Dispelling Antibiotic Myths

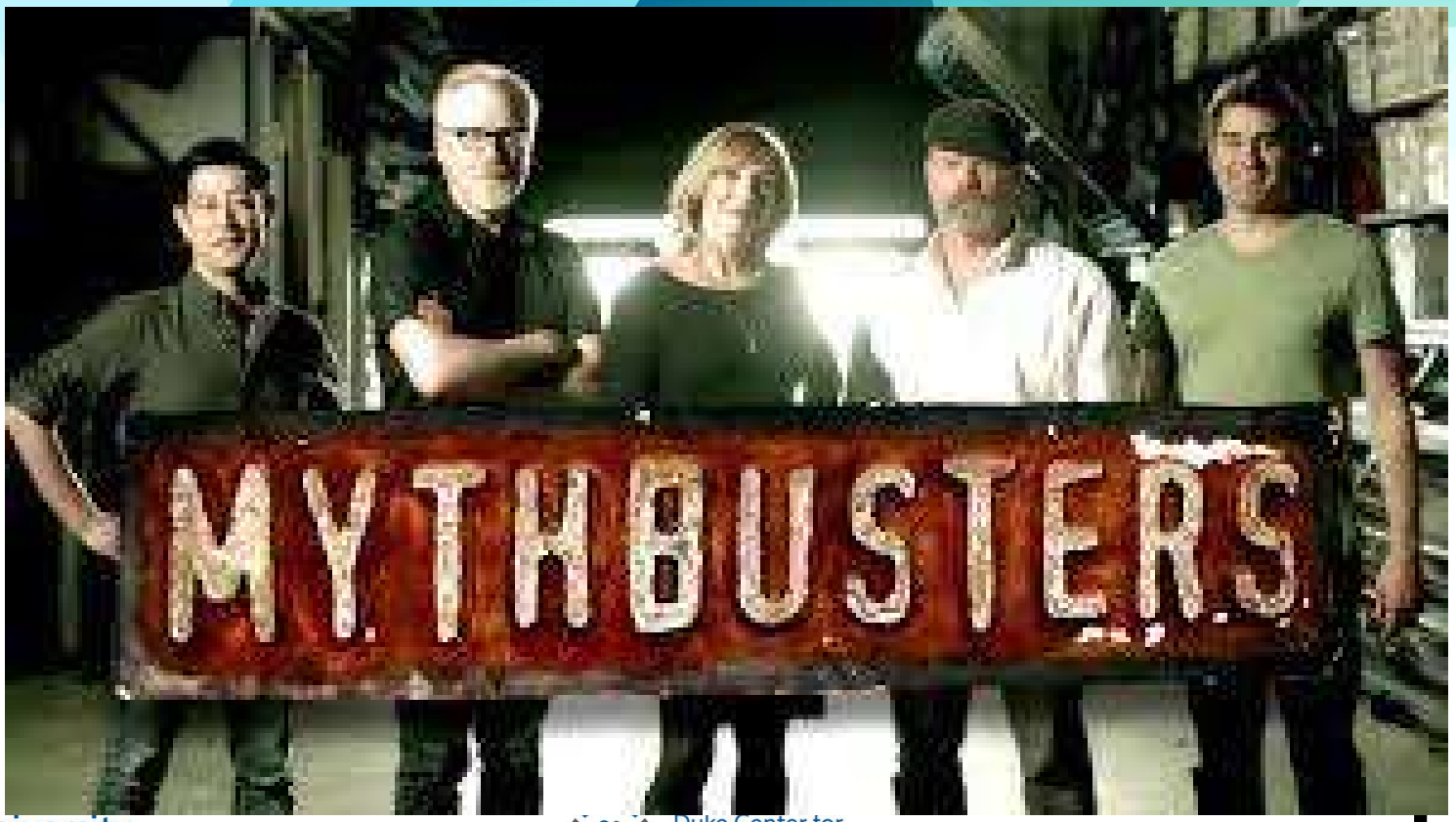
Melissa D. Johnson, PharmD, MHS, AAHIVP
Liaison Clinical Pharmacist DASON
Professor in Medicine, Duke University Medical Center

