Curbside Consults in Infectious Diseases

Management of the Hospitalized Patient
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Disclosures

- I have no disclosures.

Learning Objectives

At the end of this talk, you will be able to:

- Describe the situations in which formal in-person consultation is preferred over curbside consultation
- Outline an approach to common ID questions that arise in the inpatient setting

Roadmap

- A Brief Word on Curbsides vs. Formal Consults
- Case-Based Approach to the Top Curbside Consult Questions in ID
  1. Blood culture contaminants
  2. Oral antibiotics for ESBL cystitis
  3. Line management in CLABSI
  4. Oral therapy for pyelonephritis
  5. Antibiotics for nonpurulent cellulitis
  6. Latent TB diagnostics
  7. Zoster vaccine in immunocompromise

Roadmap

- **A Brief Word on Curbsides vs. Formal Consults**

- Case-Based Approach to the Top Curbside Consult Questions in ID
  1. Asymptomatic bacteriuria
  2. Oral antibiotics for ESBL cystitis
  3. Line management in CLABSI
  4. Oral therapy for pyelonephritis
  5. Antibiotics for nonpurulent cellulitis
  6. Latent TB diagnostics
  7. Zoster vaccine in immunocompromise

Curbsides vs Formal Consults

Study of 47 curbsides vs. formal consults

- Medicine consult
- Curbside → formal consult by a colleague
- Curbsided providers could not look in chart

Curbsides

- Information inaccurate or incomplete in 51%

Formal Consults

- Changed Rx in 60% (36% “major changes”)
- If info was inaccurate/ incomplete then it changed Rx in 92% (45% “major changes”)

Burden et al, J Hosp Med 2013, 8:31.

Are Curbsides Okay?

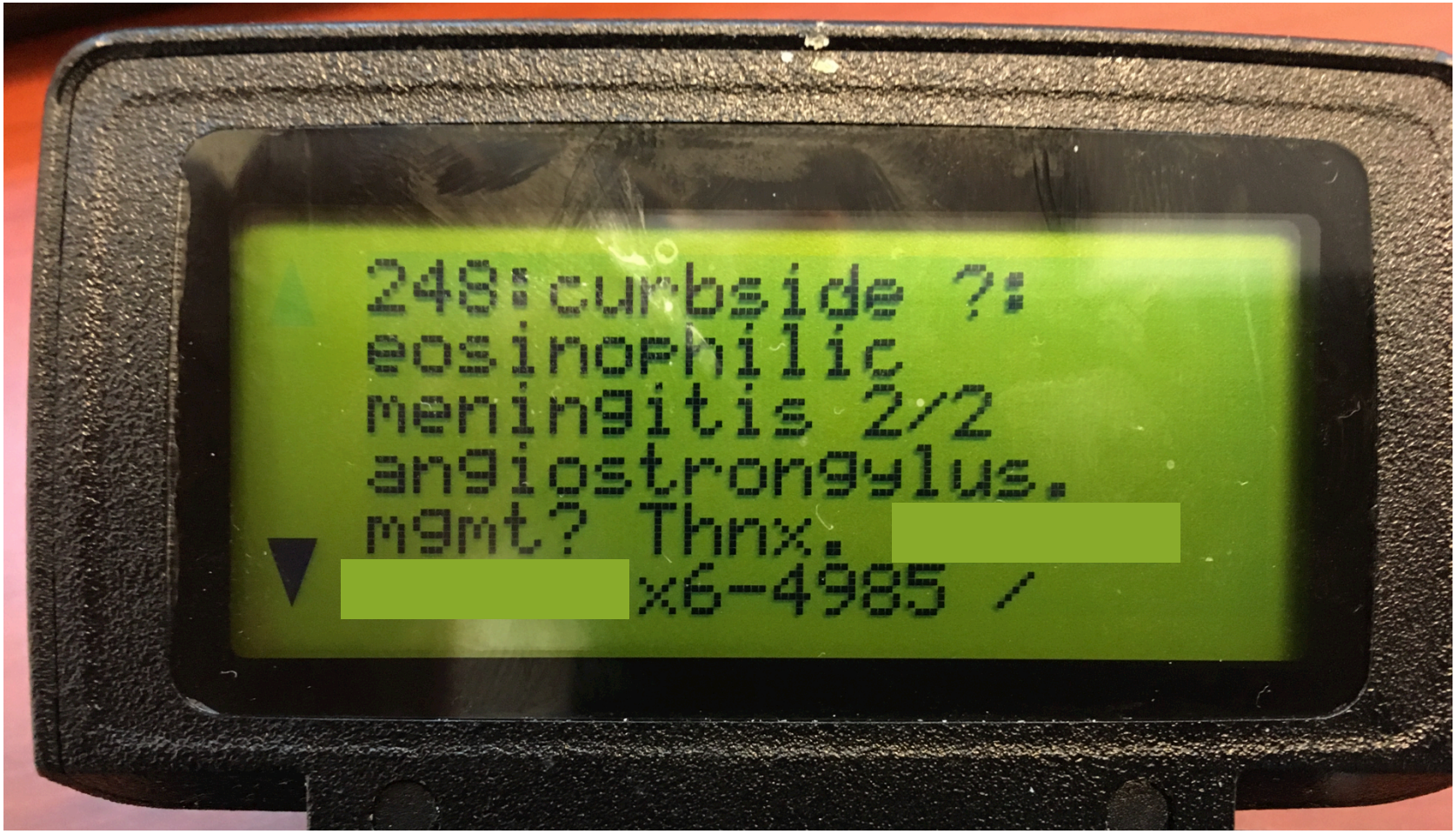
- Need to balance patient safety, provider workload, education
- Curbside volume in ID
  - In the literature: 20-120 curbsides/month
  - UCSF Medical Center: 60 curbsides/mo (15 hours/mo)
- Impossible in most practices to convert all curbsides into formal consults

Grace et al, Clin Infect Dis 2010, 51:651. Wachter, B. "The Dangers of Curbside Consults... and Why We Need Them."Wachter's World. 29 Apr. 2013.

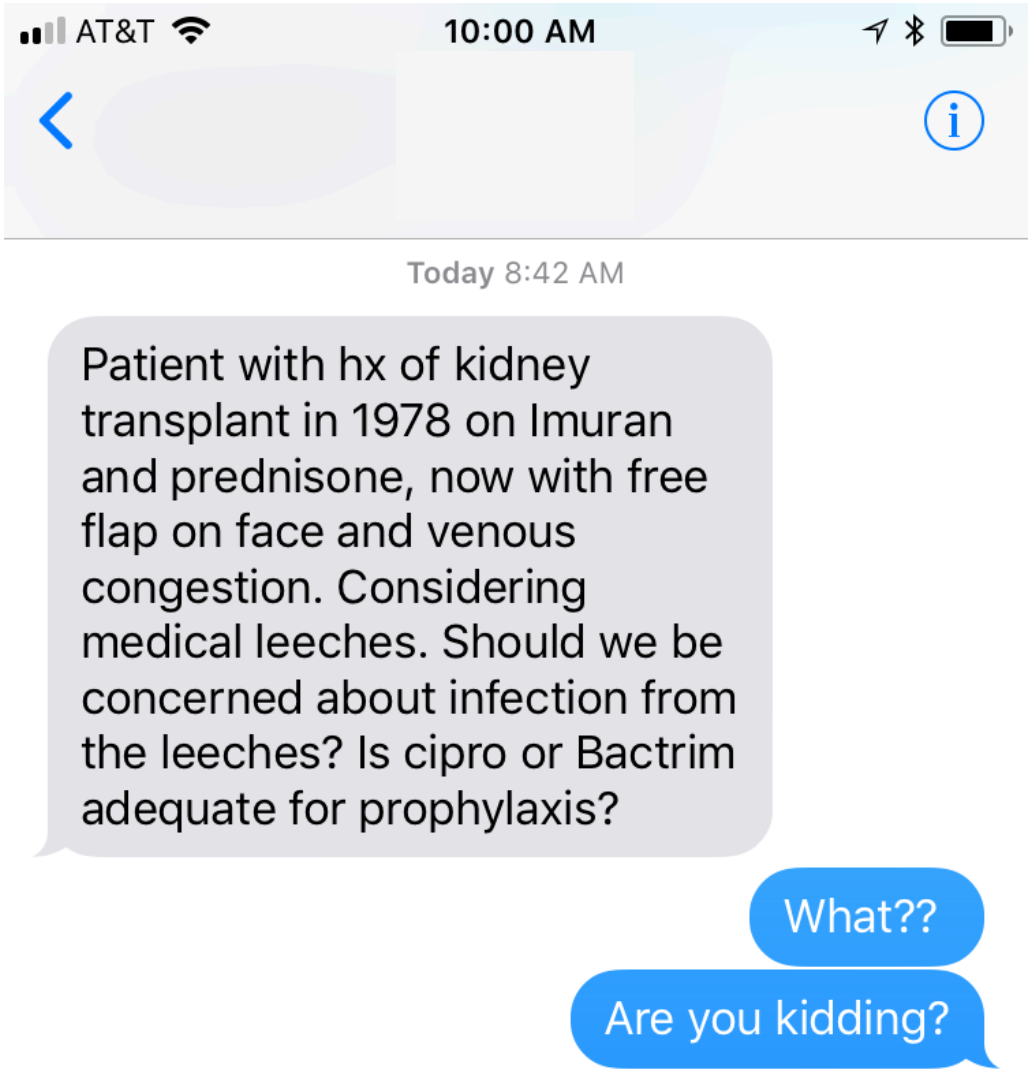
Is This An Appropriate Curbside?

What is the dose of ertapenem when the CrCl is <30?

Is This An Appropriate Curbside?



Is This An Appropriate Curbside?



Is This An Appropriate Curbside?

Theoretically, if a patient has mild cystitis due to VRE that is sensitive to doxycycline, can I use that drug to treat a VRE UTI? Does doxycycline penetrate into the urine?

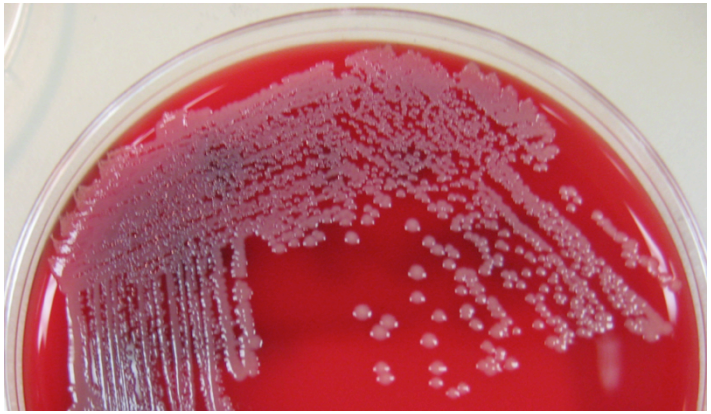
What is an Appropriate Curbside?

