An update on the treatment of skin and soft tissue infections

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Disclosure

- I do not have a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or any affiliation with an organization whose philosophy could potentially bias my presentation.

Objectives

- Describe common infections of the skin and soft tissues and recognize the clinical manifestations.
- Provide differential diagnoses of infections involving the skin and soft tissues.
- Compare and contrast the microbial etiologies in patients with various risk factors and presentations.
- Discuss general principles of antimicrobial therapy in the treatment of skin and soft tissue infections.

Patient Case

- 70F with pain in right lower leg since last night.
  - Worse with standing, walking, touch.
  - Swelling also noted.
  - Some discomfort in her LLE, but much less painful.
  - Had taken systemic steroids (unknown dose) for pain/inflammation.
- PMH: CAD, MI, HTN, RA, Bilateral Osteoporosis.

Patient Case

- Admitting Note
  - Piperacillin/tazobactam + Vancomycin x 4 days in Hospital.
  - Discharged on Day 4 with Augmentin.

- Urine Culture

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>09:00</td>
<td>Negative</td>
</tr>
<tr>
<td>Day 1</td>
<td>09:45</td>
<td>Negative</td>
</tr>
</tbody>
</table>

- Blood Culture

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 2</td>
<td>01:00</td>
<td>11.0 V</td>
</tr>
<tr>
<td>Day 2</td>
<td>01:45</td>
<td>11.0 V</td>
</tr>
<tr>
<td>Day 3</td>
<td>02:00</td>
<td>11.2 V</td>
</tr>
</tbody>
</table>
Cellulitis Pearls

- Patients with cellulitis will always have a fever or leukocytosis
- Cellulitis is NEVER EVER EVER EVER EVER bilateral
- The rubor, dolor, calor, tumor of cellulitis does not resolve with elevation
- Differentiates from stasis edema
- Cellulitis takes longer to resolve in heavier patients
- Extra day for each 50 lbs overweight
- Cellulitis progresses for a day, stabilizes for a day, and then starts to resolve

1. Rubor = redness
2. Dolor = pain
3. Calor = warmth
4. Tumor = swelling

Normal Skin Flora

- Coagulase-negative staphylococci
- Propionibacterium acnes
- Diphtheroids (Corynebacteria)
- α-hemolytic streptococci
- Bacillus spp.
- Staphylococcus aureus
- β-hemolytic streptococci

* = potential pathogen

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Beta-hemolytic Streptococci

- Group A
  - Streptococcus pyogenes
- Group C & G
  - Streptococcus dysgalactiae
- Group B
  - Streptococcus agalactiae

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Bugs and Drugs

- Beta-lactams
  - Cephalosporins
  - Penicillins
  - Carbapenems
  - Monobactams
- Lincosamides
- Oxazolidinones
- Lipopeptides
- Glycopeptides
- Lipoglycopeptides
- Glycylcyclines

TEDIZOLID

- Bacteriostatic against enterococci, staphylococci, and streptococci
- Requires neutrophils to work effectively
- ESTABLISH-1 & ESTABLISH-2 in ABSSSI
- 6 days of tedizolid vs. 10 days linezolid
- Comparable to linezolid in clinical efficacy
- Less thrombocytopenia with shorter duration

Tedizolid

- Tedizolid 200 mg PO once daily
- Tedizolid 200 mg IV q24h
- Volume of Distribution (L): 67-80
- Protein binding (%): 70-90
- Bioavailability (%): 91, N/A
- Half-life (h): 12
- AUC (mcg•hr/mL): 25.6, 29.2
- Time to peak (h): 3.5, 1.2
- Cmax (mcg/mL): 2.2, 3

Oritavancin/Dalbavancin

- Lipoglycopeptides
- Rapidly bactericidal, concentration-dependent killing

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Dalbavancin</th>
<th>Oritavancin</th>
<th>Vancomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSSA</td>
<td>0.06</td>
<td>0.23</td>
<td>2</td>
</tr>
<tr>
<td>MRSA</td>
<td>0.06</td>
<td>0.12</td>
<td>1</td>
</tr>
<tr>
<td>Group A Strp. (S. pyogenes)</td>
<td>0.03</td>
<td>0.12</td>
<td>0.5</td>
</tr>
<tr>
<td>Group B Strp. (S. agalactiae)</td>
<td>0.12</td>
<td>0.10</td>
<td>0.5</td>
</tr>
<tr>
<td>β-haemolytic Streptococce spp.</td>
<td>0.06</td>
<td>0.3</td>
<td>0.5</td>
</tr>
<tr>
<td>VanA E. faecium</td>
<td>2</td>
<td>0.29</td>
<td>57</td>
</tr>
<tr>
<td>VanB E. faecium</td>
<td>0.12</td>
<td>0.03</td>
<td>64</td>
</tr>
<tr>
<td>Clostridium spp.</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

