MANAGEMENT OF SOFT TISSUE INFECTIONS IN THE DTES

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FACULTY/PRESENTER DISCLOSURE

Faculty: Queenie Dinh

Relationships with financial sponsors:

- **None**

MITIGATING POTENTIAL BIAS

Medications discussed today are all off patent

LEARNING OBJECTIVES

Suggested subtitle: Indications for Oral and IV antibiotics

Clinical guidance on choosing oral or parenteral antibiotics for skin and soft tissue infection (SSTI)

- Guidelines
- Evidence

The resurgence of cefadroxil

When to use antibiotics in the treatment of skin abscess

Local antibiotic susceptibility patterns

Considerations for slow or non-resolving infection

CASE

ID: 45yo M

Dx: left leg cellulitis

Medical Profile: PWID, recent negative HIV test, previous SSTI, MRSA+, chronic HCV

Came to clinic yesterday and was started on cefadroxil 500 mg po bid

Has taken 2 doses so far

Returns today because not improved, and the red area is slightly larger, still ++pain

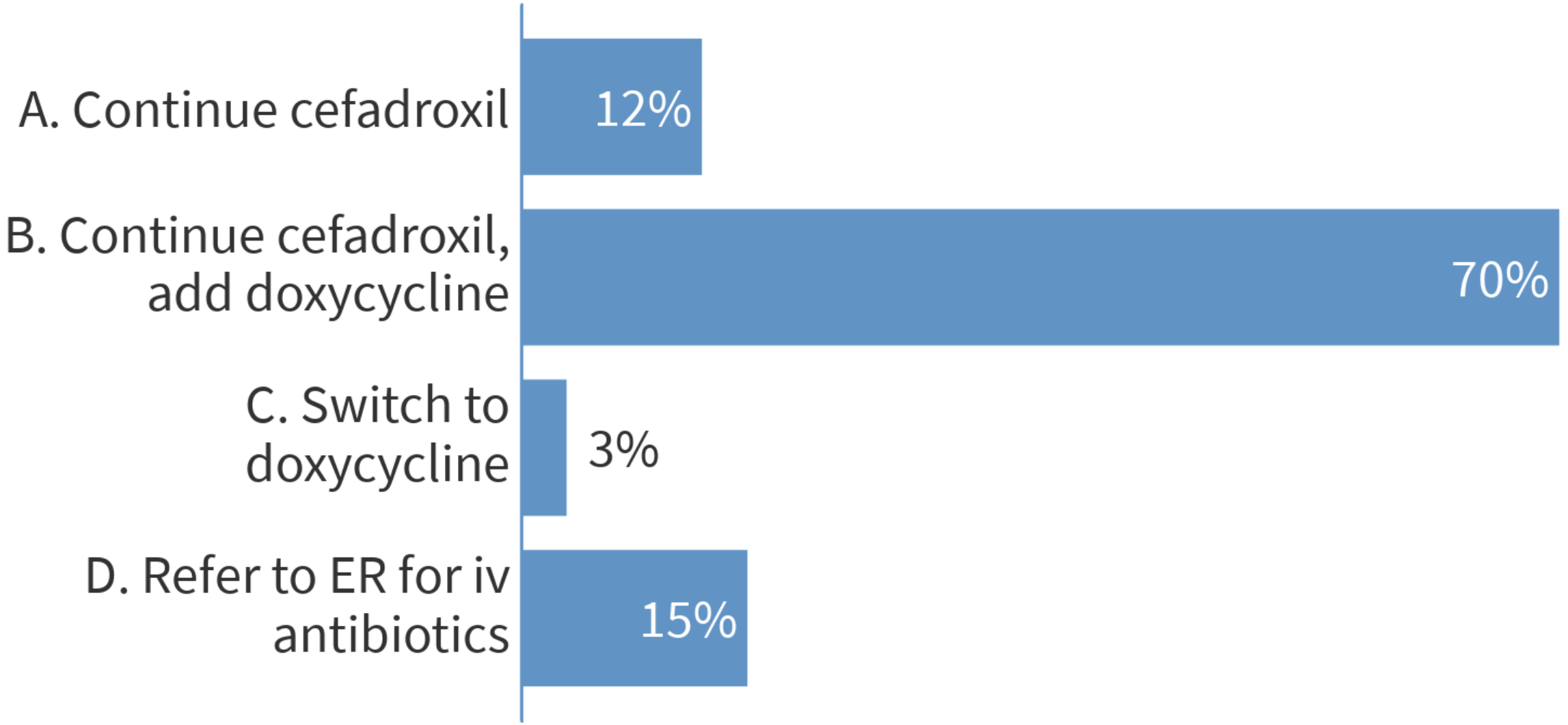
Feels generally unwell, feverish last night