- The Goldilocks of Curbside Consultation
  - Not too simple: the answer can be easily looked up
  - Not too complicated: the answer requires nuanced clinical judgment, interpretation of a lot of data, or a deep dive into the literature
  - Just right: Hypothetical, factual question

- We also tell our ID Fellows that it should probably be a consult if:
  - You need to look up the answer
  - It's early in the year
  - The team calls you back several times

The Special Case of S. *aureus* Bacteremia

- Benefit of ID consultation versus no consultation
  - ⇧ adherence to quality indicators for SAB:
    - Getting an echo, repeat blood cultures
    - Improved antibiotic choice and duration
    - ⇧ removal of prosthetic devices/source control
  - ⇧ detection of metastatic foci of infection
  - ↓ mortality (by 20-50%)



Saunderson et al, Clin Micro Infect 2015, 21:779. Forsblom et al, Clin Infect Dis 2013, 56:527. Bai et al, Clin Infect Dis 2015; 60:1451. Paulsen et al, OFID 2016. Vogel et al, J Infection 2016; 72:19.

Curbsides for *S. aureus* Bacteremia?

- Curbside consult is associated with:
  - Less identification of deep infectious foci
  - Less likely to receive the proper duration of therapy
  - ⇧ 90d mortality by > 2-fold compared to formal consult

- Formal consult for SAB is preferred if available

Forsblom et al, Clin Infect Dis 2013, 56:527.

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  2. Oral antibiotics for ESBL cystitis
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  7. Zoster vaccine in immunocompromise

Curbside #1

Do I need to worry about Bacillus if it grew in the blood? The patient is totally fine and this grew out at 3 days, right before discharge.

Do You Need to Worry about the Bacillus?

1. Yes

2. No

How to Determine a Contaminant vs True Infection

What is the clinical situation?

What is the organism? Most common contaminants:

- Coagulase-negative *Staph (*82%)
- *Corynebacterium* (not *jeikieum*) (>88%)
- *Bacillus* spp. (not *anthracis*) (>92%)
- *Propionibacterium acnes* (>94%)
- Viridans group streptococci (50-55%)

How many blood culture sets are positive?

- More likely real if 2 out of 2 sets
- Caveat: 2/2 is common for coag-neg *Staph.* Can check antibiograms (100% sensitive for same strain, 84% specific) or get species from the micro lab

When did it turn positive?

Growth at ≥3-5 days → more likely a contaminant

Number of blood culture bottles positive within a set does NOT correlate

Hall and Lyman, Clin Micro Rev 2006, 19:788. Pien et al, Am J Med 2010, 123:819.

Curbside #2

A 75 year old woman with neurogenic bladder is admitted with confusion, fever, and 2 days of suprapubic pain and dysuria.

UA shows >50 WBC/hpf and urine culture grows *E. coli*. Blood cultures are negative.

She improves on empiric ertapenem and is ready for discharge. Susceptibilities come back and the *E. coli* is an ESBL producer.

Do I need to send her home on ertapenem or are there any oral options?

Which Oral ABx Has the Best Efficacy in ESBL UTI?

1. Fosfomycin
2. Nitrofurantoin
3. Doxycycline
4. Cephalexin

Oral Options for ESBL *E. coli* in the Urine

Antibiotic	% Sensitive in vitro
Ciprofloxacin	4-36
TMP-SMX	22-43
Amoxicillin/Clavulanate	11-70
Nitrofurantoin	58-94
Fosfomycin	91-100

Caveat: susceptibilities for ESBL *Klebsiella* are lower for both fosfomycin (~54-80%) and nitrofurantoin (14%)

Prakash et al, AAC 2009, 53:1278. Liu et al, J Micro Immunol Infect 2011, 44:364. Kumar et al, Infect Dis Res Treat 2014, 7:1. Meier et al, Infect 2011, 39:333. Kresken et al, IJAA 2014, 44:295. Fournier et al, Med Mal Infect 2013, 43:62. Rodriguez-Bano, Arch Intern Med 2008, 168:1897. Linsenmeyer, AAC 2016, 60:1134.

Data for Oral ABx in *E.coli* ESBL Cystitis (Outpatient)

Fosfomycin

- 1-3 doses → 94% cure
- Can't use in pyelo/ bacteremia
- MIC not routinely performed
- Dose: 3gm PO qod x 3 (or until clinical improvement)

Nitrofurantoin

- 14d → 69% cure
- Can't use in pyelo/ bacteremia
- Avoid if CrCl<60

Amoxicillin/clav

- 5-7d → 93% cure

Falagas et al, Lancet ID 2010, 10:43. Rodriguez-Bano, Arch Intern Med 2008, 168:1897. Pullukcu et al, Int J Antimicrob Agents 2007, 29:62. Reffert and Smith, Pharmacotherapy 2014, 34:845.

What if the Patient has Pyelonephritis?

- Small study in community-acquired pyelonephritis showing non-carbapenem = carbapenem

- But, non-carbapenem group:
  - Mostly aminoglycoside or pip/tazo
  - Had much lower rates of bacteremia

- Bottom line: not enough data to support the routine use of oral antibiotics for ESBL pyelonephritis

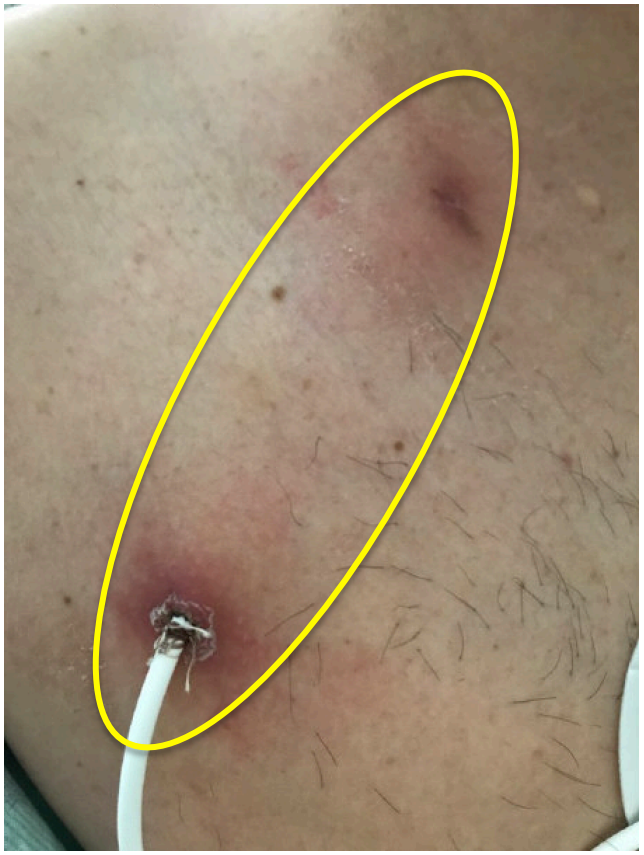
Park et al, J Antimicrob Chemother 2014, 69:2848.

Oral Options for ESBL UTI: Take-Home points

- Most data is for *E. coli* ESBL (limited data for *Klebsiella*)
- For mild-moderate cystitis:
  - Oral ABx choice dictated by susceptibilities
  - Consider empiric use of or susceptibility testing for fosfomycin
  - Caution with nitrofurantoin given poor clinical cure rates
- Would not use orals if the patient is clinically ill, has bacteremia, or cannot be followed closely
- Not enough data to support the routine use of oral antibiotics for ESBL pyelonephritis

Curbside #3

A 36 year old man with AML is s/p leukopheresis and induction therapy. He is doing well and no longer neutropenic but then spikes a fever.



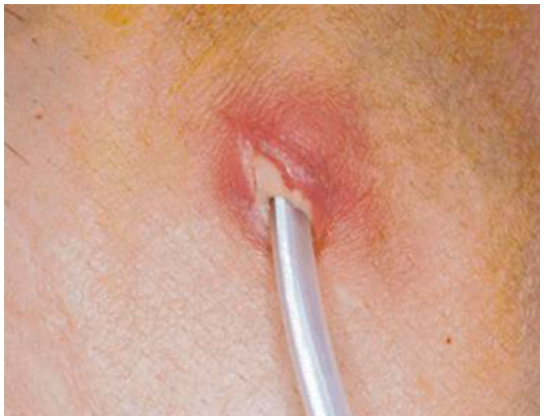
- He is bacteremic with *Staph epidermidis* from both his line and peripheral blood cultures
- He improves with vancomycin. **Can we leave the tunneled line in?**

Can You Leave the Line In?

1. Yes

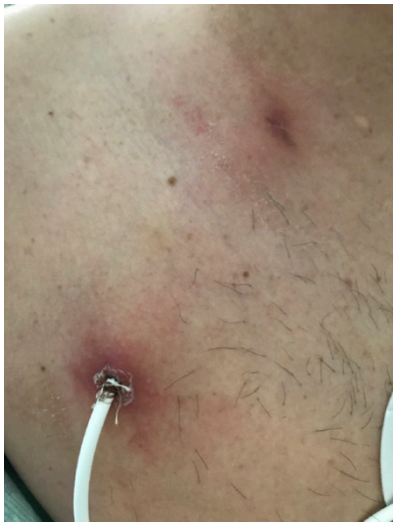
2. No

Central Line Infections



Exit site infection (<2cm from exit site)

- With or without BSI
- If blood cultures neg, can try to keep line



- **Tunnel infection (>2cm)**
- **Port pocket infection**

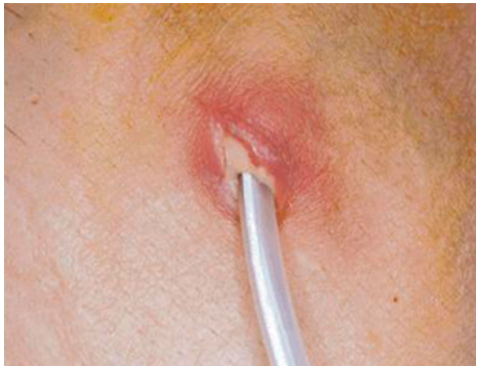
- With or without BSI
- Remove the line even if blood cultures neg

Bacteremia without overlying skin changes

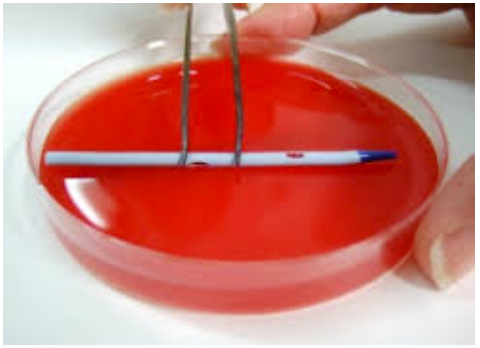
- BSI by definition
- Line removal depends on organism, clinical situation

Central-Line Associated BSI (CLABSI): Diagnosis

- Clinical findings at exit site in <3%



- Catheter tip culture:
  - (+) peripheral bcx and > 15 cfu/plate from catheter tip
  - 80% sensitive, 90% specific
  - But >80% of catheters removed unnecessarily



Mermel et al, Clin Infect Dis 2009, 49:1. Safdar and Maki, Crit Care Med 2002, 30:2632.

