Skin and Soft Tissue Infections (SSTI):
More than a skin deep review

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Objectives

• To review the anatomy and classification of SSTIs

• To understand the approach to diagnosis and management of commonly encountered pediatric SSTIs

• To incorporate recent evidence into management of SSTIs in children
  – Role of antibiotics
  – Role of adjunctive laboratory testing
ANATOMY AND CLASSIFICATION
Anatomy
Classification

• **Superficial**
  – Impetigo
  – Cellulitis
  – Erysipelas
  – Abscess (furuncles, carbuncles)

• **Deep/Necrotizing**
  – Necrotizing fasciitis
  – Pyomyositis
  – Osteomyelitis

• **Non-necrotizing**
  – Mild/moderate
  – Responsive to abx alone

• **Necrotizing**
  – Life-threatening
  – Systemic toxicity
  – Tissue necrosis
  – Requires surgical management

• **Miscellaneous**
  – Animal Contact
  – *Orbital cellulitis*
  – Immunocompromised Hosts
  – Surgical Site Infections (SSI)
Challenges in Management of SSTI

• Diagnosis
  – Overlap in clinical presentation

• Severity of illness
  – Can be subtle

• Antibiotic resistance patterns
SUPERFICIAL SSTI
Impetigo

• Anatomy: Epidermis

• Clinical Features
  – Most common skin infection in
  – Non-bullous (>70% of cases)
    • Typically on face and extremities
    • Follows local skin trauma
    • Early vesicle/pustule becomes classic “honey-crusted” plaque
    • Minimal surrounding erythema and few systemic sx

• Diagnosis – Clinical
**Impetigo**

- **Microbiology**
  - *S. pyogenes* (GAS) classic cause of non-bullous impetigo
  - *S. aureus* now the most common cause of impetigo

- **Management**
  - No labs necessary
  - Mupirocin 2% ointment – for limited number of lesions
  - Indications for oral antibiotics:
    - Multiple lesions, deeper involvement (cellulitis), perioral lesions
Erysipelas

• Anatomy: Superficial dermis

• Clinical Features:
  – Prominent lymphatic involvement
  – **Raised, sharply demarcated** borders
  – Indurated and “peau d’orange” appearance
  – Young infants/children, older adults
  – Classic: butterfly area of face; legs also common

• Microbiology: GAS most common

• Management:
  – Penicillin
  – Cephalosporin (1st generation)
Cellulitis

• “Acute spreading infection of the skin that extends deeper than erysipelas and involves the subcutaneous tissues”

• Anatomy: Deep Dermis and Subcutaneous Tissues

• Clinical Features
  – **Diffuse** inflammation with pain, warmth, erythema, edema
  – Lack of sharply demarcated borders
  – Regional lymphangitis and systemic symptoms possible
  – Systemic symptoms may start hours before skin manifestations

*Hospital Pediatrics 2013;3;103*
Cellulitis

• Diagnosis
  – Diffuse cellulitis typically not amenable to culture
  – Needle aspirates and punch biopsies not recommended\(^1\text{-}\text{2}\)
  – Ultrasound – consider to help exclude occult abscess\(^6\)
  – Blood cultures low-yield in children and adults with cellulitis\(^3\text{-}\text{4}\)

Sadow KB, *Pediatrics* 1998;101(3).
Abscess

• Anatomy: Deep dermis and subcutaneous tissues

• Clinical Features
  – Pus collection with **painful**, tender, fluctuant nodules
  – Surface pustule with surrounding erythema and edema
  – **Furuncle**, aka “boil” = infection of hair follicle
  – **Carbuncle** = coalescence of furuncles to an inflamed mass
Abscess

• Diagnosis
  – Clinical examination important but findings may be unreliable \(^5\)
  – Ultrasound can increase diagnostic accuracy \(^6\)
  – Culture of purulent fluid critical

• Microbiology
  – S. aureus is primary pathogen in 25-50% of cases
  – Often polymicrobial – skin flora, bugs (GNR, anaerobes) from adjacent mucous membranes (e.g., perioral, perianal, groin)
Abscess

• Management
  – Warm compresses
    • Adequate for small furuncles
  – I&D
    • I&D alone adequate for simple abscesses
    • Wound packing also may not be necessary

– Antibiotics
  • Simple abscesses do not require antibiotics after I&D
  • Adjunctive abx after I&D in certain situations
  • Tailor abx based on culture and susceptibility patterns
    – Include CA-MRSA coverage

– Hospitalization
  • If rapidly progressive infection or systemic toxicity
EVIDENCE UPDATE: MANAGEMENT OF SSTI
Evidence Update: Management of SSTI

