Myths and Controversies in Diagnosis & Management of Infectious Diseases

Melissa D. Johnson, PharmD, MHS, AAHIVP
Liaison Clinical Pharmacist DASON
Professor of Medicine, Duke University Medical Center

Duke University School of Medicine

Duke Center for Antimicrobial Stewardship and Infection Prevention

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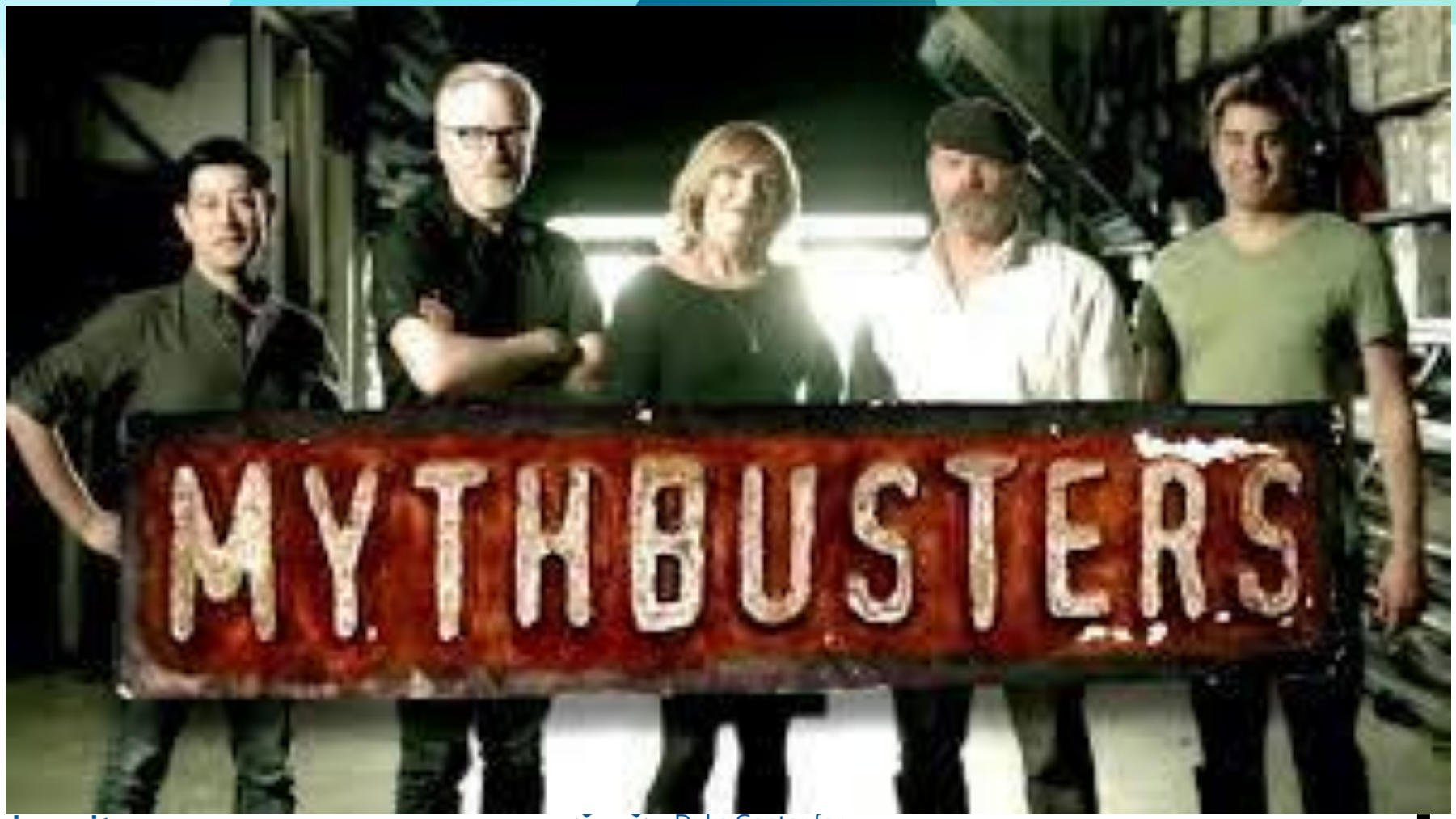
MYTHBUSTERS

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Clinical Infectious Diseases
MAJOR ARTICLE

Antibiotic Myths for the Infectious Diseases Clinician

Erin K. McCreary,[1] Melissa D. Johnson,[2] Travis M. Jones,[2] S. Shaefer Spires,[2] Angelina E. Davis,[2] April P. Dyer,[2] Elizabeth Dodds Ashley,[2] and Jason C. Gallagher[3]

[1]Division of Infectious Diseases, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; [2]Duke Antimicrobial Stewardship Outreach Network, Duke University Medical Center, Durham, North Carolina; and [3]School of Pharmacy, Temple University, Philadelphia, Pennsylvania

Clinical Infectious Diseases, 2023. ciad357, https://doi.org/10.1093/cid/ciad357

REVIEW

ELSEVIER

The American Journal of Medicine
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Top Myths of Diagnosis and Management of Infectious Diseases in Hospital Medicine

Melissa D. Johnson, PharmD, MHS, Angelina P. Davis, PharmD, MS, April P. Dyer, PharmD, MBA, MSCR, Travis M. Jones, PharmD, S. Shaefer Spires, MD, Elizabeth Dodds Ashley, PharmD, MHS

Duke Antimicrobial Stewardship Outreach Network (DASON), Duke University Medical Center, Durham, NC.

Am J Med, 2022. 135(7): 828-835. https://doi.org/10.1016/j.amjmed.2022.03.019

Open Forum Infectious Diseases
PERSPECTIVES

Can the Future of ID Escape the Inertial Dogma of Its Past? The Exemplars of Shorter Is Better and Oral Is the New IV

Kusha Davar,[1] Devin Clark,[1] Robert M. Centor,[2] Fernando Dominguez,[1] Bassam Ghanem,[3] Rachael Lee,[4] Todd C. Lee,[5] Emily G. McDonald,[6] Matthew C. Phillips,[7,8] Parham Sendi,[9] and Brad Spellberg[1]

[1]Los Angeles County + University of Southern California (LAC+USC) Medical Center, Los Angeles, California, USA, [2]Department of Medicine, Birmingham Veterans Affairs (VA) Medical Center, Birmingham, Alabama, Birmingham, Alabama, USA, [3]King Abdulaziz Medical City, Jeddah, Saudi Arabia, [4]Department of Medicine, Division of Infectious Diseases, University of Alabama at Birmingham, Birmingham, Alabama, USA, [5]Division of Infectious Diseases, Department of Medicine, McGill University, Montreal, Canada, [6]Division of General Internal Medicine, Department of Medicine, McGill University, Montreal, Quebec, Canada, [7]Division of Infectious Diseases, Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts, USA, [8]Harvard Medical School, Boston, Massachusetts, USA, and [9]Institute for Infectious Diseases, University of Bern, Bern, Switzerland

Open Forum Infectious Diseases, 2023. 10(1): ofac706. https://doi.org/10.1093/ofid/ofac706

MYTH: ANTIBIOTICS DO NO HARM

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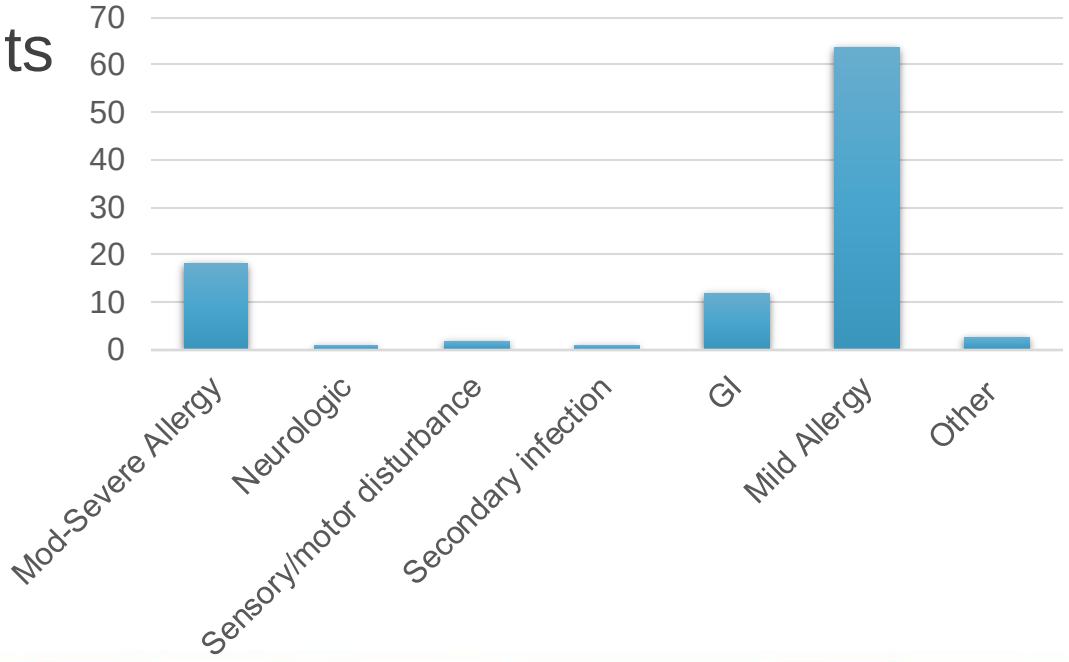
Risk of Antibiotic Adverse Drug Events (ADEs)

- In 2013-2014 approximately 16% of all ED visits for adverse drug events were due to antibiotics
  - Prevalence varies by age but this was the top ADE-related for individuals aged up to age 35 years
  - Just over 7% of antibiotic-related ADE visits to the ED result in a hospital admission



In 2006, this equated to 142,505 emergency department visits annually.