CLABSI: Differential Time to Positivity

- Allows for diagnosis without removing the line
- Culture from line + peripheral blood at the same time
- CLABSI = blood culture drawn from central line turns positive at least 2 hrs before the peripheral culture
- Test characteristics
  - 85-95% sensitive
  - 85-90% specific

Liñares, Clin Infect Dis 2007, 44:827. Bouza et al, Clin Infect Dis 2007, 44:820. Bouza et al, Clin Microbiol Infect 2013, 19: E129. Safdar et al, Ann Intern Med 2005, 142:251.

DTTP for *Candida*? → Not as good

- DTTP cut-off of 2h is 85% sensitive, 82% specific
- The special case of *C. glabrata*:
  - Most slow growing *Candida* with median TTP of 37h (other species <30h)
  - Using 2hr cut-off DTTP: sensitivity 77%, specificity 50%
  - Best DTTP cut-off = 6h → sensitivity 63%, specificity 75%

Park et al, J Clin Microbiol 2014, 52:2566.

When to Remove the Line

Complicated Infections

1. Severe sepsis
2. Persistent bacteremia (>72h of appropriate ABx)
3. Septic thrombophlebitis
4. Exit site or tunnel infection
5. Metastatic infection: endocarditis, osteomyelitis

Virulent Organisms

1. *Staphylococcus aureus*
2. *Pseudomonas*
3. *Candida*

Mermel et al, Clin Infect Dis 2009, 49:1

Line Management for Other Organisms

Less aggressive with line removal

Organism	PICC/Short-term CVC	Tunneled Cath/Port	HD Catheter
Coag-negative staphylococci	Remove or retain	Remove or retain	Remove, retain, or guidewire exchange
Enterococcus	Remove	Remove or retain	Remove, retain or guidewire exchange
Other GNRs (not *Pseudomonas*)	Remove	Remove or retain	Remove, retain or guidewire exchange

Use clinical judgment based on:

- Severity of infection
- Access options (talk to renal or onc)
- Risk of removal/replacement

Mermel et al, Clin Infect Dis 2009, 49:1

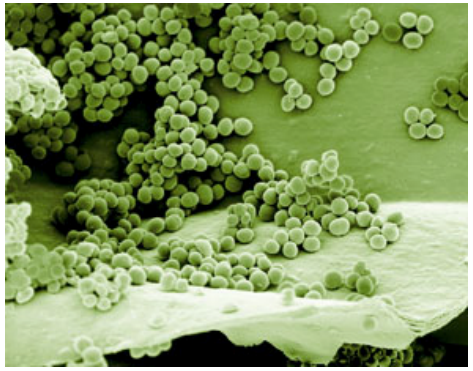
Line Salvage: General Principles

- Which patients?
  - Not for complicated infections, exit site infections, or virulent organisms
  - Only studied in long-term catheters

- How to treat?
  - Give systemic ABx + antibiotic lock therapy for 7-14 d
  - Get surveillance blood cultures (1 wk after Abx stop)

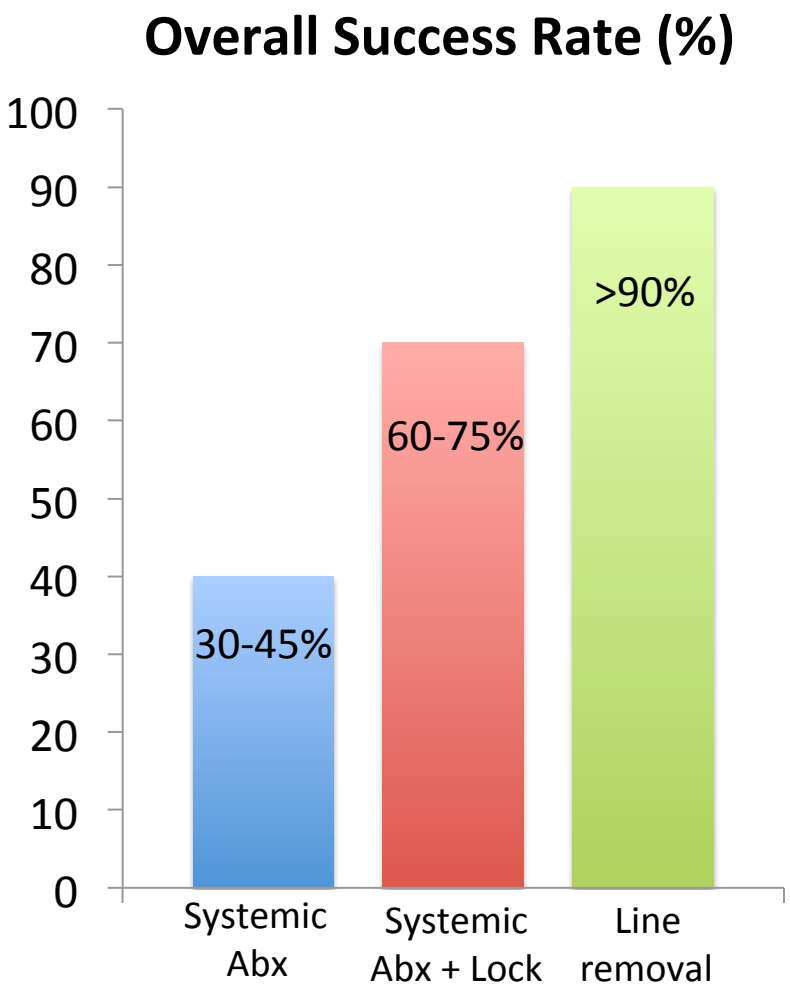
Mermel et al, Clin Infect Dis 2009, 49:1

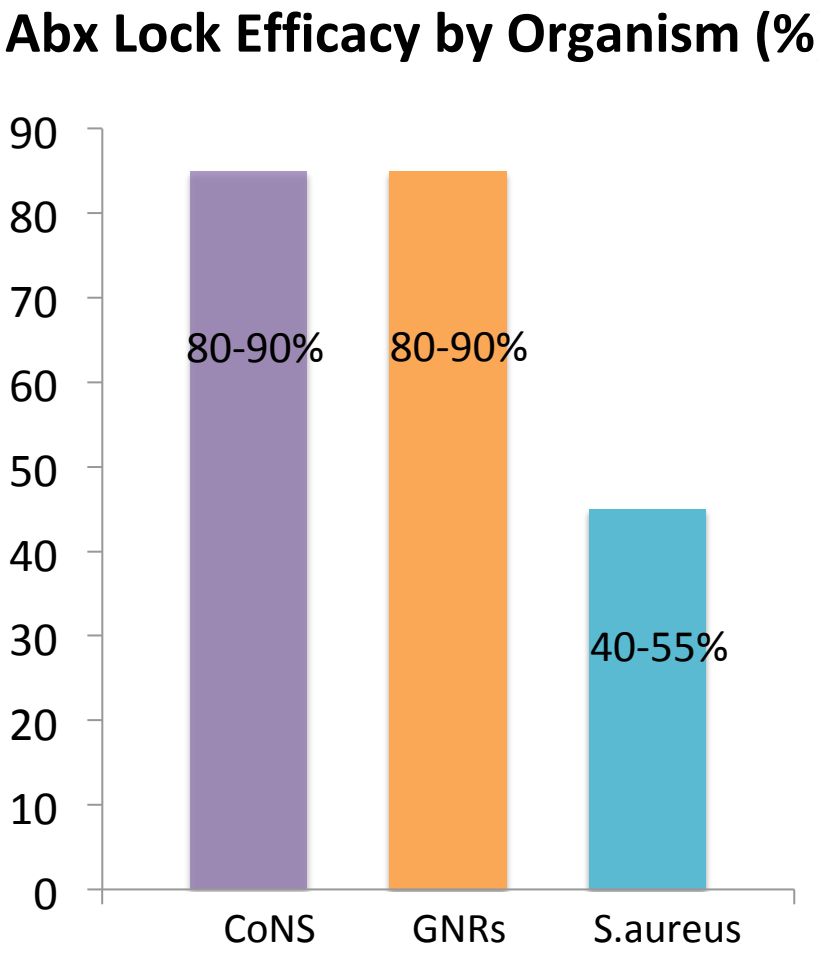
Antibiotic Lock Therapy



- Goal is to get supra-therapeutic ABx concentrations to penetrate biofilms
- Logistics
  - Work with pharmacy and nursing
  - Mix with heparin, dwell times are variable but usually <48h
  - Common Abx:
    - Gram positives: linezolid, vancomycin, cefazolin
    - Gram negatives: ceftazidime, ciprofloxacin, gentamicin

Line Salvage with Antibiotic Lock Therapy





Mermel et al, CID 2009, 49:1 Aslam et al. JASN 2014;25:2927. Fernandez-Hidalgo and Almirante, Expert Rev Anti-Infect Ther 2014, 12:117. Ashby et al, Clin J Am Soc Nephrol 2009, 4:1601. Beathard, JASN 1999, 10:1045.

What About Guidewire Exchange?

- Goal is to eliminate biofilm entirely
- How good is it?
  - Limited data, mostly HD catheters
  - At least equal to ABx lock (~70% cure), maybe better
  - Likely better than ABx lock for *S. aureus*
- When to consider using?
  - If HD catheter removal is clearly indicated but not feasible (especially for *S. aureus*)

Robinson et al, Kidney Int 1998, 53:1792. Shaffer, Am J Kid Dis 1995, 25:593. Mokrzycki et al, Dial Transpl 2006, 21:1024. Aslam et al. JASN 2014;25:2927

Line Management: Take-Home Points

- Physical exam is very insensitive for CLABSI diagnosis
- All lines should be removed for:
  - Any complicated infection
  - *S. aureus, Pseudomonas,* or *Candida*
- Line management for other organisms depends on line type (lower barrier to remove line for short term catheter > long-term catheter > HD catheter)
- Use antibiotic lock when possible for line salvage

Curbside #4

A 45 y/o woman with diabetes is admitted with pyelonephritis.