- Spectrum of Activity

Cost of Care

- Contributing factors to cost:
  - Inpatient vs. outpatient reimbursement/LOS
  - Complications from therapy
  - Cost of monitoring
  - Drug cost

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Cost Per Vial</th>
<th>Typical Regimen</th>
<th>1 Day Cost</th>
<th>7 Day Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalbavancin</td>
<td>$1,490</td>
<td>500 mg on day 1, 500 mg on day 8</td>
<td>$2,980</td>
<td>$4,470</td>
</tr>
<tr>
<td>Oritavancin</td>
<td>$920</td>
<td>1200 mg x 1 dose</td>
<td>$2,755</td>
<td>$2,760</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>$365</td>
<td>500 mg q24h</td>
<td>$365</td>
<td>$2,560</td>
</tr>
<tr>
<td>Linezolid</td>
<td>$130</td>
<td>600 mg q12h</td>
<td>$260</td>
<td>$1,820</td>
</tr>
<tr>
<td>Tedizolid</td>
<td>$235</td>
<td>200 mg q24h</td>
<td>$235</td>
<td>$1,645</td>
</tr>
<tr>
<td>Ceftaroline</td>
<td>$54</td>
<td>600 mg q12h</td>
<td>$108</td>
<td>$755</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>$5</td>
<td>1000 mg dose (plus Advantage bag)</td>
<td>$10</td>
<td>$60</td>
</tr>
</tbody>
</table>

Roadmap for Success

- Admit, Observe, or Discharge
- Intravenous or Oral Route
- Duration of Therapy
- Antimicrobial Therapy
- I&D C&S
### Eron Classification

<table>
<thead>
<tr>
<th>Class</th>
<th>Patient Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Afebrile and healthy, other than SSTI</td>
</tr>
<tr>
<td>2</td>
<td>Febrile and ill appearing, but no unstable comorbidities</td>
</tr>
<tr>
<td>3</td>
<td>Toxic appearance, one unstable comorbidity, or limb-threatening infection</td>
</tr>
<tr>
<td>4</td>
<td>Sepsis syndrome or life-threatening infection</td>
</tr>
</tbody>
</table>

#### Poor Response Predictors
- Advanced age
- Chronic liver disease
- Chronic renal disease
- Asplenia
- Alcohol abuse
- Use of abx in previous 2 weeks

#### Poor Outcome in LF Wounds
- Reduced arterial perfusion
- Neuropathy
- Chronic venous insufficiency
- Diabetes
- Obesity
- Malnutrition
- Immunocompromise

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### Additional Imaging

<table>
<thead>
<tr>
<th>Ultrasound</th>
<th>X-ray</th>
<th>CT Scan</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rule out DVT</td>
<td>Foreign bodies</td>
<td>Drainable collections</td>
<td>Investigate bone and fascia</td>
</tr>
<tr>
<td>Gas in tissues</td>
<td></td>
<td></td>
<td>Osteomyelitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Necrotizing fasciitis</td>
</tr>
</tbody>
</table>

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### The Quick Admit

- Tissue necrosis
- Sepsis
- Disproportionate pain
- AMS
- Immunocompromise
  - AIDS
  - Cancer
- Liver Failure
- Renal Failure
- Specific areas of infection

### Classifications of Infections

#### Skin and Soft Tissue Infection Classification

- Impetigo & Ecthyma
- Purulent infections
  - Cutaneous abscesses
  - Furuncles & carbuncles
- Erysipelas & cellulitis
- Necrotizing fasciitis
- Pyomyositis
- Myonecrosis & gas gangrene

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### Impetigo & Ecthyma

- Topical therapy option for impetigo if only a few lesions: mupirocin or retapamulin BID x 5 days
- PO Tx x 7 days targeted against isolated species
  - If no cultures: empiric therapy must cover both MSSA & BHS
Impetigo & Ecthyma

- **Nonbullous Impetigo**
  - BHS, MSSA, MRSA
  - No scarring
  - Starts near nose or mouth
  - Very contagious
  - Painless

- **Bullous Impetigo**
  - MSSA, MRSA
  - No scarring
  - Mainly seen in children’s arms, legs, trunk
  - Painless

- **Ecthyma**
  - BHS, MSSA, MRSA
  - Scarring
  - Painful

For mild cases, send home without antibiotics. For moderate cases, admit and administer:
- IV Daptomycin
- IV Linezolid
- IV Ceftaroline

For severe cases, do not administer initial antibiotics. Instead: 1. I & D 2. IV Vancomycin 3. IV Daptomycin 4. IV Linezolid 5. IV Ceftaroline

For recurrent abscess:
- PO abx x 5-10 days ± mupirocin/CHG decontamination x 5 days

Purulent Infections

- Painful pustules involving hair follicles and epidermis
- Treatment of choice: I & D
- If systemic signs or symptoms, treat for MRSA

