Abscessing the Evidence:
Antibiotics for the treatment of small, skin abscesses

Laura Beresford
Doctor of Pharmacy Student, Class of 2018
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Skin Abscess

- Risk Factors: immunocompromised, DM, IVDU, bacterial overgrowth, antecedent trauma.
- Pathogens: S. aureus, streptococci
- Complications: bacteremia, osteomyelitis, sepsis, endocarditis.

Mayo Clinic, 2017.

Incision and drainage

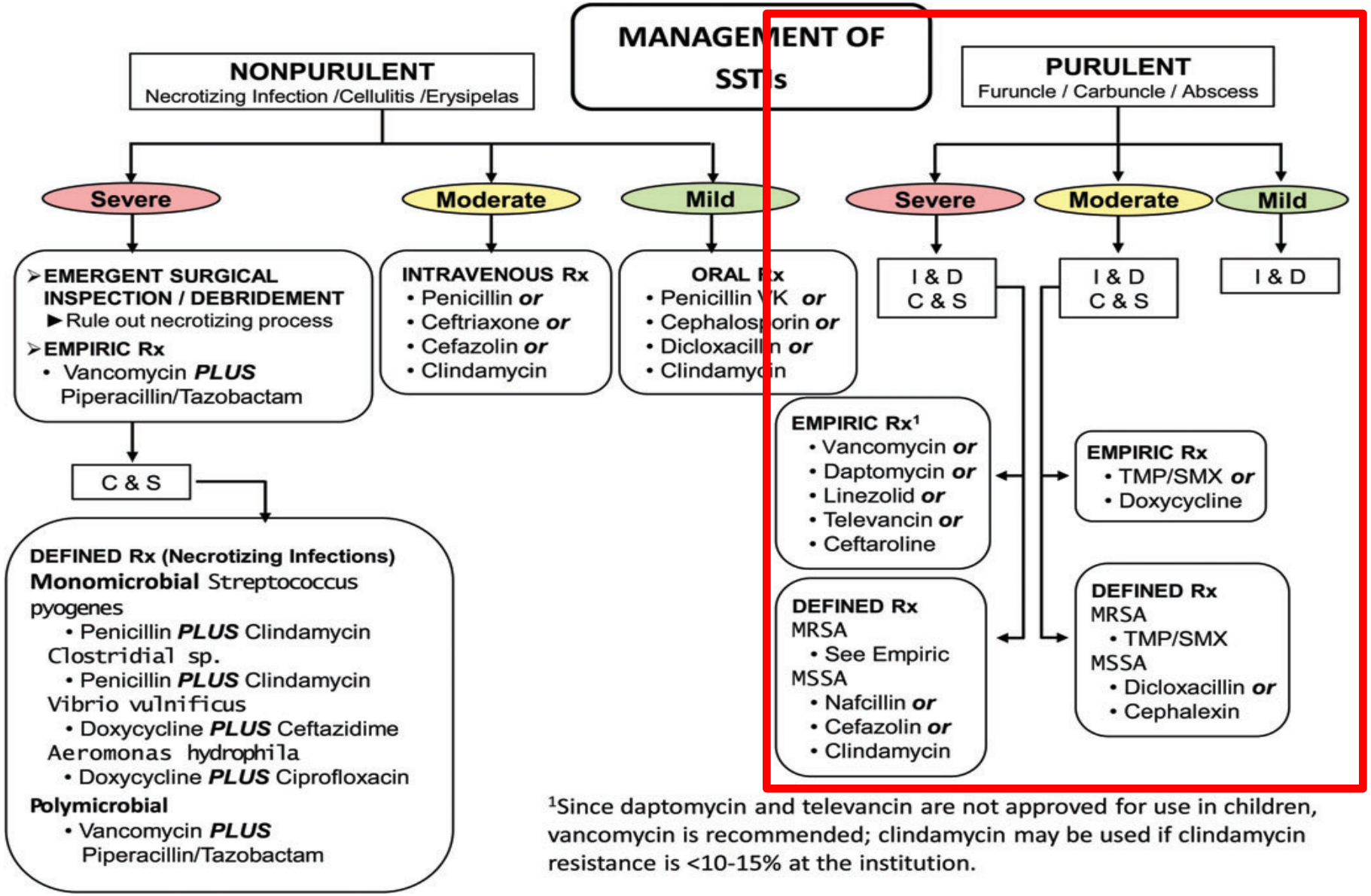
- Source control – once you identify and control the source the infection is contained and clinical cure is possible.