O/E patient is afebrile

- red confluent patch on leg, no purulence or open wounds
- Signs of tinea pedis

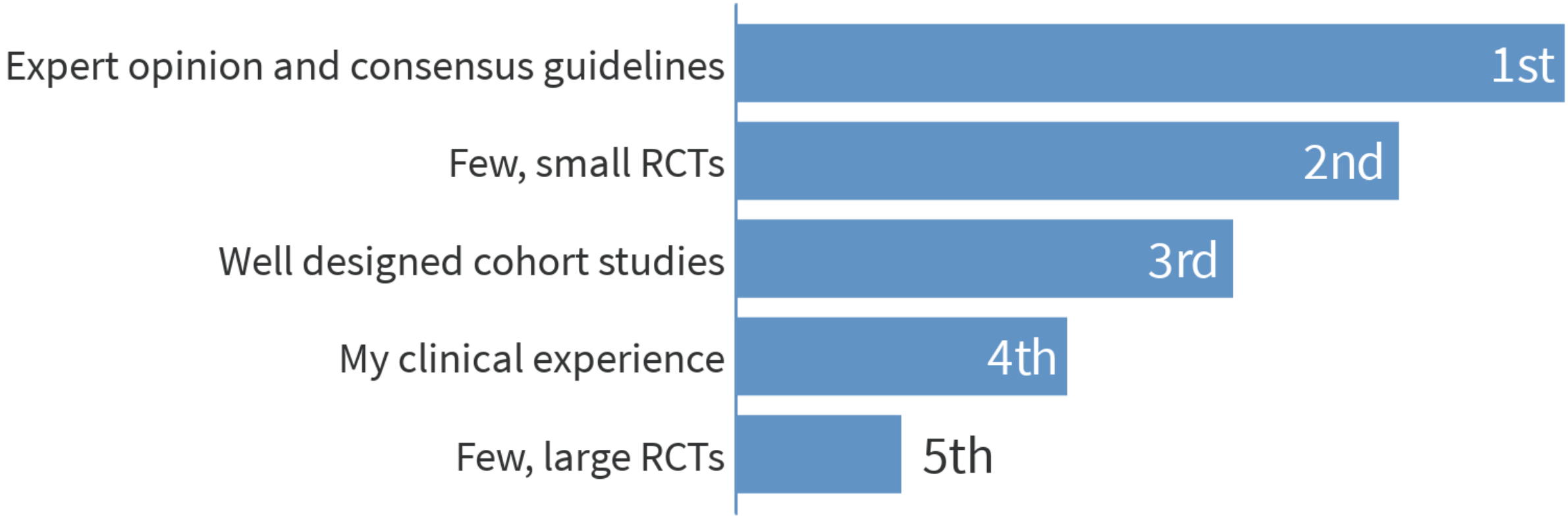
https://www.uptodate.com/contents/images/ID/82542/Erysipelas_of_leg_3.jpg