Shehab N et al. *JAMA* 2016;316:2115-25
Shehab N et al. *Clin Infect Dis* 2008;15:735-43.

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Antibiotic-Related ADE in Hospitals

- In a review of 1,488 inpatients receiving antibiotics for at least 24 hours
  - 298 patients (20%) experienced at least one antibiotic-associated ADE
    - 73% occurred during hospitalization, but up to 27% occurred after discharge (including cases of CDI and MDRO infections).
    - Each 10 days of therapy increased risk by 3%
  - More impressive was the consequences of these ADEs
    - New or prolonged hospitalization (27%)
    - Additional clinic or emergency department visits (9%)
    - Additional testing (lab, cardiac, imaging, 61%)

Tamma PD et al. *JAMA Intern Med* 2017;177:1308-15.

Truth

- Antibiotics, while generally perceived as safe agents, actually do result in direct patient harms leading to increased healthcare utilization.

- Discussing these direct risks for personal harm or additional infection (such as CDI) may be more effective tool in discussing the risks and benefits of antibiotics than more global concepts such as antibiotic resistant infections.

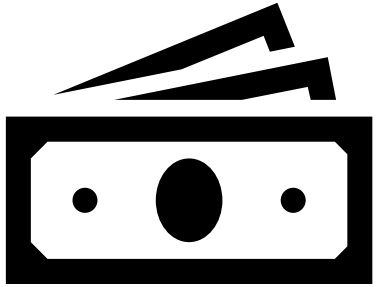
Johnson MD et al. Am J Med, 2022. 135(7): 828-835. https://doi.org/10.1016/j.amjmed.2022.03.019

MYTH: IF ONE DRUG IS GOOD TWO (OR MORE) MUST BE BETTER

Cost of Redundant Therapy to US Hospitals

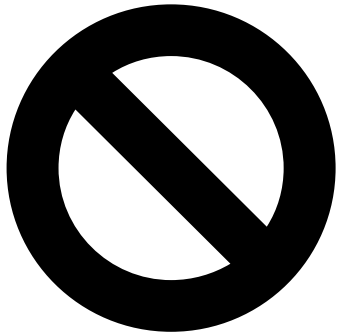
Annual avoidable cost of combination therapy to US hospitals=

$50-100 million



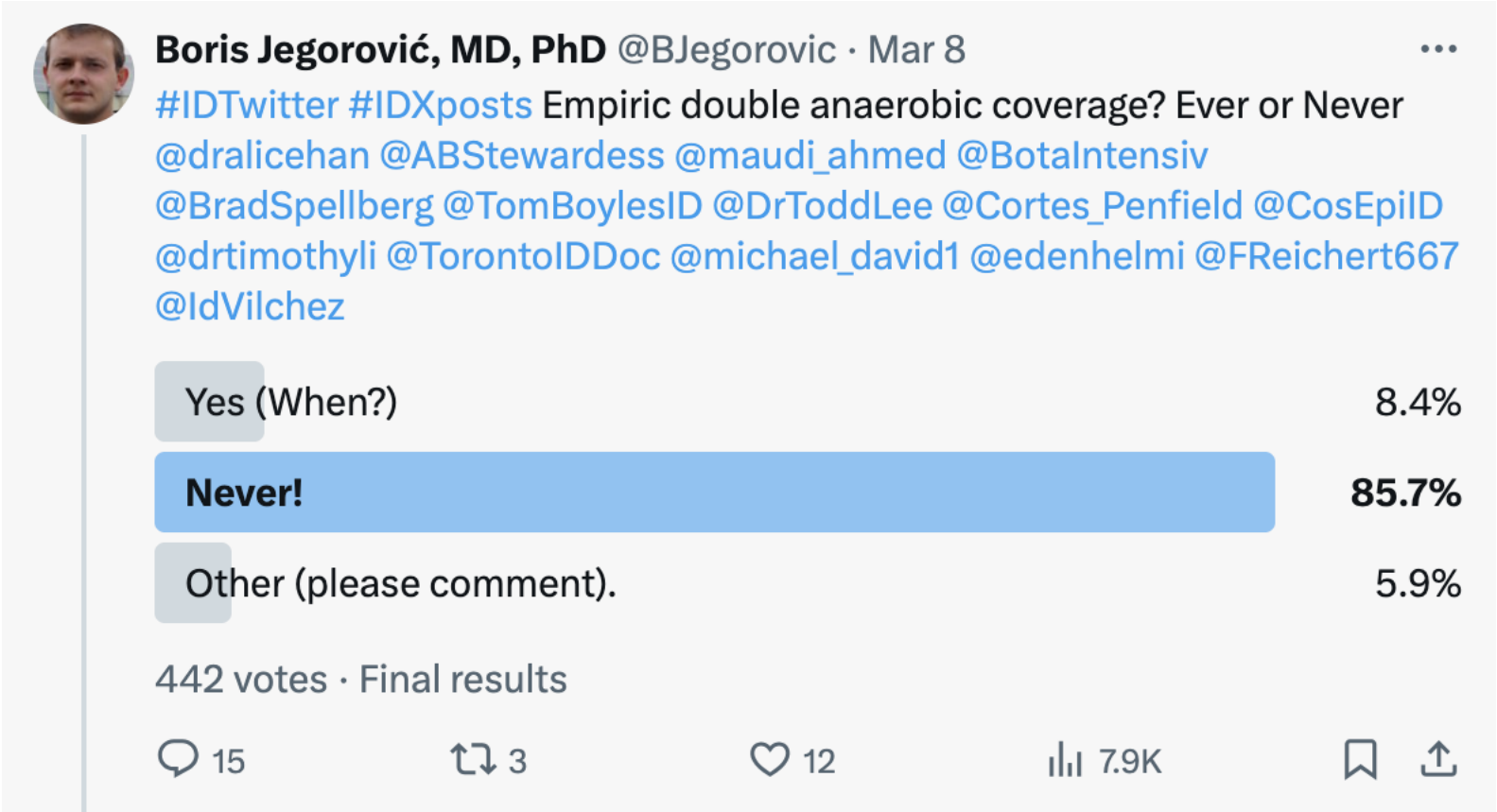
53%

of cases were due to the “never” event of piperacillin/tazobactam + metronidazole



Schultz L et al. *Infect Control Hosp Epidemiol* 2014;35:1229-35.

Empiric double anaerobic coverage?



https://twitter.com/BJegorovic/status/1766110546695184862

Acceptable Reasons for Combination Antibiotic Therapy

Anti-anaerobe	• Necrotizing fasciitis • *Clostridiodes difficile* • Select biliary tract infections
Beta-lactam	• Enterococcal endocarditis (ampicillin plus ceftriaxone) • *Listeria monogytogenes* (ampicillin plus cephalosporin)
Anti-MRSA	• Controversial, select cases of invasive MRSA infection
Gram-Negative	• Empiric therapy to increase likelihood of choosing one effective agent

Rose W et al. *Clin Infect Dis* 2021;73:2353-60.
Johnson MD et al. Am J Med 2022. https://doi.org/10.1016/j.amjmed.2022.03.019
Tamma et al. *Clin Microbiol Rev* 2012;25:450-70.

Truth

- There is little role for routine combination antibacterial therapy outside initial empiric therapy for Gram-negative infections (pending susceptibility) and targeted indications showing benefit.

- Duplicative anti-anaerobic therapy in patients without CDI is a particular target for intervention.

