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

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Sea Pines Conference

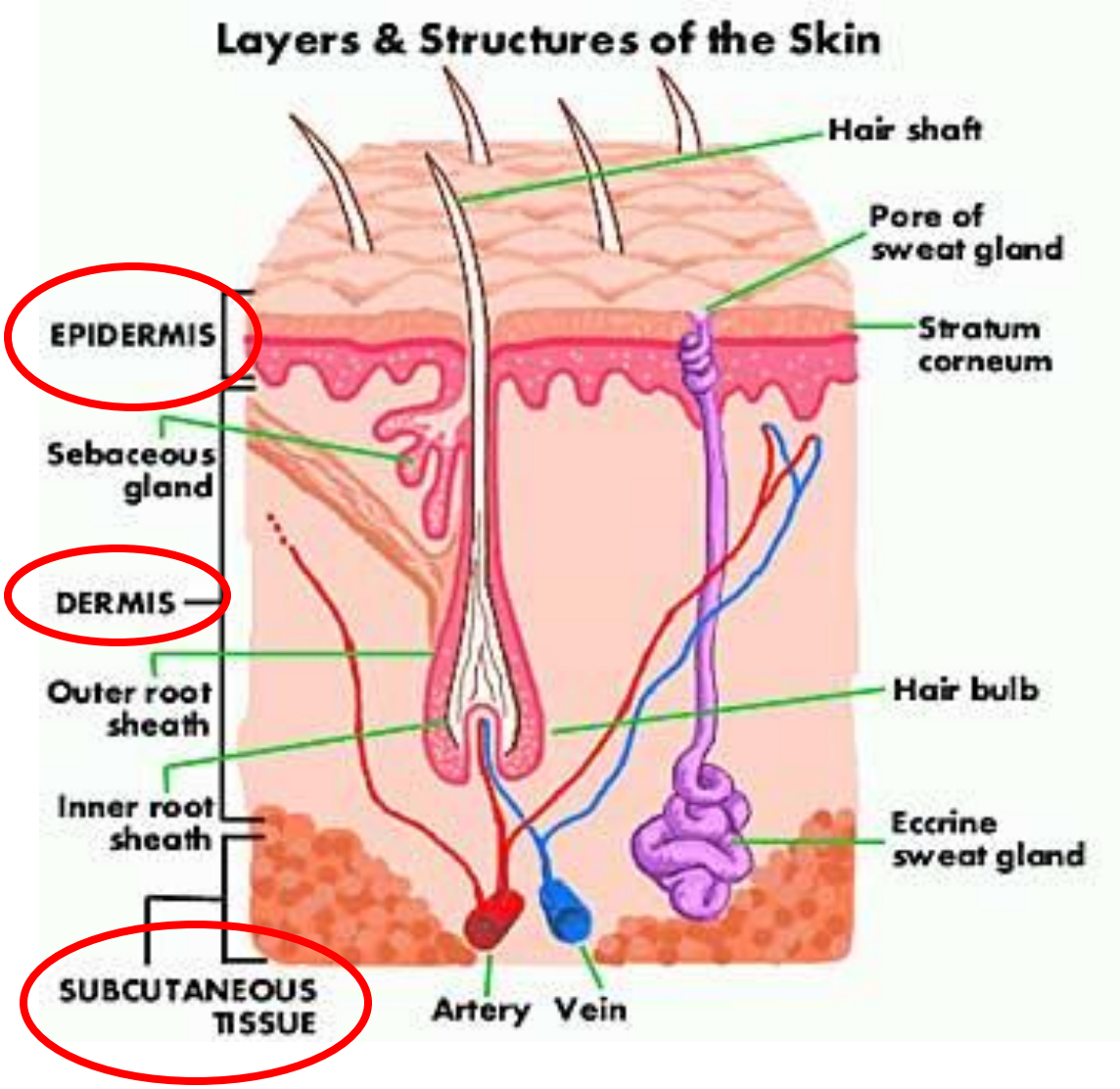
July 12th, 2018

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


Layers & Structures of the Skin
Hair shaft
Pore of sweat gland
Stratum corneum
EPIDERMIS
Sebaceous gland
DERMIS
Outer root sheath
Hair bulb
Inner root sheath
Eccrine sweat gland
SUBCUTANEOUS TISSUE
Artery
Vein