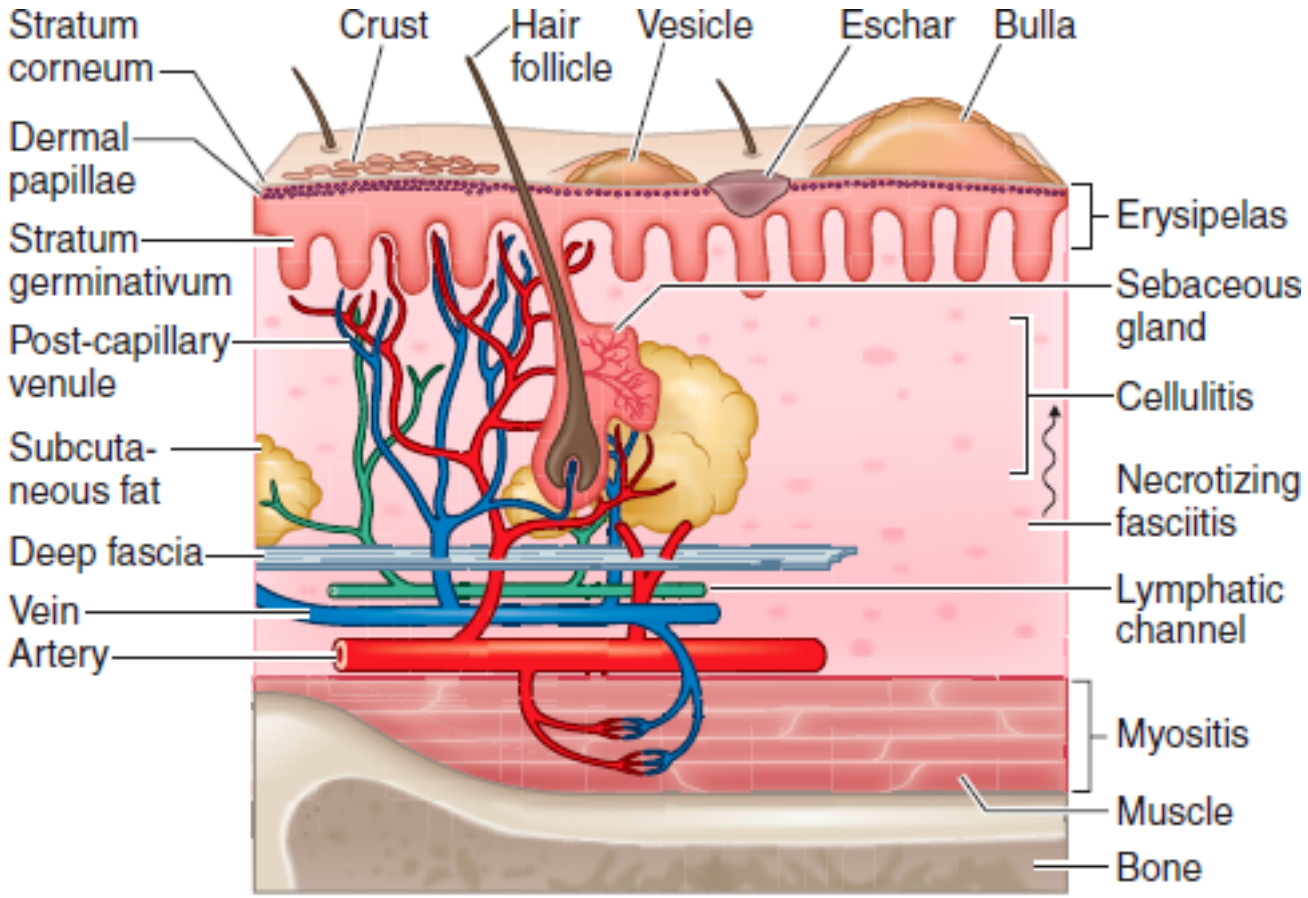
You advise the patient:



When seeing a patient with SSTI, what prompts you to recommend iv antibiotics?

Regarding clinical decision making between oral and intravenous antibiotics for SSTI, the best evidence comes from:





Structural components of the skin and soft tissues, superficial infections, and infections of the deeper structures. The rich capillary network beneath the dermal papillae plays a key role in the localization of infection and in the development of the acute inflammatory reaction.

