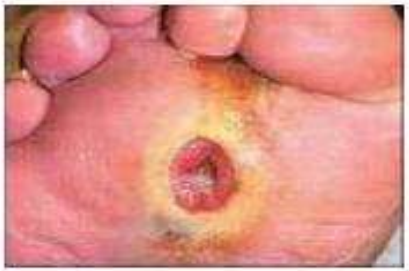
Organisms involved in diabetic foot infections

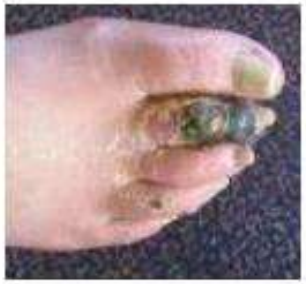
- **Cellulitis**: : beta-hemolytic streptococcus (group A,B streptococi), *S.aureus*, *Entertobacteriacae* (*E.coli*, *Klebsiella, Proteus spp.*) in chronic ulcers.
- **Macerated ulcer or nail injury** (sinus) : *P.aeruginosa* .
- **Deep soft tissue infections (**necrotizing fasciitis, or myositis):GAS & gas producing gram positive bacilli (*Clostridium*).
- **Chronic Osteomyelitis**: GAS and Group B *Sterptococcus*, *S.aureus, Enterobacteriacae* (*E.coli* ,*Proteus mirabilis* , *K.pneumoniae.) & Bacteroides fragilis*

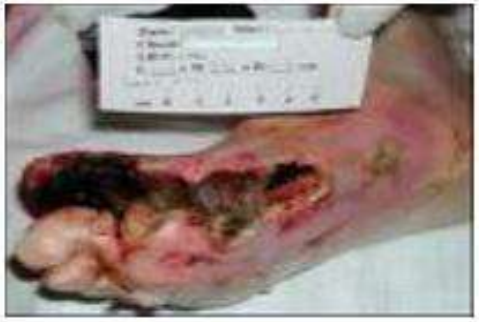
Factors that increases the development of Osteomyelitis:

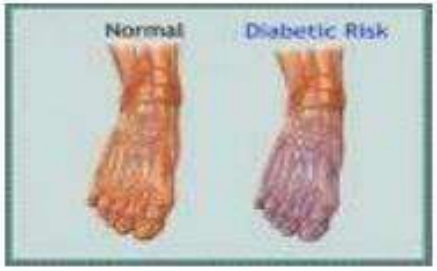
grossly visible bone or the ability to probe to bone, ulcer size >2x2 cm, ulcer depth > 3mm, ulcer duration longer than 1-2 wks, ESR >70 mm/hr







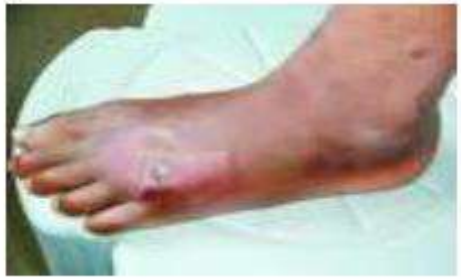




Clinical presentations of diabetic foot infections

- **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 of foot infections

- Thorough examination to evaluate the patient's vascular and neurological status.
- Radiological examination including doppler ultrasonography ,transcutaneous oxymetery, 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.

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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, Cephradine, 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.

Infection-related Mortality:

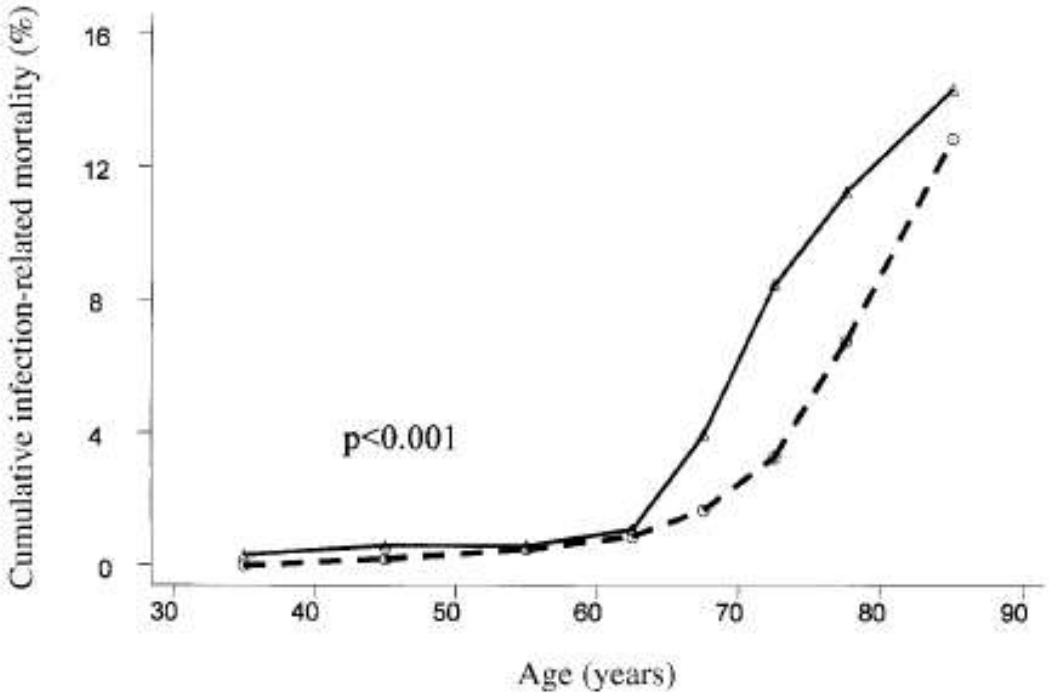
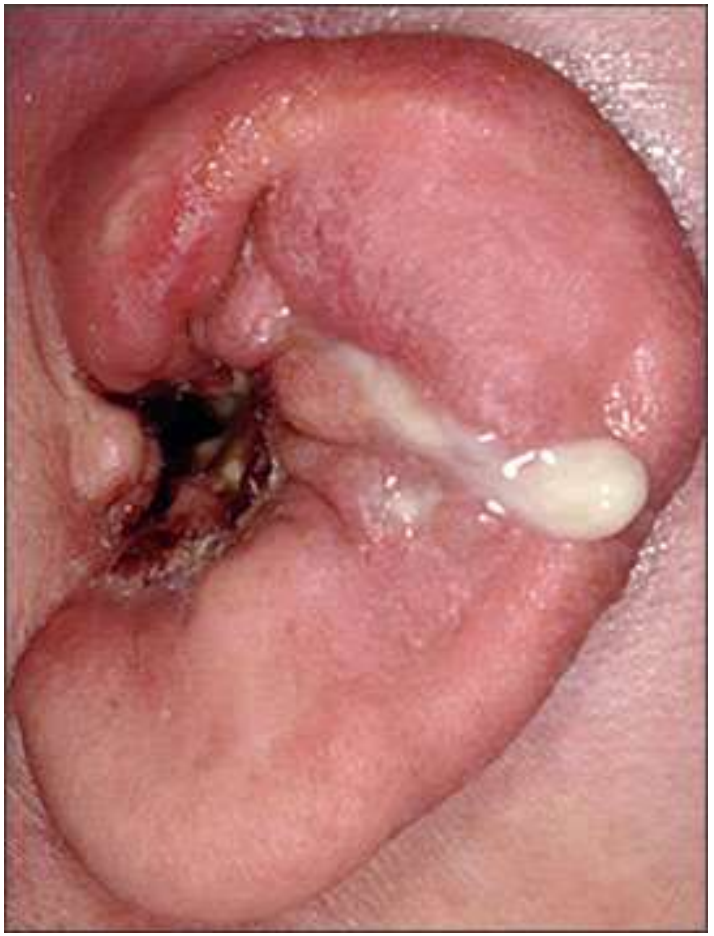


Figure 1—*Cumulative mortality related to infectious diseases in 9,208 adults by age at follow-up and diabetes status at baseline (solid line, individuals with diabetes; dashed line, nondiabetic individuals). Data for life-table calculations were based on weighted estimates to account for the complex sampling design of NHANES II and thus provide nationally representative estimates. A log-rank test was used to compare the mortality curve.*

Bertoni AG, Saydah S, Brancati FL. Diabetes and the risk of infection-related mortality in the U.S. *Diabetes Care*. 2001;24:1044-1049.

