Fighting Infection in Diabetes

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Division of Infectious Diseases

Outline
• Does DM Increase Risk of Infections?
• Diabetic Foot Ulcers
• Infections Treated Differently in DM
• Infections Increased in DM
• Other Considerations

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I have no disclosures

It's a Ruse! Nystatin Isn't a Statin After All

Does DM Increase Risk of Infection?

<table>
<thead>
<tr>
<th>Condition</th>
<th>Adj Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower Respiratory Tract Infection</td>
<td>1.32 - 1.42</td>
</tr>
<tr>
<td>UTI</td>
<td>1.24 - 1.96</td>
</tr>
<tr>
<td>GI</td>
<td>1.4</td>
</tr>
<tr>
<td>Bacterial Skin/MM Infection</td>
<td>1.33 – 1.66</td>
</tr>
<tr>
<td>Mycotic Skin/MM Infection</td>
<td>1.34 – 1.44</td>
</tr>
</tbody>
</table>

Proposed Mechanisms for Increased Infection Risk

- Decreased Cell-Mediated Immunity
- Decreased Leukocyte Function (hyperglycemia)
- Vascular Insufficiency
  - Ischemia
  - Tissue injury
- Neuropathy
  - Sensory
  - Autonomic
  - Urinary Retention
- Bacterial growth
- Impaired immune response
- Delivery
- Abx

Does DM Increase the Risk of Infection?

- **Surgical Site Infections**
  - Diabetes (OR 2.76)
  - Post-op hyperglycemia (OR 2.02)
  - Not A1c

- **Hospital-Acquired Infections**
  - DM is an independent risk factor (RR 1.76)

**Take-Away:**
- DM likely increases the risk of some infections
- Relationship of hyperglycemia is unclear
Outline

- Does DM increase risk of infections?
- Diabetic Foot Ulcers
  - Infections Treated Differently in DM
  - Infections Increased in DM
- Other Considerations

Diabetic Foot Ulcers

- Is it infected?
- How do you evaluate the infection?
  - General evaluation
  - Severity
  - Imaging
  - Culture
- How do you manage the infection?
  - What organisms should you cover?
  - Surgical management
  - Treatment duration

Question #1

When should you suspect MRSA could be playing a role in a diabetic foot infection?

A. Positive MRSA nasal carriage within last yr
B. Frequent gym use
C. Copious purulence
D. Extreme erythema
Diabetic Foot Ulcer: Is it Infected?
>2 classic signs of inflammation or purulence
- Erythema
- Warmth
- Tenderness
- Swelling/Induration
Exclude other causes
- Trauma
- Gout
- Acute Charcot
- Fracture
- Thrombosis
- Venous Stasis

Factors Associated with Infection
<table>
<thead>
<tr>
<th>Condition</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probing to bone</td>
<td>6.7</td>
</tr>
<tr>
<td>Ulcer &gt;30 days</td>
<td>4.7</td>
</tr>
<tr>
<td>History of recurrent ulcers</td>
<td>2.4</td>
</tr>
<tr>
<td>Traumatic foot wound</td>
<td>2.4</td>
</tr>
<tr>
<td>PVD (in affected limb)</td>
<td>1.9 – 5.5</td>
</tr>
<tr>
<td>Previous amputation</td>
<td>19.9</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>3.4</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td></td>
</tr>
<tr>
<td>H/o walking barefoot</td>
<td></td>
</tr>
</tbody>
</table>

### Diabetic Foot Infections: Severity?

<table>
<thead>
<tr>
<th>IDSA Infection Severity</th>
<th>Predicts risk for:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hospitalization</td>
</tr>
<tr>
<td>Uninfected</td>
<td>0%</td>
</tr>
<tr>
<td>Mild</td>
<td>4%</td>
</tr>
<tr>
<td>Moderate</td>
<td>52%</td>
</tr>
<tr>
<td>Severe</td>
<td>89%</td>
</tr>
</tbody>
</table>


### Diabetic Foot Infections: Imaging Evaluation

**Imaging**
- **XR** for new diabetic foot infections (bony abnl, gas, foreign bodies)
- **MRI** if c/f abscess, osteomyelitis
- Radionuclide bone scan + tagged WBC scan (If MRI not possible)