IDSA GUIDELINES: ASSESSING SEVERITY

Purulent SSTI	
Mild infection	Systemically well
Moderate infection	Systemic signs of infection
Severe infection	Failed incision and drainage plus oral antibiotics **OR** Systemic signs of infection (T>38°C, HR>90, RR >24 WBC >12 000 or <400 cells/μL) **OR** Immunocompromised patients.

IDSA GUIDELINES: ASSESSING SEVERITY

Non-purulent SSTI	
Mild infection	Typical cellulitis/erysipelas with no focus of purulence
Moderate infection	+ Systemic signs of infection
Severe infection	Failed oral antibiotic treatment OR Systemic signs of infection OR Immunocompromised OR Clinical signs of deeper infection such as bullae, skin sloughing, hypotension, or evidence of organ dysfunction

IDSA GUIDELINES: MANAGEMENT

Purulent SSTI	I&D	C&S	Antibiotic
Mild infection	Y	N	N
Moderate infection	Y	Y	PO
Severe infection	Y	Y	IV

IDSA GUIDELINES: MANAGEMENT

Non-purulent SSTI	
Mild infection	PO antibiotics
Moderate infection	IV abx
Severe infection	Surgical inspection +/- debridement IV antibiotics C&S

CASE

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Feels generally unwell, feverish last night

O/E patient is afebrile

- Picture red confluent patch on leg, no purulent or open wounds
- Signs of tinea pedis

YOU ADVISE THE PATIENT:

1. **Continue cefadroxil <u>with close follow-up</u>**
   - Non-purulent SSTI often looks worse in the first 24-48h on appropriate antibiotic treatment, possibly due to inflammation from released antigens
2. Continue cefadroxil, add doxycycline
   - Non-purulent SSTI unlikely due to S. aureus
   - Doxycycline doesn't cover beta-hemolytic streptococci
3. Switch to doxycycline
4. **Refer to ER for iv antibiotics**
   - Reasonable depending on patient comorbidities, and subjective feverishness

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Volume 73, Issue 11

Why isn't cefadroxil used more often? FREE

Adam H. Corson, M.D. ✉, Brian E. Myers, Pharm.D., Warren L. Dinges, M.D., Ph.D.

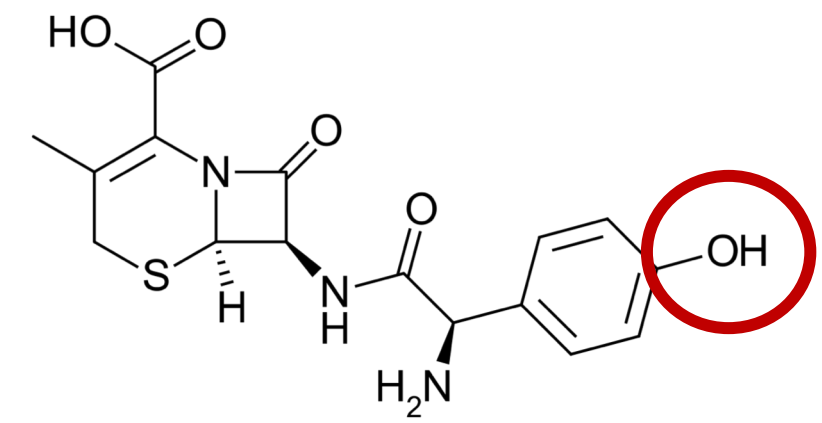
American Journal of Health-System Pharmacy, Volume 73, Issue 11, 1 June 2016, Pages 754–755, https://doi.org/10.2146/ajhp150841

