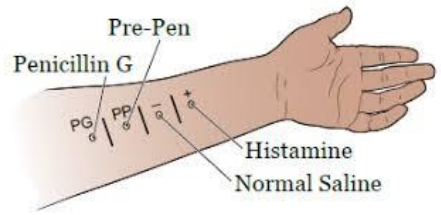

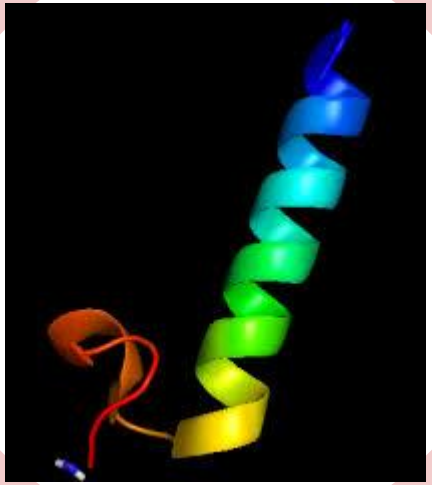

Modifying Antibiotics: Tools to Improve Stewardship

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Learning Objectives

- Identify patients who are candidates for oral antibiotics for the management of osteomyelitis, endocarditis, and bacteremia

- Assess the impact of appropriate allergy assessment/penicillin skin testing on antibiotic use in the inpatient setting

- Identify opportunities to use rapid diagnostic/laboratory tests to deescalate antibiotics

Disclosure: Husband is employed by Merck

Question #1

Would you streamline IV therapy to oral therapy in a patient with left-sided endocarditis?

Yes

No

Let’s start with the basics….

High Bioavailability (≥90%)	Moderate Bioavailability (75–89%)	Low Bioavailability (<75%)
Levofloxacin Moxifloxacin Doxycycline Minocycline Linezolid Tedizolid Clindamycin Metronidazole Rifampin	Ciprofloxacin TMP-SMX	Cefuroxime axetil Cefdinir Cefpodoxime proxetil Delafloxacin

Where do amoxicillin, amoxicillin-clavulanate, and cephalexin fit in?

Start at the Guidelines

Endocarditis	Infectious Diseases Society of America 2015	European Society of Cardiology 2015
Right Sided *S. aureus*	"may be achieved with relatively short courses of either parenteral oral treatment for 2-4 weeks"	*Staphylococcus sp* TMP-SMX (4800mg/TMP 960)/day + Clindamycin IV (1 week IV and 5 weeks oral)
	Right sided *S. aureus* (no prosthetic material/IVDU): oral 4 week antibiotic regimen of Ciprofloxacin and Rifampin	Ciprofloxacin 750mg BID + Rifampin 300mg BID
Native or Prosthetic Valve: *Enterococcus sp* (resistant to penicillin, aminoglycosides, and Vancomycin):	Linezolid 600mg IV/PO q 12h > 6 weeks (Class IIB, Level of Evidence C)	Linezolid 600mg BID ≥ 8 weeks
Native or Prosthetic Valve: HACEK	Ciprofloxacin 500mg po q 12h/400mg IV q 12h (Class IIB, Level of Evidence C)	Ciprofloxacin 750mg BID is a less validated alternative

Circulation 2015;132:1435-1486 Eur Heart J 2015;36:3075-3128

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Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

Kasper Iversen, M.D., D.M.Sc., Nikolaj Ihlemann, M.D., Ph.D., Sabine U. Gill, M.D., Ph.D., Trine Madsen, M.D., Ph.D., Hanne Elming, M.D., Ph.D., Kaare T. Jensen, M.D., Ph.D., Niels E. Bruun, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Kurt Fursted, M.D., D.M.Sc., Jens J. Christensen, M.D., D.M.Sc., Martin Schultz, M.D., Christine F. Klein, M.D., Emil L. Fosbøll, M.D., Ph.D., Flemming Rosenvinge, M.D., Henrik C. Schønheyder, M.D., D.M.Sc., Lars Køber, M.D., D.M.Sc., Christian Torp-Pedersen, M.D., D.M.Sc., Jannik Helweg-Larsen, M.D., D.M.Sc., Niels Tønder, M.D., D.M.Sc., Claus Moser, M.D., Ph.D., and Henning Bundgaard, M.D., D.M.Sc.

N Engl J Med 2019;380;5:415-423

Does your patient fit the criteria?

	Inclusion Criteria
✖	≥ 18 years
✖	Satisfactory response to treatment: Afebrile >2 days, CRP <25% of peak level or <20 mg/L, and WBC <15 x 10^9/L
✖	Left-s
✖	Fulfill
✖	Blood S s gative
✖	IV antibiotics for at least 10 days or at least 7 days post valve surgery; At least 10 days of scheduled antibiotics needed to remain
✖	TEE no signs of abscess formation or valve abnormality that would require surgery
✖	Exclusion: Suspected reduced gastro-intestinal uptake or BMI > 40 kg/m^2

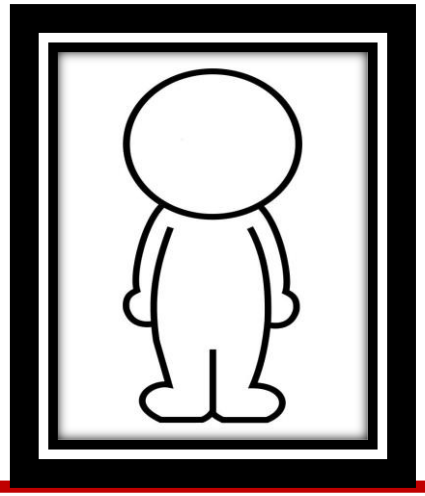
Note: Only 20% of the 1957 patients screened were enrolled

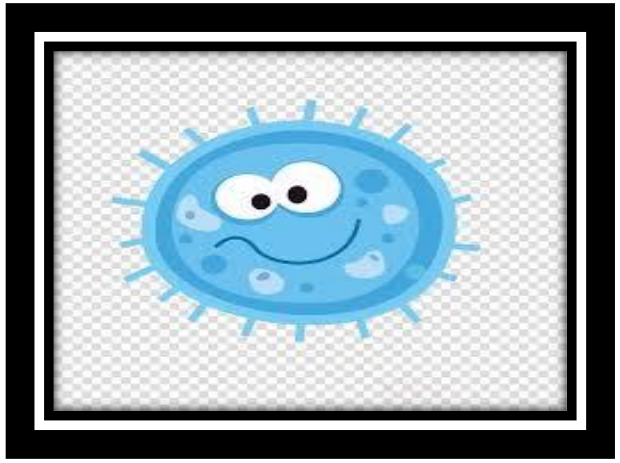
N Engl J Med 2019;380;5:415-423

What Oral Antibiotics Did they Use?

Organism	Oral Regimen
Penicillin sensitive MSSA/ Coagulase-Negative *Staphylococci sp.*	Amoxicillin 1g po 4 times daily + Rifampin 600mg po BID Linezolid 600mg po twice daily + Rifampin 600mg po BID
MSSA and Coagulase-negative *Staphylococci sp.*	Dicloxacillin 1g PO 4 times daily + Rifampin 600mg po BID Linezolid 600mg po twice daily + Rifampin 600mg po BID
MR Coagulase Negative *Staphylococci*	Linezolid 600mg po twice daily + Rifampin 600mg po BID
Enterococcus faecalis	Amoxicillin 1000mg po 4 times daily + Rifampin 600mg po BID Amoxicillin 1000mg po 4 times daily + Moxifloxacin 400mg po daily Linezolid 600mg po twice daily + Rifampin 600mg po BID Linezolid 600mg po twice daily + Moxifloxacin 400mg po daily
Streptococci sp. (PCN MIC < 1 mg/L)	Amoxicillin 1g po 4 times daily + Rifampin 600mg po twice daily Linezolid 600mg po twice daily + Rifampin 600mg po twice daily Linezolid 600mg po twice daily + Moxifloxacin 400mg po daily
Streptococci sp. (PCN MIC ≥ 1 mg/L)	Linezolid 600mg po twice daily + Rifampin 600mg po twice daily Moxifloxacin 400mg po daily + Rifampin 600mg po twice daily Moxifloxacin 400mg po daily + Clindamycin 600mg po 3 times daily