### Diabetic Foot Infections: Osteomyelitis Evaluation

<table>
<thead>
<tr>
<th>Diagnostic Tool</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDG-PET Scan</td>
<td>89%</td>
<td>92%</td>
</tr>
<tr>
<td>WBC Scan (\textsuperscript{111}In-Oxine)</td>
<td>92%</td>
<td>75%</td>
</tr>
<tr>
<td>WBC Scan (\textsuperscript{99m}Tc-HMPAO)</td>
<td>91%</td>
<td>92%</td>
</tr>
<tr>
<td>MRI</td>
<td>93%</td>
<td>75%</td>
</tr>
<tr>
<td>XR</td>
<td>54%</td>
<td>68%</td>
</tr>
<tr>
<td>Probe To Bone</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Gold Standard:** Bone biopsy with pathology and culture

*Consider inflammatory markers (for monitoring)*


### Diabetic Foot Infections: Culture Evaluation

**Culture**
- **No infection = No need for culture**
- If debridement, try to obtain culture
- Deep Tissue Biopsy/Curettage
- *After debridement & cleansing*
- Drain purulence
- **NO wound swabs**
- Prior to abx if possible

IDSA Diabetic Foot Infections Guidelines 2012.
Diabetic Foot Infections: Management

- Determine care setting
- Debride (necrotic tissue, callus, etc)
- Offload
- Wound Care
- Antibiotics

Diabetic Foot Infections: Management

When to hospitalize?

- Severe infections
- Moderate infections with complications
- Social factors
- Failure of outpatient therapy

Diabetic Foot Infections: What organisms should be covered?

Mild/Moderate Infections

- Staph, Strep
- Not anaerobes or other resistant organism

<table>
<thead>
<tr>
<th>Organism(s)</th>
<th>Situation</th>
</tr>
</thead>
<tbody>
<tr>
<td>GNRs</td>
<td>Warm climate, Severe infections</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>Warm climate, Water exposure, Severe Infections</td>
</tr>
<tr>
<td>Anaerobes</td>
<td>Chronic, Previously Tx’d, Severe Infections</td>
</tr>
<tr>
<td>MRSA</td>
<td>H/o MRSA infxn or carriage (last 1y), Severe Infections</td>
</tr>
<tr>
<td>ESBL</td>
<td>When prevalent***</td>
</tr>
</tbody>
</table>
Diabetic Foot Infections: Surgical Management

Balancing of risks & benefits
- Pt preference?
- Surgical target?
- Chance for function?
- Location?
- Surgical risk?
- Prolonged abx risk?
- Sepsis/disseminated infection?

Involve vascular surgeon if ischemia

Diabetic Foot Infections: Surgical Management

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- Pt preference?
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- Chance for function?
- Location?
- Surgical risk?
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Involve vascular surgeon if ischemia

Diabetic Foot Infections: Antibiotic Duration

<table>
<thead>
<tr>
<th>SSTI Infection Severity</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>1-2 weeks</td>
</tr>
<tr>
<td>Moderate</td>
<td>1-3 weeks</td>
</tr>
<tr>
<td>Severe</td>
<td>2-4 weeks</td>
</tr>
</tbody>
</table>

Diabetic Foot Infections: Antibiotic Duration

<table>
<thead>
<tr>
<th>Osteomyelitis</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>No remaining infection</td>
<td>2-5 days*</td>
</tr>
<tr>
<td>Residual soft tissue infxn</td>
<td>1-3 weeks*</td>
</tr>
<tr>
<td>Residual infected but reliable bone</td>
<td>4-6 weeks**</td>
</tr>
<tr>
<td>No debridement &amp; residual infected bone</td>
<td>≥ 3 months**</td>
</tr>
</tbody>
</table>

*PO or IV
**IV -> consider PO

Diabetic Foot Ulcers

Take-Aways:
- Not every ulcer is infected
- Infected ulcers need multipronged assessment
- Obtain deep culture when feasible
- Mild/moderate are typically 2/2 Staph, Strep
- Surgery requires risk/benefit evaluation
- Abx duration varies based on severity
Outline

- Does DM increase risk of infections?
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Question #2

A 62yo gentleman with T2DM presents with a 2d history of cough and fevers. He is febrile but otherwise stable and is diagnosed with community-acquired pneumonia. \textbf{Which is the most appropriate therapy?}

A. Azithromycin
B. Levofloxacin
C. Doxycycline
D. Ceftriaxone + Azithromycin

Infections Treated Differently

\textbf{CAP} \\
Empiric therapy: FQ vs. (B-Lactam + Macrolide)