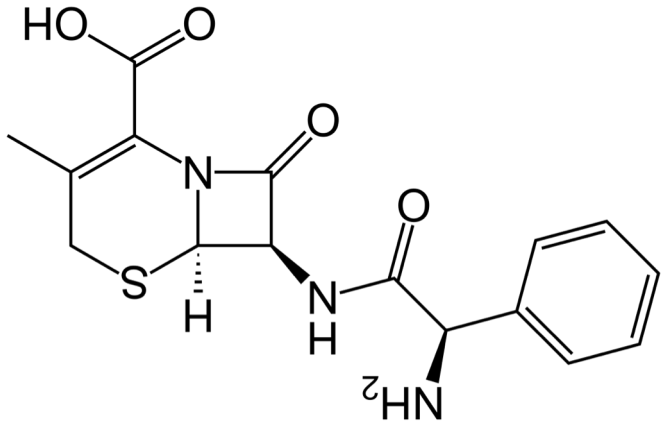
Published: 01 June 2016

Medicare data suggest cephalexin is prescribed 23x more than cefadroxil

https://doi.org/10.2146/ajhp150841

CEFADROXIL





In use since 1978

Compared to cephalexin:

Hydroxy derivative

Longer half life

Similar oral bioavailability 90%

Dosing for SSTI 1000mg daily or divided bid

A handful of old trials suggest similar efficacy in SSTI

Uncomplicated UTI

https://www.accessdata.fda.gov/drugsatfda_docs/label/2002/50512s44lbl.pdf

BACK TO THE PATIENT

Plan to continue cefadroxil

Patient doesn't return to see you and in 2 days you get an ER note stating patient was given iv antibiotics.

Can we predict which patients will fail oral antibiotics for SSTI?

ORAL ANTIBIOTIC FAILURE IN NONPURULENT SSTI

500 patients with non-purulent SSTI in 2 Ottawa EDs

288 patients took oral antibiotics for >=48hrs

85 patients had failure of oral antibiotics **29.5%**

1. Changed to intravenous therapy* (60%)
2. Hospital admission for a SSTI (35%)

*owing to progression of infection and not due to intolerance or allergy.

Among the 288 patients who took oral antibiotics >=48hrs

Only 5.6% History of MRSA

Only 1.4% PWID

Academic Emergency Medicine 2019; 26: 51– 59. https://doi.org/10.1111/acem.13492

ORAL ANTIBIOTIC FAILURE IN NONPURULENT SSTI

Predictor	Adjusted OR	95% CI	p-value
Tachypnea at triage (RR > 20)	6.31	1.80–22.08	0.004
Chronic ulcers	4.90	1.68–14.27	0.004
History of MRSA colonization or infection	4.83	1.51–15.44	0.008
Cellulitis in the past 12 months	2.23	1.01–4.96	0.05
Chronic kidney disease	2.60	0.82–8.22	0.10
Diabetes mellitus	1.70	0.87–3.32	0.12

A previous study also identified **chronic leg ulcers** as a predictor of treatment failure for SSTI in ED (Acad Emerg Med 2014;21:526)

ORAL VERSUS PARENTERAL

- Non-inferiority RCT conducted in Australia, published in 2015

Population	47 ED patients with uncomplicated SSTI	
Intervention	cephalexin 500mg po qid	1.29
Control	cefazolin 2g iv and probenecid 1g po daily	1.78
Outcome		**days until no advancement of the area of cellulitis**

Not a particularly clinically meaningful outcome

- **Conclusion: oral is non-inferior**

https://academic.oup.com/jac/article/70/2/581/2911262

ORAL VERSUS PARENTERAL

- Non-inferiority RCT conducted in Kelowna, Halifax and published in 2018

Population	206 ED patients with uncomplicated mild–moderate SSTI		
Intervention	cephalexin 500mg po qid	4.2%	100%
Control	cefazolin 2g iv and probenecid 1g po daily	6.1%	97.7%
Outcomes		**Failure of therapy at 72 hours**	**Clinical cure at 7 days**

Generalizability: excluded abscess requiring I&D, hx MRSA (local MRSA rates <20%)