Treatment Alternatives

- Incision and drainage (I+D)
- I+D plus antibiotics (oral/IV)

CONTROVERSY

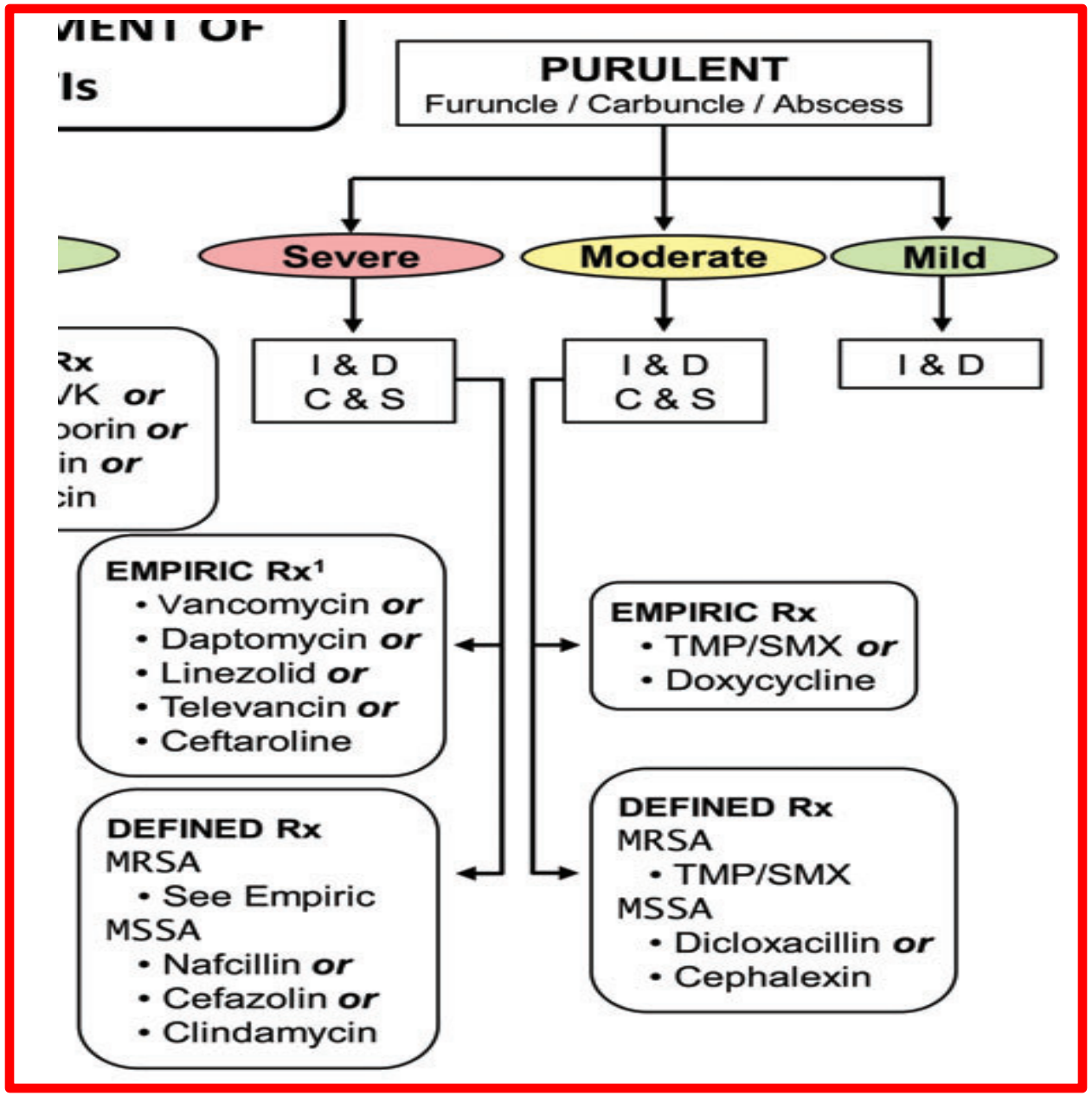
2014 IDSA Criteria



[1]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.