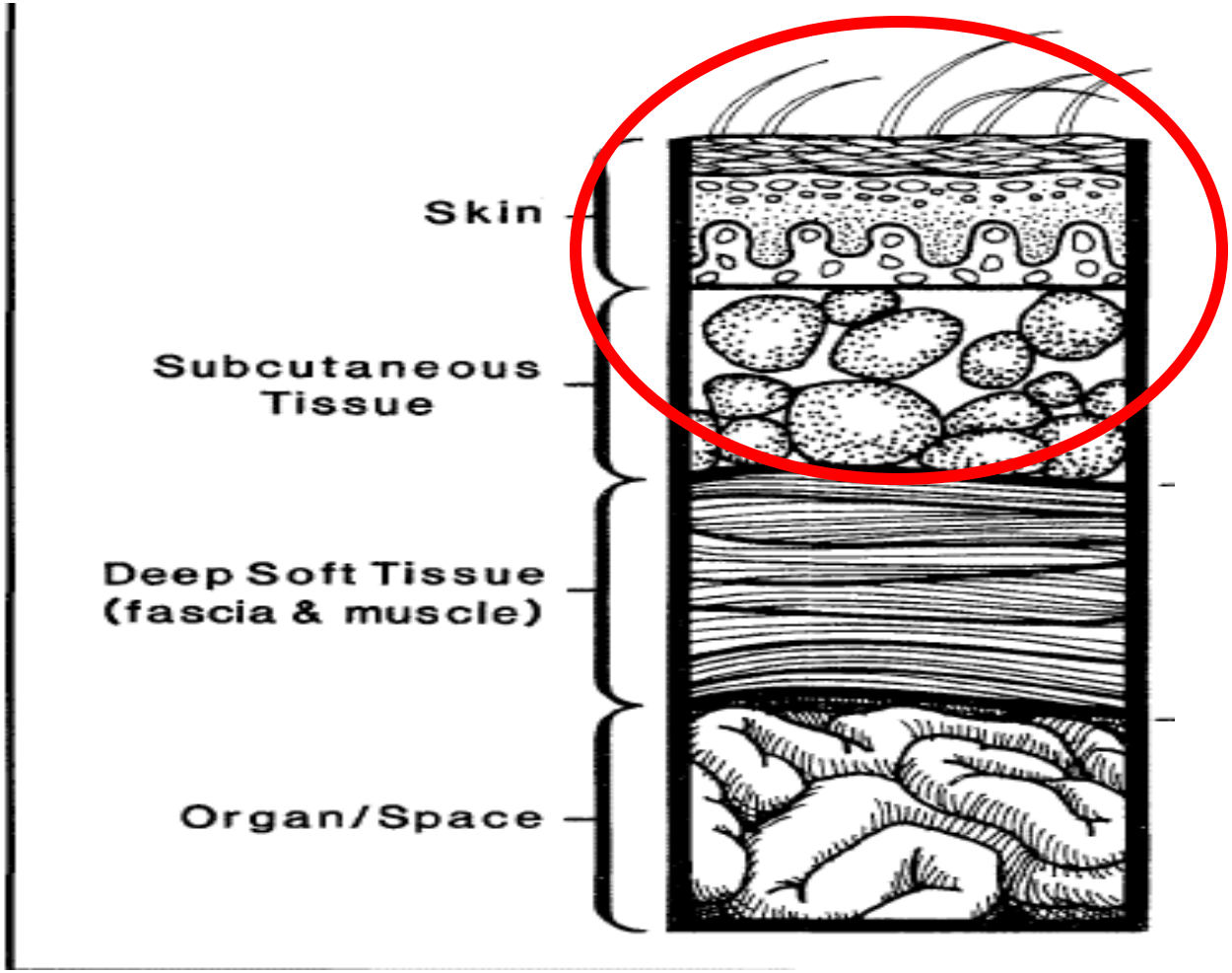
Classification

- **Superficial**
  - Impetigo
  - Cellulitis
  - Erysipelas
  - Abscess (furuncles, carbuncles)
- **Deep/Necrotizing**
  - Necrotizing fasciitis
  - Pyomyositis
  - Osteomyelitis
- **Miscellaneous**
  - Animal Contact
  - *Orbital cellulitis*
  - Immunocompromised Hosts
  - Surgical Site Infections (SSI)
- **Non-necrotizing**
  - Mild/moderate
  - Responsive to abx alone
- **Necrotizing**
  - Life-threatening
  - Systemic toxicity
  - Tissue necrosis
  - Requires surgical management

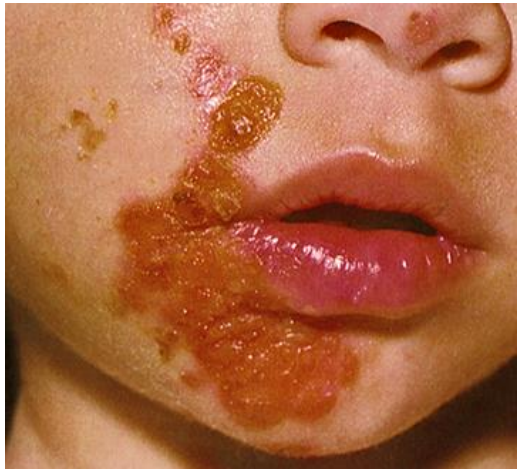
Challenges in Management of SSTI