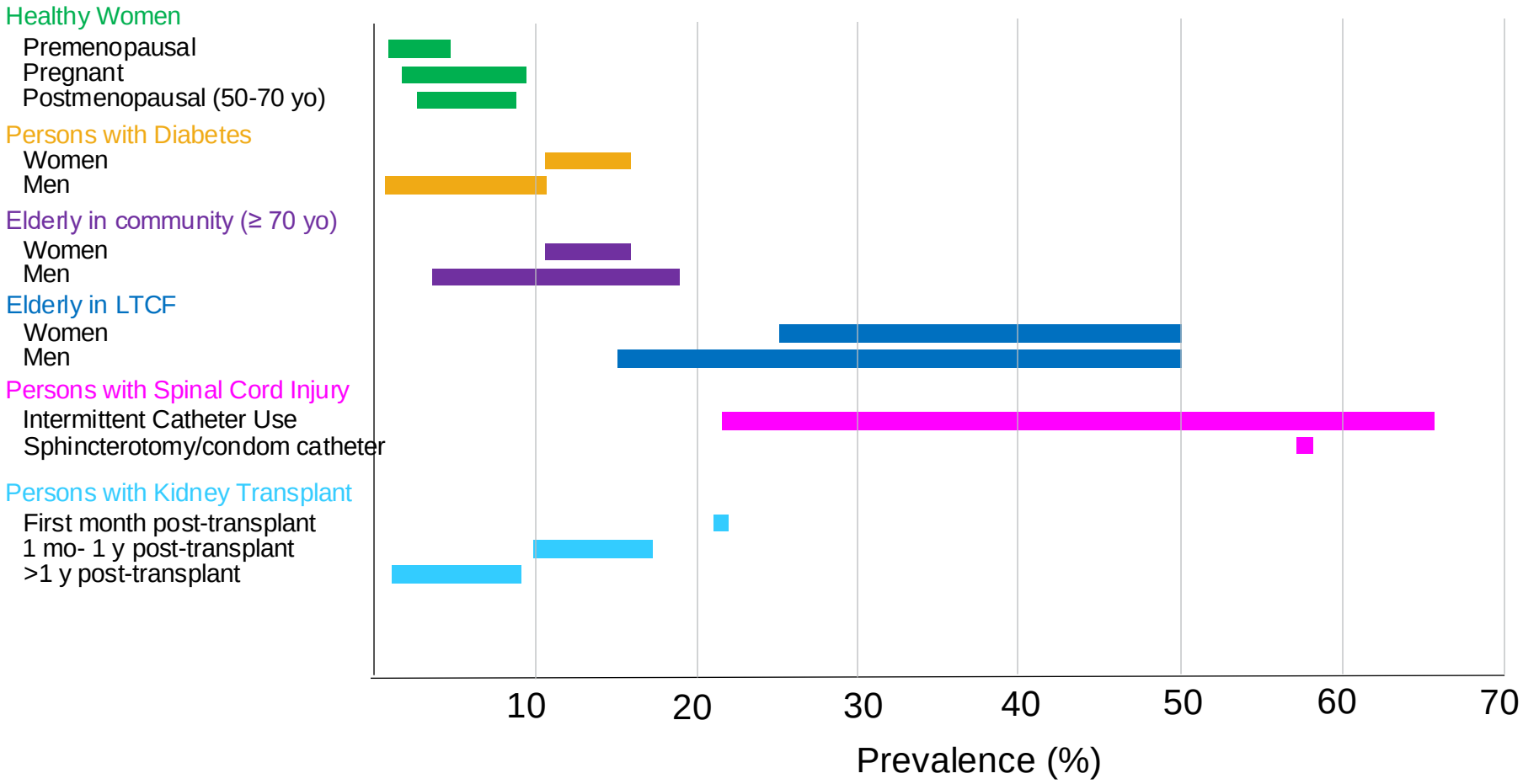
Johnson MD et al. Am J Med, 2022. 135(7): 828-835. https://doi.org/10.1016/j.amjmed.2022.03.019

MYTH: BACTERIA IN THE URINE SIGNIFIES A UTI AND SHOULD BE TREATED; RELATED MYTH: CLOUDY AND/OR SMELLY URINE INDICATES YOUR PATIENT HAS A UTI

Bacteria in the Urine is a Common Finding

It does not necessarily indicate a UTI

Prevalence of Asymptomatic Bacteriuria in Different Populations



Persons with indwelling catheter use:
short term: 3-5% per catheter day long term: **100%** !

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Adapted from: Nicolle LE et al. Clin Infect Dis 2019;68(10): e83-110.

Treatment of Asymptomatic Bacteriuria (ASB)

Unnecessary treatment of ASB is common

- 20% (ED) to 83% (nursing homes or hospitalized) of cases

One of “Top 5 excessive healthcare practices in geriatric patients”

Recent study demonstrated 71% of primary care clinicians would inappropriately prescribe antibiotics for case scenarios of ASB

Leads to immediate and downstream consequences:

- Increased risk of adverse drug events
- Increased risk of infections due to MDRO
- Ecological damage in the health care setting and community
- Increased health care costs
- Increased risk of future UTIs

Trautner BW and Grigoryan L. Infect Dis Clin North Am. 2014. 28(1): 15-31.
ABIM Foundation. Choosing Wisely: An initiative of the ABIM foundation. 2010
Petty LA et al. JAMA Intern Med. 2019;179(11):1519-1527.
Baghdadi JD et al. JAMA Netw Open. 2022;5(5):e2214268.

Vast Majority of Patients Do Not Require Screening/Treatment for ASB

SHOULD NOT BE ROUTINELY SCREENED/PRESCRIBED ANTIBIOTICS	SHOULD BE SCREENED/TREATED
• Nonpregnant women • Women with diabetes mellitus • Elderly patients living in the community • Patients with spinal cord injury • Patients with an indwelling catheter in place • Renal transplant recipients >1 month post-transplant • Non-renal solid organ transplant recipients • Patients undergoing elective neurologic surgery	• Pregnant Women • Patients undergoing select urologic procedures (endoscopic urologic procedures associated with mucosal trauma)

Johnson MD et al. Am J Med 2022. https://doi.org/10.1016/j.amjmed.2022.03.019
Trautner BW and Grigoryan L. Infect Dis Clin North Am. 2014. 28(1): 15-31.
Nicolle LE et al. Clin Infect Dis. 2019; 68(10)e83-110.

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Urinalysis- interpretation

Element	Findings of Interest	Comments/Interpretation
WBC	Presence of WBC	• If WBC negative, UTI absent • Optimal threshold for diagnosis undefined; threshold of pyuria [e.g. WBCs >5/high-powered field (hpf) vs WBCs >10/hpf] does not reliably distinguish ASB from infection • Pyuria + bacteriuria does not necessitate treatment if otherwise healthy & asymptomatic • May be positive in patients with indwelling catheters, oliguria/anuria (e.g. hemodialysis patients), acute renal failure, STIs, and in the presence of moderate hematuria; does not distinguish ASB from UTI • May be artificially low in neutropenic/leukopenic patients
Leukocyte esterase (LE)	Positive = pyuria	• If both LE and Nitrite negative, high negative predictive value (UTI unlikely) • May be elevated due to genitourinary inflammation, irritation from instrumentation/catheterization, glomerulonephritis, UTIs and sexually transmitted infections
Nitrite	Positive = presence of bacteria that reduce nitrate (*E.coli*, *Proteus*)	• *Enterococci*, *S. saphrophyticus*, *Candida* UTI likely to be nitrite negative • A negative test does not rule out UTI • False positives possible due to exposure to air or phenazopyridine, or from preanalytic contamination • A positive test does not rule in UTI in the absence of symptoms
Epithelial cells	<5 = good urine sample	• Many epithelial cells= contamination • The presence of renal epithelial cells may represent acute renal injury
pH	High	• Higher with urea-splitting organisms like Proteus and Providencia (pH >6.5)
RBCs	>2-3 RBCs	• Nonspecific, many other causes • May be present due to acute glomerulonephritis, stone disease, trauma, malignancy, or menstruation

DASON Newsletter, April 2018; Advani SD et al. *Antimicrob Steward Healthc Epidemiol*. 2021;1(1).