Clinical Infectious Diseases 2014;59(2):e10-52

2014 IDSA Criteria



Clinical Infectious Diseases 2014;59(2):e10-52

IDSA Guidelines - 2014

- "Incision and drainage is the recommended Tx of inflamed, epidermoid cysts, carbuncles, abscesses, and large furuncles (strong, high)"

- "The decision to administer Abx directed against S. aureus as an adjunct to I+D should be made based upon presence or absence of systemic inflammatory response syndrome (SIRS) (strong, low)"

Clinical Infectious Diseases 2014;59(2):e10-52

PICO Question

P	Children and adults with skin abscesses <5cm
I	Antibiotics + incision/drainage
C	Incision/drainage
O	Clinical Cure ADRs

Search Strategy

Databases	EMBASE, Medline, CENTRAL, clinicaltrials.gov, Google Scholar
Search Terms	Small or uncomplicated, skin, abscess, antibiotic, incision or drainage
Limits	English, humans, RCTs
Results	6 Trials

Trials before 2014 IDSA Guidelines

Study	Sample Size	Abscess Size	Intervention	Outcome	Results
Llera et al. (1985)	N = 81 LTF = 31	Not stated	Cephradine vs placebo x 7d	Clinical improvement @ 7d	Cephradine – 96% Placebo – 96% NSS
Rajendran et al. (2007)	N = 166 LTF = 4	>2cm	Cephalexin vs placebo x 7d	Clinical cure or failure def. by 10% diff. in groups	Cephal-84.1%, placebo-90.5% NSS
Schmitz et al. (2010)	N = 212 LTF = 22	Median diameter: 2.8cm – placebo, 2.5cm – SMX/TMP	SMX/TMP vs placebo x 7d	Clinical cure @ 7d def. as 15% diff. in groups	SMX/TMP-83% Placebo-74% NSS
Duong et al. (2010)	N = 161 LTF = 12	Mean diameter: 2.2 $\pm$ 1.5cm	SMX/TMP vs placebo x 10d	Clinical resolution or failure	Failure rate placebo-5.3%, SMX/TMP-4.1%, non-inferior

Antimicrobial agents and Chemotherapy. 2007;51(11):4044-48
Annals of Emerg Med. 1985;14:15-19
Annals of Emerg Med. 2010:55;5:401-07
Annals of Emerg Med. 2010;56(3):283-87

Trimethoprim-Sulfamethoxazole versus Placebo for Uncomplicated Skin Abscess

Talan DA, Mower WR, Krishnadasan A, et al.

D	DB, PC, multi-centre U.S, **N =1265**
P	Inclusion criteria: >12y/o, >2cm cutaneous lesion <1wk w/ purulent material. Exclusion criteria: indwelling devices, bite wound, wound w/ foreign body, IVDU in prev month and fever, LTC home, CrCl <50ml/min, immunocompromised, taking meds that interact w/ SMX/TMP.
I	I/D + SMX/TMP 1600/320mg po BID x 7d
C	I/D + placebo x 7d
O	Primary: Clinical cure at 7 to 14 days after end of Tx period Secondary: composite cure, surgical drainage procedures, skin infections at same/diff site, hospitalizations, ADRs

NEJM. 2016;374(9):823-32

Baseline Characteristics

	SMX/TMP (n=630)	Placebo (n=617)
Median Age (IQR)	35 (26-47)	35 (26-48)
Diabetes, N (%)	69 (11.0)	68 (11.0)
Median length of abscess, cm (IQR)	2.5 (2.0-3.5)	2.5 (2.0-3.5)
Median width of abscess, cm (IQR)	2.0 (1.5-3.0)	2.0 (1.5-3.0)
Median length of erythema, cm (IQR)	7.0 (4.3-10.0)	6.5 (4.0-10.0)
Median width of erythema, cm (IQR)	5.0 (3.5-8.0)	5.0 (3.0 -7.5)

NEJM. 2016;374(9):823-32

Culture Results

	SMX/TMP (n=630)	Placebo (n=617)
MRSA, N (%)	274 (43.5)	291 (47.2)
MSSA, N (%)	100 (15.9)	102 (16.5)
CoNS, N (%)	80 (12.7)	61 (9.9)
Streptococci spp., N (%)	41 (6.5)	22 (3.6)
Other, N (%)	104 (16.5)	69 (11.2)

NEJM. 2016;374(9):823-32

Results – Primary Outcome

	Clinical Cure at TOC Visit			
	SMX/TMP (n=636)	Placebo (n=629)	Difference (95% CI) *percentage points*	P-value
Modified ITT - 1	507/630 (80.5%)	454/617 (73.6%)	6.9 (2.1 – 11.7)	0.005
Modified ITT - 2	562/606 (92.7%)	526/607 (86.7%)	6.1 (2.5 – 9.7)	<0.001
Per-protocol	487/524 (92.9%)	457/533 (85.7%)	7.2 (3.2 – 11.2)	<0.001