- 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

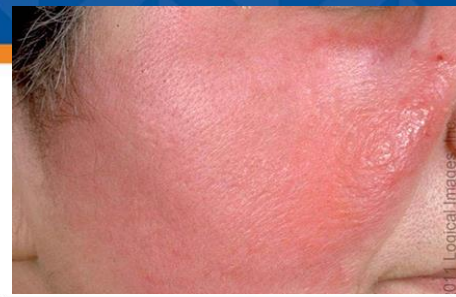
Erysipelas

- Anatomy: Superficial dermis

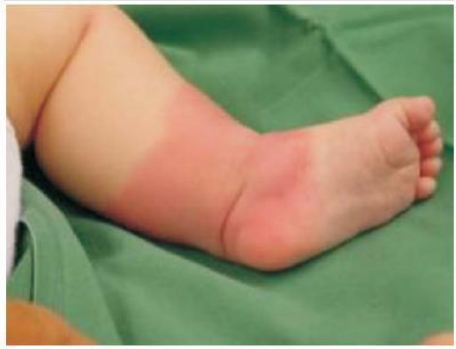
- Clinical Features:
  - Prominent lymphatic involvement
  - **Raised, sharply demarcated** borders
  - Indurated and "peau d'orange" appearance
  - Young infants/children, older adults
  - Classic: butterfly area of face; legs also cor

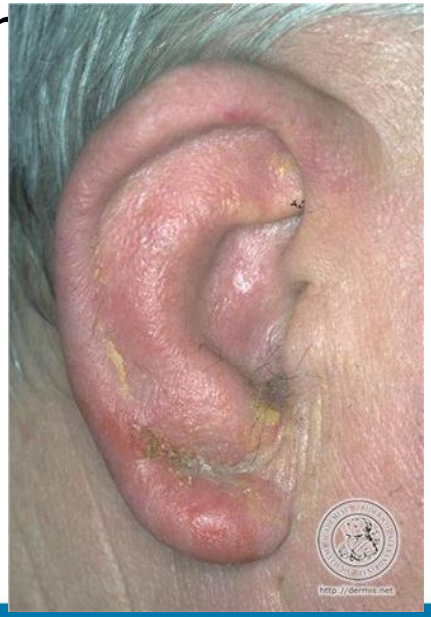
- Microbiology: GAS most common

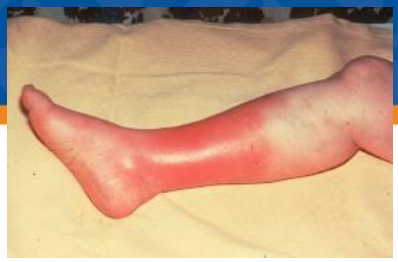
- Management:
  - Penicillin
  - Cephalosporin (1st generation)



