INFECTION AND
DIABETES MELLITUS
Alterations in Immune Mechanisms in Diabetic Patients
Individuals with DM have a greater frequency and severity of infection. The reasons for this include incompletely defined abnormalities in cell-mediated immunity and phagocyte function associated with hyperglycemia, as well as diminished vascularization. Hyperglycemia aids the colonization and growth of a variety of organisms (Candida and other fungal species). Many common infections are more frequent and severe in the diabetic population, whereas several rare infections are seen almost exclusively in the diabetic population. Examples of this latter category include rhinocerebral mucormycosis, emphysematous infections of the gallbladder and urinary tract, and “malignant” or invasive otitis externa. Invasive otitis externa is usually secondary to Pseudomonas aeruginosa infection in the soft tissue surrounding the external auditory canal, usually begins with pain and discharge, and may rapidly progress to osteomyelitis and meningitis. These infections should be sought, in particular, in patients presenting with severe hyperglycemia.
Pneumonia, urinary tract infections, and skin and soft tissue infections are all more common in the diabetic population. In general, the organisms that cause pulmonary infections are similar to those found in the nondiabetic population; however, gram-negative organisms, S. aureus, and Mycobacterium tuberculosis are more frequent pathogens. Urinary tract infections (either lower tract or pyelonephritis) are the result of common bacterial agents such as Escherichia coli, although several yeast species (Candida albicans and Torulopsis glabrata) are commonly observed. Complications of urinary tract infections include emphysematous pyelonephritis and emphysematous cystitis. Bacteriuria occurs frequently in individuals with diabetic cystopathy and does not require antibiotic therapy. Susceptibility to furunculosis, superficial candidal infections, and vulvovaginitis are increased. Poor glycemic control is a common denominator in individuals with these infections. Individuals with diabetes have an increased rate of colonization of S. aureus in the skinfolds and nares. Individuals with diabetes also have a greater risk of postoperative wound infections.
Infection in diabetic patients:

- Frequent
- Potentially life-threatening
- UTI, TB, Candidiasis, gram – negative pneumonia occur with greater frequency in diabetics
Common infections in diabetics may be poorly tolerated due to:

1) alterations in host defense mechanisms
2) high prevalence of coexistent disease
Vicious cycle may ensue:

- stress of infection complicates management of the diabetes
- worsening metabolic control exacerbate the infectious process.
Hyperglycemia (FBS > 126 or RBS > 200 mg/dL) on general medical and surgical units was associated with:

1) An 18 – fold increase in in-hospital mortality
2) A larger length of stay in hospital (9 VS 4.5 days)
3) More subsequent nursing home care
4) Greater risk of infection

JCEM 2002; 87: 978 - 982
Over the short-term, hyperglycemia may adversely affect:

1) fluid balance
2) immune function,
3) inflammation, and
4) outcome in patients after stroke, myocardial infarction, CABG and critical illness.

Diabetes 1990; 39: 271
Infect Dis Clin of N Amer 9: 1 – 9 1995
Hyperglycemic patients undergoing cardiac surgery suffer:

1) Greater mortality
2) Increased chance of deep – wound infection
3) More overall infection rate

*Hyperglycemia, on the first and second postoperative days, was the single most important predictor of serious infectious complications*

Circulation 1999; 100: I – 591

Ann Thorac surg 1997; 63: 356
Deep sternal wound infection rates in cardiac surgery patients are:

1) Directly correlated with increasing postoperative glucose levels.

2) The rate of this serious complication was reduced by 66% with intensive IV insulin infusion for 3 – days postoperatively.
This body of evidence strongly suggests that hyperglycemia in the hospital is associated with adverse outcomes, particularly:

1) **Death**

2) **Disability after stroke and acute cardiovascular events, and**

3) **infections.**
Intensive insulin therapy in ICU patients resulted in decreases in:

1) Sepsis rate 46%
2) ARF 41%
3) Transfusions rate 50%
4) Critical illness-related polyneuropathy 44%

NEJM 2001; 345: 1359
High glucose levels in the brood and body fluids promote the overgrowth of certain fungal pathogens especially:

*Candida and zygomycetes*

Zygomycetes grows more rapidly under conditions of *acidosis*, making DKA a major predisposing factor.
2) Subtle alterations in cell-mediated immunity predispose the diabetic patient to:

- Tuberculosis and
- Certain fungal infections
Factors that Increase the Diabetic Patient's Susceptibility to Infection

- Increased cutaneous and mucous membrane carriage of potential pathogens
- Abnormal phagocyte function
- Abnormal cell-mediated immunity
- Hyperglycemia and acidosis
- Coexisting medical conditions
  - Neuropathy
  - Angiopathy
HOST FACTORS PREDISPOSING TO INFECTION

A) are incompletely understood

B) several defects in the immune defense mechanisms:

1) cutaneous and mucous membrane carriage of potential organisms is increased in diabetic patients. (staph. aureus, gram-negative bacilli, and candidia)
3) Alterations in monocyte phagocytosis and in PMN leukocyte functions including:

- Mobilization
- Chemotaxis
- Adherence
- Phagocytosis
- And bactericidal function

Some defects clearly improve with aggressive glycemic control.
Reversible defects in immune system in hyperglycemic patients:

1) Inactivation of immunoglobulins

2) Impaired complement system function (opsonization)

3) Neutrophil dysfunction
   - Impaired chemotaxis
   - Impaired phagocytosis
   - Impaired intracellular killing

Diabetes. 1974; 23: 9
1978; 27: 677
1988; 37: 544
1978; 27: 889
Therefore it is critical that metabolic derangements be promptly corrected in all diabetic patients who present with infection.
Measures to Prevent Infection in Diabetic Patients

Normalization of blood glucose
Avoidance of acidosis
Treatment of coexisting atherosclerotic cardiovascular risk factors (hypertension, hyperlipidemia, obesity, smoking)
Proper foot care
Prophylaxis
  Isoniazid for patients with positive tuberculin skin test
  Pneumococcal vaccine
  Influenza vaccine
Reductions of infectious complications due to:

Apparent eradication of nonenzymatic glycation of proteins critical to adequate function of immune system

Diabetes. 1995; 39: 271
J Trauma 1995; 30: 830
A number of unusual infections occur predominantly in diabetics (table)

Many of these can be life-threatening and constitute medical emergencies
# Infections Associated with Diabetes Mellitus

<table>
<thead>
<tr>
<th>Type of Infection</th>
<th>Approximate Percentage of Patients with Diabetes Mellitus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant otitis externa</td>
<td>90</td>
</tr>
<tr>
<td>Emphysematous pyelonephritis</td>
<td>92</td>
</tr>
<tr>
<td>Emphysematous cystitis</td>
<td>80</td>
</tr>
<tr>
<td>Rhinocerebral mucormycosis</td>
<td>75</td>
</tr>
<tr>
<td>Necrotizing fasciitis</td>
<td>75</td>
</tr>
<tr>
<td>Papillary necrosis</td>
<td>57</td>
</tr>
<tr>
<td>Perinephric abscess</td>
<td>36</td>
</tr>
<tr>
<td>Emphysematous cholecystitis</td>
<td>35</td>
</tr>
</tbody>
</table>
## LIFE-THREATENING INFECTIONS IN DIABETICS: SUMMARY OF KEY CLINICAL FEATURES