N Engl J Med 2019;380;5:415-423





Mean Age: 67 ± 12 y

Female: 20-25%

Diabetic: 15-18%

Renal Failure: 10-12%

Dialysis: 6.5-7.5%

Streptococcus: 45-52%

MSSA: 20-23%

Enterococcus: 23-25%

CoNS: 5%

Prosthetic Valve: 26%

Aortic Valve: 54%

Vegetation size
> 9mm: 3-5.5%

Surgery: 37-38%

Primary Outcome

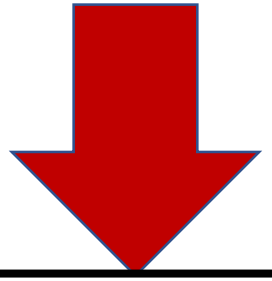
Component	IV Treatment N=199	PO Treatment N=201	Difference % points (95% CI)	Hazard Ratio (95% CI)
Composite outcome	24 (12.1%)	18 (9.0%)	3.1 (-3.4 – 9.6)	0.72 (0.37 – 1.36)
All-cause mortality	13 (6.5%)	7 (3.5%)	3.0 (-1.4 to 7.7)	0.53 (0.21 to 1.32)
Unplanned cardiac surgery	6 (3.0%)	6 (3.0%)	0 (-3.3 to 3.4)	0.99 (0.32 to 3.07)
Embolic Event	3 (1.5%)	3 (1.5%)	0 (-2.4 to 2.4)	0.97 (0.20 to 4.82)
Relapse of the + blood culture	5 (2.5%)	5 (2.5%)	0 (-3.1 to 3.1)	0.97 (0.28 to 3.33)

N Engl J Med 2019;380;5:415-423

Long Term Adverse Reactions

- **Fluoroquinolones**
  - Aortic Dissection/Retinal detachment
  - hypoglycemia/mental health
  - tendonitis, peripheral neuropathy, CNS, Cardiac
- **Linezolid**
  - Hematologic
  - Optic Neuritis/Lactic Acidosis
  - Peripheral Neuropathy
- **Rifampin**
  - Liver Function Abnormalities
  - GI Intolerance
- **Ampicillin**
  - Neutropenia @ 4-6g/day
  - GI tolerance

Therapeutic Drug Monitoring

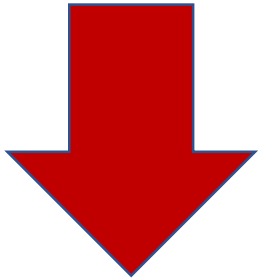


Oral Group: 7 patients antibiotic concentrations were below desired level (only 1 of the 2 antibiotics)

- Rifampin n=3
- Moxifloxacin n=2
- Linezolid n=1
- Dicloxacillin n=1

No effect on primary outcome

Clinical Follow up



Oral Group: Seen 2 to 3 times per week in Clinic

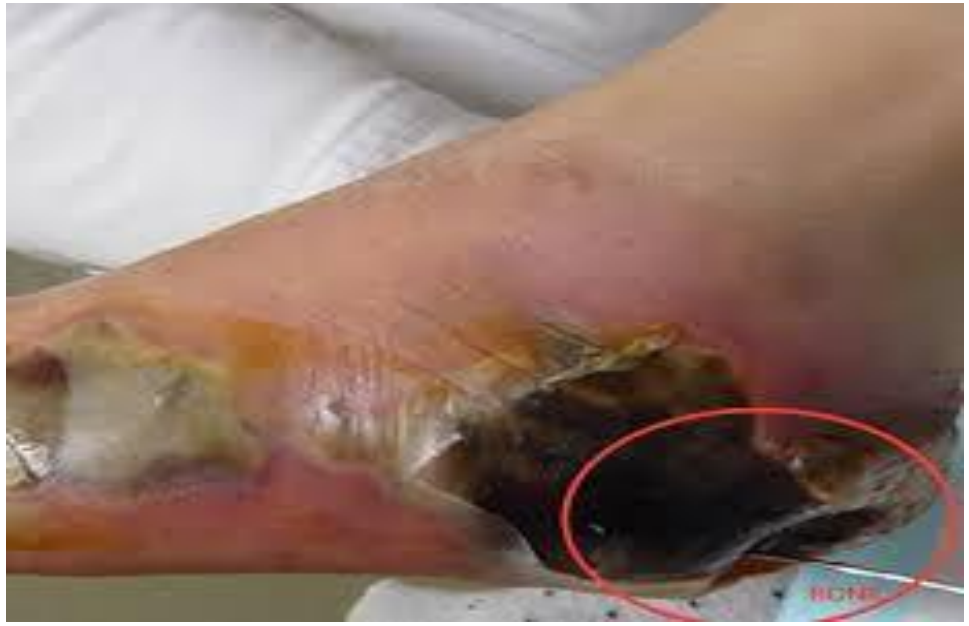
N Engl J Med 2019;380;5:415-423

Question #2

Would you streamline IV therapy to oral therapy in a patient with osteomyelitis after debridement?

Yes

No



IDSA Diabetic Foot Guidelines

- "For osteomyelitis, some initial parenteral antibiotic therapy may be beneficial, especially if an agent with suboptimal bioavailability is selected, but predominantly oral therapy with a highly bioavailable agent is probably adequate."

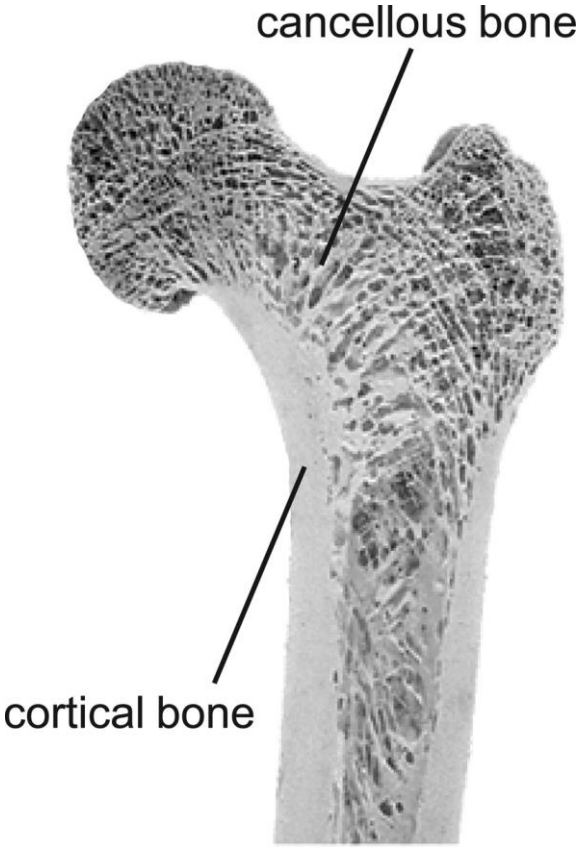
Table 11. Suggested Route, Setting, and Duration of Antibiotic Therapy, by Clinical Syndrome

Site of Infection, by Severity or Extent	Route of Administration	Setting	Duration of Therapy
Soft-tissue only			
Mild	Topical or oral	Outpatient	1–2 wk; may extend up to 4 wk if slow to resolve
Moderate	Oral (or initial parenteral)	Outpatient/ inpatient	1–3 wk
Severe	Initial parenteral, switch to oral when possible	Inpatient, then outpatient	2–4 wk
Bone or joint			
No residual infected tissue (eg, postamputation)	Parenteral or oral	…	2–5 d
Residual infected soft tissue (but not bone)	Parenteral or oral	…	1–3 wk
Residual infected (but viable) bone	Initial parenteral, then consider oral switch	…	4–6 wk
No surgery, or residual dead bone postoperatively	Initial parenteral, then consider oral switch	…	≥3 mo

CID 2012;54(12):132-173

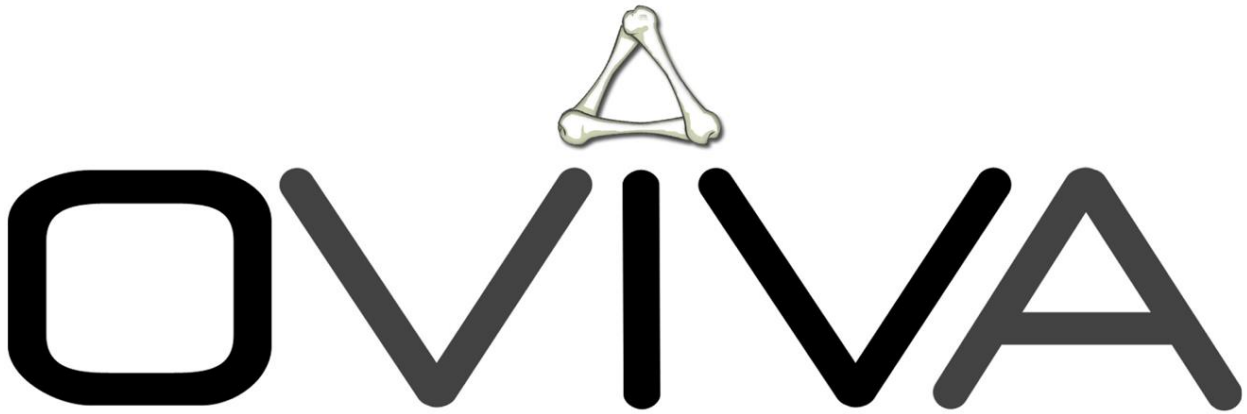
Highly Bioavailable, but do they penetrate into the bone?