Erysipelas







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

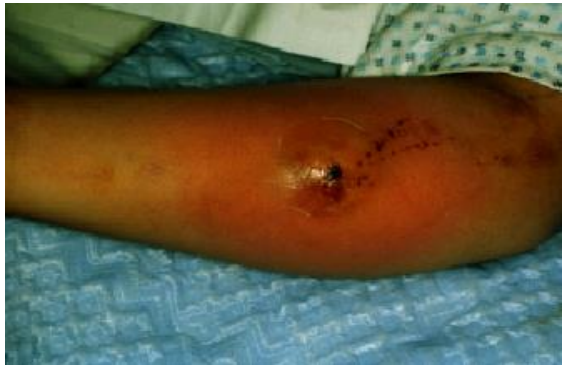
Hospital Pediatrics 2013;3;103

Cellulitis

- Diagnosis
  - Diffuse cellulitis typically not amenable to culture
  - Needle aspirates and punch biopsies not recommended [1-2]
  - Ultrasound – consider to help exclude occult abscess [6]
  - Blood cultures low-yield in children and adults with cellulitis [3-4]

Jeng A, *Medicine (Baltimore)* 2010;89:217-226.
Stevens DL, *Clin Infect Dis* 2005;41:1373-1406.
Sadow KB, *Pediatrics* 1998;101(3).
Swartz MN, *NEJM* 2004;350(9):904-912.
Squire BJ, *Acad Emerg Med* 2005;12:601-606.

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 2 SSTI Hospitalizations and I&Ds: 1997, 2000, 20(

	1997 *N* (wt)	Weight, %	2009 *N* (wt)	Weight, %	*P*
No. of hospitalizations					
All US hospitalizations	1 905 797 (6 657 325)	—	3 407 146 (7 370 203)	—	
SSTI	13 225 (30 653)	0.46	49 834 (74 443)	1.01	<.01
Receiving I&D	2779 (6284)	20.5	21 544 (32 431)	43.6	<.01
Asthma	86 698 (200 699)	3.01	97 117 (143 641)	1.95	<.01
Pneumonia	77 936 (197 584)	2.97	118 317 (176 145)	2.39	<.01

wt, weighted.

Miller LG, *N Engl J Med* 2015;372:1093-103
Lopez MA, *Pediatrics* 2013;131:e718

I. Antibiotics for SSTI: MRSA is common

Table 1. Bacterial Isolates from Purulent Skin and Soft-Tissue Infections in 11 U.S. Emergency Departments.*

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

N Engl J Med 2006;355:666-74.

- 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

Moran GJ, *NEJM* 2006;366:666-674

N Engl J Med 2007;357:380-90.

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

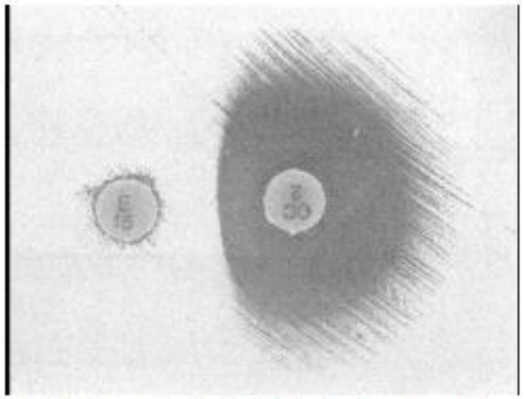


FIGURE 2. D-zone test for inducible clindamycin resistance.

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 cephalexin
  - 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 cephalexin and 97% of clindamycin groups

Chen AE, et al, *Pediatrics* 2011;127:e573

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?