Malignant Otitis Externa

- Almost exclusively in patients with diabetes
- More common if >35 years
- Caused by *Pseudomonas aeruginosa*
- Presents as severe ear pain and drainage/pus from the ear



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http://www.aafp.org/afp/2006/1101/p1510.html

Malignant Otitis Externa Treatment

- Surgical consult to rule out cancer
- Fluoroquinolones are the drug of choice
- Initially: IV ciprofloxacin 400mg every 8 hours until clinical response is seen or a decrease in ESR
- Maintenance: Ciprofloxacin 750mg by mouth twice daily for a total treatment duration of 6-8 weeks
- Topical antibiotics are not indicated

Khardori R. Infection in patients with diabetes mellitus. Medscape reference. WebMD 2011.
Grandis JR, Yu VL. Malignant (necrotizing) external otitis. In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA. 2012.
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HOSPITAL CARE DELIVERY STANDARDS

15.1 **Perform an A1C test on all patients with diabetes or hyperglycemia (blood glucose >140 mg/dL [7.8 mmol/L]) admitted to the hospital if not performed in the prior 3 months. B**

15.2 Insulin should be administered using validated written or computerized protocols that allow for predefined adjustments in the insulin dosage based on glycemic fluctuations. C

DIABETES CARE PROVIDERS IN THE HOSPITAL

15.3 When caring for hospitalized patients with diabetes, consult with a specialized diabetes or glucose management team when possible. C

GLYCEMIC TARGETS IN HOSPITALIZED PATIENTS

15.4 Insulin therapy should be initiated for treatment of persistent hyperglycemia starting at a threshold ≥180 mg/dL (10.0 mmol/L). Once insulin therapy is started, a target glucose range of 140–180 mg/dL (7.8–10.0 mmol/L) is recommended for the majority of critically ill patients and noncritically ill patients. A

15.5 More stringent goals, such as 110–140 mg/dL (6.1–7.8 mmol/L), may be appropriate for selected patients if they can be achieved without significant hypoglycemia. C

GLUCOSE-LOWERING TREATMENT IN HOSPITALIZED PATIENTS

15.6 Basal insulin or a basal plus bolus correction insulin regimen is the preferred treatment for noncritically ill hospitalized patients with poor oral intake or those who are taking nothing by mouth. A

15.7 An insulin regimen with basal, prandial, and correction components is the preferred treatment for noncritically ill hospitalized patients with good nutritional intake. A

15.8 Use of only a sliding scale insulin regimen in the inpatient hospital setting is strongly discouraged. A

HYPOGLYCEMIA

15.9 A hypoglycemia management protocol should be adopted and implemented by each patient. A plan for preventing and treating hypoglycemia should be established for each patient. Episodes of hypoglycemia in the hospital should be documented in the medical record and tracked. E

15.10 The treatment regimen should be reviewed and changed as necessary to prevent further hypoglycemia when a blood glucose value of <70 mg/dL (3.9 mmol/L) is documented. C

Transition from the Hospital Setting to the Ambulatory Setting

15.11 There should be a structured discharge plan tailored to the individual patient with diabetes. B

The Agency for Healthcare Research and Quality (AHRQ) recommends that, at a minimum, discharge plans include the following:

Medication Reconciliation

- The patient's medications must be cross-checked to ensure that no chronic medications were stopped and to ensure the safety of new prescriptions.
- Prescriptions for new or changed medication should be filled and reviewed with the patient and family at or before discharge.

The Agency for Healthcare Research and Quality (AHRQ) recommends that, at a minimum, discharge plans include the following (continued):

Structured Discharge Communication

- Information on medication changes, pending tests and studies, and follow up needs must be accurately and promptly communicated to outpatient physicians.
- Discharge summaries should be transmitted to the primary care provider as soon as possible after discharge.
- Scheduling follow-up appointments prior to discharge increases the likelihood that patients will attend.

It is recommended that the following areas of knowledge be reviewed and addressed prior to hospital discharge:

- Identification of the health care provider who will provide diabetes care after discharge.
- Level of understanding related to the diabetes diagnosis, self-monitoring of blood glucose, home blood glucose goals, and when to call the provider.
- Definition, recognition, treatment, and prevention of hyperglycemia and hypoglycemia.
- Information on making healthy food choices at home and referral to an outpatient RD/RDN to guide individualization of meal plan, if needed.
- If relevant, when and how to take blood glucose–lowering medications, including insulin administration.
- Sick-day management.
- Proper use and disposal of needles and syringes.