<table>
<thead>
<tr>
<th>Entity</th>
<th>Predisposing factors</th>
<th>Signs and Symptoms</th>
<th>Causative Organism (Diagnostic Specimen)</th>
<th>Preferred Radiographic Studies</th>
<th>Treatment</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Malignant otitis externa</strong></td>
<td>Swimming in fresh water</td>
<td>Otalgia, Otorrhea, Temporal headache, TMJ pain, granulation tissue in EAC</td>
<td>Pseudomonas aeruginosa (Cultures of ear drainage, EAC, or surgical biopsy)</td>
<td>Cranial CT or MR</td>
<td>Antipseudomonal antibiotics (piperacillin/tobramycin or ciprofloxacin/rifampin) Local debridement</td>
<td>10% to 20%</td>
</tr>
<tr>
<td><strong>Rhinocerebral mucormycosis</strong></td>
<td>Poorly controlled diabetes with hyperglycemia and ketoacidosis, Corticosteroids</td>
<td>Lethargy, Fever, Headache, Facial pain and swelling, Nasal drainage, Proptosis, Black mucosal eschars</td>
<td>Fungi of the order Mucorales (Histology on tissue biopsy)</td>
<td>Cranial CT or MR</td>
<td>Control of hyperglycemia and acidosis Amphotericin B Excisional surgery</td>
<td>50%</td>
</tr>
<tr>
<td><strong>Emphysematous cholecystitis</strong></td>
<td>Prior cholecystitis (No relationship to glucose control)</td>
<td>Clostridia SP, Or E. col (Cultures of bile)</td>
<td>KUB CT of abdomen</td>
<td>Ampicillin, clindamycin, and an aminoglycoside Cholecystectomy</td>
<td>15%</td>
<td></td>
</tr>
<tr>
<td>Entity</td>
<td>Predisposing factors</td>
<td>Signs and Symptoms</td>
<td>Causative Organism (Diagnostic Specimen)</td>
<td>Preferred Radiographic Studies</td>
<td>Treatment</td>
<td>Mortality</td>
</tr>
<tr>
<td>--------------------------------------------</td>
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</tr>
<tr>
<td><strong>Emphysematous pyelonephritis</strong></td>
<td>Ureteral obstruction? Poor glucose control</td>
<td>Fever</td>
<td>E. Coli and other GNRs (Cultures of urine and blood)</td>
<td>KUB CT of abdomen</td>
<td>Third-generation cephalosporin, imipenem or ciprofloxacin Nephrectomy or percutaneous drainage</td>
<td>10% to 37%</td>
</tr>
<tr>
<td><strong>Necrotizing soft tissue infections</strong></td>
<td>Minor trauma, Local cutaneous infections, Surgery (especially abdominal), Perineal/perirectal infections, Poorly controlled diabetes with/without ketoacidosis</td>
<td>High fever, Local pain, Skin anesthesia, Edema, Skin necrosis, Draining wounds, Crepitus</td>
<td>Mixed aerobic anaerobic flora (Culture of tissue biopsy)</td>
<td>Plain films of involved area</td>
<td>Imipenem, Extensive surgical debridement; amputation occasionally required Hyperbaric oxygen</td>
<td>20% to 60%</td>
</tr>
</tbody>
</table>
### NECROTIZING SOFT TISSUE INFECTIONS SEEN IN DIABETICS

<table>
<thead>
<tr>
<th>Predisposing factors</th>
<th>Nonclostridial Gas Gangrene'</th>
<th>Necrotizing Fasciitis</th>
<th>Necrotizing Cellulitis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prior localized infection</td>
<td>Local skin infection Surgery (especially abdominal)</td>
<td>Obesity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Perineal infection</td>
<td>Renal disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Minor trauma</td>
<td>Perirectal infection</td>
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<tr>
<td></td>
<td></td>
<td>? Injections</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Onset</th>
<th>Gradual or rapid</th>
<th>Rapid</th>
<th>Rapid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>Mild</td>
<td>Moderate to severe</td>
<td>Severe</td>
</tr>
<tr>
<td></td>
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<td></td>
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<tr>
<td>Skin appearance</td>
<td>Minimal discoloration</td>
<td>Erythematous; areas of necrosis</td>
<td>Areas of necrosis</td>
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<tr>
<td></td>
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<tr>
<td>Exudate</td>
<td>Dark pus</td>
<td>Seropurulent drainage</td>
<td>&quot;Dishwater&quot; pus</td>
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<td></td>
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</tr>
<tr>
<td>Gas</td>
<td>Extensive</td>
<td>Mild</td>
<td>Mild</td>
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<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Odor</td>
<td>Foul</td>
<td>Foul</td>
<td>Foul</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle involvement</td>
<td>None</td>
<td>None</td>
<td>Mild</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>20%</td>
<td>25% to 50</td>
<td>≥ 60%</td>
</tr>
</tbody>
</table>