Cardinal Rules for UTI Workup

- Evaluate carefully for symptoms before sending urinalysis
- The presence of cloudy or foul-smelling urine alone is an unreliable indicator of UTI
- Pyuria and bacteriuria are expected in patients with chronic indwelling urinary catheters and do not help distinguish between ASB and UTI
- The use of more stringent urine testing algorithms and reporting may help reduce overprescribing of antibiotics for ASB
- Treating Asymptomatic Bacteriuria/Pyuria may increase risk of a future UTI

Johnson MD et al. Am J Med 2022. https://doi.org/10.1016/j.amjmed.2022.03.019
Nicolle LE et al. Clin Infect Dis 2019;68(10): e83-110.
ASB FAQ: https://sites.google.com/view/asphds/asb-faq

Urinary Tract Infections/ASB

Research

JAMA Internal Medicine | Original Investigation

A Statewide Quality Initiative to Reduce Unnecessary Antibiotic Treatment of Asymptomatic Bacteriuria

Valerie M. Vaughn, MD, MSc; Ashwin Gupta, MD; Lindsay A. Petty, MD; Anurag N. Malani, MD; Danielle Osterholzer, MD; Payal
Mariam Younas, MD; Steven J. Bernstein, MD, MPH; Stephanie Burdick, MD; David Ratz, MS; Julia E. Szymczak, PhD; Elizabet
Tawny Czilok, MHI, RN; Tanima Basu, MA, MS; Jennifer K. Horowitz, MA; Scott A. Flanders, MD; Tejal N. Gandhi, MD

Michigan Hospital Medicine Safety Consortium, 46 hospitals

3 year prospective QI study

Diagnostic stewardship vs antibiotic stewardship to reduce antibiotic use for ASB

14,572 patients with + urine culture, 28.4% had ASB; 76.8% with ASB got antibiotics for a median of 6 days

Vaughn VM et al. JAMA Intern Med. 2023;183(9):933-941. doi:10.1001/jamainternmed.2023.2749

Urinary Tract Infections/ASB

- Overall, percent of patients treated as UTI that had ASB declined from 29.1% to 17.1%

- Diagnostic Stewardship outcome
- percent of patients with + urine culture who had ASB declined from 34.1% to 22.5%

- Antimicrobial Stewardship outcome
- percent of patients with ASB that got antibiotics was not significantly changed over the study period (82% to 76.3%) & mean duration was similar (6.38 days to 5.93 days)

Diagnostic stewardship (reducing unnecessary urine cultures) was more impactful in reducing ASB overtreatment

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Vaughn VM et al. JAMA Intern Med. 2023;183(9):933-941. doi:10.1001/jamainternmed.2023.2749

Truth

- Bacteria in the urine in the absence of symptoms indicates asymptomatic bacteriuria, and with few exceptions, does not require antibiotic treatment.

Johnson MD et al. Am J Med 2022. https://doi.org/10.1016/j.amjmed.2022.03.019

MYTH: ORAL FOSFOMYCIN IS AN EXCELLENT DRUG FOR UNCOMPLICATED CYSTITIS

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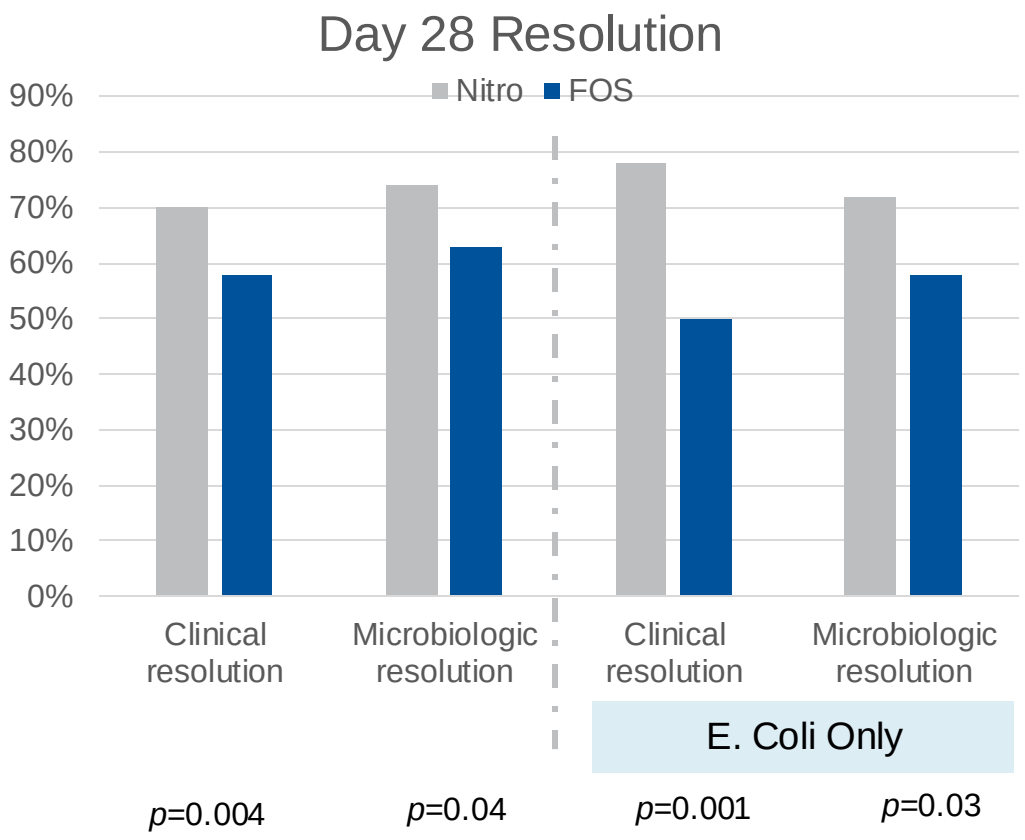
Fosfomycin features

- US: only orally available (IV ex-US)
- One-time dose (3 g) for cystitis
- Rapidly bactericidal (?)
- PK: ~35-40% of a 3 g dose excreted in urine by 24h
  - ~60-83% have measurable concentrations in urine at 48h after a 3 g dose
- Limited spectrum- low collateral damage
- Early RCT: similar efficacy as 7-day course of nitrofurantoin
  - 521 females with cystitis, >80% E. coli

Stein GE. Clin Therapeut 21(11): 1999.
Wenzler E. Antimicrob Agents Chemother. 2018 Jul 27;62(8):e00464-18.

So what's the problem?

- 2018 RCT- multinational, open label
- Single dose Fosfomycin 3 g vs nitrofurantoin 100 mg TID x 5 days
- 513 nonpregnant women with lower UTI symptoms and positive LE/nitrites
  - 475 completed the study, 377 (73%) positive baseline urine culture
    - 61% *E. coli*, 7% *Klebsiella* spp.*, 7% *Enterococcus* spp., 5% *Proteus* spp.*



Proteus spp. are intrinsically resistant & *Klebsiella* spp. are often resistant to nitrofurantoin

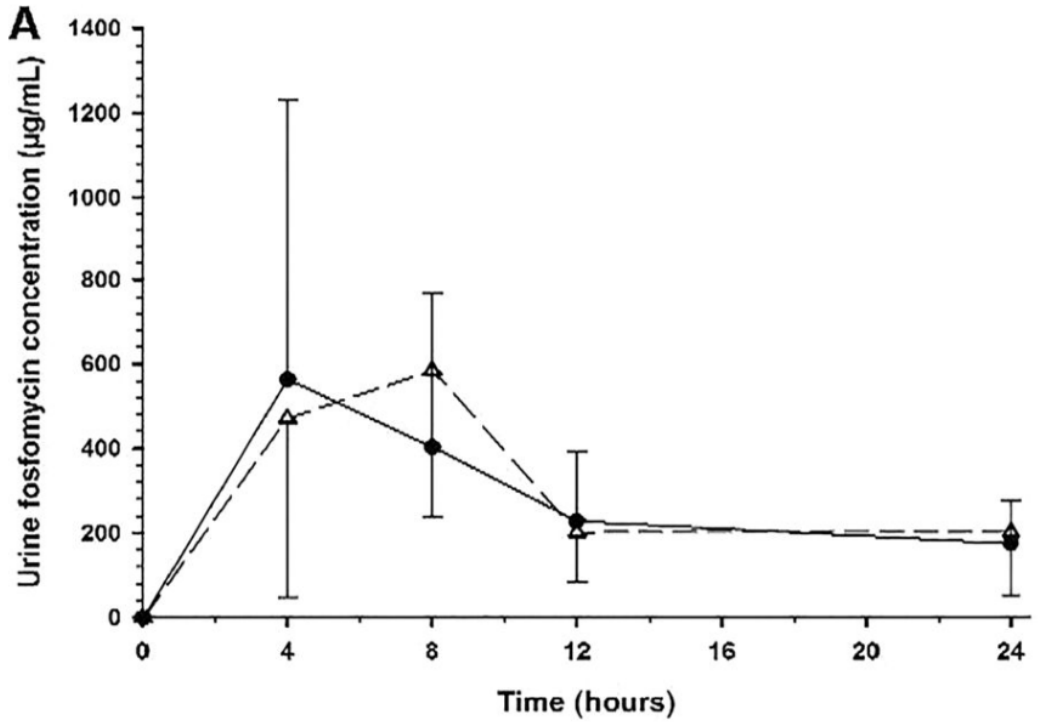
Huttner A et al. JAMA 2018; 319(17): 1781-1789.

What might explain suboptimal effects?

- *In vitro* dynamic bladder infection model:
  - regrowth of *E. coli*, *Klebsiella* spp., and other uropathogens after a single dose
  - Amplification of resistant subpopulations
- Baseline fosfomycin resistance might be higher than anticipated
  - Spain: increase from 4% in 1997 to 11% in 2009
- Antimicrobial susceptibility testing methods were not reliable
  - Require Glucose-6-Phosphate (G6P) supplementation for agar dilution
  - Other methods are suboptimal
  - G6P not present in human urine
    - Impaired antibacterial activity and pharmacodynamics *in vivo*
- PK/PD variability - may be related to timing of oral drug administration relative to bladder emptying, and urinary output

Huttner A et al. JAMA 2018; 319(17): 1781-1789.
Wenzler E. Antimicrob Agents Chemother. 2018 Jul 27;62(8):e00464-18.