Antibiotic	Cancellous Bone µg/mL	Cortical Bone µg/mL	Serum-Bone Ratio (%)	CLSI breakpoint µg/mL *Staphylococcus*
Rifampin	6.5	1.3	>100%	≤1
Levofloxacin	10	4.6	38-99%	≤1
Ciprofloxacin	13.8		30-48%	≤1
Moxifloxacin	2.8		49%	0.5
Linezolid*	6.4		37-51%	≤4
TMP-SMX	6.3/35.8		50/15%	≤2/38
Clindamycin*	6.9		40-45%	≤0.5
Doxycycline*	3		2-6%	≤4



* Penetration with ischemia

Int J Infect Dis 2019;81:128-136 CID 2012;54(3):393-407

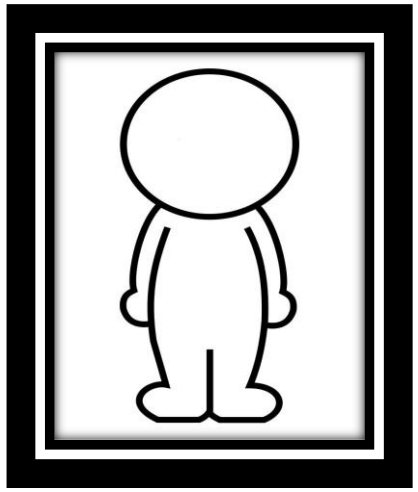


Oral versus Intravenous Antibiotics for Bone and Joint Infection

Ho-Kwong Li, M.R.C.P., Ines Rombach, D.Phil., Rhea Zambellas, M.Sc., A. Sarah Walker, Ph.D., Martin A. McNally, F.R.C.S.(Orth.), Bridget L. Atkins, F.R.C.P., Benjamin A. Lipsky, M.D., Harriet C. Hughes, M.A.(Cantab.), Deepa Bose, F.R.C.S., Michelle Kümin, Ph.D., Claire Scarborough, M.R.C.P., Philippa C. Matthews, D.Phil., et al., for the OVIVA Trial Collaborators*

N Engl J Med 2019;380;5:425-436

Inclusion Criteria



> 18 years old

- Acute or chronic bone or joint infections

Managed by an ID specialist!!!!

Received ≤ 7 days of IV antibiotic therapy from the date of definitive surgery or start of treatment if no surgery

N Engl J Med 2019;380;5:425-436 Trial 2015;15:583:1-12

Exclusion Criteria

- *Staphylococcus aureus* bacteremia on presentation or within the last 1 month
- Bacterial endocarditis (presentation or within the last month)
- Concomitant infection
- Mild Osteomyelitis (opinion of investigator)
- Only sensitive to IV antibiotics
- Septic shock or systemic features requiring IV therapy
- Evidence of being unlikely to comply with trial requirements

N Engl J Med 2019;380;5:425-436 Trial 2015;15:583:1-12

Oral Antibiotics Utilized

Antibiotic	Number of Patients (%)
Penicillins	83 (15.9%)
Fluoroquinolones	**191 (36.5%)**
Ciprofloxacin	**189**
Moxifloxacin	**1**
Levofloxacin	**1**
Combination with rifampin	**84%**
Doxycycline	57 (10.9%)
Macrolide/Clindamycin	68 (13.0%)
Clarithromycin/Erythromycin	6
Other	54 (10.3%)
Combination	87 (16.6%)

N Engl J Med 2019;380;5:425-436 Trial 2015;15:583:1-12

Primary Outcome

	Intravenous Group	Oral Group	Difference in Risk (90% CI)
Definitive Treatment Failure at 1 year	74/506 (14.6%)	67/509 (13.2%)	-1.4 (-4.9-2.2)

Secondary Outcomes

	Intravenous Group (n=527)	Oral Group (n=527)
Participants who experienced one serious adverse event	146 (27.7%)	138/527 (26.9%)
Antibiotic-related serious adverse events	30/220 (13.6%)	15/224 (6.7%)
IV catheter complications	49/523 (9.4%)	5/523 (1.0%)
Episode of *C.difficile* diarrhea	9/523 (1.7%)	5/523 (1.0%)
Early discontinuation of randomly assigned treatment strategy	99/523 (18.9%)	67/523 (12.8%)

N Engl J Med 2019;380;5:425-436 Trial 2015;15:583:1-12

Are you comfortable with long term Fluoroquinolones for MSSA?

- Emergence of resistance can occur with *Staphylococcus* (particularly MRSA) when exposed to fluoroquinolones.
  - Combine with rifampin
- Local sensitivities of Fluoroquinolones
- Adverse events with long term use
- What about Delafloxacin?

Other options

TMP-SMX ± rifampin

- Need for higher doses (trimethoprim) 7-10mg/kg/day
- ADEs: rashes, GI intolerance, hyperkalemia, renal, and LFT elevation

Doxycycline ± rifampin

- More data with suppressive therapy
- Less clinical data

Linezolid ± rifampin

- ADEs: anemia, thrombocytopenia, peripheral neuropathy, optic neuropathy
- Cost

Question #3

Would you streamline IV therapy to an oral beta-lactam in a patient with gram negative bacteremia?

Yes

No

Systematic Review and Meta-analysis

- 8 retrospective cohort studies of adult hospitalized patients
- Beta Lactams vs Fluoroquinolone/trimethoprim sulfamethoxazole

  - **All Cause Mortality**
    - OR 1.13 (0.69 – 1.87)

  - **Infection Recurrence Rate (same genus and species)**
    - OR 2.05 (1.17-3.61)

  - **Recurrent Bacteremia**
    - OR 2.15 (0.93 – 4.99)

Open Forum Infect Dis. 2019 Aug 14. pii: ofz364. doi: 10.1093/ofid/ofz364

Gram Negative Bacteremia Studies: Retrospective Cohort Studies

Study	UTI Source	All cause Mortality		Recurrent Infections	
		FQ/TMP SMX	Beta-lactams	FQ/TMP	**Beta-lactams**
Sessa 2018	77.8%	0/57 (0%)	0/151 (0%)	3/57 (5.3%)	**14/151 (9.3%)**
Kutob 2016	70.2%	9/285 (3.2%)	3/77 (3.9%)	12/285 (4.2%)	**7/77 (9.0%)**
Mercuro 2018	70.85%	1/140 (0.71%)	1/84 (1.2%)	3/140 (2.1%)	**5/84 (6.0%)**
Rieger 2018	100%	2/84 (2.4%)	0/30 (0%)	2/84 (2.3%)	**1/30 (3.3%)**
Tamma 2019	40.2%	68/617 (11%)	15/122 (12%)	4/617* (0.65%)	**0/122 (0%)**
Thurber 2019	100%	0/250 (0%)	0/14 (0%)	4/250 (1.6%)	**0/14 (0%)**

Punjabi C et al Open Forum Infect Dis. 2019 Aug 14. pii: ofz364. doi: 10.1093/ofid/ofz364OFID