• Commonly encountered clinical questions:
  1. When are antibiotics necessary? IV vs PO?
  2. Is one class of antibiotics preferred over another? (Should I cover for MRSA?)
  3. What additional testing is useful/high-yield?
I. Evidence Update: Antibiotics for SSTI

- SSTI are common (>14M clinic visits + >850K admissions annually)
- Serious complications can occur (bacteremia, need for surgical procedures, morbidity/mortality)
- Clinical presentation and severity of illness can be subtle

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>SSTI Hospitalizations and I&amp;Ds: 1997, 2000, 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1997 N (wt)</td>
</tr>
<tr>
<td></td>
<td>1905 797 (6 657 325)</td>
</tr>
<tr>
<td>All US hospitalizations</td>
<td>13 225 (30 653)</td>
</tr>
<tr>
<td>SSTI</td>
<td></td>
</tr>
<tr>
<td>Receiving I&amp;D</td>
<td>2779 (6 284)</td>
</tr>
<tr>
<td>Asthma</td>
<td>86 698 (200 699)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>77 936 (197 584)</td>
</tr>
</tbody>
</table>

wt, weighted.

Lopez MA, *Pediatrics* 2013;131:e718
I. Antibiotics for SSTI: MRSA is common

- MRSA is most prevalent organism in SSTIs (59%)
- Many w/CA-MRSA have no RF
- Presence of RF for CA-MRSA raise suspicion but are not 100% reliable

<table>
<thead>
<tr>
<th>Site</th>
<th>No. of Patients Enrolled (N=422)</th>
<th>MRSA (N=249)†</th>
<th>MSSA (N=71)</th>
<th>Other Bacteria (N=64)‡</th>
<th>No Bacterial Growth (N=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albuquerque</td>
<td>42</td>
<td>25 (60)</td>
<td>10 (24)</td>
<td>3 (7)</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Atlanta</td>
<td>32</td>
<td>23 (72)</td>
<td>4 (12)</td>
<td>3 (9)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Charlotte, N.C.</td>
<td>25</td>
<td>17 (68)</td>
<td>0</td>
<td>4 (16)</td>
<td>4 (16)</td>
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<tr>
<td>Kansas City, Mo.</td>
<td>58</td>
<td>43 (74)</td>
<td>6 (10)</td>
<td>4 (7)</td>
<td>5 (9)</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>47</td>
<td>24 (51)</td>
<td>6 (13)</td>
<td>8 (17)</td>
<td>9 (19)</td>
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<tr>
<td>Minneapolis</td>
<td>28</td>
<td>11 (39)</td>
<td>4 (14)</td>
<td>9 (32)</td>
<td>4 (14)</td>
</tr>
<tr>
<td>New Orleans</td>
<td>69</td>
<td>46 (67)</td>
<td>11 (16)</td>
<td>9 (13)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>New York</td>
<td>20</td>
<td>3 (15)</td>
<td>8 (40)</td>
<td>5 (25)</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Philadelphia</td>
<td>58</td>
<td>32 (55)</td>
<td>12 (21)</td>
<td>12 (21)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Phoenix, Ariz.</td>
<td>30</td>
<td>18 (60)</td>
<td>8 (27)</td>
<td>4 (13)</td>
<td>0</td>
</tr>
<tr>
<td>Portland, Oreg.</td>
<td>13</td>
<td>7 (54)</td>
<td>2 (15)</td>
<td>3 (23)</td>
<td>1 (8)</td>
</tr>
</tbody>
</table>

Peds study of empiric antibiotics for SSTIs

• Studies:
  – Trends in invasive MRSA (infants!)
    • Common cause of bacteremia in infants
  – Empiric antibiotics often have gram negative coverage
Staph vs Strep: Classic Clinical Features

• CA-MSSA ("classic" *S. aureus*)
  – Pyogenic infections
  – Localized swelling and erythema
  – Less rapid with less systemic toxicity

• *Streptococcus* (usually GAS)
  – Rapid onset (hours)
  – Progressive, well-demarcated erythema along tissue planes
  – Often associated lymphangitis
  – Systemic symptoms (chills, fever) and toxicity

• CA-MRSA
  – Mimics GAS → rapid onset, systemic toxicity
  – Very pyogenic infection
Community Acquired MRSA (CA-MRSA)

- Oral Antibiotic Options
  - Clindamycin
  - TMP-SMX
    - No activity against GAS
  - Tetracyclines (Doxycycline, Minocycline)
  - Linezolid
  - “Triple Coverage” → only with clindamycin or linezolid
I. Antibiotics for SSTI: Beta-lactams work just fine in the CA-MRSA era