PK exposures



Urine AUC: 4800 µg h /ml
Stasis at MICs up to 128 mcg/mL, 1- log kill up to 32 mcg/mL

Urine Concentrations in other PK studies of oral Fosfomycin 3 g

Dose	Timepoint	Urine Concentration
3 g	0-4h	1,053 to 4,415 µg/ml
50 mg/kg (~4g)	2 h	2000-2500 µg/ml (bioassay)
3 g	6-8 h 24h	537.7 ± 251.8 163.5 ± 99.3

PD parameter of interest: neutropenic thigh model: AUC/MIC
Stasis: 23, 1-log Kill: 83

Wenzler E. Antimicrob Agents Chemother. 2018 Jul 27;62(8):e00464-18.

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Fosfomycin Breakpoints

Organization	MIC (mcg/mL)		
	Susceptible	Intermediate	Resistant
EUCAST pre-2024 Oral IV	 ≤ 8 ≤ 32	 NA NA	 > 8 > 32
EUCAST 2024 Oral and IV	≤ 8	NA	>8
CLSI* & FDA	≤ 64	128	≥ 256

**E. coli*, *Enterococcus faecalis*

CLSI M 100, 2025. EUCAST www.eucast.org

Fosfomycin clinical use – complicated UTIs

- Multicenter retrospective cohort, adults
  - Fosfomycin at hospital discharge, n =110
  - Ertapenem, n=212
- Mostly ESBL+ *E. coli /K. pneumoniae*
- Included repeat episodes
- Excluded prostatitis
- Fosfomycin susceptibility performed by disk-diffusion, only on ESBL + isolates

Open Forum Infectious Diseases
MAJOR ARTICLE

Fosfomycin vs Ertapenem for Outpatient Treatment of Complicated Urinary Tract Infections: A Multicenter, Retrospective Cohort Study

Noah Wald-Dickler,[1,2] Todd C. Lee,[3] Soodtida Tangpraphaphorn,[1] Susan M. Butler-Wu,[1,4] Nina Wang,[1] Tyler Degener,[1,2] Carolyn Kan,[1,2] Matthew C. Phillips,[1,2] Edward Cho,[1,2] Catherine Canamar,[1] Paul Holtom,[1,2] and Brad Spellberg[1]

[1]Los Angeles County - University of Southern California Medical Center (LAC-USC Medical Center), Los Angeles, California, USA, [2]Department of Medicine, Keck School of Medicine of USC, Los Angeles, California, USA, [3]Clinical Practice Assessment Unit, McGill University, Montreal, Quebec, Canada, and [4]Department of Pathology, Keck School of Medicine of USC, Los Angeles, California, USA

30-day clinical success
Fosfomycin: 72/110 (65.4%)
Ertapenem: 157/212 (74.1%)
$p = 0.1$

Wald-Dickler N. OFID 2022. 9(1): ofab620. https://doi.org/10.1093/ofid/ofab620

Truth

- Erin McCreary: “Fosfomycin is the best ASB drug in the world”
- Oral packets of Fosfomycin are quite costly compared to other oral options for uncomplicated cystitis
- Susceptibility testing for fosfomycin is a challenge
  - it remains to be seen if this is reliably predictive of clinical outcomes and what optimal breakpoints are
- Fosfomycin has the same eGFR limitations as nitrofurantoin
- May be an oral alternative to carbapenem for outpatient treatment of ESBL+ (E.coli / K. pneumo) UTIs

MYTH: A history of a penicillin allergy means the patient can never receive a beta-lactam antibiotic

True incidence of anaphylactic reactions to beta-lactams is between 1 in 25,000 to 1 in 6,700 patients

10% of the population reports a penicillin allergy, but *less than 1%* of the whole population is truly allergic

Figure adapted from www.cdc/gov/getsmart.

Is it Harmful to Use Penicillin Alternatives?

- Treatment with alternative, broad-spectrum agents has significant collateral damage
- Retrospective study matched 51,582 unique penicillin “allergic” hospitalized individuals to 2 unique control subjects each
  - Kaiser Foundation South California Hospitals 2010-2012
- Results, penicillin-allergic patients vs matched controls:
  - More fluoroquinolones, clindamycin, and vancomycin prescribed
  - Longer hospital stays by 0.59 days/person
  - 23.4% more *C. difficile*
  - 14.1% more MRSA
  - 30.1% more VRE infections
  - $20 million increase cost/year for this group of patients

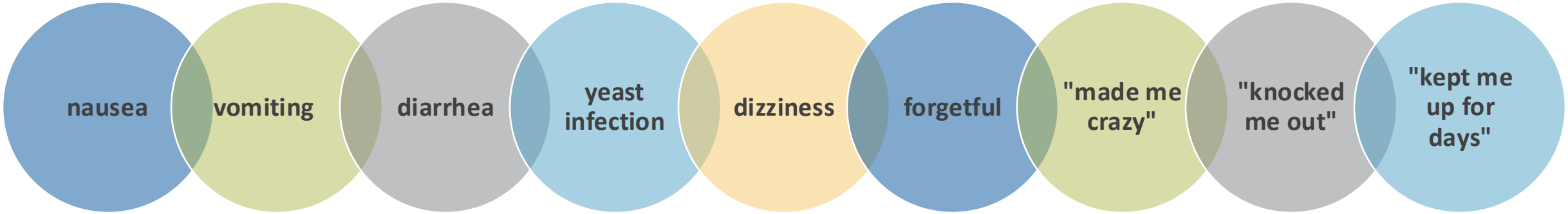
Macy E et al. J Allergy Clin Immunol 2014;133:790-96.

Overview of Hypersensitivity Reactions:

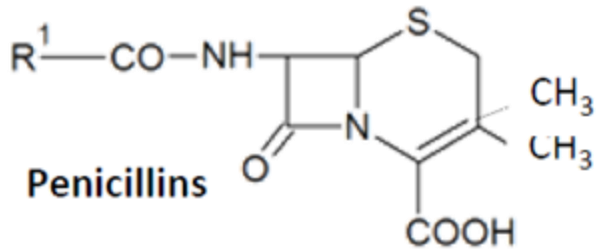
	Immediate	Delayed		
	Type I	**Type II**	**Type III**	**Type IV**
	IgE-mediated	IgG-mediated cell destruction	IgG drug immune complex deposition	IgG-mediated cell destruction
	anaphylaxis, hypotension, angioedema	hemolytic anemia, thrombocytopenia, neutropenia	serum sickness, vasculitis, drug fever	contact dermatitis, SJS, TEN, DIHS
	almost always occurs within 1 hour of administration	*almost always occurs greater than 72 hours after first administration*		

SJS, Stevens Johnson Syndrome; TEN, toxic epidermal necrolysis; DIHS, drug-induced hypersensitivity syndrome

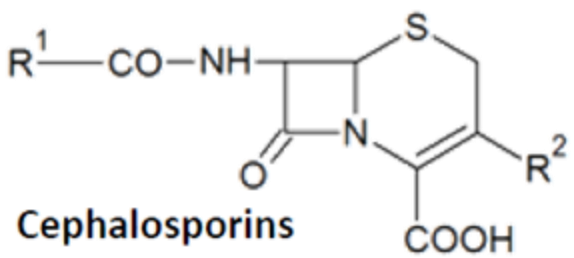
Overview of Intolerances:



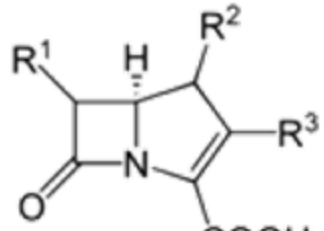
Cross-reactivity Among Beta-lactams



Penicillins



Cephalosporins



Carbapenems

Aminopenicillins:

93.7% patients with allergic reaction to ampicillin cross-react with benzyl penicillin and/or amoxicillin determinants

Cephalosporins:

0.17% to 8.4%

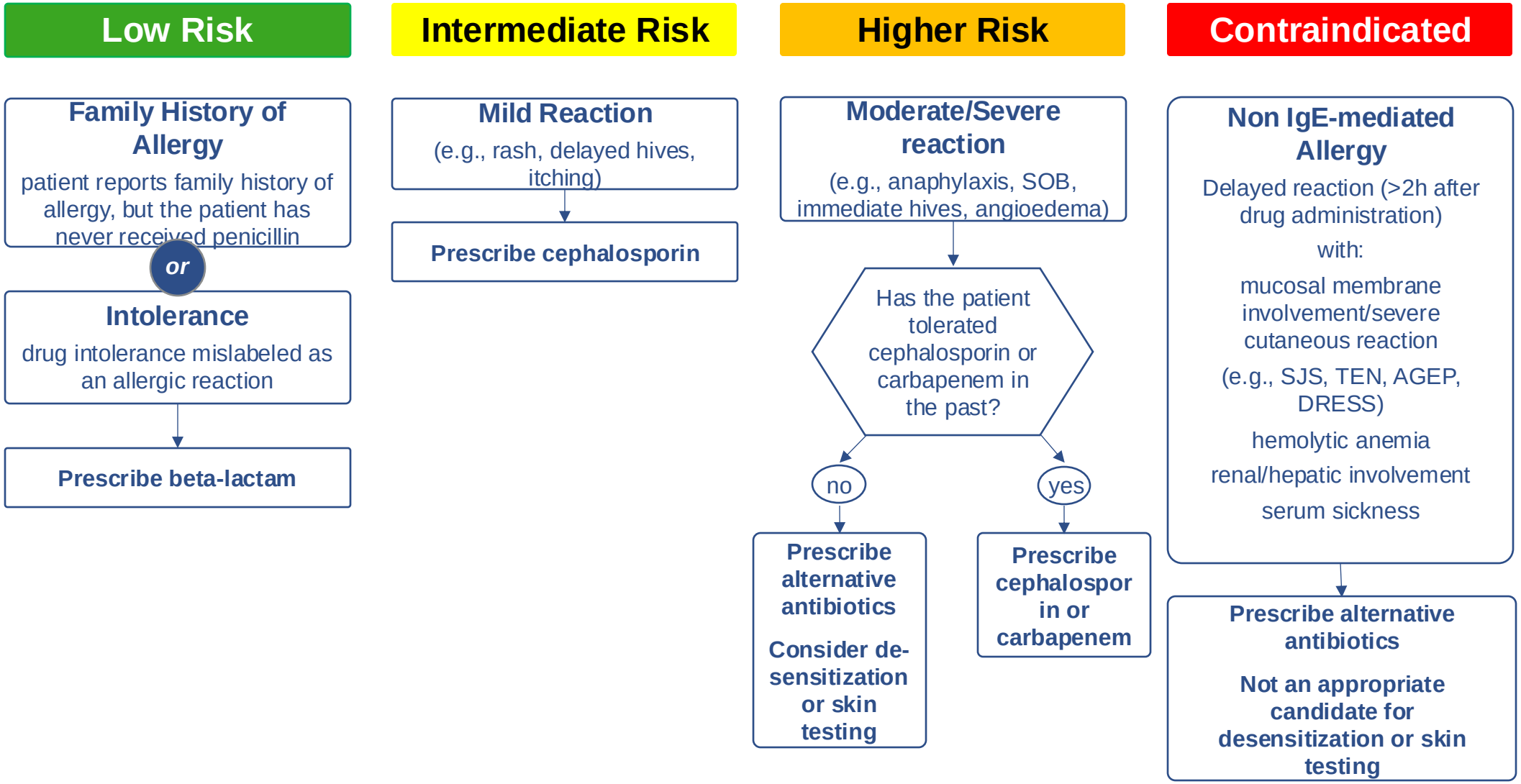
Carbapenems:

< 1%

Petz LD. J Infect Dis. 1978;137 Suppl:S74.
Dash CH. J Antimicrob Chemother. 1975;1(3 Suppl):107.
Daulat S et al. J Allergy Clin Immunol. 2004;113(6):1220.
Goodman EJ et al. J Clin Anesth. 2001;13(8):561.
Fonacier L et al. Allergy Asthma Proc. 2005;26(2):135.

Kula B et al. Clin Infect Dis. 2014;59(8):1113.
Atanasković-Marković M et al. Allergy. 2008;63(2):237.
Romano A et al. Ann Intern Med. 2007;146(4):266.
Romano A et al. N Engl J Med. 2006;354(26):2835.
Marković M et al. J Allergy Clin Immunol. 2009;124(1):167.

Example Penicillin Allergy Assessment Algorithm for Adults



SOB, shortness of breath; SJS, Stevens Johnson Syndrome; TEN, toxic epidermal necrolysis; AGEP, acute generalized exanthematous pustulosis; DRESS, Drug reaction with eosinophilia and systemic symptoms

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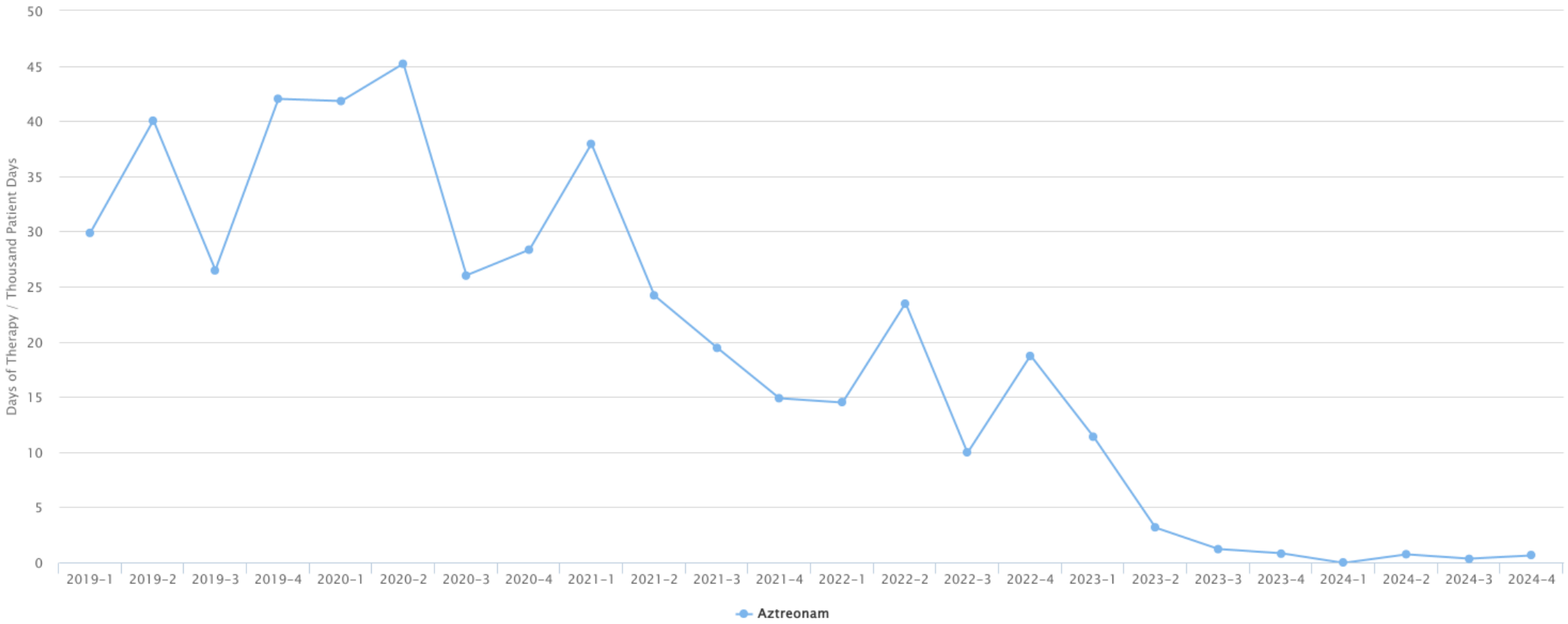
Johnson MD et al. Am J Med 2022; 135(7): 828-835.

Impact of Penicillin-Allergy Assessment on Aztreonam Use



Unpublished data, DASON (2025)

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Penicillin-Allergy Assessment

Research

JAMA Internal Medicine | Original Investigation

Efficacy of a Clinical Decision Rule to Enable Direct Oral Challenge in Patients With Low-Risk Penicillin Allergy

The PALACE Randomized Clinical Trial

Ana Maria Copaescu, MD; Sara Vogrin, MBiostat; Fiona James, BBiomedSci; Kyra Y. L. Chua, PhD; Morgan T. Rose, MBBS; Joseph De Luca, MBBS; Jamie Waldron, MD; Andrew Awad, MD; Jack Godsell, MBBS; Elise Mitri, BPharm; Belinda Lambros, MAdvNursPrac; Abby Douglas, PhD; Rabea Youcef Khoudja, MD; Ghislaine A. C. Isabwe, MD; Genevieve Genest, MD; Michael Fein, MD; Cristine Radojicic, MD; Ann Collier, MD; Patricia Lugar, MD; Cosby Stone, MD; Moshe Ben-Shoshan, MD; Nicholas A. Turner, MD; Natasha E. Holmes, PhD; Elizabeth J. Phillips, MD; Jason A. Trubiano, PhD

Multicenter non-inferiority clinical trial in outpatient adults with low-risk penicillin allergy history (PEN-FAST score <3)

Compared Direct oral challenge vs pinprick testing followed by oral challenge

Outcome: physician verified positive oral penicillin challenge (immediate reaction/anaphylaxis)

1/187 oral challenge (0.5%) vs
1/190 (0.5%) pinprick + oral challenge

Copaescu AM et al. JAMA Intern Med. 2023;183(9):944-952. doi:10.1001/jamainternmed.2023.2986
Rose M et al. J All Clin Immunol. 2024; 153(2): Supplement, AB375. https://doi.org/10.1016/j.jaci.2023.11.901

PEN-FAST Calculator

PEN-FAST - Penicillin Allergy Risk

PEN	*Penicillin allergy reported by patient*	*If yes, proceed with assessment*
F	*Five years or less since reaction*[a]	**2 points**
A	*Anaphylaxis or angioedema*	**2 points**
	OR	
S	Severe cutaneous adverse reaction[b]	
T	*Treatment required for reaction*[a]	**1 point**
		Total points

Interpretation

Points	
0	**Very low risk** of positive penicillin allergy test <1% (<1 in 100 patients reporting penicillin allergy)
1-2	**Low risk** of positive penicillin allergy test 5% (1 in 20 patients)
3	**Moderate risk** of positive penicillin allergy test 20% (1 in 5 patients)
4-5	**High risk** of positive penicillin allergy test 50% (1 in 2 patients)

https://qxmd.com/calculate/calculator_752/pen-fast-penicillin-allergy-risk-tool

Cefazolin for patients with penicillin allergy history?