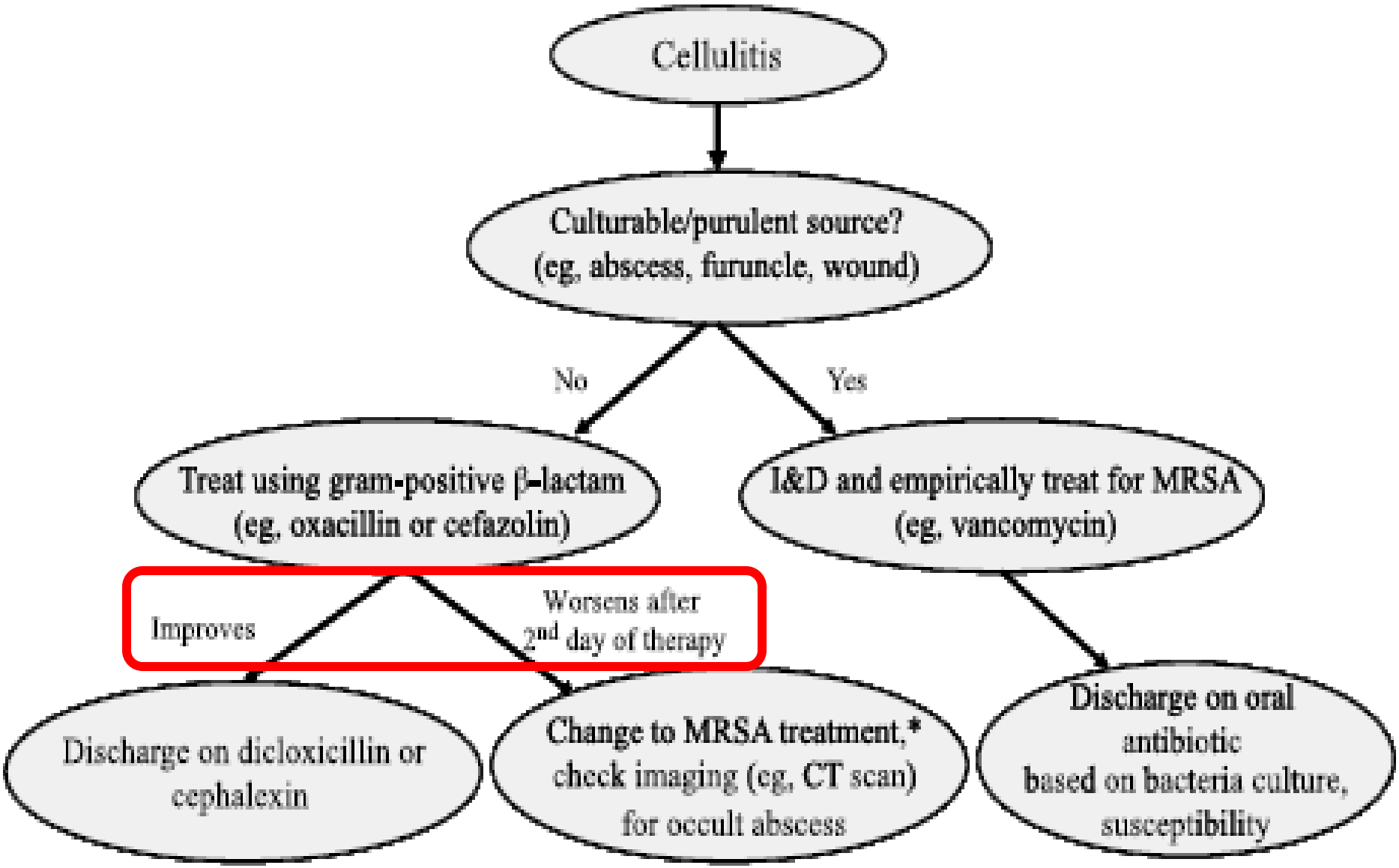
GABHS still the most common cause of cellulitis

- 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)