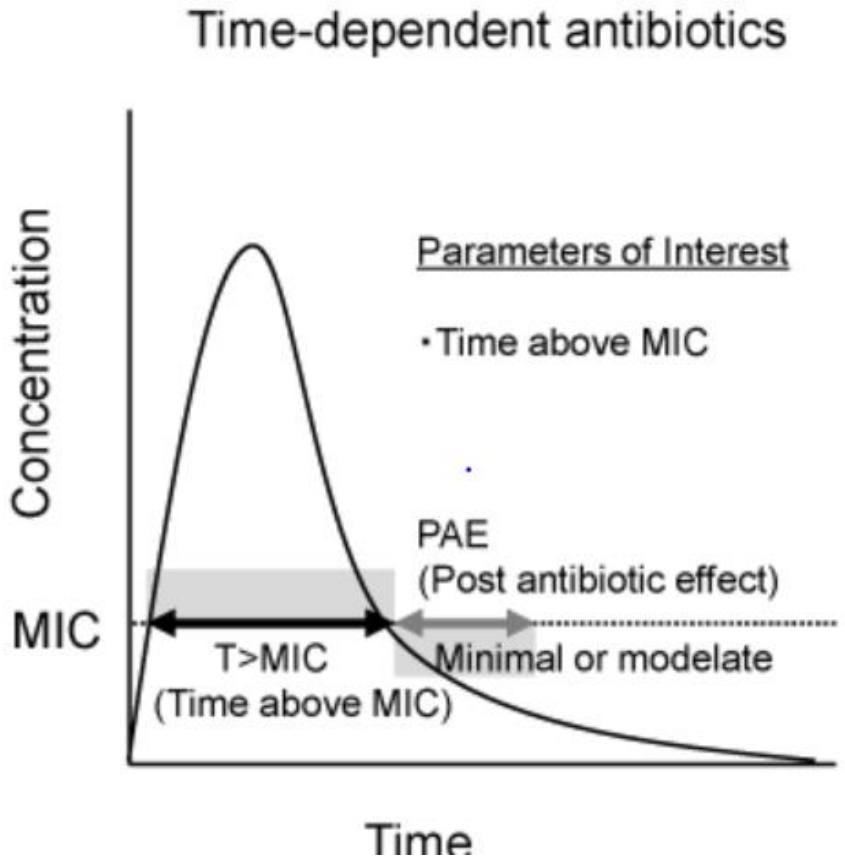
Why are there more recurrences with BL?

Study	UTI Source	Bacteremia caused by:	BMI	CrCl <30 ml/min	Received "high dose" beta-lactam regimen
Sessa 2018	77.8%	E. coli	>30 65/151 (43%)	52/151 34%	33/50 (66%)
Kutob 2016	70.2%	Enterobactericiae	ND	ND	30/58 (52%)
Mercuro 2018	70.85%	Enterobactericiae	30.9 ± 8.7	11/75 15%	46/74 (61%)
Rieger 2017	100%	Enterobactericiae	ND	ND	ND

Punjabi C et al Open Forum Infect Dis. 2019 Aug 14. pii: ofz364. doi: 10.1093/ofid/ofz364OFID

Why don’t beta-lactams work as well?

DOSES are TOO low?



Microbiologic Testing not beta-lactam specific

Pharmacodynamic Target: fT > MIC >50% penicillins >60% cephalosporins

	Frequency	MIC breakpoint (CLSI) mg/L	Cmax (mg/L)	Protein Binding	Half-life (hrs)
Amoxicillin	TID	8	500mg = 5.5-7.5 1000mg = 16	20%	1.0
Ce					
Ce axe					
Cefdinir	BID/Qday	1	300mg = 1.6 ± 0.55 600mg = 2.9 ± 1.01	60-70%	1.7
Cefpodoxime proxetil	BID	2	100mg = 1.2 ± 1.2 200mg = 2.3 ± 2.2 400mg = 3.8 ± 3.6	40%	2.8

Cefazolin	Sensitive	<=4	Final

Comment: FOR UNCOMPLICATED UTI'S, CEFAZOLIN MIC RESULTS LESS THAN OR EQUAL TO 16 MCG/ML PREDICT SUSCEPTIBILITY OF THE FOLLOWING ORAL CEPHALOSPORINS: CEFACLOR, CEFDINIR, CEFPODOXIME, CEFPROZIL, CEFUROXIME AND CEPHALEXIN.

Method: MIC

MacGregor RR Clin Infect Dis 1997;24:457-467

It's Pharmacodynamics

Antibiotic	Dose (mg)/dosing interval (h)	%fT>MIC							Maximum MIC allowing for target attainment	Highest frequency wild-type MIC for *E. coli**
		16 mg/L	8 mg/L	4 mg/L	2 mg/L	1 mg/L	0.5 mg/L	0.25 mg/L		
Amoxicillin	500/8	–	13.0	23.0	33.0	43.0	53.0	63.0	0.5 mg/L	4 mg/L
Amoxicillin	1000/8	–	23.0	33.0	43.0	53.0	63.0	73.0	1 mg/L	4 mg/L
Amoxicillin-clavulanate	875/12	–	11.0	17.6	24.3	31.0	37.6	44.3	–	4 mg/L
Amoxicillin-clavulanate	875/8	–	16.4	26.4	36.4	46.4	56.4	66.4	0.5 mg/L	4 mg/L
Cephalexin	500/6	3.30	22.7	42.1	61.5	80.9	100	100	2 mg/L	4 mg/L
Cephalexin	1000/6	22.7	42.1	61.5	80.9	100	100	100	4 mg/L	4 mg/L
Cefaclor	500/6	–	11.0	23.5	36.0	48.5	61.0	73.5	0.5 mg/L	1 mg/L
Cefprozil	500/12	–	12.6	20.1	27.5	35.0	42.5	50.0	–	N/A
Cefuroxime	500/12	–	–	0.43	10.2	20.5	29.7	39.5	–	4 mg/L
Cefdinir	300/12	–	–	–	–	7.41	12.4	17.3	–	N/A
Cefpodoxime	400/12	–	–	–	22.8	39.7	56.6	73.5	0.25 mg/L	0.5 mg/L

Mogle B Expert Opinion on Pharmacotherapy, 20:8, 903-907,

Question #4

Do you recommend an oral challenge with a beta-lactam or cephalosporin in a patient with a penicillin allergy?

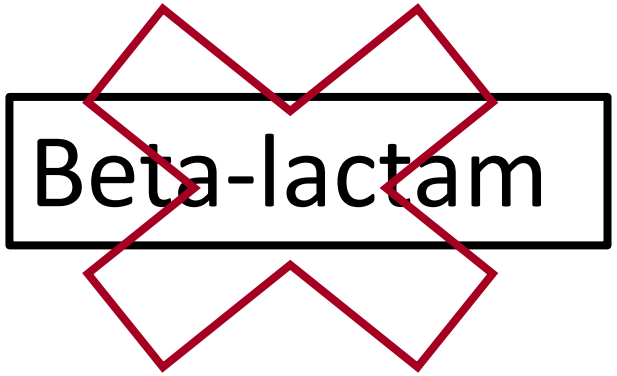
Yes

No

Facts:

- 50% of patients with a true penicillin allergy will lose sensitivity to penicillin within 5 years
- 80% of patients will lose sensitivity to penicillin within 10 years

https://www.cdc.gov/antibiotic-use/community/pdfs/penicillin-factsheet.pdfStaicu, *Ann Allergy Asthma Immunol* 2017
Drug Allergy Practice Guidelines. *Ann Allergy Asthma Immunol* 2010