Her urine and 2 blood cultures are positive for pan-sensitive *Klebsiella pneumoniae*. She was treated empirically with ceftriaxone and has improved (defervesced, normalized her WBC count, resolution of symptoms).

When can she change to PO therapy and how long do we need to treat for?

I want to use cephalexin because this is the most narrow antibiotic – is this okay?

She Should Finish a Treatment Course With:

1. Ceftriaxone IV x 14 days
2. Ciprofloxacin PO x 14 days
3. Ciprofloxacin PO x 7 days
4. Cephalexin PO x 5 days

New! Oral Step Down Therapy for GNR Bacteremia

JAMA Internal Medicine | Original Investigation | LESS IS MORE

Association of 30-Day Mortality With Oral Step-Down vs Continued Intravenous Therapy in Patients Hospitalized With Enterobacteriaceae Bacteremia

Retrospective study of 1478 adults with Enterobacteriaceae bacteremia:

- Clinically stable
- Mix of infections (GI,GU,lines)
- Had source control

- Oral step-down by day 5 vs continued IV
- Both groups got 14d (oral group: 3 days IV)
- Oral group: FQ (70%), TMP-SMX (13%), beta-lactams (17%)

- No difference in mortality, recurrent bacteremia
- Oral group had shorter LOS (5 vs 7d)
- No difference between Abx types

Bottom line: ok to change to PO when clinically stable, have source control (and know susceptibilities). Most data is for FQ.

Tamma et al, JAMA IM 2019, Jan 22 Epub.

What About Duration? RCTs on Short Course Therapy

Study	ABx Results	Patients	Bacteremia
Talan et al 2000	Cipro 500mg PO bid x 7d superior to TMP-SMX 1 DS PO bid x 14d	Uncomplicated pyelo	5%
Peterson et al 2008	Levo 750mg PO qday x 5d = cipro 500mg PO bid x 10d	Uncomplicated and complicated pyelo	2%
Sandberg et al 2012	Cipro 500mg PO bid for 7d = cipro 500mg PO bid for 14d	Uncomplicated pyelo	27%

Talan et al, JAMA 2000, 283:1583. Peterson et al, Urology 2008, 71:17. Sandberg et al, Lancet 2012, 380:48.

New! Antibiotic Duration for GNR Bacteremia

Clinical Infectious Diseases

Seven versus fourteen Days of Antibiotic Therapy for uncomplicated Gram-negative Bacteremia: a Non-inferiority Randomized Controlled Trial

RCT of 604 adults with GNR bacteremia:

- Afebrile, stable by day 5, had source control
- 70% GU source
- 90% Enterobacteriaceae

- Randomized to 7 vs. 14 days of antibiotics
- IV to PO transition not standardized
- IV Abx (ceph or BL/BLI)
- PO Abx (74% FQ, 18% beta lactams)

No difference in mortality, clinical failure, re-admission, LOS, adverse effects, Cdiff

Bottom line: a 7d course of Abx is sufficient for Enterobacteriaceae bacteremia from a GU source if stable and have source control

Yahav et al, Clin Infect Dis 2018. Dec 11 Epub.

Treatment Recommendations for Pyelonephritis

Uncomplicated Pyelo (IDSA)

- Fluoroquinolones
  - Cipro 500mg PO bid x 7 days (A-I)
  - Levo 750mg PO daily x 5 days (B-II)
- TMP-SMX
  - TMP-SMX 1 DS PO bid x 14 d (A-I)
- Beta-lactams
  - Oral beta lactam x 10-14 days (B-III)
  - Lower efficacy than other regimens
  - Probably ok with bacteremia based on newer data

Complicated Pyelo

- No guidelines exist
- Most would treat for 7-14 days as per uncomplicated pyelo
- Reasonable to follow these guidelines on duration of therapy for non-FQ, although 7 days also likely sufficient based on newer data

Gupta et al, Clin Infect Dis 2011, 52:e103..

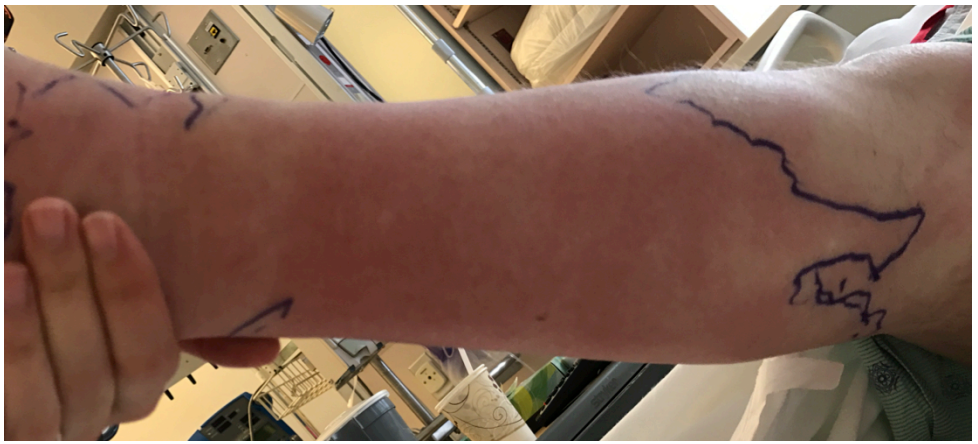
PO Therapy for Pyelonephritis: Take-Home Points

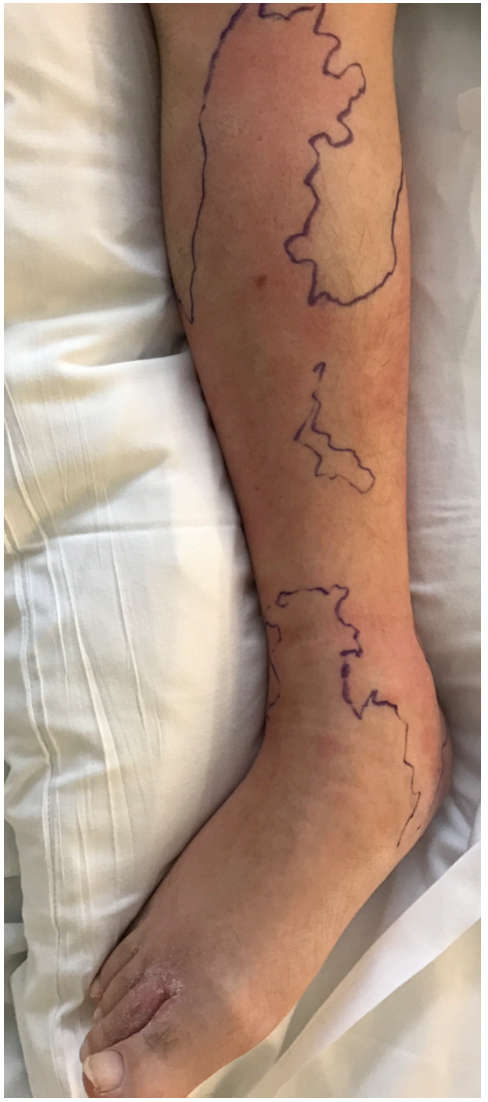
- Ok to change to PO therapy once the patient is improving clinically and you have source control
- If you can use a FQ for stepdown: drug of choice, duration can be 7 days, ok if bacteremic
- If you need to use a beta-lactam for stepdown: would do 7-14 days based on IDSA guidelines (10-14d) and newer data on GNR bacteremia (7d), likely ok if bacteremic but less data than FQ

Curbside #5

45 year old man with no significant PMH is admitted with fever to 38.6˚C and a red painful leg. Other vitals stable. WBC is 12.

He is started on vancomycin.





Curbside #5 Continued

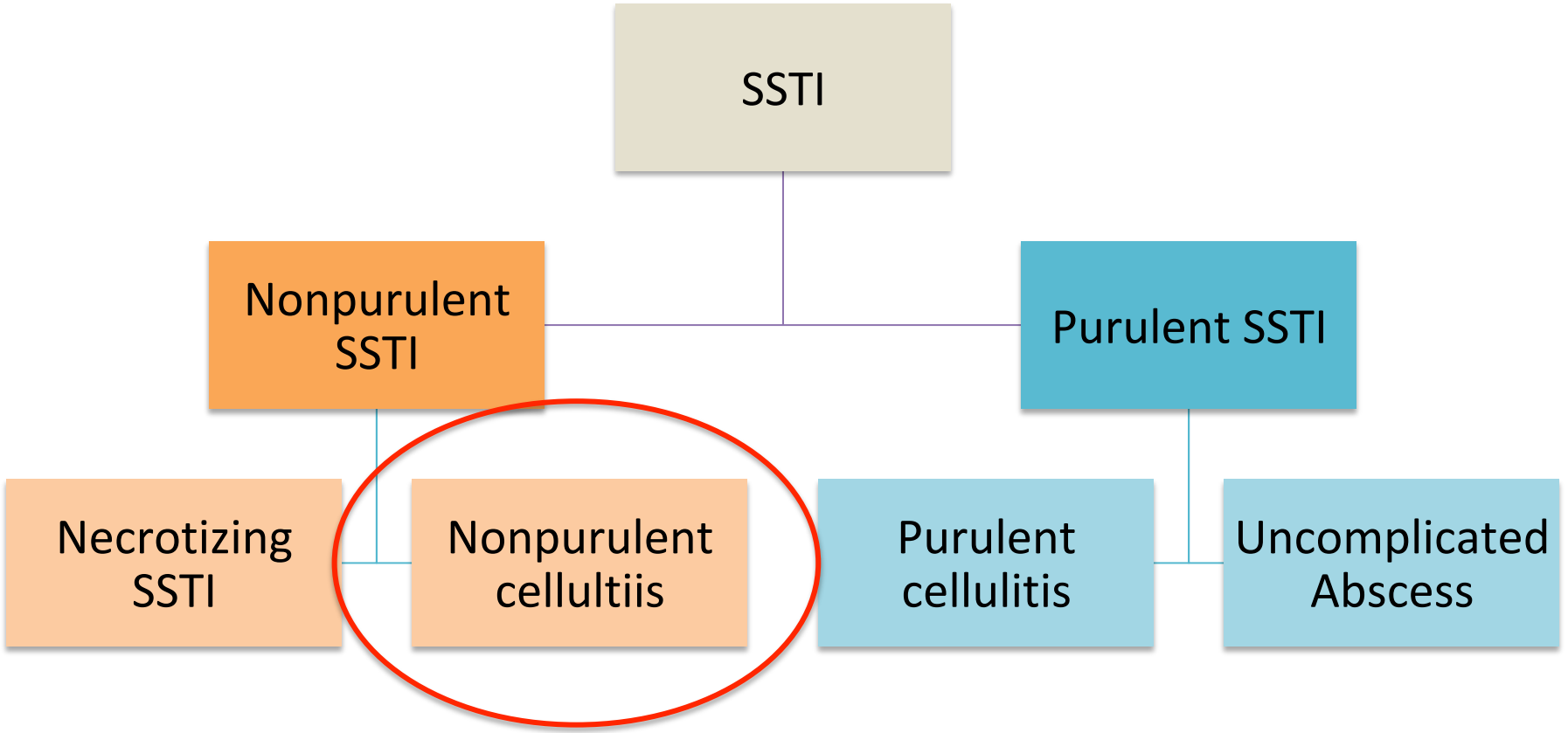
The next morning his exam is unchanged (slightly worse?) and so pip/tazo is added.