2 PWID, 1 homeless, 0 HIV

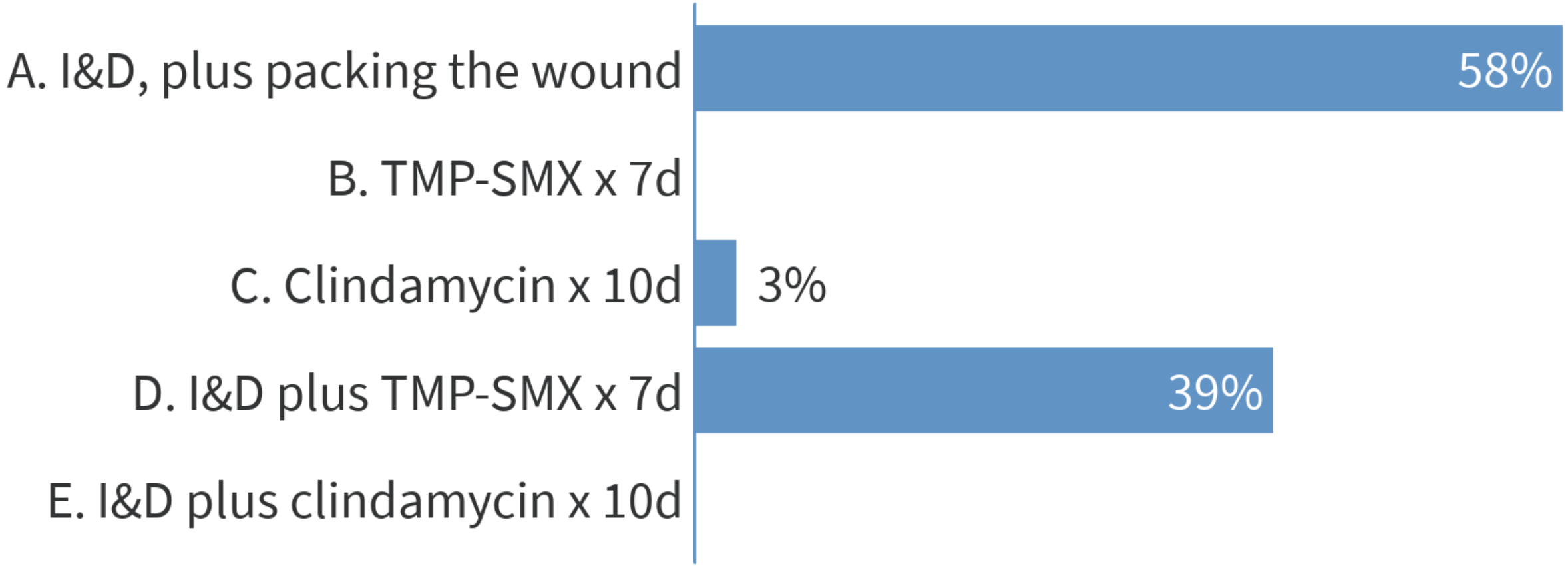
Failure: Evaluated between 72 and 96 hours after antibiotic therapy started

Hospital admission, change in antibiotics, or persistent or worsening signs and symptoms of SSTI

- **Conclusion: oral is non-inferior**

Dalen D, et al. Emerg Med J 2018;35:492–498. doi:10.1136/emermed-2017-207420

Case: A 25 yo M presents to your office with a 3 day hx of pain & swelling L. forearm, related to missed injection. Exam shows T36.6C. 3-4cm tender, red, fluctuant area. You recommend:



SKIN ABSCESS

Talan et al.: 1247 patients in ER, treated with I&D

	TMP-SMX (7d)	**Placebo**	
Clinical cure	80.5%	73.6%	p=0.005

Notes: 8% known MRSA, 97.4% of MRSA in study susceptible to TMP-SMX

- <5% related to IDU
- 2 patients in each arm subsequently had invasive infection

Daum et al.: 786 outpatients patients with abscesses <5cm, got I&D

	TMP-SMX (10d)	**Clindamycin (10d)**	**Placebo**	
Clinical cure	81.7%	83.1%	68.9%	p<0.001

Notes: PWID generally excluded

CASE

A 25 yo M presents to your office with a 3 day hx of pain & swelling L. forearm, related to a missed injection.