Carbapenems
Vancomycin
Daptomycin
Fluoroquinolones
Aztreonam
Azithromycin

↑ Abx exposure + ↑ MDRO + ↑ Adverse reactions + ↑ Drug costs + ↑ LOS, Readmits

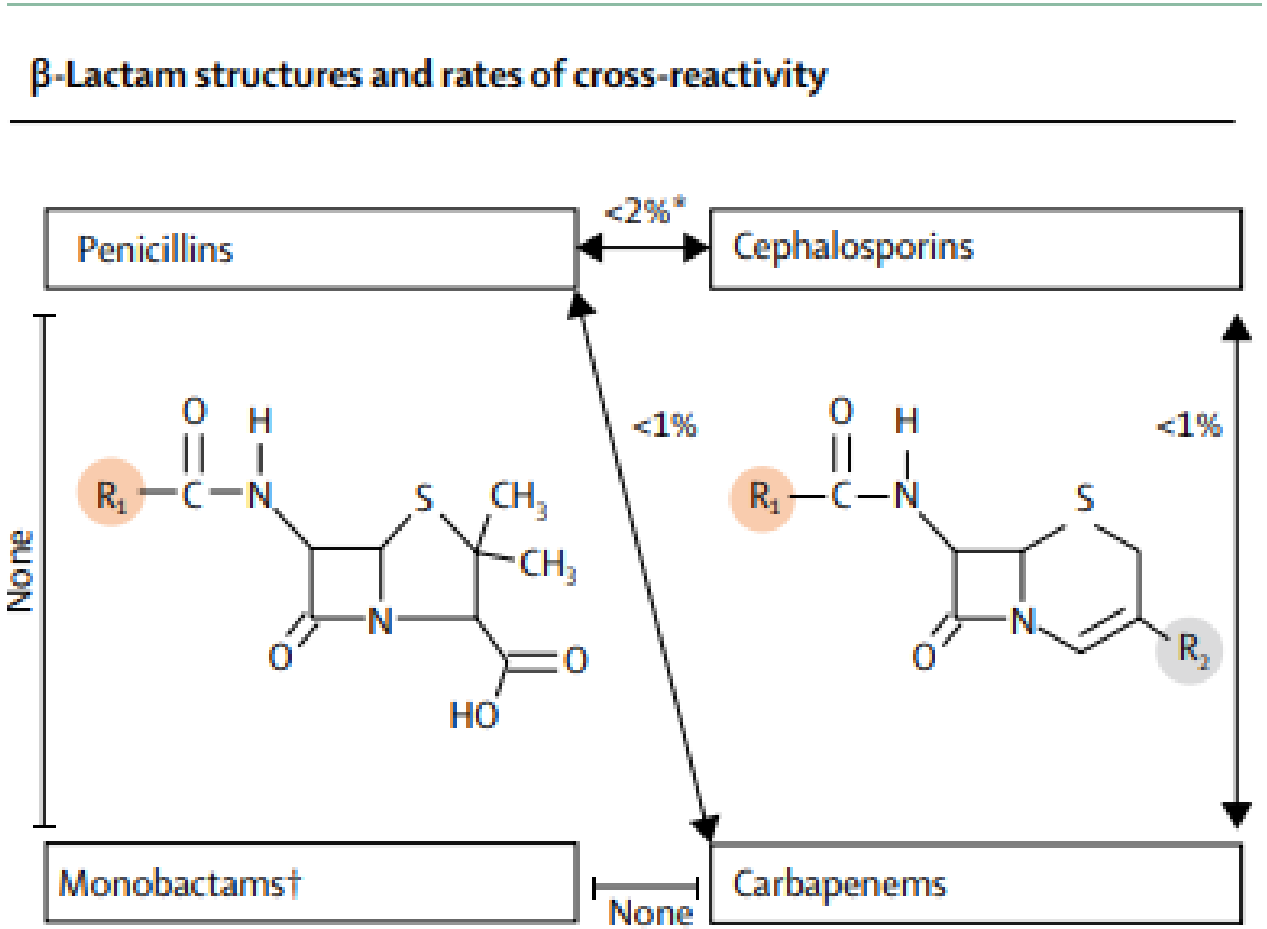
FACT: The PCN allergy label has many implications across the healthcare spectrum.

Staicu, *Ann Allergy Asthma Immunol* 2017 Van Dijk, *J Allergy Clin Immunol Pract* 2016 Blumenthal, *BMJ* 2018 Blumenthal, *Ann Allergy Asthma Immunol* 2015 McFadden, *Clin Infect Dis* 2016 Blumenthal, *Clin Infect Dis* 2015 Macy, *J All Clin Immunol* 2014 Mattingly, *J Allergy Clin Immunol Pract* 2018

Perform Allergy History

- What is the reaction?
- How long after you took the medication did it occur?
- How long ago did the reaction occur
- Have you tolerated other beta-lactam antibiotics?

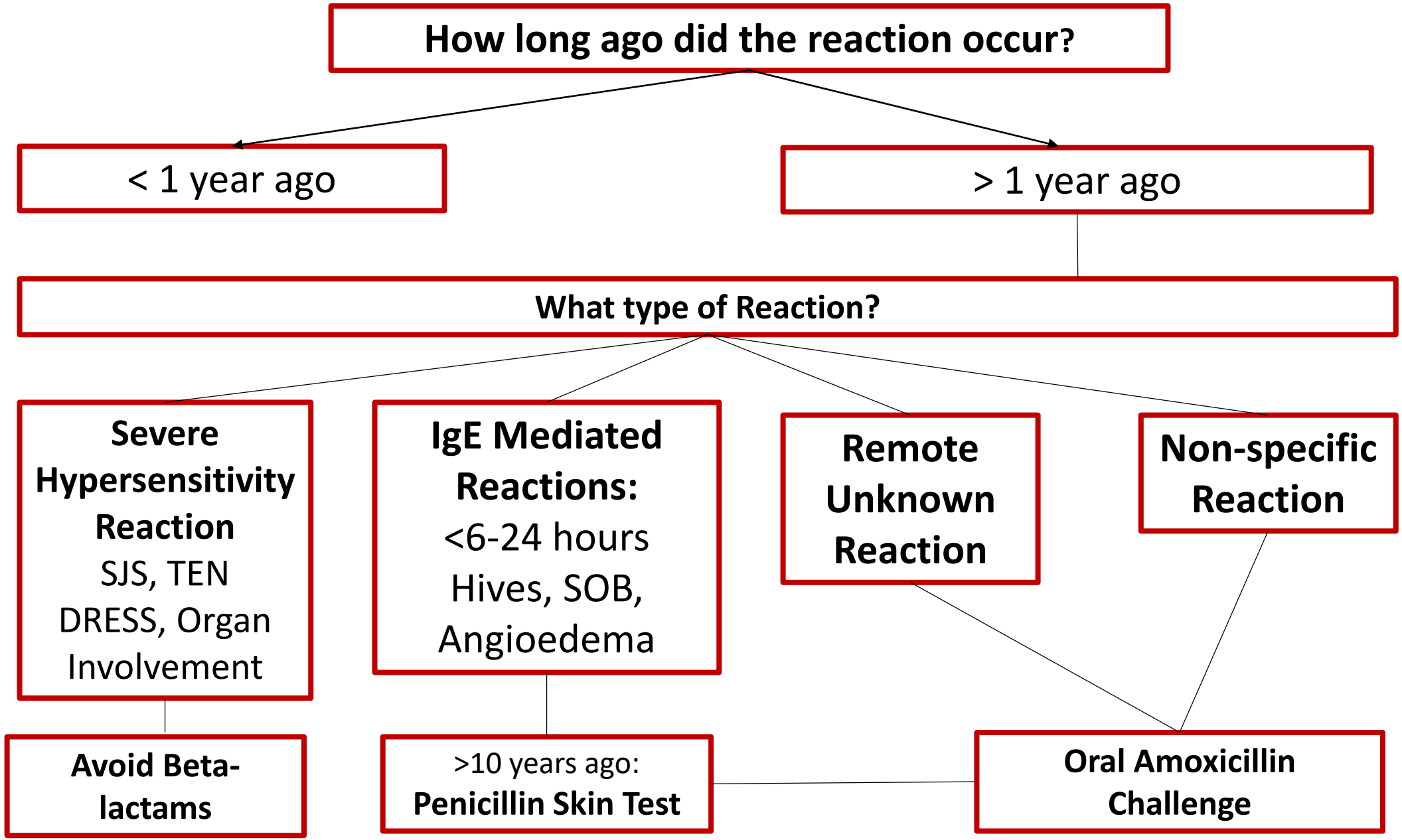
Are patients with a PCN allergy allergic to cephalosporins?