By hospital day #3 he is significantly improved and now ready for discharge. What oral antibiotics should we send him home on?

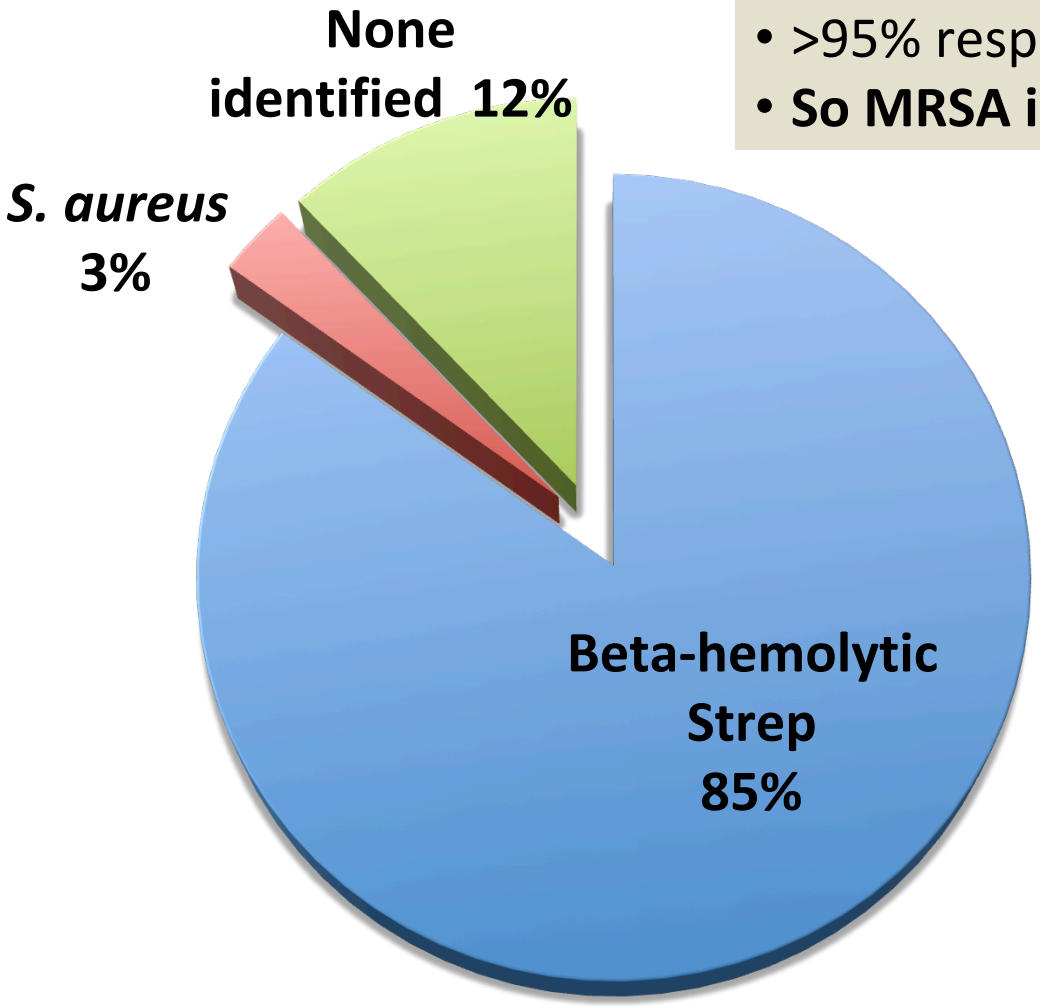
What Antibiotics Would You Send Him Home On?

1. TMP-SMX for 7 days
2. Levofloxacin + clindamycin for 10 days
3. Cephalexin for 5 days
4. Amox/clav + doxycycline for 14 days

Overview of Skin and Soft Tissue Infections



Nonpurulent SSTI: Microbiology

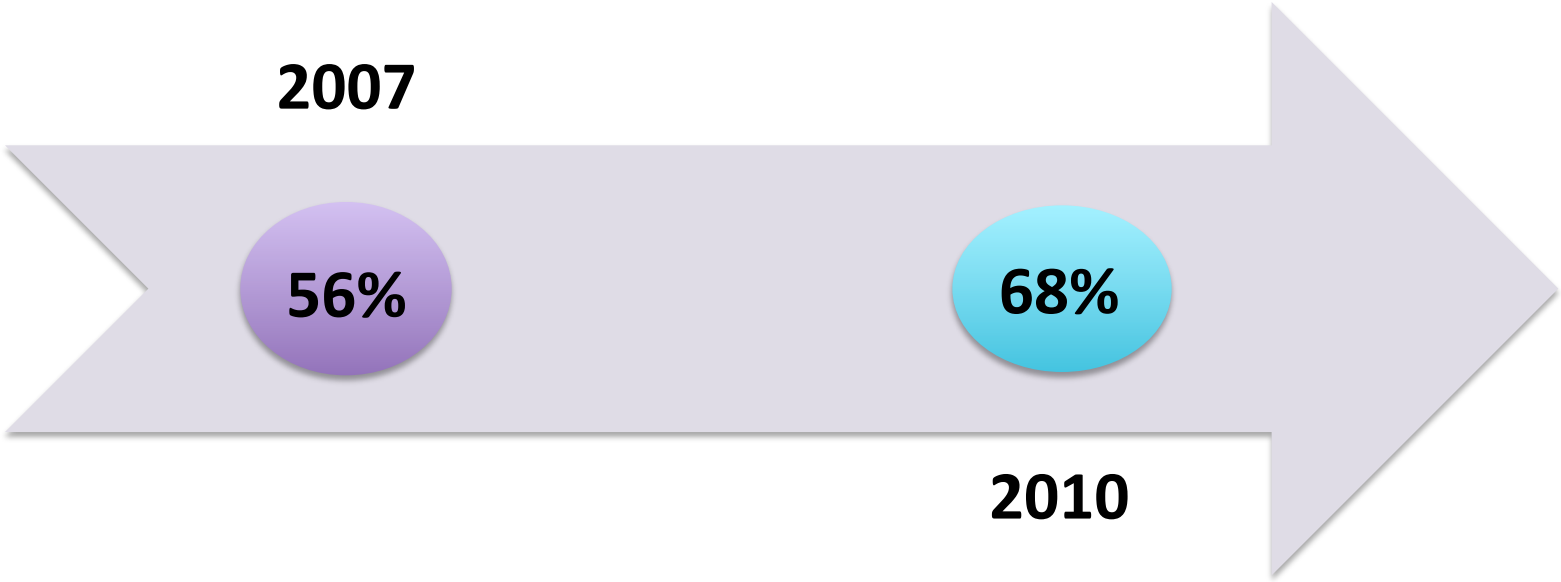


- >95% response to beta-lactams
- **So MRSA is not a major player**

Bruun et al, Open Forum Infect Dis 2016. Jeng et al, Medicine 2010, 89:217.

No MRSA Coverage Needed: How Are We Doing?

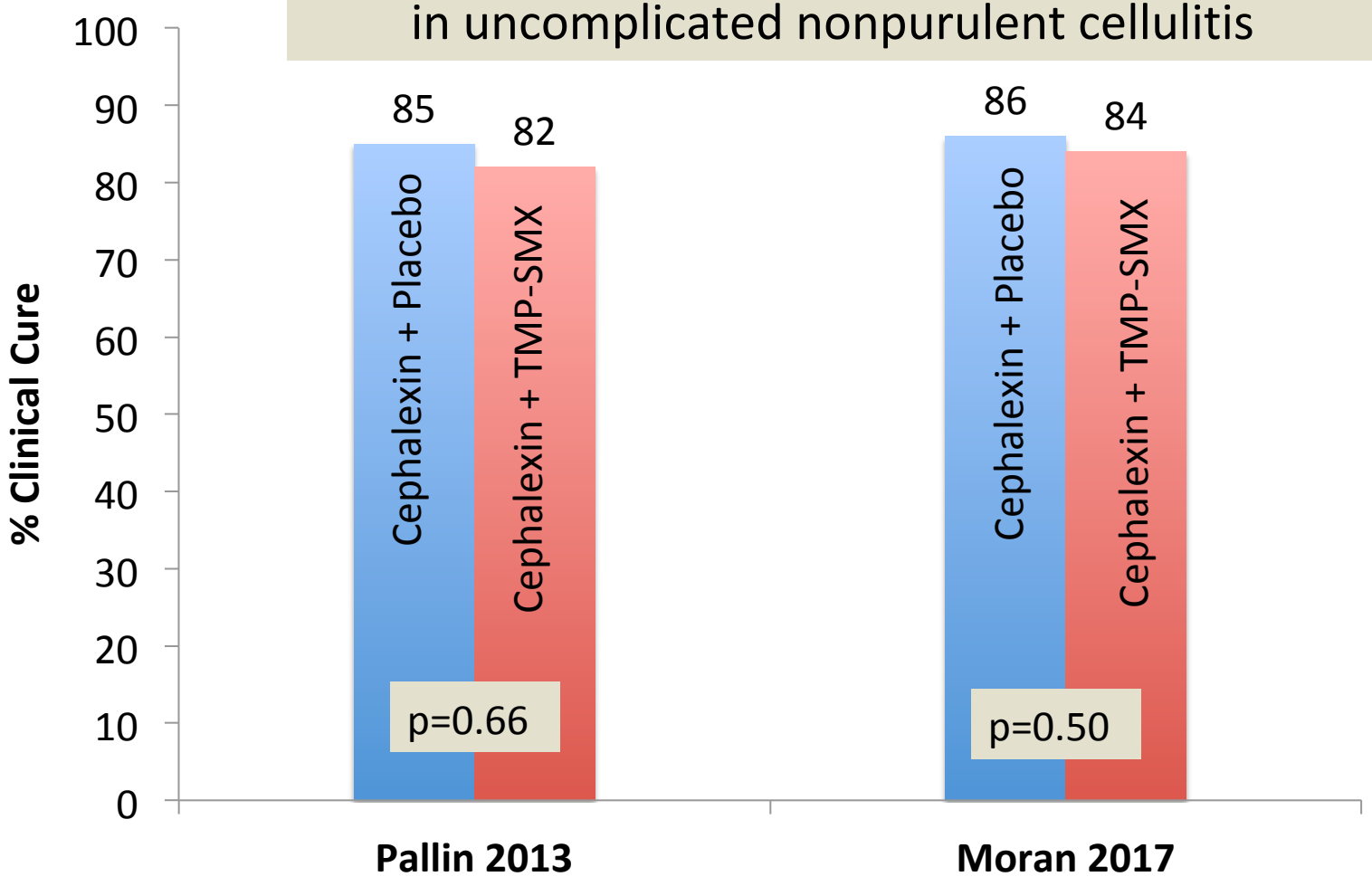
Regimens for nonpurulent cellulitis in ED visits that include MRSA coverage:



Pallin et al, West J Emerg Med 2014, 15:282.