Purulent Infections

- Furuncle
- Carbuncle
- Cutaneous Abscess

Diagnosis

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (diagnose purulent infection without systemic signs of infection)</td>
<td>Purulent infection with 1 systemic sign (implies only 2 criteria be met)</td>
<td>Purulent infection with SIRS response (implies 2 or more criteria must be met)</td>
</tr>
</tbody>
</table>

Treatment

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV Vancomycin, no antibiotics</td>
<td>IV + PO MRSA active agent</td>
<td>Not defined</td>
</tr>
</tbody>
</table>

Admit and Administer:
- IV Vancomycin
- IV Daptomycin
- IV Linezolid
- IV Ceftaroline

Send home without antibiotics.
**Non-Purulent Infections**

- **Erysipelas**
  - Clearly demarcated
  - Usually on face

- **Cellulitis**
  - Diffuse erythema with less delineated borders
  - Commonly found on lower extremities

**Non-Purulent Cellulitis**

- Streptococci
- Staphylococci

**Non-Purulent Infections**

- No skin or blood cultures indicated
  - Except in immunosuppressed, immersion injuries, animal bites
- Treat x 5 days unless not resolved in this time
- Elevate affected area
- Treat predisposing factors
  - Edema
  - Skin disorders
  - Examine interdigital toe space in patients with lower extremity cellulitis to prevent recurrence

**Indications for Hospitalization**

- Outpatient treatment is failing*
- Concerns over poor adherence to therapy*
- Severely immunocompromised
- SIRS
- Hemodynamic instability
- Altered mental status
- Concern for deeper or necrotizing infection

*May be candidates for quick acting IV lipoglycopeptides in 23 hour observation unit
Necrotizing Fasciitis
- Infection spreads rapidly through fascial plane to surrounding tissues
- Often a predisposing condition in lower extremities
- Most infections are community-acquired & highly fatal
- Common pathogens: Streplococcus pyogenes, S. aureus, Vibrio, Aeromonas, Peptostreptococcus
  - Isolated from deep tissue specimen or exudate aspiration
  - Can be polymicrobial
  - Perianal abscess or other areas involving genitalia
  - Surgical procedures involving the bowel
  - Decubitus ulcers
  - IVDU
- Differentiated from cellulitis by:
  - Severe pain disproportionate to clinical findings
  - Nonresponse to antimicrobial therapy
  - Hard wooden feel of subQ tissue
  - Systemic toxicity
  - Edema extending beyond erythema
  - Crepitus
  - Bullous lesions
  - Skin necrosis or ecchymoses
- Treatment:
  - Repeat surgical debridement daily
  - Aggressive fluid replenishment
  - Empiric antibiotic choices
  - Streamline once etiology known and treat until:
    - Fever resolved x 48-72 hours
    - Clinical improvement
    - No further need for debridement
  - S. pyogenes should be treated with penicillin + clindamycin

Pyomyositis
- Differentiated from cellulitis by:
  - Severe pain disproportionate to clinical findings
  - Nonresponse to antimicrobial therapy
  - Hard wooden feel of subQ tissue
  - Systemic toxicity
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Pyomyositis

- Infection (pus) in the muscle
  - Mainly in extremity but can be found in any muscle
  - Presents with extreme pain, muscle tenderness, fever
  - CK remains normal if no trauma (hematogenous seeding)
  - Diagnosis confirmed by MRI
- Etiologies
  - > 90% Staphylococcus aureus (CA-MRSA)
  - Streptococcus pyogenes
  - Streptococcus pneumoniae
  - Gram negative enteric bacteria
- Vancomycin is empiric treatment of choice

Myonecrosis & Gas Gangrene

- Clostridial infection with rapid onset
  - C. perfringens: trauma associated
  - C. septicum: GI malignancy associated
  - Increasingly severe pain
  - Skin can be pale at first but then changes to bronze, then purple-red color
  - Gas is detected in the tissue by palpation (crepitus) or imaging
  - SIRS → Shock → Multi-organ failure

Non-Purulent Infections

- Rapid surgical debridement can be life-saving
- Broad spectrum antimicrobials initiated immediately until diagnosis confirmed
- Vancomycin PLUS
  - Piperacillin/tazobactam
  - Ampicillin/subbactam
  - Carbapenem
  - Definitive therapy: clindamycin
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C&S

23 Hour Observation Status, Administer:
- IV Dalbavancin
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- IV Vancomycin
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Yes
No

Admit and Administer:
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EXIT NOW

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*May only need therapy against MSSA/BHS (not MRSA)

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Patients who are Eron class 3 solely due to unstable comorbidities may be treated with MSSA/BHS active agents, similar to Eron class 2 options.

Discharge with:
- PO Penicillin VK
- PO Cephalexin
- PO Dicloxacillin
- PO Clindamycin

Admit and Administer:
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- IV Oritavancin
- IV Vancomycin
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Admit and Administer:
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