• Diffuse, Non-culturable SSTIs
  – Case-control study of 2096 patients at PCP clinic and ED sites
  – All enrolled patients had non-drained, non-cultured SSTI
  – High prevalence of MRSA (>50%)

  – Conclusion: β-Lactams are reasonable first-line agents for non-culturable outpatient SSTIs
    • TMP-SMX associated with higher odds of treatment failure than β-lactams
    • Clindamycin provides no additional benefit over β-lactams

Elliott DJ, et al, Pediatrics 2009;123:e95
I. Antibiotics for SSTI: Draining pus matters more than the antibiotic

- **Purulent, Culturable SSTIs**
  - RCT of 161 children with uncomplicated skin abscess at large peds ED
    - Randomized to placebo vs TMP-SMX x 7-10 days *after I&D*
    - No difference – high success rate in both arms (94.7% vs 95.9%)
    - More new lesions at 10 days in placebo (26% vs 13%) but not at 3 mo
    - 129/161 (80.1%) had CA-MRSA, 13/161 (8.1%) MSSA

- **Conclusion: I&D alone is adequate for simple abscess**
  - Placebo non-inferior to TMP-SMX after I&D of simple abscess
  - Adjunctive abx are not necessary for drained simple abscesses

*Ann Emerg Med 2010; 55:401-407*
I. Antibiotics for SSTI:
Even abx that don’t work for MRSA are just fine... as long as you drain pus

- Purulent, Culturable SSTIs
  - RCT 200 patients with uncomplicated, *purulent* outpatient SSTI
  - Randomized to clindamycin vs cephalaxin
  - 69% of cultured wounds MRSA+
  - 96% had drainage procedure (manual expression of pus or I&D)
  - **No difference in clinical outcomes** (2-3 days and 7 days)
    - Improvement in 94% of cephalaxin and 97% of clindamycin groups

Fine. MRSA is a common cause of abscesses and draining pus when present gives you more bang for your buck than antibiotics.

But if MRSA is so common, shouldn’t it also be a big cause of non-purulent cellulitis as well?
GABHS still the most common cause of cellulitis

**Design**
- Prospective cohort
- 248 adults at an LA county hospital 2004-2007 with diffuse cellulitis
- High prevalence of MRSA (>50%)
- 179 completed → acute + convalescent titers for β-hemolytic strep (BHS)

**Results**
- 73% had evidence (serology or +blood culture) of BHS infection
- 96% of patients who got ≤1 dose anti-MRSA abx responded to β-lactams
- Includes 27% of patients who had no evidence of BHS

**Bottom Line**
- BHS is still predominant cause of diffuse, non-culturable cellulitis
- MSSA more important than MRSA in diffuse cellulitis
- Empiric treatment with β-lactams effective for most cases

*(Medicine 2010;89: 217–226)*
2011 IDSA Guidelines – Mgmt of MRSA

Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant *Staphylococcus Aureus* Infections in Adults and Children

- I&D alone for simple cutaneous abscesses
- Antibiotics only for certain situations when treating abscess
  - Definitive conclusion on role of antibiotics (if any) unknown

- Purulent cellulitis → empiric anti-MRSA abx x 5-10 days
- Non-purulent cellulitis → empiric anti-strep abx x 5-10 days
  - Expand to cover CA-MRSA if no response or systemic toxicity
Abscess

Conditions in which Antimicrobial Therapy is Recommended after Incision and Drainage of an Abscess due to Community-Associated Methicillin-Resistant *Staphylococcus aureus*

<table>
<thead>
<tr>
<th>Severe or extensive disease (eg, involving multiple sites of infection) or rapid progression in presence of associated cellulitis</th>
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<tbody>
<tr>
<td>Signs and symptoms of systemic illness</td>
</tr>
<tr>
<td>Associated comorbidities or immunosuppression (diabetes mellitus, human immunodeficiency virus infection/AIDS, neoplasm)</td>
</tr>
<tr>
<td>Extremes of age</td>
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<tr>
<td>Abscess in area difficult to drain completely (eg, face, hand, and genitalia)</td>
</tr>
<tr>
<td>Associated septic phlebitis</td>
</tr>
<tr>
<td>Lack of response to incision and drainage alone</td>
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</table>
Newest Guideline – 2014 IDSA SSTI Guideline

• Clarity around cellulitis – gone is the “purulent cellulitis” term

• Skin abscess with surrounding redness, warmth, tenderness = “abscess with surrounding inflammation”, not “abscess with surrounding cellulitis”

• Is this an important distinction or just semantics?
  – Primary therapy for pus = drainage
  – Primary therapy for cellulitis = antibiotics aimed at streptococci (except in specific circumstances)
  – MRSA is an unusual cause of typical cellulitis, even if MRSA SSTI rates are high
  – For cellulitis, cover for MRSA only if:
    • Penetrating trauma, MRSA elsewhere (including nasal swab), IVDU, immunosuppressed?, SIRS?