So Do You Need MRSA Coverage or Not?

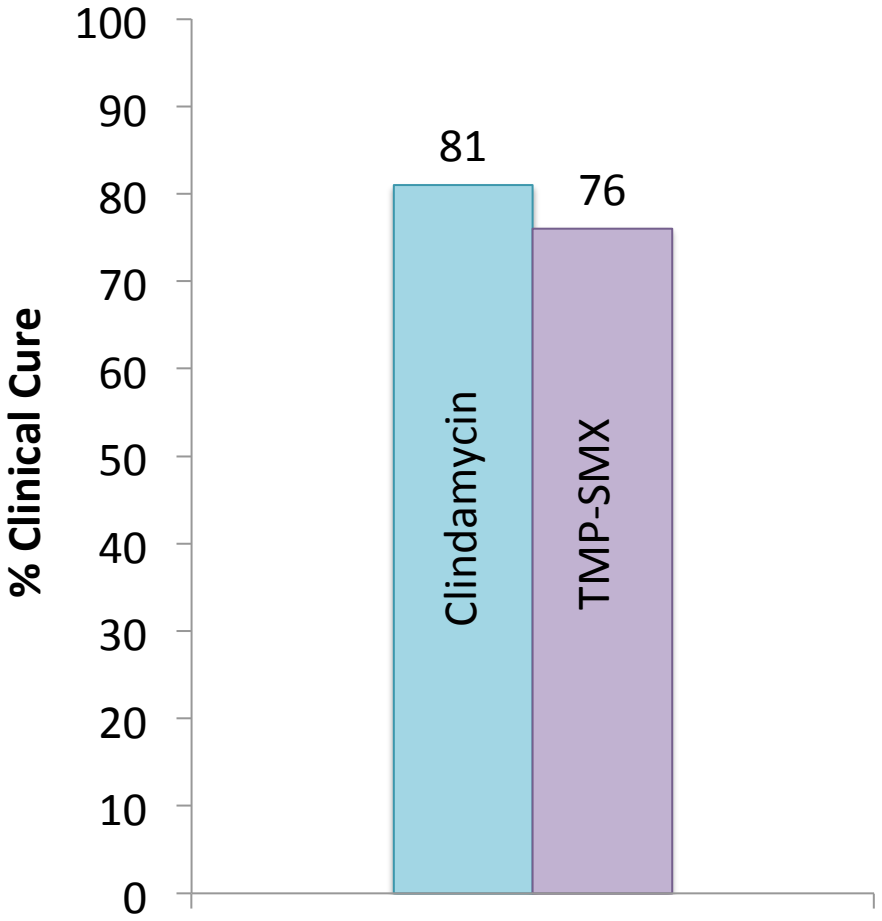
Bottom Line: MRSA coverage is NOT needed in uncomplicated nonpurulent cellulitis



Pallin et al, CID 2013, 56:1754. Moran et al, JAMA 2017, 317:2088.

Can You Use TMP-SMX alone?

- Study of TMP-SMX vs clindamycin for uncomplicated SSTI in outpatients
- In nonpurulent cellulitis subgroup (n=280) → no difference
- So maybe TMP-SMX okay for Strep?



Miller et al, NEJM 2015.

Empiric Abx for Nonpurulent SSTI

Oral

- Penicillin
- Amoxicillin
- Cephalexin
- Dicloxacillin
- Clindamycin

IV

- Penicillin
- Cefazolin
- Ceftriaxone
- Clindamycin

Stevens et al, Clin Infect Dis 2014, 59:e10.

When to Expand Coverage?

When to Cover for MRSA?

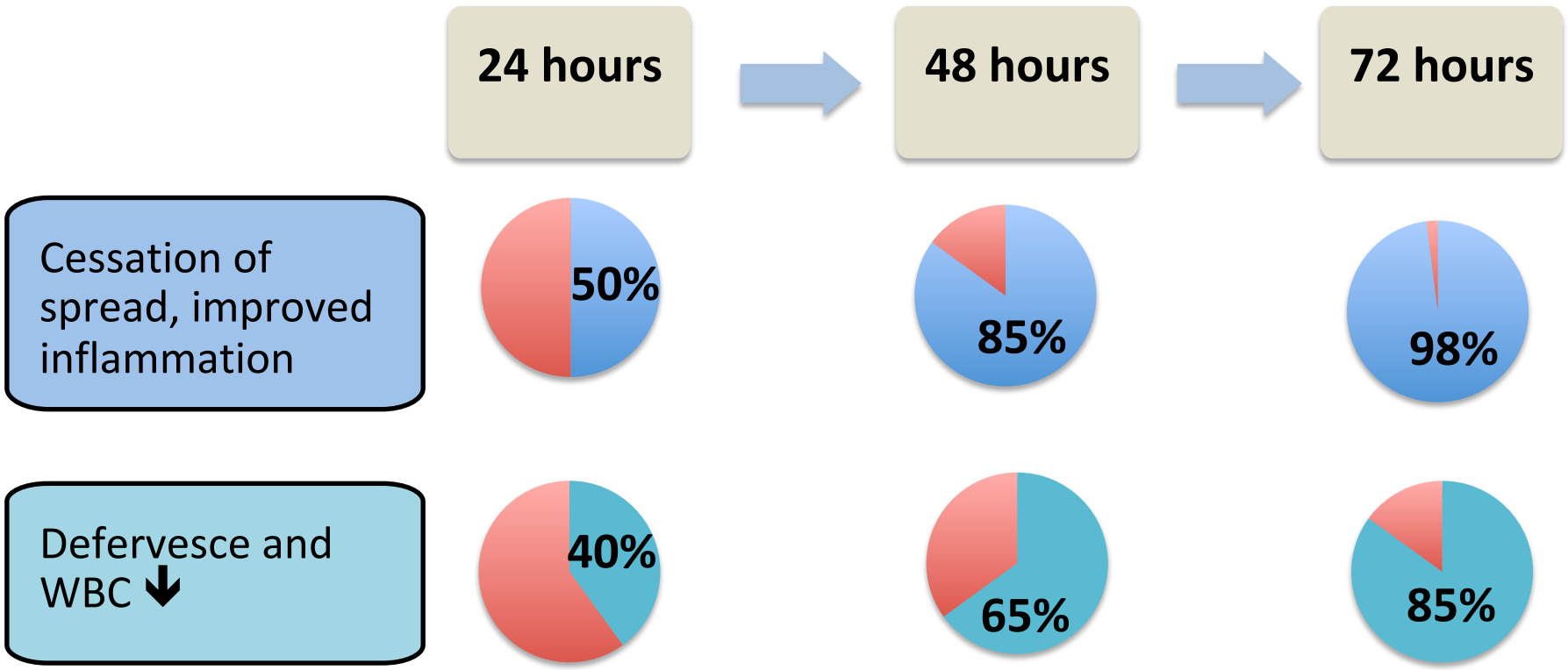
- Severe infection
- Severe immunocompromise
- Penetrating trauma (surgical site infection, injection drug use)
- Presence of wounds
- Concurrent MRSA elsewhere
- Not getting better without it

When to Cover for GNRs?

- Severe infection
- Severe immunocompromise
- Surgical site infections in abdomen or axilla
- Orbital cellulitis
- Not getting better without it

Stevens et al, Clin Infect Dis 2014, 59:e10.

When Should Cellulitis Get Better?

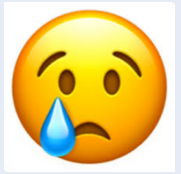


Escalation of Abx within 2 days was common but <u>not</u> associated with ⇧ response → likely was premature

Bruun et al, Clin Infect Dis 2016, 63:1034.

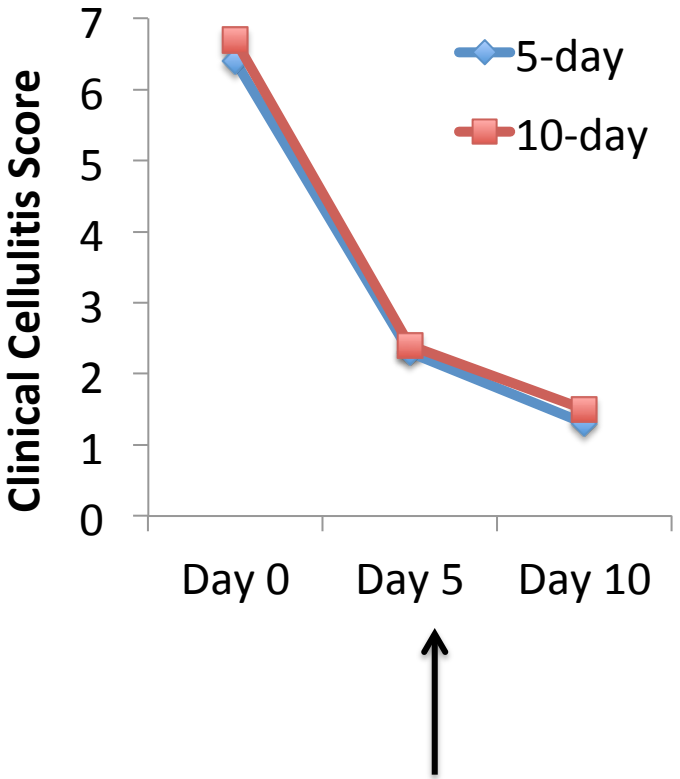
What Are Oral Step Down Options?