Duke University School of Medicine

Duke Center for Antimicrobial Stewardship and Infection Prevention

dason DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK

dason.medicine.duke.edu



Duke University School of Medicine

Duke Center for Antimicrobial Stewardship and Infection Prevention

dason DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK

dason.medicine.duke.edu

Duke University School of Medicine

Duke Center for Antimicrobial Stewardship and Infection Prevention

dason DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK

dason.medicine.duke.edu

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

The American Journal of Medicine
Volume 135, Issue 7, July 2022, Pages 828-835

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

Review

Legends, dogmas, presumptions, and demystifications in antibiotic therapy

Leyendas, dogmas, presunciones y desmitificaciones en antibioterapia

Rosa Blanes Hernández[1], Santiago de Cossio Tejido[1], Francesc Puchades Gimeno[2,3], Víctor García-Bustos[1,2], Miguel Salavert Lletí[1,2*]

[1]Infectious Diseases Unit, La Fe University and Polytechnic Hospital, Valencia, Spain
[2]Accredited Research Group on Severe Infection; La Fe Health Research Institute (IIS-La Fe), Valencia, Spain
[3]Internal Medicine Department. Valencia General University Hospital Consortium, Valencia, Spain

Rev Esp Quimioter 2025; 38(Suppl. 1): 70-79
https://doi.org/10.37201/req/s01.11.2025

dason DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK

MYTH: ANTIBIOTICS DO NO HARM

Duke University School of Medicine

Duke Center for Antimicrobial Stewardship and Infection Prevention

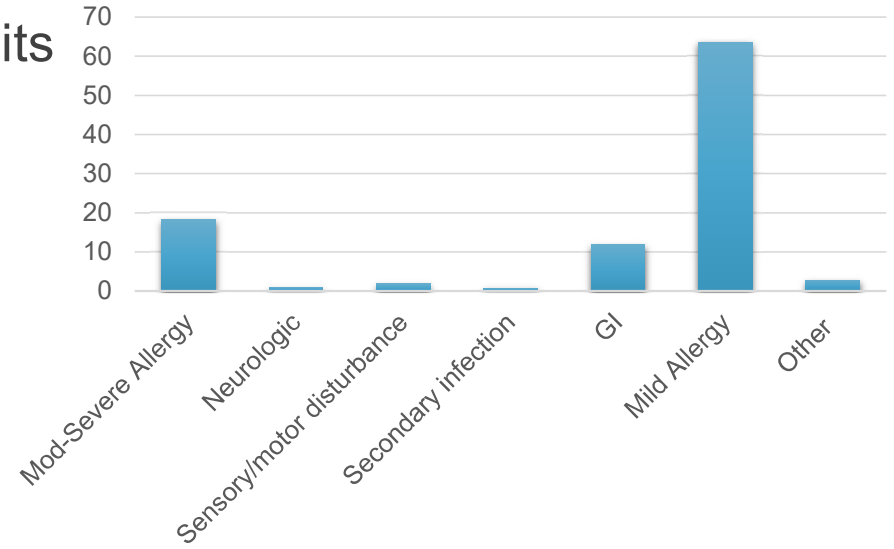
dason DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK

dason.medicine.duke.edu

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.

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: ANTIBIOTIC DURATIONS OF 7, 14, 21 DAYS ARE TYPICALLY NECESSARY

Duke University School of Medicine

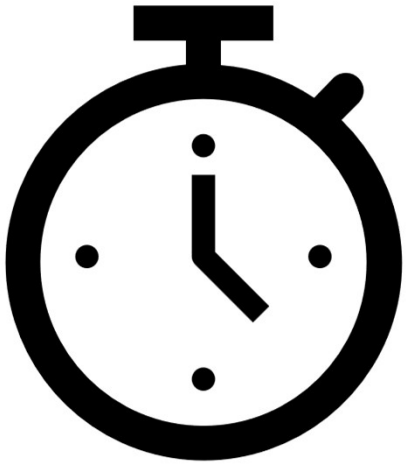
Duke Center for Antimicrobial Stewardship and Infection Prevention