• Recommended duration for cellulitis: 5 days, as long as patient improving
Since daptomycin and televancin are not approved for use in children, vancomycin is recommended; clindamycin may be used if clindamycin resistance is <10-15% at the institution.
Recent studies also supportive of guidelines

- **Clindamycin vs TMP-SMX for uncomplicated SSTI**
  - RCT of 524 patients at urgent cares, EDs, and clinics @ 4 US sites
  - 6 months – 85 years old; mean age 27; **30% children**
  - Cellulitis and/or abscess (30% abscess only; 15% abscess + cellulitis)
  - Clindamycin or TMP-SMX given for 10 days to primary outcome of clinical cure at 7-10 days post-treatment
  - **Conclusion**: no difference in cure rates or adverse events

![Table showing outcomes of Clindamycin vs TMP-SMX](image)

*Cellulitis and/or abscess (30% abscess only; 15% abscess + cellulitis)*

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Event rates</th>
<th>At 7 to 10 d after completion of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical cure§</td>
<td>90%</td>
<td>1.4% (−5 to 8)</td>
</tr>
<tr>
<td>Adverse events</td>
<td>18.9%</td>
<td>1.7% (−29 to 45)</td>
</tr>
</tbody>
</table>

*Clindamycin vs trimethoprim–sulfamethoxazole (TMP-SMX) in outpatients with uncomplicated skin infections‡*

*Ann Int Med; ACP Journal Club Jul 21, 2015*
Wait...now TMP-SMX is maybe better than I&D?!?

• **TMP-SMX vs Placebo for Uncomplicated Skin Abscess**
  
  – RCT of 1265 patients at 5 US sites with uncomplicated skin abscess that were incised and drained
  – Following I&D, randomized to TMP-SMX or placebo x 7 days
  – Median age 35 (range 14-73); 45% +MRSA wound cultures
  – Primary outcome: clinical cure at 7-14 days post-treatment
  – TMP-SMX group cure rate 6.9% higher than placebo group

<table>
<thead>
<tr>
<th>Table 3. Cure Rates among Patients with a Drained Cutaneous Abscess in Three Trial Populations.*</th>
</tr>
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<tbody>
<tr>
<td><strong>Trial Population</strong></td>
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<tr>
<td></td>
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<tr>
<td>Modified intention-to-treat</td>
</tr>
<tr>
<td>Per-protocol‡</td>
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<tr>
<td>FDAGEEP</td>
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Enough with the “evidence”...what’s the bottom line?
I. Antibiotics for SSTI: Clinical Bottom Line

• Pus matters
  – If purulent → think Staph (include MRSA)
  – If non-purulent → think Strep

• Always I&D and obtain culture data whenever possible

• Antibiotics _not_ absolutely necessary after I&D of uncomplicated abscesses

• If given, tailor abx based on culture results
I. Antibiotics for SSTI: Clinical Bottom Line

- Cephalosporins are reasonable first-line agents for uncomplicated SSTI (especially if nonpurulent, nonculturable)

- Expand to cover CA-MRSA if no response in first 48 hrs

- Use local micro/epi data to guide empiric abx selection
  - Rates of CA-MRSA resistance to clindamycin and TMP-SMX

- Follow-up (“wound checks”) and anticipatory guidance is key
II. Additional Testing for SSTI: Cellulitis ≠ Bacteremia

- Blood cultures commonly done for children admitted with cellulitis, esp those who will receive IV abx

- Prevalence SSTI-associated bacteremia ~20% (pre-Hib era)

- Following introduction of Hib vaccine, SSTI-associated bacteremia rates fell to ~2%
  - Largely driven by superinfection of active VZV lesions

*Pediatrics 2013;132:454-459
*Pediatrics 1998;101(3):
II. Additional Testing for SSTI: Cellulitis ≠ Bacteremia

- Two recent studies evaluated prevalence of SSTI-associated bacteremia in the modern (MRSA) era
  - Prevalence in ED patients with uncomplicated cellulitis: 0%
  - Prevalence in inpatients admitted with uncomplicated SSTI: 0%
  - Ratio of contaminant: pathogen in +Bcx: 3-4:1
  - Cost of 4 contaminated Bcx (in one study): $2280
  - Sending a Bcx in SSTI inpatients increases LOS by 1 day