You have to make a decision on what is most likely (3 options):

Escalation was not needed → cover Strep	Cover for both MRSA and Streptococcus	Cover for MRSA, Strep and GNRs
• Penicillin • Amoxicillin • Cephalexin • Dicloxacillin • Clindamycin	• Clindamycin alone • TMP-SMX alone • Beta-lactam + (doxy or TMP-SMX)	• Amox/clav + (doxy or TMP-SMX) • Levofloxacin + (doxy or TMP-SMX) 

How Long Should You Treat?

- RCT of 5 vs 10 days levofloxacin in uncomplicated nonpurulent cellulitis (10-20% inpatient)
- No difference in clinical response
- Bottom line (and IDSA Guidelines): Treat for 5 days as long as there is clinical improvement

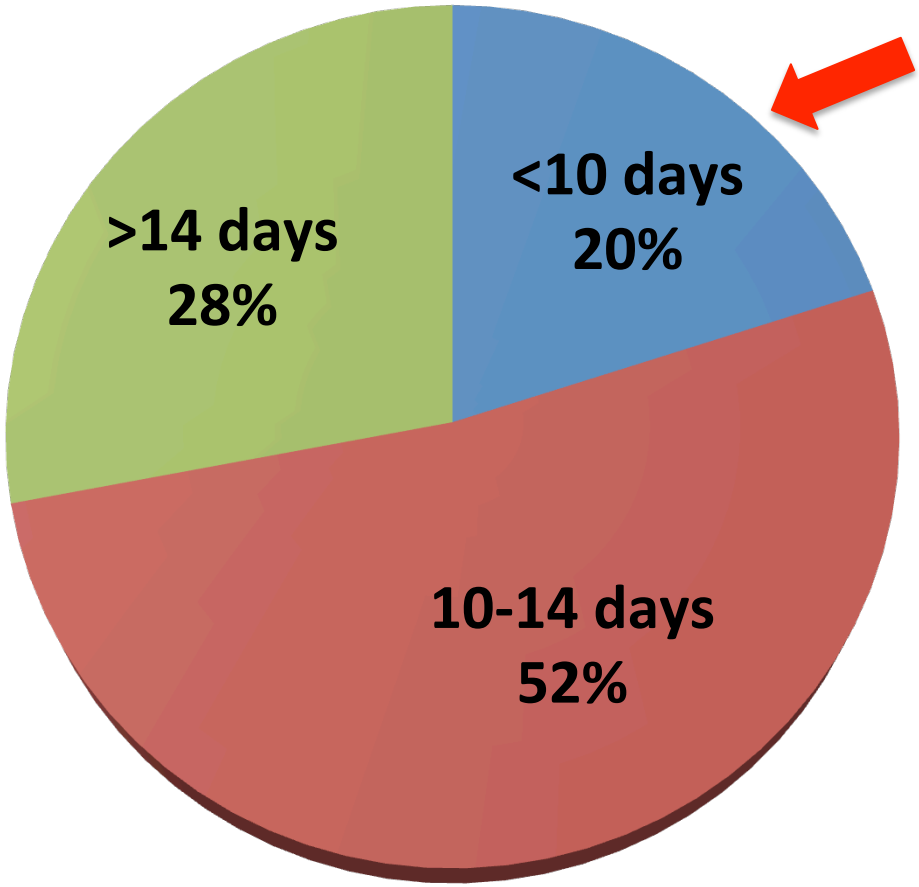


Small residual inflammation that resolved w/o ABx

Hepburn et al, Arch Intern Med 2004, 164:1669. Stevens et al, Clin Infect Dis 2014, 59:e10.

Duration of Therapy: How Are We Doing?

Duration of Therapy for Uncomplicated SSTI in Hospitalized Adults



Only 20% had an "appropriate" duration

Walsh et al, BMC Infec Dis 2016, 16:721.

Nonpurulent SSTI: Take Home Points

1. The majority of nonpurulent cellulitis is caused by beta-hemolytic *Streptococcus*

2. Antibiotics should target beta-hemolytic Strep; MRSA coverage is not indicated in most patients

3. Duration of therapy = 5 days as long as there is clinical improvement

Curbside #6

Date: Thursday, March 24, 2016 at 7:30 PM
To: Jennifer Babik <jennifer.babik@ucsf.edu>
Subject: SECURE: ID question

Hi Jen,

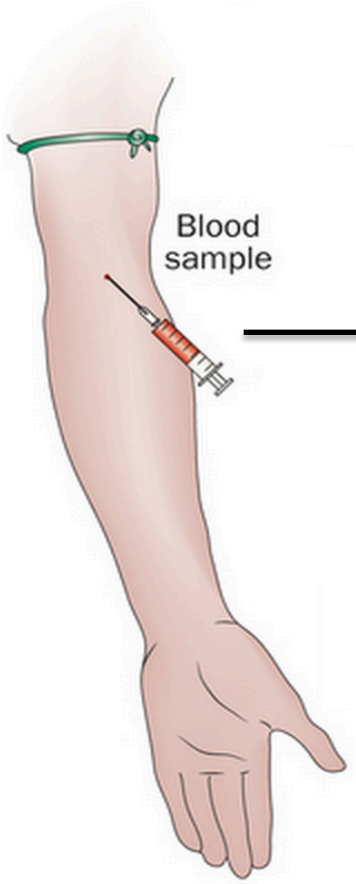
I have an ID question about a patient of mine that I am hoping to run by you. The question is whether she needs to be treated for LTBI before starting TNF inhibitor therapy.

23 y/o woman with Takayasu arteritis on prednisone who needs escalation of immunosuppression to infliximab. She has had an indeterminate QuantiFERON (QFT) x 2, negative PPD, and no lung pathology on chest CT. She is US-born and has no known TB exposures or other risk factors. Should she be treated for latent TB infection (LTBI)?

An Indeterminate QFT Means:

1. Intermediate probability of LTBI
2. Borderline/equivocal result
3. Low level positive result
4. The test didn’t work

QuantiFERON Interferon Gamma Release Assay (IGRA)



Incubate

Measure IFN-γ by ELISA

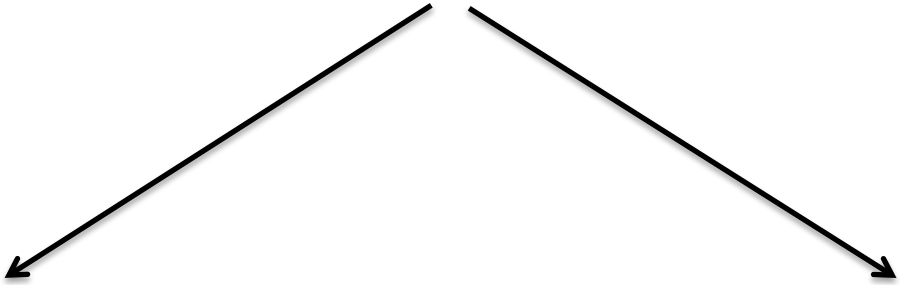
1) **Nil tube**: Negative control
2) **TB antigen tube**:
   - ESAT-6 + CEP-10
   - Not in BCG or most NTM
3) **Mitogen tube**: Positive control

<u>Test Readout</u>

- Positive
- Negative
- Indeterminate

Definition of an Indeterminate Assay

Indeterminate = TEST FAILURE



Positive control (mitogen) didn't work

Negative control (nil) had too much background IFN-γ

>85% of indeterminate results

How Common is an Indeterminate QFT?

- HCWs and TB Screening Programs: 1%

- Tertiary care inpatient settings: 20%

Fabre, Open Forum Infect Dis 2014. Lucet al al, Infect Contrl Hosp Epi 2015, 36:569. Simpson et al, J Immigrant Minorty Health 2013, 15:686.

Reasons for an Indeterminate QFT

Test Factors

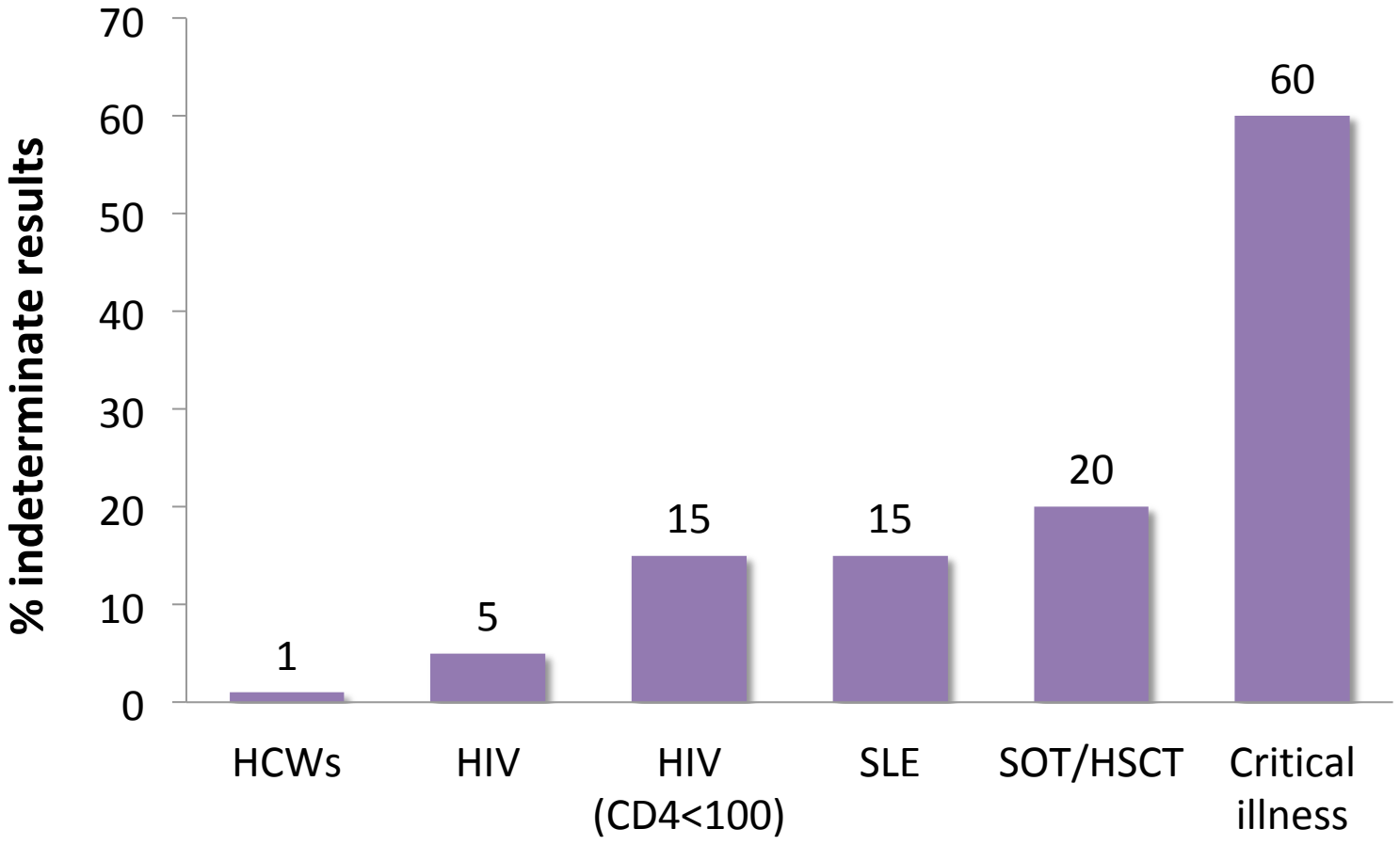
- Volume of blood drawn
- Suboptimal handling
- Delays from blood draw to incubation step

Patient Factors

- Immunocompromise impairs ability of T cells to produce IFN-γ in response to mitogen

Pai et al, Clin Micro Rev 2014, 27:3.