Exam shows T36.6C. 3-4 cm tender, red, fluctuant area.

You recommend:

1. ***I&D, plus packing the wound***
2. TMP-SMX x 7d
3. Clindamycin x 10d
4. **I&D plus TMP-SMX x 7d**
5. **I&D plus clindamycin x 10d**

LIFELABS 2019 ANTIBIOGRAM (2018 CALENDAR YR, VANCOUVER OUTPATIENT/COMMUNITY)

Skin and Soft Tissue Pathogens

ORGANISM	Number of isolates tested	ANTIBIOTIC (% susceptible)													
		Ampicillin	Azithromycin	Ceftriaxone	Cephalothin / Cephalexin	Clarithromycin	Clindamycin	Cloxacillin	Erythromycin	Levofloxacin	Linezolid	Penicillin	Tetracycline[1]	TMX	Vancomycin
S. aureus (MSSA)	8454				100		84	100	79				95	99	
S. aureus (MRSA)	2136	R		R	R		73	R	26		100	R	81	96	100
Group A Streptococcus[2]	227	100	78	100	100	78	79		78	100		100		R	100
Group B Streptococcus[2]	77	100	47	100	100	47	51		47	97		100		R	100

[1]Isolates susceptible to tetracycline are predictably susceptible to doxycycline; however, some isolates that are resistant to tetracycline may be susceptible to doxycycline.

[2]Groups A, B, C and G streptococcal isolates are predictably susceptible to penicillin, amoxicillin and cephalosporins, therefore antimicrobial susceptibility testing is not routinely performed.

Providence antibiogram is pretty similar to this, but generally MRSA susceptibilities to clindamycin, tetracycline, and TMP-SMX is lower

https://lifelabs.azureedge.net/lifelabs-wp-cdn/2019/03/2019-Antibiogram-Lower-Mainland.pdf

SLOW TO RESPOND SSTI

Medication adherence

Correct drug

Correct dose

Non-pharmacologic

- Rest
- Compress
- Elevate

Is there a deeper infection?

Is there a concurrent dx? eg DVT

NON-RESPONDING SSTI

Hints to other etiologies

- DM
- Cirrhosis
- Neutropenia
- Bites
- Marine exposure
- Etc…

SSTI mimics

- Herpes zoster
- Erythema migrans (Lyme disease)
- Gout
- Erythema nodosum
- Contact dermatitis
- Insect bite/stings
- Drug reaction
- Vascular

ADDRESS PRECIPITANTS AND PREVENTION

Treat precipitants like tinea pedis

Review safe injection practices

- Safe injection site associated with reduced rate of admission to hospital for cutaneous injection-related infections

Can Fam Physician. 2017 Nov; 63(11): 866.

https://www.oneandonlycampaign.org/sites/default/files/upload/pdf/SIPC_logoposter_patient.pdf

TAKE HOME POINTS

Who should be referred for iv antibiotics?

- Complicated SSTI (eg systemic symptoms, concern for necrotizing infection)
- Requires I&D that cannot be done in the clinic setting, e.g. procedural sedation
- patients at increased risk of failure
  - Factors like chronic leg ulcers, MRSA hx, previous cellulitis have limited predictive power
- Failure of oral antibiotics at 48-72h

TAKE HOME POINTS

Skin abscess: who needs antibiotics?

Small/uncomplicated abscess:

- Many patients have clinical cure without antibiotics (over 2/3)
- Antibiotics increase the cure rate by 10-15%
- Shared-decision making

Larger or complicated abscess: give antibiotics

I&D recommended for all

TAKE HOME POINTS

Cephalexin and cefadroxil are very similar and effective for non-purulent SSTI

- Cefadroxil has the advantage of bid dosing

In choosing empiric anti-MRSA coverage for SSTI, consider the local antibiogram

- In addition to allergy, drug interactions, etc
- TMP-SMX has highest rate of susceptibility among available oral agents

PWID and our other marginalized patients are not well represented in clinical trials of SSTI management

- How large is the gap between trial efficacy and real-world effectiveness?