NEJM. 2016;374(9):823-32

Results – Secondary Outcomes

	SMX/TMP (n=636)	Placebo (n=629)	Difference (95% CI) *percentage points*
Composite clinical cure by TOC (%)	86.5	74.3	12.2 (7.2 – 17.1)
Hospitalization by TOC (%)	3.6	6.4	-2.8 (-5.6 – 0.1)
New skin infection at different site (%)	3.1	10.3	-7.2 (-10.4 – -4.1)
Additional surgical drainage procedure	3.4	8.6	-5.2 (-8.2 – -2.2)

NEJM. 2016;374(9):823-32

Adverse Events

	SMX/TMP (n=636)	Placebo (n=629)
Any ADR, N (%)	412 (65.4)	402 (65.2)
GI disorders, N (%)	269 (42.7)	223 (36.1)
Diarrhea, N (%)	94 (14.9)	96 (15.6)
Nausea, N (%)	134 (21.3)	102 (16.5)
Headache, N (%)	100 (15.9)	76 (12.3)
Rash, N (%)	16 (2.5)	9 (1.5)

NEJM. 2016;374(9):823-32

Authors Conclusions

- Patients who received SMX/TMP at doses of 1600/320mg orally twice daily, had a higher cure rate than those who received placebo. We also found that many secondary outcomes were better in the SMX/TMP group compared to placebo.

Critique

Randomization?	Web-based central randomization
Allocation Concealment?	2 antibiotics looked similar
Baseline Characteristics?	Similar
Blinded?	Double blinded
Attrition Bias?	252 pts did not complete extended F/U visit
ITT or Per-protocol?	Modified ITT
Power Calculation?	Stated in protocol
Generalizability?	Excluded immunocompromised pts
Funding?	National Institute of Allergy and Infectious Diseases

NEJM. 2016;374(9):823-32

Further Limitations

- Dose of SMX/TMP is quite high
- Some non-adherence – 64.7% were 100% adherent, 17.2% were 75-99% adherent

NEJM. 2016;374(9):823-32

A Placebo-Controlled Trial of Antibiotics for Smaller Skin Abscesses.

Daum RS, Miller LG, Immergluck L et al.

D	R, DB, PC, Multi-centre U.S, May 2009-January 2015, **N=786**
P	Inclusion criteria: single abscess <5cm w/ 2 of the following: erythema, swelling, induration, local warmth, purulent drainage & tenderness. Exclusion criteria: bite wounds, systemic anti-staph Abx in prev 14d, immunocompromised in prev 12 mo.
I	Arm 1: I/D + clindamycin 300mg po TID x 10d Arm 2: I/D + SMX/TMP 800/160mg po BID x 10d
C	Arm 3: I/D + placebo x 10d
O	Primary outcome: Clinical cure by test-of-cure visit Secondary outcomes: Cure rates at the end-of-treatment and 1-mo. F/U visits, cure rates in adults & children, cure rates for MRSA or other strains and ADEs.

NEJM. 2017;376:2545-55.

Baseline Characteristics

	Clindamycin (n=266)	SMX/TMP (n=263)	Placebo (n=257)
Mean Age (yrs)	30.1±8.8	28.2±8.0	30.2±8.1
Black or African American, N (%)	165 (62.0)	152 (57.8)	167 (65.0)
>18 yrs , N (%)	165 (62.0)	172 (65.4)	168 (65.4)
Body Temperature (◦C)	36.67±0.47	36.63±0.47	36.63±0.46
Area of wound (cm^2)	3.88±4.90	3.76±3.44	4.04±4.43
Area of erythema (cm^2)	26.85±104.34	29.68±93.76	25.76±53.11

NEJM. 2017;376:2545-55.