\textbf{Coccidioidomycosis} \\
Treat newly-diagnosed, uncomplicated PNA

\textbf{Latent TB infection} \\
DM is an indication for treatment
Outline

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Urinary Tract Infection

\[
\text{A1c} = \text{risk UTI} \quad (1 \text{ unit} \ 	riangleq 21\% \ \text{of UTI frequency})
\]

Asymptomatic Bacteriuria is common

<table>
<thead>
<tr>
<th>Group</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-menopausal women</td>
<td>1-5%</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>2-10%</td>
</tr>
<tr>
<td>Post-menopausal women, 50-70 yrs</td>
<td>3-9%</td>
</tr>
<tr>
<td>Pts with DM</td>
<td>9-27%</td>
</tr>
<tr>
<td>Elderly in LTC facilities (women; men)</td>
<td>15-50%</td>
</tr>
<tr>
<td>Pts with spinal cord injuries</td>
<td>23-89%</td>
</tr>
<tr>
<td>Pts undergoing HD</td>
<td>28%</td>
</tr>
<tr>
<td>Pts with indwelling catheters</td>
<td>25-100%</td>
</tr>
</tbody>
</table>

Urinary Tract Infection

No treatment for asymptomatic bacteriuria

RCT:
- DM women with axs bacteriuria
- TMP/SMX vs Placebo
- 40% (placebo) vs 42% (tx) symptomatic UTI

Treatment
- If DM well-controlled, treat as uncomplicated?
- Otherwise: cipro or levo x7-14d
- If pregnant: nitrofurantoin or cephalexin

Skin & Soft Tissue Infections

Most commonly due to Staph and Strep
- <10% of cases due to GNRs (same as non-Diabetics)

Higher complication rate in DM
- Predisposing factor for necrotizing fascitis, Fournier’s

Higher hospitalization rate in DM

Tx: Consider abx after I&D of MRSA abscesses
Vulvovaginal Candidiasis

Likely associated with:
- Glycosuria
- HgbA1c
- Blood glucose & glycosuria (even w/o DM)

Less Common Infections

Mucor
- 36% due to DM
- 66% of pts with DM had sinus dz
- since 1990s, potentially 2/2 statin

Malignant Otitis Externa
- ~90% pts have DM
- Associated with poor DM control
- Typically Pseudomonas

Infections Increased in DM

Take-Aways:
- Asymptomatic bacteriuria is common
  - Don’t treat it!
- SSTIs are likely due to Staph, Strep
- Consider I&D plus abx with all abscesses
- Vulvovaginal candidiasis a/w poor DM control
- Malignant OE a/w poor DM control

Outline

- Does DM increase risk of infections?
- Diabetic Foot Infections
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- Other Considerations
  - Vaccinations
  - Fluoroquinolone therapy
Question #3

How do the vaccination recommendations differ for a 55yo woman with DM compared to a 55yo woman without DM?

A. Menactra vaccination recommended
B. Hepatitis B vaccination recommended
C. Hep B and Pneumovax recommended
D. Pneumovax recommended

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Vaccinations in DM

Age 19-64y
- 1 dose PPSV23, then:
  - 1 dose PCV13 at 65y (if none previously)
  - 2nd dose PPSV23
  (1y post-PCV13 & 5y after PPSV23)
- Hepatitis B series (esp if <60y)

Fluoroquinolones

FQs have been associated with dysglycemia

Cohort Study: Macrolides vs FQs

<table>
<thead>
<tr>
<th>FQ</th>
<th>Hyperglycemia Adj Odds Ratio</th>
<th>Hypoglycemia Adj Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levofloxacin</td>
<td>1.75</td>
<td>1.79</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>1.87</td>
<td>1.46</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>2.48</td>
<td>2.13</td>
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</table>

CDC Immunization Schedule: https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html#DM
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Summary
- DM likely increases the risk of some infections
- Relationship of hyperglycemia is unclear
- Diabetic Ulcers
  - Not every ulcer is infected
  - Infected ulcers need multipronged assessment
  - Obtain deep culture when feasible
  - Mild/moderate are typically 2/2 Staph, Strep
  - Surgery requires risk/benefit evaluation
  - Abx duration varies based on severity

Summary
- Treat differently: CAP, Cocci, LTBI, ?UTIs
- Asymptomatic bacteriuria is common
- SSTIs are likely due to Staph, Strep
- Consider I&D plus abx with all abscesses
- Association with poor DM control
  - UTIs
  - Vulvovaginal candidiasis
  - Malignant OM a/w poor DM control

Questions?

Questions

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