Jeng, A*; Medicine (Baltimore)* 2010;89:217

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*

Severe or extensive disease (eg, involving multiple sites of infection) or rapid progression in presence of associated cellulitis
Signs and symptoms of systemic illness
Associated comorbidities or immunosuppression (diabetes mellitus, human immunodeficiency virus infection/AIDS, neoplasm)
Extremes of age
Abscess in area difficult to drain completely (eg, face, hand, and genitalia)
Associated septic phlebitis
Lack of response to incision and drainage alone

Newest Guideline – 2014 IDSA SSTI Guideline

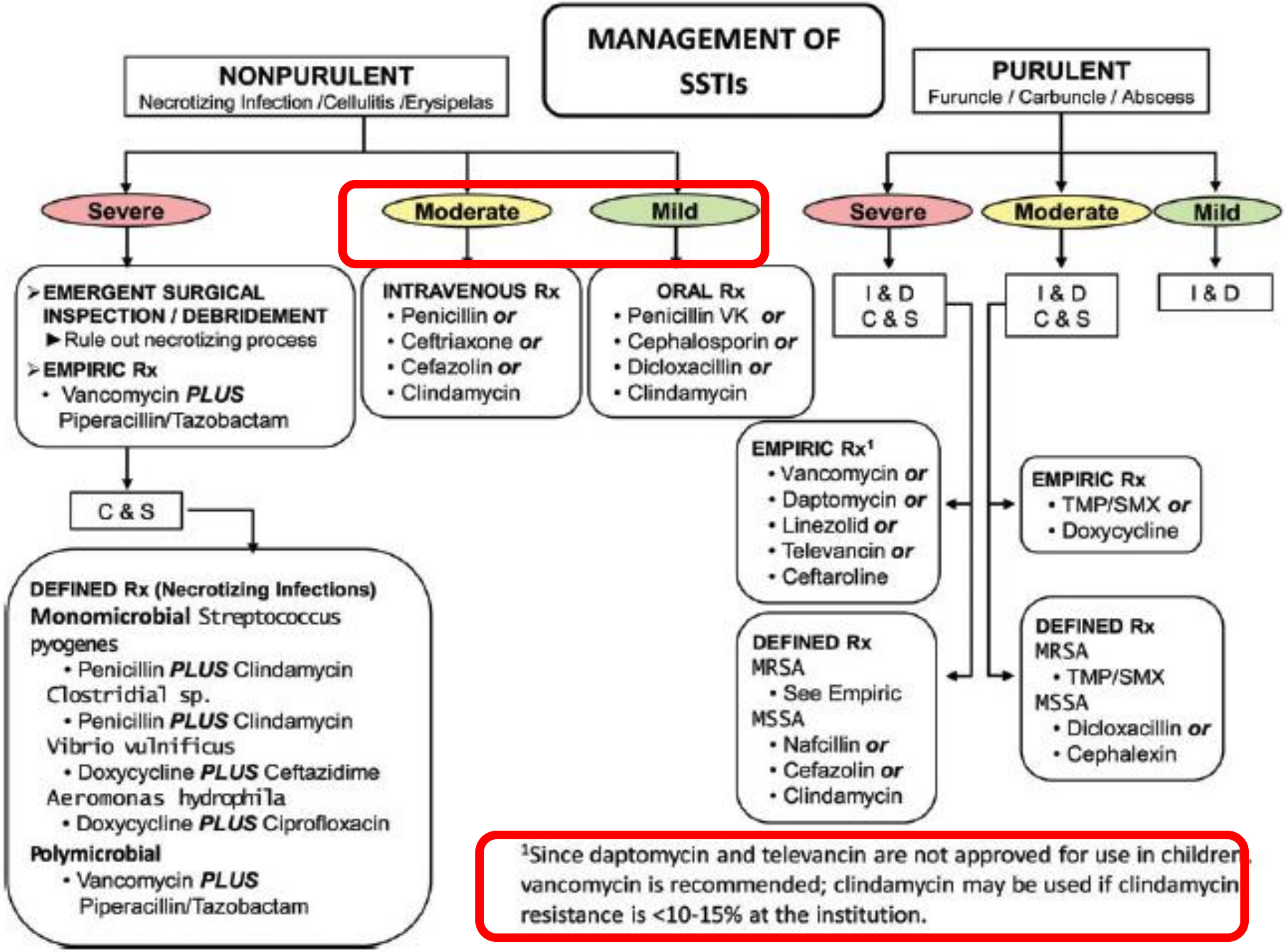
- Clarity around cellulitis – gone is the "purulent cellulitis" term