- Consider if penicillin allergy was childhood reaction, intolerance, rash or IgE mediated reaction

- Examples:
- Lessard S et al. Am J Health-Syst Pharm 2023. 80: 532-536.
- VanderVelde KA et al. Antimicrob Steward Healthc Epidemiol. 2023 Jan 11;3(1):e11.
- Macy E et al. JAMA Netw Open. 2021;4(4):e218367.

Beta-lactam Cross-Reactivity- Example

Antibiotic Ordered	Antibiotic Allergy: "Penicillin"	"Cephalosporin"	Amoxicillin/Amox/clav	Ampicillin/Amp/sulb	Aztreonam	Cefaclor	Cefazolin	Cefepime	Cefotaxime	Cefoxitin	Cefdinir	Ceftaroline	Ceftriaxone	Cefuroxime	Cephalexin	Ceftazidime/avibactam	Ceftolozane/tazobactam	Nafcillin	Penicillin G	Piperacillin/tazobactam
Amoxicillin/Amox/clav [16-21]	N	CP a, b		N b	Y b	N a, b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	N b	Y b	Y b	CP b	N b	CP b
Ampicillin/Amp/sulb [16-21]	N	Cp a, b	N b		Y b	N a, b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	N b	Y b	Y b	CP b	N b	CP b
Aztreonam [17, 19, 21]	Y b	Y b	Y b	Y b		Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	N b	CP b	Y b	Y b	Y b
Cefaclor [16-21]	N	N	N a, b	N a, b	Y b		Y b	Y a, b	Y b	Y b	Y b	Y b	UA a	UA a	N a, b	Y b	Y b	Y b	UA b	CP b
Cefazolin [16-21]	Y a, b	N	Y b	Y b	Y b	Y b		Y b	Y b	Y a, b	Y b	Y b	Y a, b	Y a, b	Y b	Y b	Y b	Y b	Y b	Y b
Cefepime [16-19, 21]	Y a, b	N	Y b	Y b	Y b	Y a, b	Y b		N b	Y b	UA b	UA b	N a, b	N a, b	Y b	CP b	CP b	Y b	Y b	Y b
Cefotaxime [16-21]	Y a, b	N	Y b	Y b	Y b	Y b	Y b	N b		UA b	UA b	UA b	N a, b	N a, b	Y a, b	N a, b	CP b	Y b	Y b	Y b
Cefoxitin [16-21]	UA b	N	Y b	Y b	Y b	Y b	Y a, b	Y b	UA b		Y b	Y b	UA b	N b	Y a, b	Y b	Y b	Y b	N b	Y b
Cefdinir [16-19, 21]	Y b	N	Y b	Y b	Y b	Y b	Y b	UA b	UA b	Y b		UA b	UA b	Y b	Y b	UA b	UA b	Y b	Y b	Y b
Ceftaroline [17-19, 21]	Y b	N	Y b	Y b	Y b	Y b	Y b	UA b	UA b	Y b	UA b		UA b	UA b	Y b	UA b	UA b	Y b	Y b	Y b
Ceftriaxone [16-21]	Y a, b	N	Y b	Y b	Y b	UA a	Y a, b	N a, b	N a, b	UA b	UA b	UA b		N a, b	UA a, b	N a, b	UA b	Y b	Y b	Y b
Cefuroxime [16-21]	Y a, b	N	Y b	Y b	Y b	UA a	Y a, b	N a, b	N a, b	N b	Y b	UA b	N a, b		Y a, b	UA a, b	UA b	Y b	Y b	Y b
Cephalexin [16-21]	N a, b	N	N b	N b	Y b	N a, b	Y b	Y b	Y a, b	Y a, b	Y b	Y b	UA a, b	Y a, b		UA a	Y b	CP a	N b	CP b
Ceftazidime/avibactam [16-21]	Y a, b	N	Y b	Y b	N b	Y b	Y b	CP b	N a, b	Y b	UA b	UA b	N a, b	UA a, b	UA a		N b	Y b	Y b	Y b
Ceftolozane/tazobactam [17, 19, 21]	Y b	N	Y b	Y b	CP b	Y b	Y b	CP b	CP b	Y b	UA b	UA b	UA b	UA b	Y b	N b		Y b	Y b	N c
Ertapenem [18]	Y a, b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b
Meropenem [18]	Y a, b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b
Nafcillin [17, 19]	CP b	Y b	CP b	CP b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	CP a	Y b	Y b		CP b	CP b
Penicillin G [16-21]	N	CP b	N b	N b	Y b	UA b	Y b	Y b	Y b	N b	Y b	Y b	Y b	Y b	N b	Y b	Y b	CP b		CP b
Piperacillin/tazobactam [17-19]	N	UA	CP b	CP b	Y b	CP b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	Y b	CP b	Y b	N c	CP b	CP b	

- Ok for any but Type II-IV HSR, if type I contact provider (may be ok)
- Ok for any but Type I-IV HSR- similar side chain or limited data
- Higher likelihood of cross-reactivity
- Limited/conflicting information or similar side chain- contact provider to discuss

Collins CD et al. *Clinical Infectious Diseases*, Volume 72, Issue 8, 15 April 2021, Pages 1404 1412, https://doi.org/10.1093/cid/ciaa232

Truth

- The incidence true penicillin allergy is quite low, and the rate of cross-reactivity between members of the beta-lactam family are much lower than originally believed
- The overwhelming majority of patients that report penicillin allergy can tolerate alternative beta-lactams

Johnson MD et al. Am J Med, 2022. 135(7): 828-835. https://doi.org/10.1016/j.amjmed.2022.03.019

MYTH: CLINDAMYCIN IS A FIRST-LINE DRUG FOR PREVENTION OF SURGICAL SITE INFECTIONS IN PATIENTS WITH REPORTED PENICILLIN ALLERGIES

Duke University School of Medicine

Duke Center for Antimicrobial Stewardship and Infection Prevention

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dason.medicine.duke.edu

Background

- Clindamycin is often selected as an alternative agent for surgical prophylaxis in penicillin-allergic patients
- Recent data have demonstrated that many penicillin-allergic patients can receive cefazolin safely, and centers have incorporated this into their workflows for surgical prophylaxis
- Rate of intraoperative hypersensitivity reactions to clindamycin and/or vancomycin vs cefazolin as surgical prophylaxis was 1.3% vs 0.2%

McCreary E et al. Clinical Infectious Diseases, 2023. ciad357, https://doi.org/10.1093/cid/ciad357
Norvell MR et al. OFID 2023. 10(6): ofad224.