Share Side Chains

- Amoxicillin
- Ampicillin
- Cephalexin
- Cefadroxil
- Cefprozil
- Cefaclor

http://dx.doi.org/10.1016/ S0140-6736(18)32218-9



Kuruvilla et al Allergy Asthma Proc 2019;40:57-61

First rule out SCAR, hemolytic anemia, organ specific reactions, drug fever, serum sickness

Low Risk

GI Symptoms
Pruritus without rash
Remote history > 10 years ago
Unknown Reaction
Family History

Oral Challenge

Medium Risk

Urticarial or pruritic rash

Immediate reaction ≤ 6 hours after exposure – isolated urticarial

Delayed reactions > 6-24 hours after exposure: Isolated urticarial or benign exanthum

Oral challenge
Skin test/oral challenge

High Risk

Anaphylactic Reaction
+ Skin Test
Recurrent Reactions
Reaction to multiple antibiotics

Allergy Referral
Desensitization

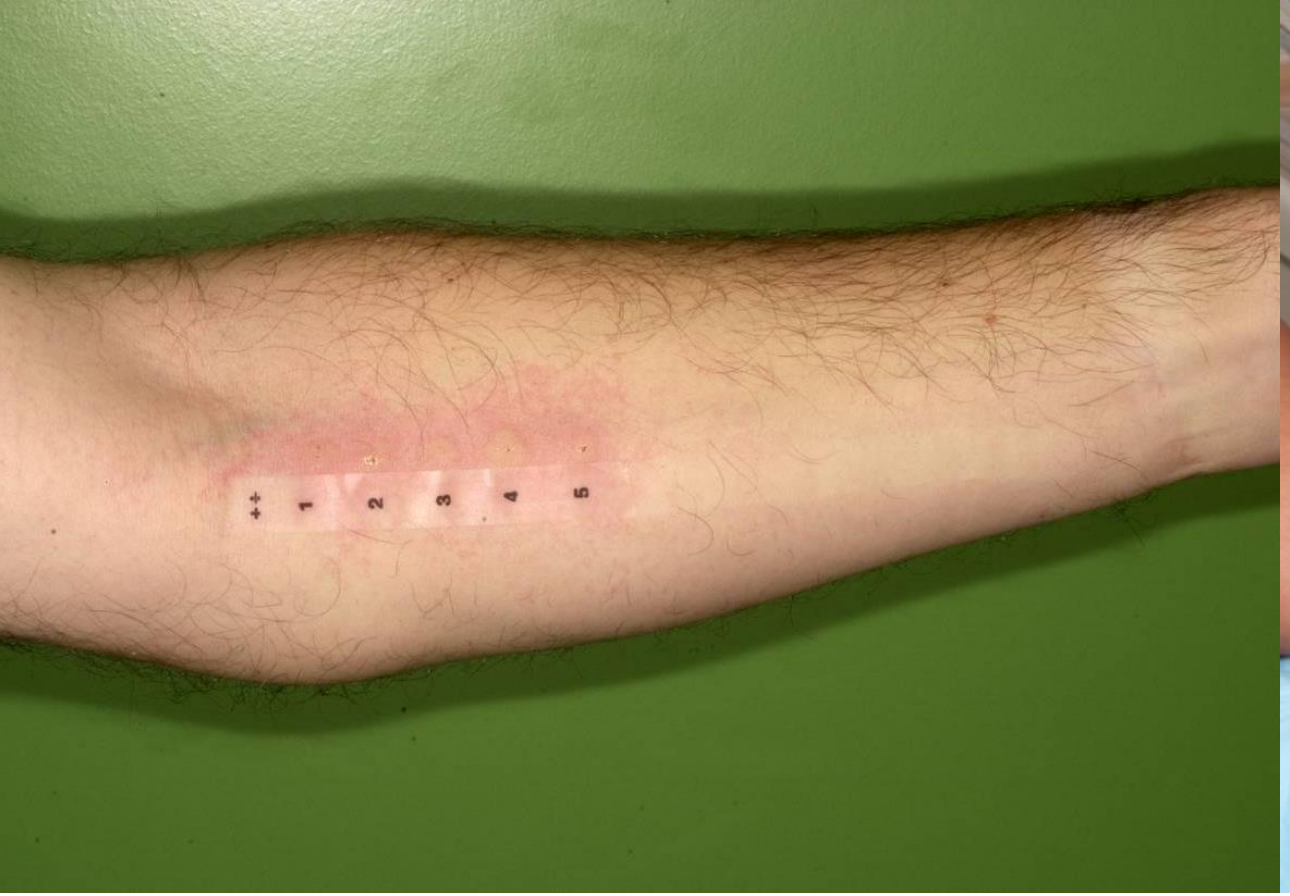
JAMA 2019;321(2):188-199 N Engl J med 2019;381-2338-51