- 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

Slide courtesy of Dr. Tom Holland



CID 2014:59 (15 July)

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

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

Outcomes	*Event rates*		*At 7 to 10 d after completion of treatment*
	Clindamycin	*TMP-SMX*	*RRI (95% CI)*
Clinical cure§	90%	88%	1.4% (−5 to 8)
Adverse events	18.9%	18.6%	1.7% (−29 to 45)

N Engl J Med 2015;372:1093-103
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 3. Cure Rates among Patients with a Drained Cutaneous Abscess in Three Trial Populations.*

Trial Population	Cure of Abscess		Difference (95% CI)	P Value†
	Trimethoprim–Sulfamethoxazole	Placebo		
	no./total no. (%)		*percentage points*	
Modified intention-to-treat 1	507/630 (80.5)	454/617 (73.6)	6.9 (2.1 to 11.7)	0.005
Per-protocol‡	487/524 (92.9)	457/533 (85.7)	7.2 (3.2 to 11.2)	<0.001
FDAGEEP	218/601 (36.3)	204/605 (33.7)	2.6 (–3.0 to 8.1)	0.38

N Engl J Med 2016;374:823-32.

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):

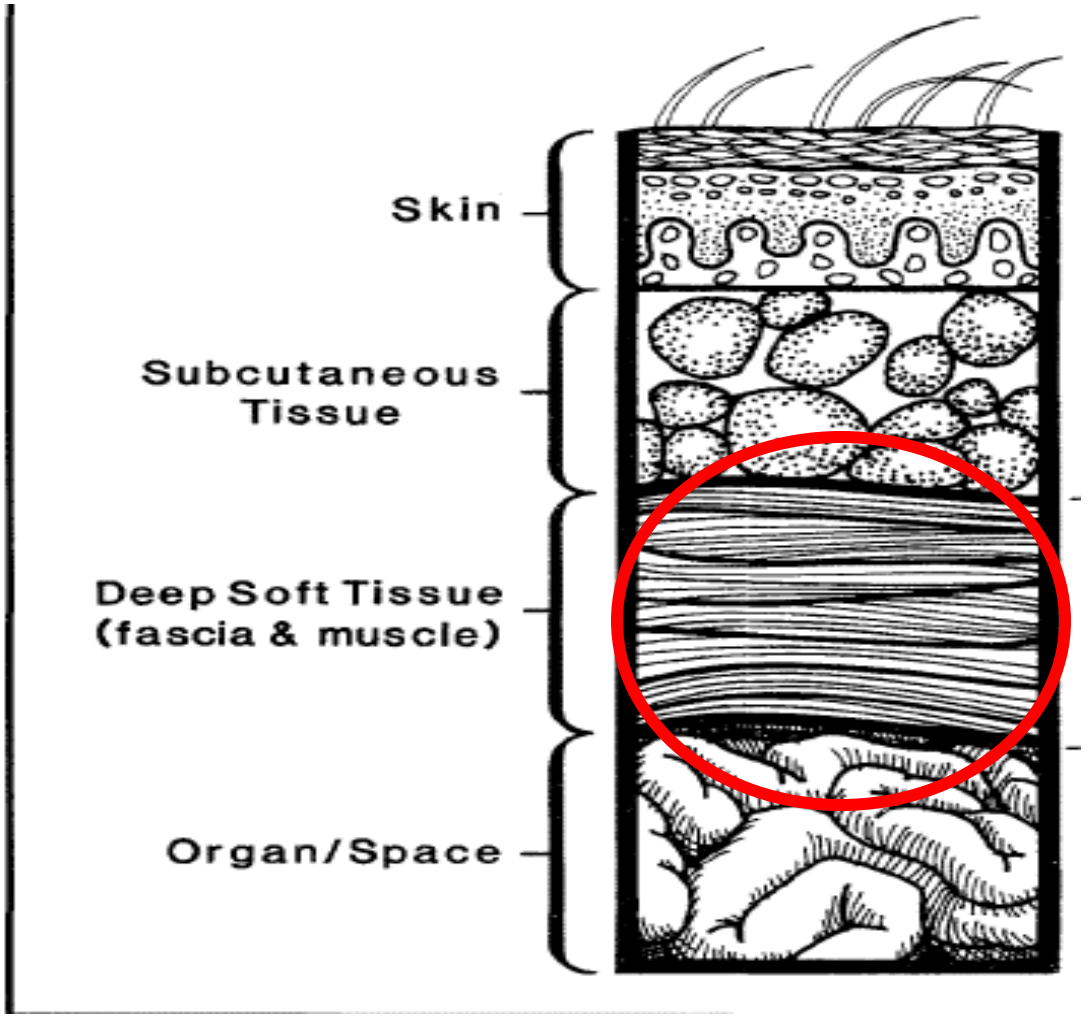
II. Additional Testing for SSTI: Cellulitis ≠Bacteremia