dason DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK

dason.medicine.duke.edu

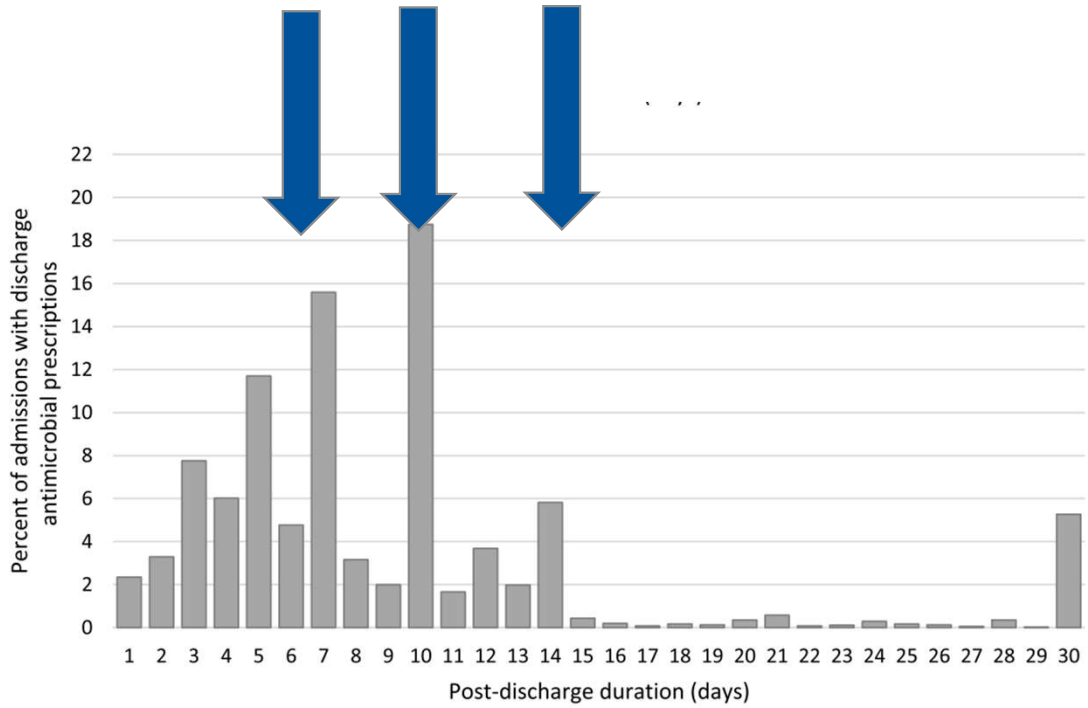
Misconceptions Leading to Prolonged Antibiotic Durations

1. Concerns over infection relapse
   - Shorter durations do not lead to relapse in pneumonia:
     - Rice LB. CID 2018;66(7):1004-12.
2. Myth that treating beyond symptom resolutions prevents antibiotic resistance
   - Longer courses lead to antibiotic resistance:
     - Chastre J, et al. JAMA 2003;290(19):2588-98.
     - Singh N, et al. Am J Resp Crit Care Med 2000;162(2 Pt 1):505-11.
3. Belief that longer durations of therapy are more effective
   - Shorter durations are just as effective for many common infections:
     - Spellberg B. JAMA Intern Med. 2016;176(9):1254-1255.
     - Spellberg B. et. al. Ann Intern Med 2019;171(3):210-11.



Common post-discharge durations

3 DASON hospitals



Duke Center for Antimicrobial Stewardship and Infection Prevention

Dyer A, et al. ICHE, 2019. 40(8): 847-54. https://doi.org/10.1017/ice.2019.118

Controlled Trials Demonstrating Short Course Therapy is Just as Effective as Longer Courses For Common Infections

Infection	Short (days)	Long (days)	Number of Supporting Randomized Controlled Trials
CAP	3-5	7-14	14
Ventilator-associated pneumonia	5-8	10-15	3
Pyelonephritis & Complicated UTI	5-7	10-14	11
Intra-abdominal infection	4	8-10	3
Gram-negative bacteremia	7	14	3
Acute exacerbation of Chronic Bronchitis & Sinusitis	≤5	≥7	>25
Cellulitis (ABSSSI)	5-6	10	4
Chronic osteomyelitis	42	84	2
Septic arthritis	14	28	1
Osteomyelitis w/ removed implant	28	42	1
Neutropenic fever	AF X 72h	Once ANC >500	2

https://www.bradspellberg.com/shorter-is-better; Hernandez RB. Rev Esp Quimioter 2025; 38(Suppl. 1): 70-79 https://doi.org/10.37201/req/s01.11.2025

Dangers of excessive antibiotic durations

There is evidence concluding that “shorter is better” in terms of duration.