Indeterminate QFT and Immunocompromise

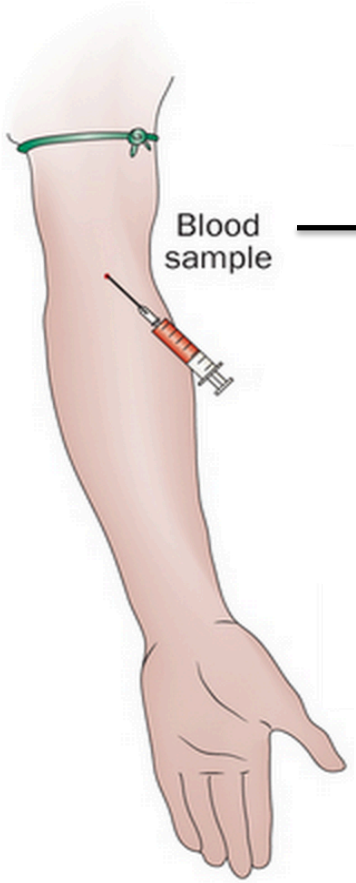


Cho et al, Lupus 2016; 0:1. Huang et al, Sci Rep 2016; 6:19972. Sester et al, Am J Respir Crit Care Med 2014, 190:1168. Leutkemeyer et al, Am J Respir Crit Care Med 2007, 175:737.

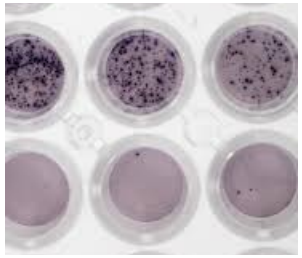
How to Manage Indeterminate QFT?

- If high risk patient → repeat and/or perform a PPD
- Repeat QFT
  - May eliminate possibility of lab-related factors
  - Many will still be indeterminate (40-70%)
  - Consider waiting until CD4 is higher or immunosuppression is decreased
- In a high risk patient, use epidemiologic risk factors, clinical history, chest imaging

T-SPOT TB Test: This DOES Have a Borderline Result



Mix blood PBMC and TB antigens
Check for IFN-γ production by ELISPOT
Also uses a positive and negative control



Test Readout

- Positive (>8 spots)
- Negative (<4 spots)
- Borderline (5-7 spots)
- Invalid (failure of positive or negative control)

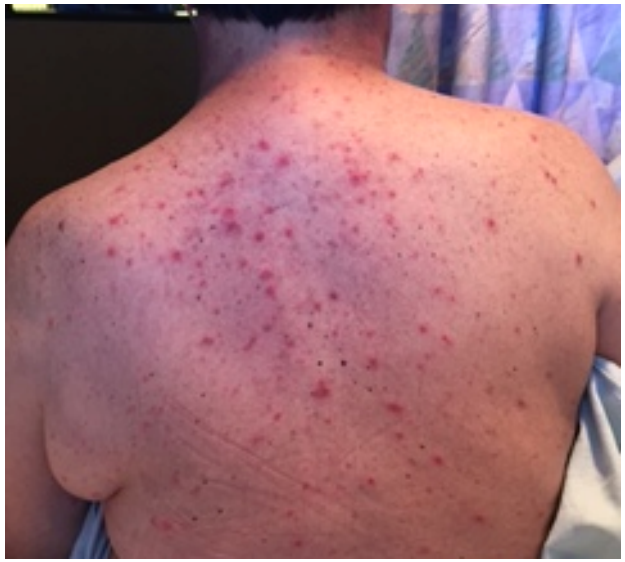
Indeterminate QFT: Take-Home Point

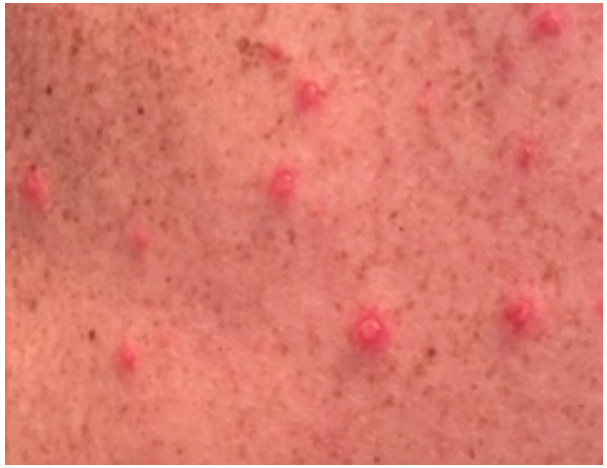
- Indeterminate QFT = test failure due to failure of either the positive (most likely) or negative control

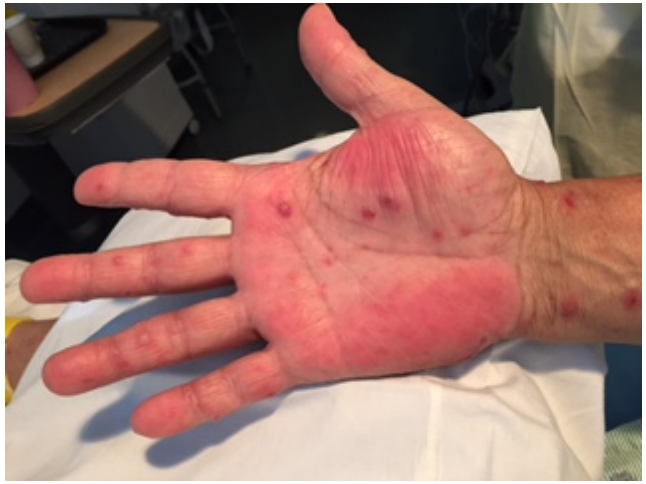
Curbside #7

A 59 year old man with SLE on cellcept and prednisone (10 mg/day) presents with disseminated VZV.

Should he get the new shingles vaccine?







Should This Patient Get the New Shingles Vaccine?

1. Yes

2. No

VZV Vaccines

	Zostavax (ZVL)	Shingrix (RZV)
Type	Live-attenuated	Recombinant
# Doses	One dose SC	Two doses IM (2-6 mo apart)
Vaccine efficacy against zoster	70% (50-59 years) 64% (60-69 years) 38% (≥70 years)	97% (50-59 years) 97% (60-69 years) 90% (≥70 years)
Vaccine efficacy against PHN	67%	89%
Wanes over time?	Yes , significant	No or modest ↓ (at 4 yr)

Oxman et al, NEJM 2005. Lal et al, NEJM 2015.Cunningham et al, NEJM 2016.

ACIP Recommendations

- Shingrix is preferred over Zostavax (as of January 2018)

- Indications:
  - All people ≥50 years old without contraindications
  - Give even if a prior episode of zoster
  - Give even if a prior dose of Zostavax (studied at 5 yrs afterward, likely can give earlier but wait at least 8 weeks)
  - Don't need to screen for prior varicella

- Contraindications:
  - Allergy to the vaccine or its components
  - Not yet studied in pregnancy

Dooling et al, MMWR 2018, 67:103. ACIP, January 2018.

Shingrix in Immunocompromised?

- ACIP: okay in “low dose immunosuppressive therapy” (≤ 20mg/day prednisone or equivalent)

- What about other kinds of immunocompromise?
  - These patients were excluded from the original RCTs
  - Phase I and II studies show it is safe
  - Phase III efficacy studies underway…and some now done!

Dooling et al, MMWR 2018, 67:103. ACIP, January 2018

Shingrix in Renal Transplant Patients

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

Immunogenicity and Safety of the Adjuvanted Recombinant Zoster Vaccine in Chronically Immunosuppressed Adults Following Renal Transplant: A Phase 3, Randomized Clinical Trial

- RCT of RZV vs placebo in 264 renal transplant patients (>75% on triple immunosuppression)
- Vaccine was immunogenic
- More local reactions in RZV arm but no serious adverse effects or safety concerns

Vink et al, Clin Infect Dis 2019, epub.

Singrix in HSCT Patients

JAMA | Original Investigation

Effect of Recombinant Zoster Vaccine on Incidence of Herpes Zoster After Autologous Stem Cell Transplantation

A Randomized Clinical Trial

- RCT of RZV vs placebo in 1846 HSCT recipients (mean 60 days from transplant; mostly MM and NHL)
- Incidence of zoster significantly reduced at 21 months (30 vs 94 per1000 person-years); 68% vaccine efficacy
- Injection site reactions more common but otherwise no significant adverse effects or safety concerns

Bastidas et al, JAMA 2019, 322:123.

New Shingrix Vaccine: Take-Home Points

- Shingrix is the preferred zoster vaccine

- Early studies show it is effective and safe in various types of immunocompromise (but watch for more studies coming in different populations)

Roadmap Revisited

- Remember the Goldilocks Rule for curbsides and avoid them in *S. aureus* bacteremia if possible

- Top Curbside Consult Questions in ID
  1. Blood culture contaminants: Consider clinical situation, organism, time to positivity, how many sets positive
  2. Oral Abx for ESBL cystitis: Fosfomycin has best data
  3. Line management in CLABSI: remove for virulent organisms and complicated infections
  4. Oral therapy for pyelo: Short course (7 days) ok even if bacteremic, especially for fluoroquinolones
  5. Nonpurulent cellulitis: cover beta-hemolytic *Streptococcus*
  6. Latent TB: An indeterminate QFT means test failure
  7. Zoster vaccines: Shingrix is the preferred vaccine and appears to be safe and effective in immunocompromised patients

Thanks For Your Attention!

- Questions?