- 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?

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- 2 days redness and swelling of foot
- No fevers/chills, n/v

- Exam:
  - Afebrile
  - Mild erythema
  - Normal gait

- Management?

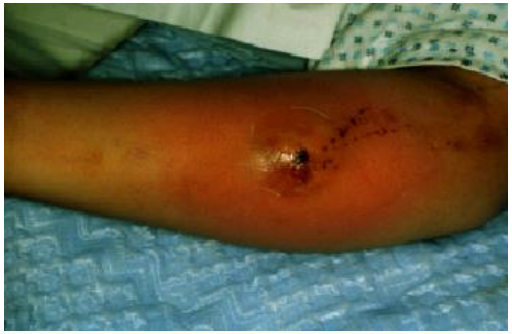
- Case Considerations
  - Classification?
    Cellulitis
  - Management?
    - Antibiotics? PO – e.g., cephalexin
    - Blood cultures? No
    - Imaging? No
    - Dispo – Admit vs DC? DC
    - What type of follow-up?
      F/U if no response/worsens

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

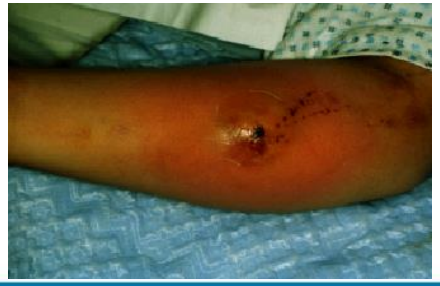
- 11 yo healthy M w/2 days redness and pain to L arm
- Subjective fever last night

- 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 + infllammation

  - 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

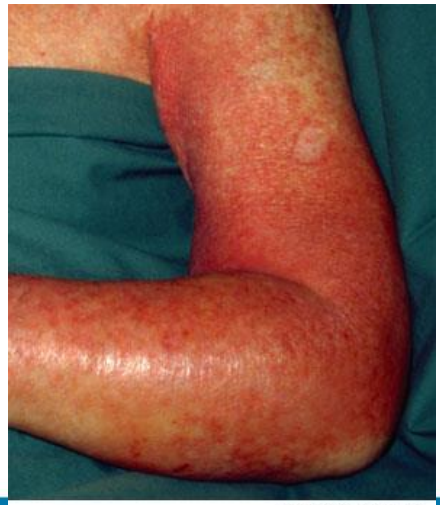


Case #3

- 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?

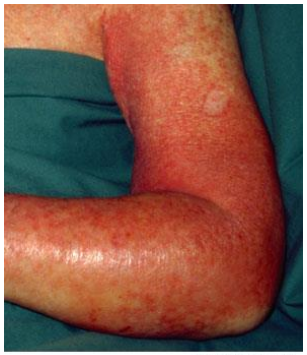


Case #3

- 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?

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