Oral Challenge

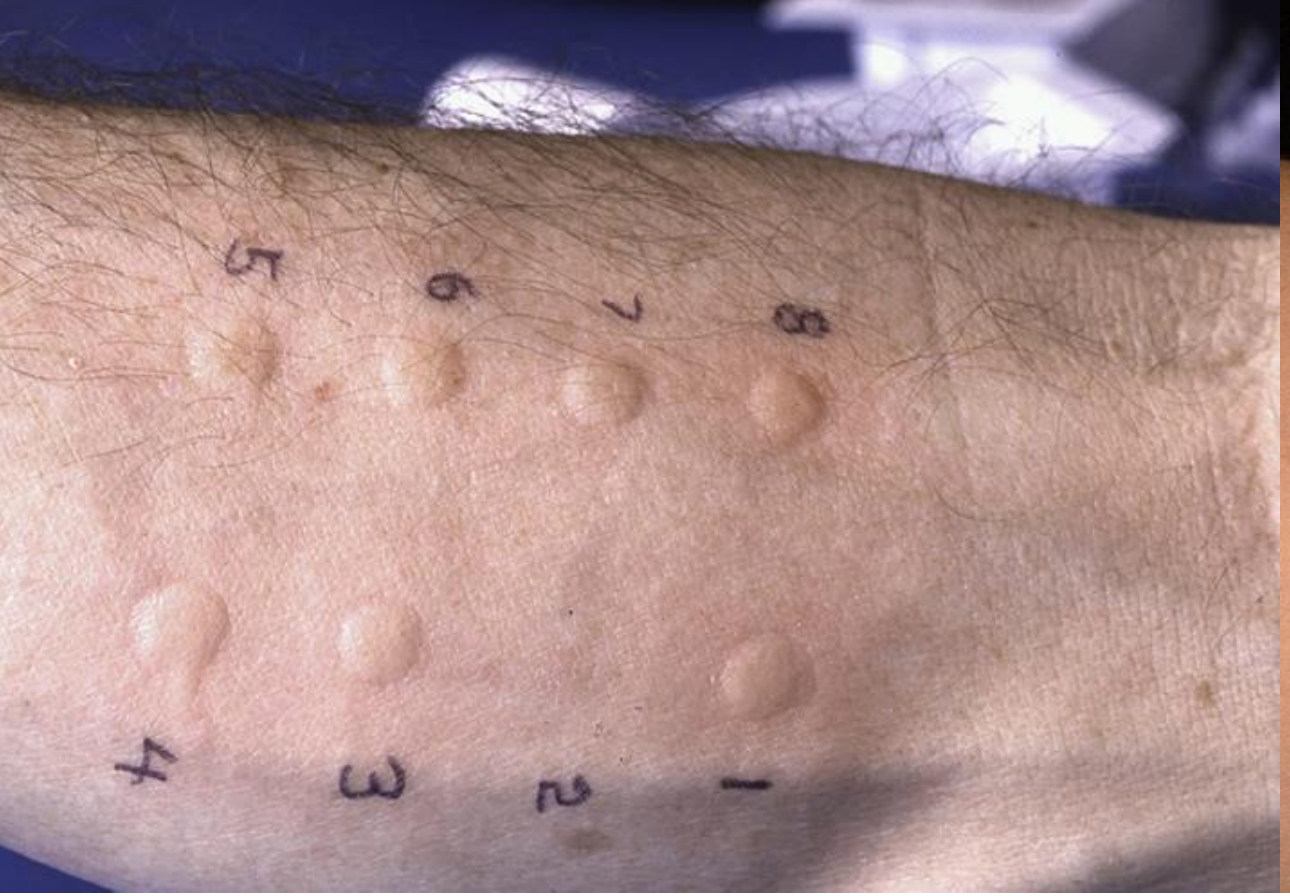
2 Step Challenge

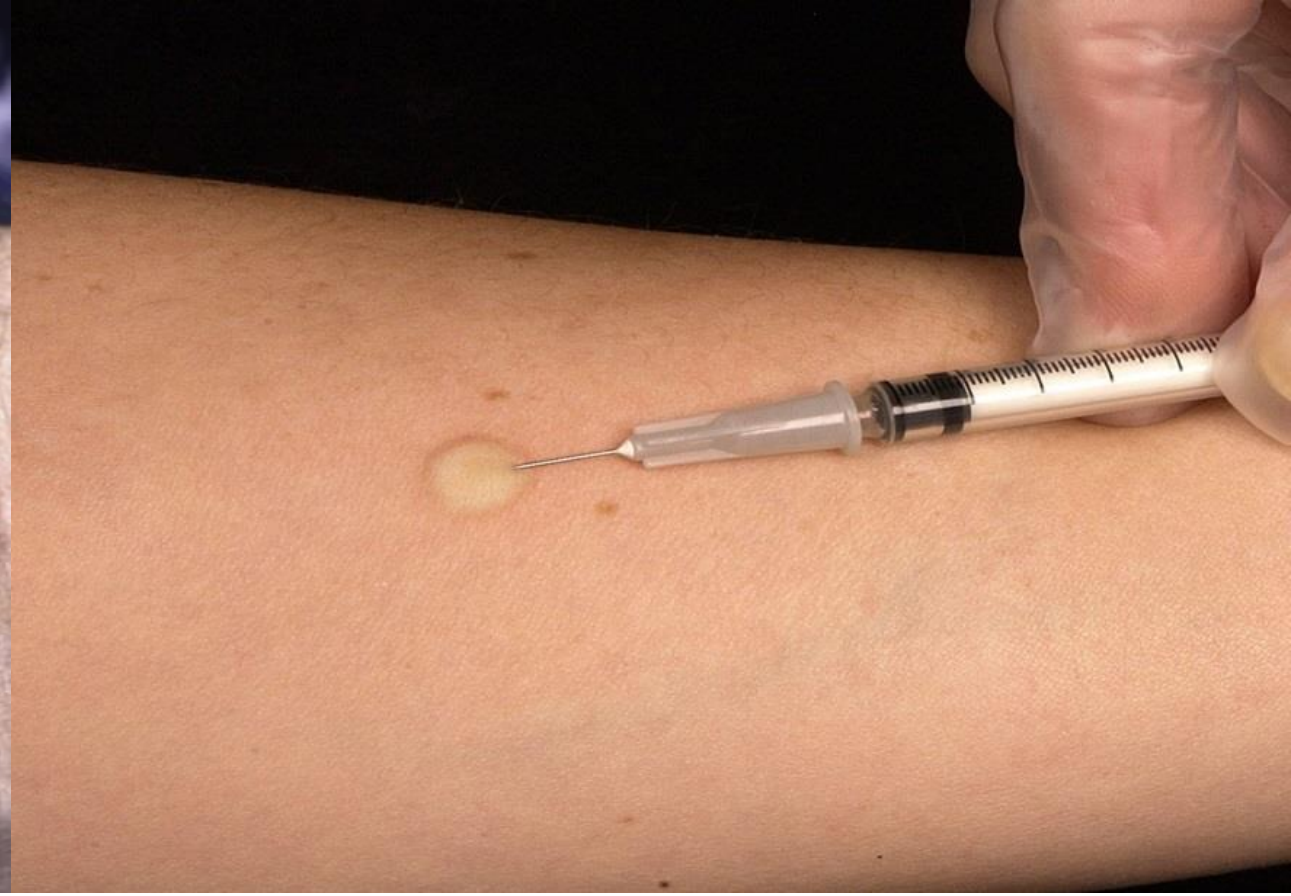
- Amoxicillin 25mg or 50mg (1/10th of the dose)
  - Wait 30 to 60 min
- Amoxicillin 250mg or 500mg (Full dose)
  - Wait 30 to 60 min

IF NEGATIVE: DELABEL!!!!!



Penicillin Allergy – Skin Prick Testing





Penicillin Skin Testing – Intradermal Test

ORAL CHALLENGE:
Follow with amoxicillin 250 to 500mg and observe for 1 hour

Interpretation of Penicillin Skin Testing

Result	Chance of IgE-Mediated Reaction	Penicillin Administration
Positive	50/50 chance of reaction	Avoid
Negative	Risk of reaction same as the baseline population	Give

Note: Penicillin skin testing does not address other types of reactions

Negative Predictive Value ranges from 97 to 99%

Systemic reactions are uncommon (<1%) – Scratch Test improves Safety

Unger NR, 2013 Pharmacotherapy Solensky and Khan et al. 2010. Annals of Allergy Asthma & Immunology.

Legislation Proposal

- Section 1. Section 6802 of the education law is amended to read as follows:
-
- "Administer", for the purpose of section sixty-eight hundred one of this article, means:
  - the direct application of an immunizing agent to adults, whether by injection, ingestion, inhalation or any other means, pursuant to a patient specific order or non-patient specific regimen prescribed or ordered by a physician or certified nurse practitioner, who has a practice site in the county or adjoining county in which the immunization is administered, for immunizations to prevent influenza, pneumococcal, acute herpes zoster, meningococcal, tetanus, diphtheria or pertussis disease and medications required for emergency treatment of anaphylaxis. If the commissioner of health determines that there is an outbreak of disease, or that there is the imminent threat of an outbreak of disease, then the commissioner of health may issue a non-patient specific regimen applicable statewide.
  - the direct application of an immunizing agent to children between the ages of two and eighteen years of age, whether by injection, ingestion, inhalation or any other means, pursuant to a patient specific order or non-patient specific regimen prescribed or ordered by a physician or certified nurse practitioner, who has a practice site in the county or adjoining county in which the immunization is administered, for immunization to prevent influenza and medications required for emergency treatment of anaphylaxis resulting from such immunization. If the commissioner of health determines that there is an outbreak of influenza, or that there is the imminent threat of an outbreak of influenza, then the commissioner of health may issue a non-patient specific regimen applicable statewide.
  - the direct application of antigen to determine immune status or allergy, whether by injection, ingestion, inhalation or any other means, pursuant to a patient specific order or non-patient specific regimen prescribed or ordered by a physician or certified nurse practitioner, for penicillin allergy, tuberculosis, and medications required for emergency treatment of anaphylaxis resulting from such skin test, or other condition identified by the commissioner of health

Myths….

- “The notion that penicillin-allergic patients must avoid all cephalosporins because of potential cross-reactivity among the molecules should be dismissed as a myth.”
  - Due to similarities in the R1 side chain

- “The notion that a patient allergic to a specific cephalosporin must avoid all cephalosporins because of potential cross-reactivity among the molecules should be dismissed as a myth.”
  - Due to similarities in the R1 or R2 side chains

Zagursky RJ J Allergy Clin Immunol Practice 2018;6:72-81

(+) Known cross-reactive (X) Similar or same side chain	Penicillin	Amoxicillin	Ampicillin	Cephalexin	Cefazolin	Cefuroxime	Cefoxitin	Ceftriaxone	Cefotaxime	Ceftazidime	Cefepime	Cefiderocol	Aztreonam
Penicillin		+	+	+									
Amoxicillin	+		+	+									
Ampicillin	+	+		X									
Cephalexin	+	+	X										
Cefazolin													
Cefuroxime							X	X	X		X		
Cefoxitin						X							
Ceftriaxone						X			X		X		
Cefotaxime						X		X			X		
Ceftazidime												X	X
Cefepime						X		X	X				
Cefiderocol										X			X
Aztreonam										X		X	

Slide from Rachel Ruehl (ALK) Picard M 2019 J Allergy Clin Immun Pract

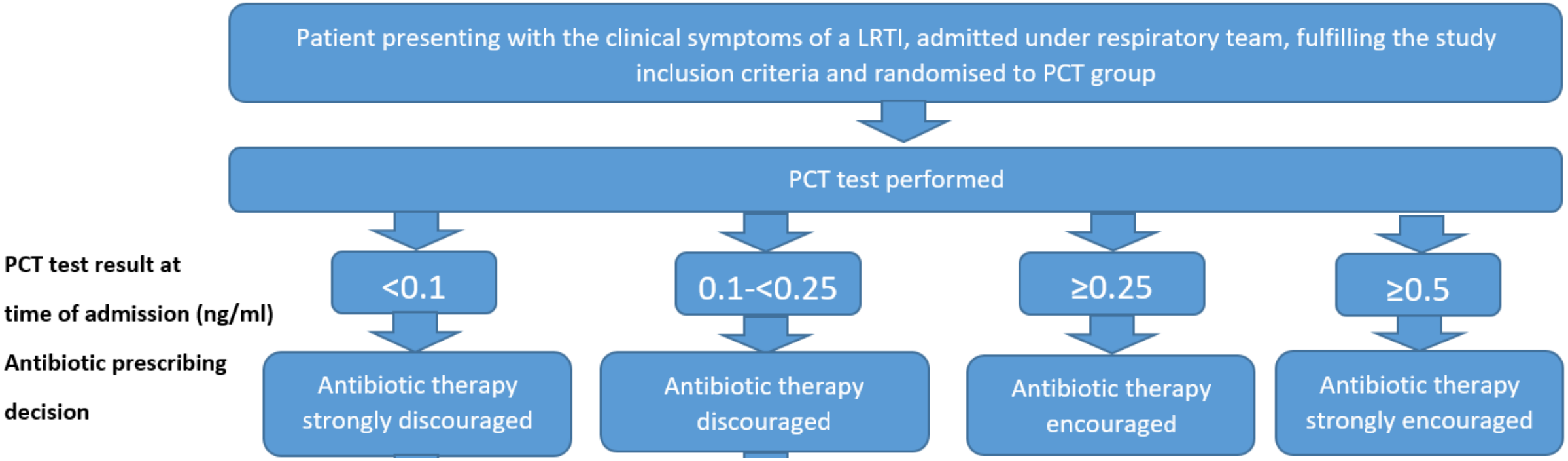
Question #5

Would you recommend the use of procalcitonin to discontinue antibiotic therapy in a patient with community acquired pneumonia?