Baseline Abscess Size

Abscess size, greatest dimension (cm)	Age Group				
	<1 yr (n=17)	1 - 8 yr (n=166)	9 - 17 yrs (n=98)	≥18 yrs (n=505)	All ages (n=785)
0.0 - <1.0, N (%)	5 (29.4%)	49 (29.5%)	16 (16.3%)	81 (16.0%)	151 (19.2%)
>1.0 - ≤2.0, N (%)	5 (29.4%)	38 (22.9%)	21 (21.4%)	136 (26.9%)	200 (25.4%)
>2.0 - ≤3.0, N (%)	7 (41.2%)	47 (41.2%)	23 (23.5%)	150 (29.7%)	227 (28.9%)
>3.0 - ≤4.0, N (%)	0	31 (18.7%)	19 (19.4%)	81 (16.0%)	131 (16.7%)
>4.0 - ≤5.0, N (%)	0	1 (0.6%)	19 (19.4%)	56 (11.1%)	76 (9.7%)

NEJM. 2017;376:2545-55.

Results - ITT

	Clinical Cure at TOC Visit		
	Clindamycin	SMX/TMP	Placebo
All Participants	221/266 (83.1%)	215/263 (81.7%)	177/257 (68.9%)
Children	90/101 (89.1%)	75/91 (82.4%)	61/89 (68.5%)
Adults	131/165 (79.4%)	140/172 (81.4%)	116/168 (69.0%)

NEJM. 2017;376:2545-55.

Results - ITT

	Clinical Cure at TOC Visit		
	Clindamycin	SMX/TMP	Placebo
S. *aureus* isolated	157/188 (83.5%)	149/179 (83.2%)	102/160 (63.8%)
MRSA isolated	116/142 (81.7%)	110/130 (84.6%)	73/116 (62.9%)
MSSA isolated	41/46 (89.1%)	39/49 (79.6%)	29/44 (65.9%)
No S. *aureus* isolated	57/68 (83.8%)	59/72 (81.9%)	69/83 (83.1%)*

*NSS

NEJM. 2017;376:2545-55.

Adverse Events

	Clindamycin (n=266)	SMX/TMP (n=263)	Placebo (n=257)
Any ADR, N (%)	58 (21.9)	29 (11.1)	32 (12.5)
GI disorders, N (%)	52 (19.6)	26 (10.0)	27 (10.6)
Diarrhea, N (%)	43 (16.2)	14 (5.4)	17 (6.7)
Nausea, N (%)	6 (2.3)	11 (4.2)	6 (2.4)
Headache, N (%)	4 (1.5)	5 (1.9)	1 (0.4)
Rash, N (%)	6 (2.3)	1 (0.4)	1 (0.4)

NEJM. 2017;376:2545-55.

Authors Conclusions

- Patients with small abscesses (<5cm) who grow S. aureus may benefit from receiving 10 days of clindamycin or SMP/TMX taking into account the risk vs. benefit of receiving antibiotics.

Critique

Randomization?	Stated but not specified
Allocation Concealment?	Concealed
Baseline Characteristics?	Similar between groups
Blinded?	Participants, site personnel and investigators blinded
Attrition Bias?	31 pts did not complete the study
ITT or Per-protocol?	ITT
Power Calculation?	Specified and met sample size
Generalizability?	Majority Black/African American, resistance patterns
Funding?	National Institute of Allergy and ID/National Center for Research Resources

NEJM. 2017;376:2545-55.

Further Limitations

- Generalizability
  - 35.8% pediatric participants
  - Majority black/African American population
  - Resistance patterns differ
- Only studied SMX/TMP and clindamycin
- F/U was limited to 1 month
- Duration of 10 days of Abx
- Did not tailor to susceptibilities

Summary

Study	Regimen	Efficacy	Safety
Llera et al. (1985)	Cephradine vs placebo x 7d		Unable to assess
Rajendran et al. (2007)	Cephalexin vs placebo x 7d		Unable to assess
Schmitz et al. (2010)	SMX/TMP vs placebo x 7d		
Duong et al. (2010)	SMX/TMP vs placebo x 10d	Non-inferiority	
Talan et al. (2016)	SMX/TMP vs placebo x 7d		
Daum et al. (2017)	SMX/TMP vs clinda vs placebo x 10d	S. aureus isolates only	> in clinda group

Take home points

- S. aureus cultured – consider Tx
- Skin abscesses <5cm were studied
- Further trials are needed to see if a shorter duration is appropriate
- Factors to consider:
  - Patient/parent preference
  - Antimicrobial stewardship/duration of Abx Tx
  - If the patient is clinically unwell (oral temp >38.3)
  - Tailoring to susceptibilities

Back to my clinical question…

- Based off the evidence, I would consider using Abx in an uncomplicated skin abscess which grows S. aureus taking into account the previously stated factors.
- There is not enough evidence at this time to recommend Abx in skin abscesses that grow other pathogens.

Questions?