RESOURCES

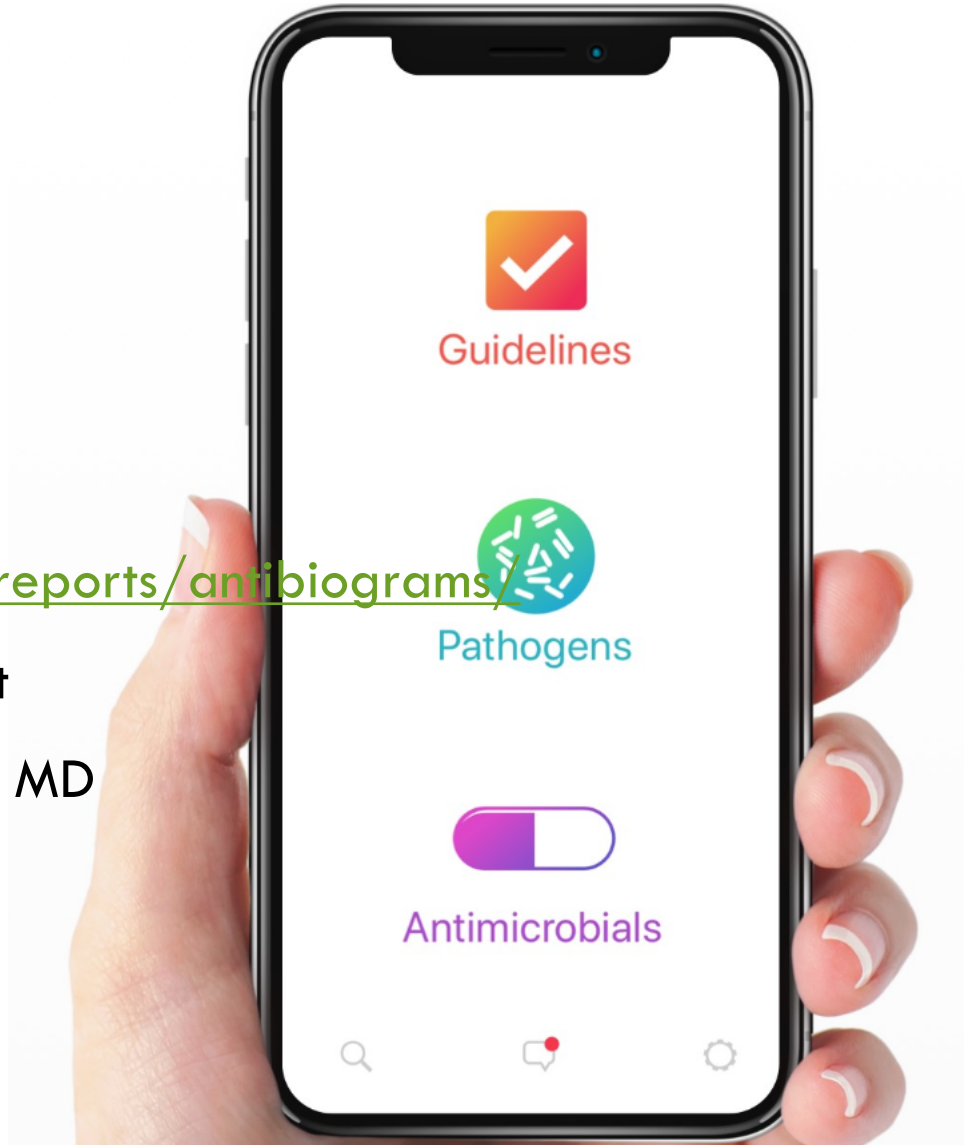
Antibiograms

Lifelabs: https://www.lifelabs.com/healthcare-providers/reports/antibiograms/

Health authorities: try spectrum app in addition to intranet

SPH OPAT: 604-682-2344, x63580 and ask for the OPAT MD

RACE line



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