Increased duration of therapy means increased:

- Risk of adverse effects including *C. difficile* infection
- Risk for developing antibiotic resistance
- Burden on healthcare resources (time and cost)

Spellberg B. The New Antibiotic Mantra- "Shorter Is Better". JAMA Intern Med. 2016;176(9):1254-1255.

Stewardship interventions targeted at durations

- Antibiotic “time out” / prospective audit-feedback
- Automatic stop orders (35% decrease in antibiotic use)
- Display of buttons for shorter durations
- Removal of default durations from EHR order panels
- Transition of care interventions aimed at impacting overall duration

Sun S et al. Pediatrics 2021. 147(6): e2020034819. doi: 10.1542/peds.2020-034819.
Wrenn RH et al. Infec Control Hosp Epi 2024; Feb 13. doi: 10.1017/ice.2024.16

Transitions of Care Example

eFigure 1. Institutional Guidelines for Antimicrobial Selection and Duration of Therapies at the Time of Intervention Implementation

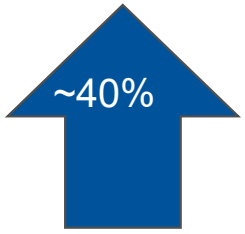
Institutional Oral Antimicrobial Selection and Duration Guidance*			
Respiratory Tract Infections	Community-acquired pneumonia, with or without risk factors (without microbiologic data)	• Amoxicillin-clavulanic acid 1000/62.5 mg 2 tabs BID + (azithromycin 500 mg daily or doxycycline 100 mg BID) • Cefuroxime 500 mg BID OR cefpodoxime 400 mg BID + (azithromycin 500 mg daily or doxycycline 100 mg BID) • Doxycycline 100 mg BID • Moxifloxacin 400 mg OR levofloxacin 750 mg daily	5 days in patients with prompt clinical response 7-10 days in patients with structural lung disease or delayed response
	Acute exacerbation of COPD (AECOPD)	• Doxycycline 100 mg BID • Azithromycin 500 mg x1 then 250 mg daily	5-7 days
	Hospital acquired pneumonia	• Moxifloxacin 400 mg OR levofloxacin 750 mg daily	7 days w/ prompt clinical response: tailor therapy to microbiologic data
	Influenza	• Oseltamivir 75 mg BID	5 days
Urinary Tract Infections	Uncomplicated UTI/cystitis: Align with organism susceptibility	• Nitrofurantoin (NFT) 100 mg BID • Sulfamethoxazole/trimethoprim (SMT) 1 DS tab BID • Beta-lactam (targeted to organism) • Fosfomycin 3 gm oral sachet (MDRO history only)	• NFT: 5 days • SMT: 3 days • Beta-lactams: 3-7 days • Fosfomycin: 2-3 doses
	Complicated UTI/ pyelonephritis Align with organism susceptibility	• Sulfamethoxazole/trimethoprim (SMT) 1-2 DS tab BID • Ciprofloxacin 500 mg BID • Beta-lactams (targeted to organism)	• SMT: 10-14 days* • Fluoroquinolones: 7 days • Beta-lactams: 10-14 days
	Asymptomatic bacteriuria	• Do not treat if not pregnant, or perioperative prophylaxis	0 days