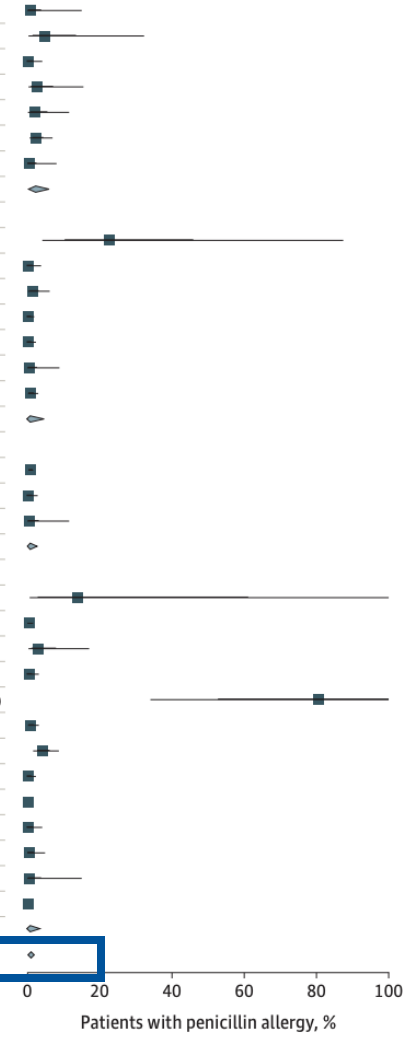
Dual allergy to penicillin & cefazolin was 0.7%

Meta-analysis of 77 studies

6147 patients

A Cefazolin allergy in patients with allergy to penicillins

Study	Patients with penicillin allergy, No./total No.	Patients with penicillin allergy, % (95% CrI)
Inpatients and ED patients		
Castleton et al,[24] 1976	0/5	0.4 (0-13.5)
Pines et al,[37] 1977	1/10	4.4 (0.2-32.6)
Fonacier et al,[28] 2005	0/37	0.2 (0-3.6)
Blumenthal et al,[23] 2015	1/21	2.5 (0.1-15.1)
Turner et al,[45] 2018	1/29	1.9 (0.1-11.2)
Blumenthal et al,[22] 2019	3/106	2.4 (0.6-6.6)
Maguire et al,[32] 2020	0/14	0.3 (0-7.2)
Subtotal 2.7% (95% CrI, 0.7%-6.1%); I^2 = 16.8%		
Mixed outpatients		
Aihara and Ikezawa,[18] 1987	3/11	23.4 (4.4-88.6)
Novalbos et al,[34] 2001	0/41	0.2 (0-3.4)
Park et al,[36] 2010	1/59	1.1 (0.1-5.8)
Ponvert et al,[38] 2011	0/150	0.1 (0-1.2)
Jimenez-Rodriguez et al,[39] 2019	0/86	0.2 (0-1.9)
Trubiano et al,[44] 2019	0/12	0.3 (0-8.0)
Romano et al,[40] 2020	1/131	0.6 (0-1.7)
Subtotal 1.0% (95% CrI, 0%-4.8%); I^2 = 81.1%		
Pregnant women		
Desai et al,[26] 2017	10/1332	0.7 (0.4-1.3)
Desravines et al,[27] 2019	0/65	0.2 (0-2.3)
Thellier et al,[43] 2020	0/8	0.4 (0-10.3)
Subtotal 0.7% (95% CrI, 0%-2.3%); I^2 = 29.2%		
Surgical patients		
Beam and Spooner,[20] 1984	1/2	14.9 (0.4-100)
Goodman et al,[29] 2001	1/299	0.3 (0-1.3)
Park et al,[35] 2006	1/19	2.7 (0.2-16.9)
Haslam et al,[30] 2012	0/54	0.2 (0-2.7)
Cook et al,[25] 2014	11/22	82.6 (34.6-100)
Beltran et al,[21] 2015	1/127	0.6 (0.1-2.8)
Laaouaj et al,[31] 2016	6/139	4.0 (1.5-8.5)
Michaud and Yen,[33] 2017	0/81	0.2 (0-2.0)
Anstey et al,[19] 2019	2/2570	0.1 (0-0.2)
Schlosser et al,[41] 2020	0/38	0.2 (0-3.5)
Stone et al,[42] 2019	0/28	0.3 (0-4.4)
Ahmad et al,[17] 2020	0/5	0.4 (0-13.6)
Lam et al,[46] 2020	0/500	0.1 (0-0.5)
Subtotal 0.7% (95% CrI, 0%-3.3%); I^2 = 85.5%		
All studies 0.7% (95% CrI, 0.1%-1.7%); I^2 = 74.9%		



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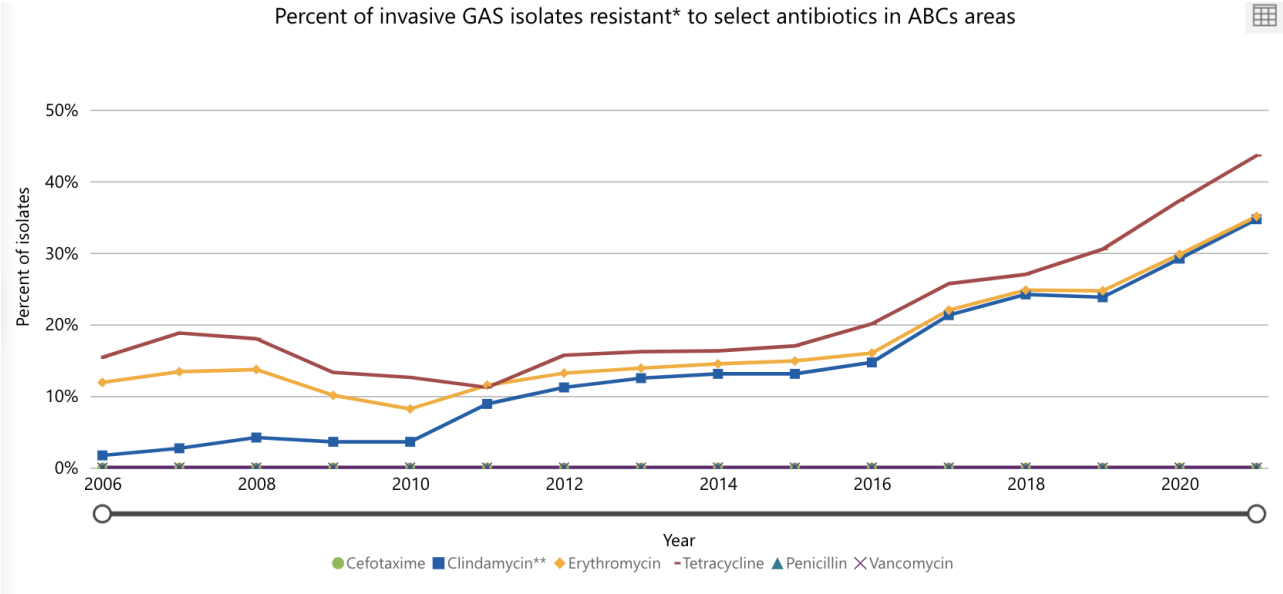
Sousa-Pinto B et al. JAMA Surg. 2021;156(4):e210021. doi:10.1001/jamasurg.2021.0021

Resistance to clindamycin has increased



https://www.cdc.gov/abcs/bact-facts-interactive-dashboard.html

White BA et al. The Lancet. 2021. 21:1208-1209.

	Clindamycin % Susceptible
MRSA	64
MSSA	70
CoNS	56

TABLE 7. Anaerobes, Percent Susceptible, National Surveillance Data[a]

Organisms	Ampicillin-Sulbactam	Clindamycin	Imipenem	Meropenem	Metronidazole	Moxifloxacin	Piperacillin-tazobactam	Penicillin
Anaerobic gram-positive cocci	N/A	97	99	100	100	72	99	100
Bacteroides fragilis	84	26	97	93	100	61	96	N/A
Bacteroides thetaiotamicron	82	28	100	99	100	54	87	N/A
Bacteroides ovatus	80	46	100	95	100	41	94	N/A
Bacteroides vulgatus	45[b]	53	97	96	100	31[b]	92	N/A
Bacteroides uniformis	84[b]	45	100[b]	100	100	48[b]	96	N/A
Parabacteroides distasonis	59[b]	43	100[b]	97	100	62	95	N/A
C. acnes (formerly P. acnes)	N/A	53[b]	94[b]	N/A	R	95	100[b]	N/A
Fusobacterium sp.	100[b]	77	95	100[b]	95	68	96	N/A
Prevotella sp.	97[b]	69[b]	100	98	99	66	100	100

2022 DUH Antibiogram, Inpatient Adult

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Truth

- The Joint Task Force of Practice Parameters suggests using structurally dissimilar cephalosporins as 1st line antibiotic agents of choice for surgical prophylaxis in patients with a history of anaphylaxis to penicillin
- The need for clindamycin in surgical prophylaxis is limited, and reduced given its increasing resistance and potential for adverse effects

Conclusions

- We have identified common myths in diagnosis and management of infectious diseases and presented evidence to dispel these myths
- This evidence-based information and the tools discussed will provide support as you continue stewardship efforts in your practice
- We encourage you to work to share this information in your hospital and leverage this to optimize antimicrobial use

Want More?

Breakpoints: The SIDP Podcast

The Society of Infectious Diseases Pharmacists provides a free educational podcast to discuss current literature, share information from infectious diseases meetings, advocate for optimal patient care, and lead antimicrobial stewardship efforts.

#85 – Who You Gonna Call? Mythbusters! Antibiotic Myths For Infectious Diseases Clinicians

MYTHBUSTERS

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https://breakpoints-sidp.org/85-who-you-gonna-call-mythbusters-antibiotic-myths-for-infectious-diseases-clinicians/

THANK YOU!

Libby Dodds Ashley

Angelina Davis

April Dyer

Jason Gallagher

Travis Jones

Erin McCreary

Shaefer Spires

Duke Center for Antimicrobial Stewardship and Infection Prevention