Yes

No

Protocol



O'Riodan F J Antimicrob Chemother 2019;74:3352-3361

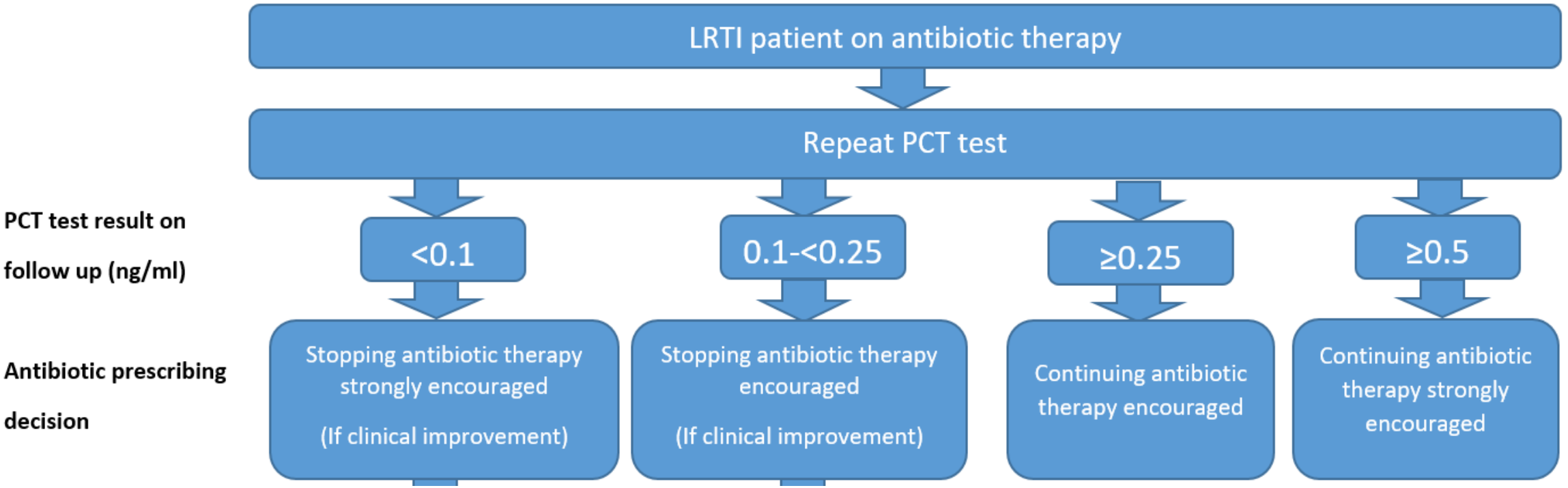
IDSA CAP Guidelines

Question 5: In Adults with CAP, Should Serum Procalcitonin plus Clinical Judgment versus Clinical Judgment Alone Be Used to Withhold Initiation of Antibiotic Treatment?

Recommendation. We recommend that empiric antibiotic therapy should be initiated in adults with clinically suspected and radiographically confirmed CAP regardless of initial serum procalcitonin level (strong recommendation, moderate quality of evidence).

Am J Respir Crit Care Med Vol 200, Iss 7, pp e45–e67, Oct 1, 2019

Antibiotic Continuation



O'Riodan F J Antimicrob Chemother 2019;74:3352-3361

Issues with Procalcitonin

- Average antibiotic length of therapy decreased
  - Average LOT was in excess of current US standards of 5-7 days

- May not be elevated in certain circumstances:
  - Viral infection with concomitant bacterial infection
  - *Legionella sp*
  - *Mycoplasma sp*

Question #6

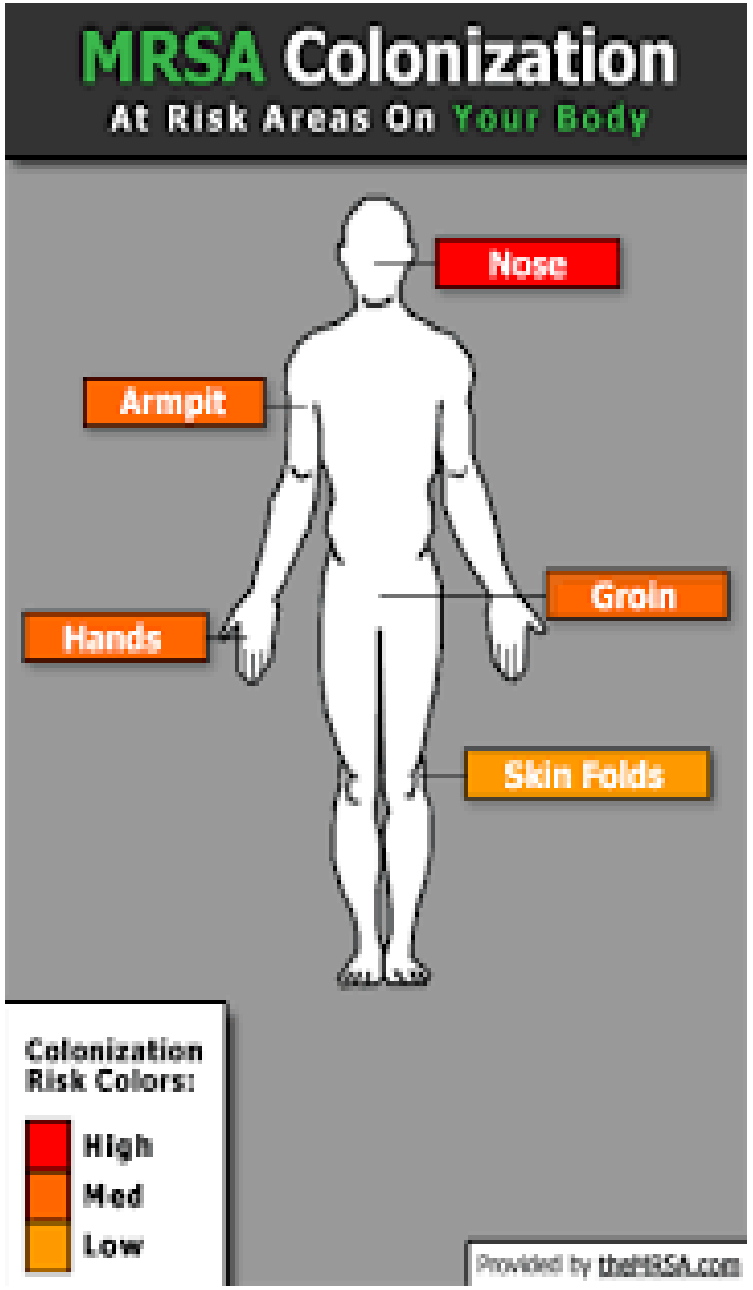
We use MRSA nasal screens to de-escalate vancomycin in patients with pneumonia, but can it be used to discontinue vancomycin in patients with skin and soft tissue infections?

Yes

No

MRSA Colonization

- 20% of people are **persistently** colonized with *S. aureus*
- 60% of people are **intermittent** carriers of *S. aureus*



Antimicrobial Agents Chemother. 2014;58(2):859-62

Study	N	Prevalence	Sensitivity	Specificity	PPV	NPV
Jones M	NR	17.7%	58%	84%	44%	90%
Robicsek A	1393	Extremity 22%	61%	94%	76%	90%
		Ulcers 27%	70%	89%	70%	89%
		Non-extremity 8.7%	60%	96%	61%	96%
Uckay I	102	NR	58%	85%	71%	76%

Pharmacotherapy 2018;38(12):1216-1228

Questions

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