- **Clinical bottom line:**
  - Bacteremia rare in ED and inpatients with uncomp SSTI (<1%)
  - Unnecessary Bcx are costly and increase hospital LOS
  - No role for routine Bcx in uncomplicated SSTI

*Pediatrics 2013;132:454-459
Hospital Pediatrics 2013;3;103*
DEEP/NECROTIZING SSTI
Necrotizing Fasciitis

• Anatomy: All layers from skin to underlying muscle

• Clinical Features
  – Severe pain out of proportion to exam
  – Erythema → Ecchymosis and bullae (late)
  – Crepitus
  – Cutaneous anesthesia
  – Woody/firm feeling of skin
  – Systemic toxicity, fever, AMS
  – Can develop after initial minor skin lesions

• Microbiology
  – Type I = Polymicrobial (mixed aerobes and anaerobes)
  – Type II = Monomicrobial – usually GAS
Necrotizing Fasciitis

• Diagnosis
  – Clinical/Labs
    • “Hard” signs often absent → Maintain a high clinical suspicion
    • Risk scores can aid in decision for surgical exploration
  – Imaging
    • XR (tissue gas very specific), CT, MRI
    • Imaging should NOT delay surgery
  – Operative
    • Gold standard for diagnosis

• Management
  – Medical → Broad spectrum abx
  – Surgical → prompt surgery saves lives
Common Pitfalls in Management of SSTIs

1. Typical cellulitis caused by MRSA is unusual

2. TMP-SMX does not reliably cover streptococcus

3. Pay close attention to susceptibility pattern on cultures – if Clinda-S + Erythro-R, look for D-Test

4. Routine blood cx unnecessary for uncomplicated SSTI

5. Necrotizing SSTIs cause high mortality– call surgery early
Case #1

• 6 yo healthy female brought to SDC
• 2 days redness and swelling of foot
• No fevers/chills, n/v

• Exam:
  – Afebrile
  – Mild erythema
  – Normal gait

• Management?
Case #1

- 6 yo healthy female brought to SDC
- 2 days redness and swelling of foot
- No fevers/chills, n/v

Exam:
- Afebrile
- Mild erythema
- Normal gait

Management?

Case Considerations
- Classification?
  Cellulitis
- Management?
  - Antibiotics? PO – e.g., cephalexin
  - Blood cultures? No
  - Imaging? No
  - Dispo – Admit vs DC? DC
  - What type of follow-up? F/U if no response/worsens
Case #2

• 11 yo healthy M w/2 days redness and pain to L arm
• Subjective fever last night

• Exam
  – Afebrile / Rest of VS normal
  – 3 x 5 cm area of warmth, tenderness, and erythema L arm
  – Central area of ~2 cm fluctuance

• Management?
Case #2

• 11 yo healthy M w/ 2 days redness and pain to L arm
• Subjective fever last night

• Exam
  – Afebrile / Rest of VS normal
  – 3 x 5 cm area of warmth, tenderness, and erythema L arm
  – Central area of ~2 cm fluctuance

• Management?

• Case Considerations
  – Classification?
    Abscess + inflammation
  – Management?
    • Antibiotics? No (if drained)
    • Blood cultures? No
    • Imaging? +/- U/S
    • Dispo – Admit vs DC? DC
  • What type of follow-up?
    Wound check in 1-2 days
Case #3

- 18 yo healthy male with 2-3 days of progressive erythema, edema, and pain of LUE
- Associated fevers, chills, malaise starting same day as onset of skin sx

- Exam:
  - T 39/ BP 115/70 / HR 120
  - LUE diffusely swollen, firm, and red
  - Exquisitely tender with minimal palpation on exam
  - No crepitus

- Management?
Case #3

- 18 yo healthy male with 2-3 days of progressive erythema, edema, and pain of LUE
- Associated fevers, chills, malaise starting same day as onset of skin sx

Exam:
- T 39/ BP 115/70 / HR 120
- LUE diffusely swollen, firm, and red
- Exquisitely tender with minimal palpation on exam
- No crepitus

Management?

Case Considerations
- Classification?
  Deep/complicated SSTI
- Management?
  - Antibiotics? Yes – include MRSA coverage
  - Blood cultures? Yes
  - Imaging?
    Maybe, but not at expense of urgent surgical C/S
- Dispo – Admit vs DC? Admit
- What type of follow-up?
  Serial evaluations as IP (potentially SICK patient)
QUESTIONS?
References