Institutional Oral Antimicrobial Selection and Duration Guidance			
Skin Structure Infection	Non-purulent cellulitis	• Cephalexin 500 mg QID, Cefuroxime 500 mg BID • Dicloxacillin 500 mg QID • Clindamycin 300-450 mg TID (severe beta lactam allergy)	5 days with prompt clinical response
	Purulent cellulitis/cutaneous abscess (suspected MRSA)	• Doxycycline 100 mg BID • Sulfamethoxazole/trimethoprim 1-2 DS BID	5 days with prompt clinical response
Intra-abdominal infection	Spontaneous bacterial peritonitis	• Moxifloxacin 400 mg or levofloxacin 750 mg daily	5 days
	Complicated, community acquired intra-abdominal infection **with source control** e.g., appendicitis, cholecystitis, diverticulitis s/p removal of foci	• Moxifloxacin 400 mg daily • Ciprofloxacin 500 mg BID + metronidazole 500 mg BID/TID • Cefuroxime 500 mg BID + metronidazole 500 mg BID • Amoxicillin-clavulanic acid 875/125 mg BID	4-7 days after source control 7 days targeted therapy in transient bacteremia after foci removed

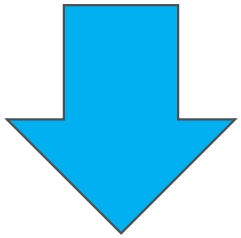
*Disclaimer: Guidelines for oral antimicrobial selection and duration were developed at the time of the intervention implementation. Local guidance should be considered with antibiogram and updated literature.

Mercurio NJ et al. JAMA Netw Open. 2022 May 2;5(5):e2211331. doi: 10.1001/jamanetworkopen.2022.11331.

Transitions of Care Stewardship



Optimal prescribing



Severe Antimicrobial-Related Adverse Events

3.2% post-intervention vs 9% pre-intervention

Decreased total antimicrobial duration (time-adjusted absolute difference, −1.1 [95% CI, −1.7 to −0.6] antibiotic days)

Duration of antimicrobial therapy for respiratory tract infection was reduced (time-adjusted absolute difference, −1.8 [95% CI, −2.3 to −1.2] antibiotic-days)

No differences in clinical resolution or mortality

Duke Center for Antimicrobial Stewardship and Infection Prevention

Mercurio NJ et al. JAMA Netw Open. 2022 May 2;5(5):e2211331. doi: 10.1001/jamanetworkopen.2022.11331.

Truth

- Durations of therapy should be based on best available evidence and the patient's clinical course, rather than an arbitrary number such as 7, 14, or 21 days.

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

Duke University School of Medicine

Duke Center for Antimicrobial Stewardship and Infection Prevention

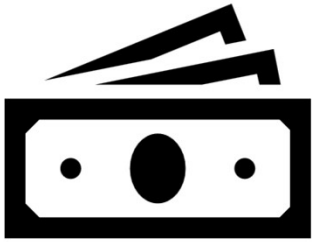
dason DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK

dason.medicine.duke.edu

Cost of Redundant Therapy to US Hospitals

Annual avoidable cost of combination therapy to US hospitals=

$50-100 million

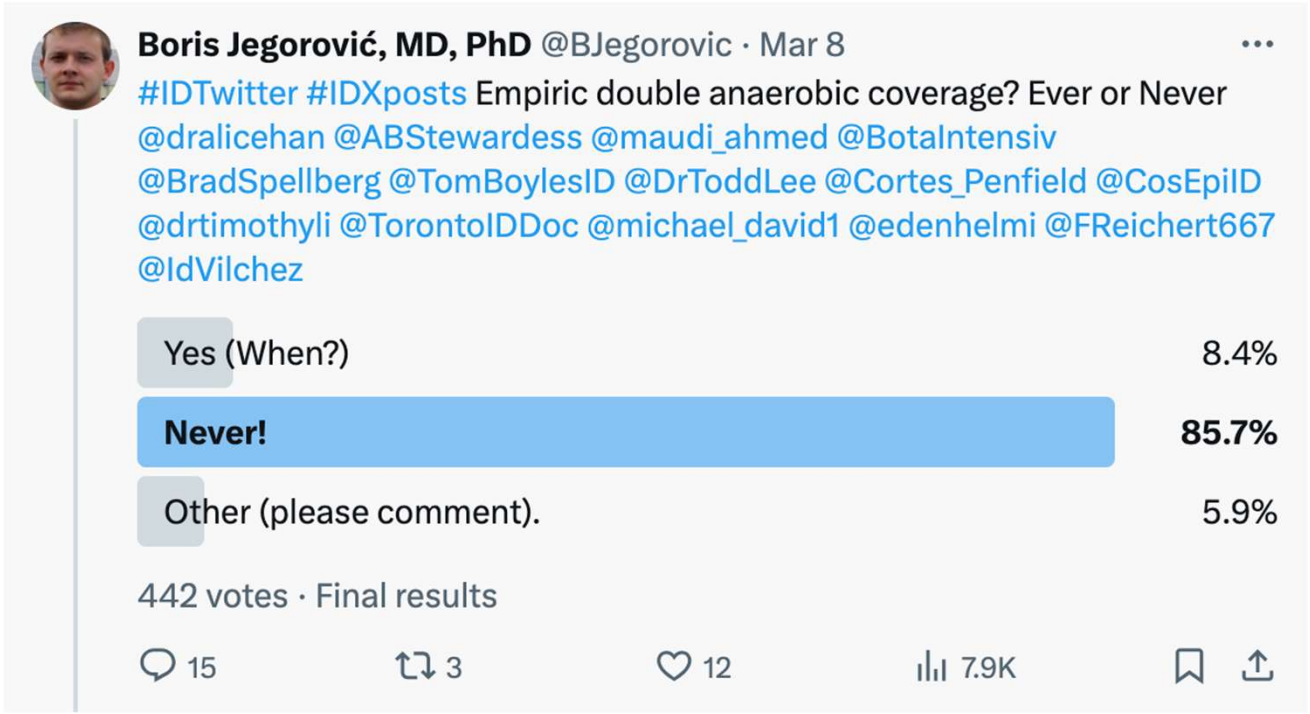


53%

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: ORAL ANTIBIOTICS ARE NOT AS GOOD AS IV ANTIBIOTICS FOR HOSPITALIZED PATIENTS

Duke University School of Medicine

Duke Center for Antimicrobial Stewardship and Infection Prevention

dason DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK

dason.medicine.duke.edu

Background

- Intravenous (IV) administration allows for rapid attainment of peak drug levels for optimal treatment of serious infections.
- For this reason, IV antibiotics are often prescribed for hospitalized patients.
- However, routine use is not indicated solely based on hospital admission.

Factors to consider:

- Bioavailability of the oral agent
- Ability to swallow or absorb medications via the oral route
- Severity of illness
- Clinical stability
- Isolated pathogen
- Site of infection

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

What are the data?

PRO

- Some serious infections (ie, chronic osteomyelitis, infective endocarditis, bacteremia from a urinary source) can be successfully managed with a step-down to a highly bioavailable oral agent
- Full oral antibiotic therapy has been successful in periprosthetic joint infections and streptococcal bacteremia

CON

- Clinical failure has been observed with oral step-down prior to day 3 and low-dose oral stepdown therapy in streptococcal bacteremia

Gram Negative Bacteremia

Antimicrobial Stewardship & Healthcare Epidemiology (2023), **3**, e148, 1–6
doi:10.1017/ash.2023.435

SHEA

Original Article

Outcomes of high-dose oral beta-lactam definitive therapy compared to fluoroquinolone or trimethoprim-sulfamethoxazole oral therapy for bacteremia secondary to a urinary tract infection

Abigail C. Geyer PharmD[1], Kali M. VanLangen PharmD[1,2], Andrew P. Jameson MD[3,4] and Lisa E. Dumkow PharmD[1]

[1]Department of Pharmacy, Trinity Health Grand Rapids, Grand Rapids, MI, USA, [2]Ferris State University, College of Pharmacy, Grand Rapids, MI, USA, [3]Division of Infectious Disease, Trinity Health Grand Rapids, Grand Rapids, MI, USA and [4]Department of Medicine, Michigan State College of Human Medicine, Grand Rapids, MI, USA

Oral Antibiotic	Dose for CrCL ≥50 ml/min
Amoxicillin	1000 mg TID
Cephalexin	1000 mg TID
Ciprofloxacin	500-750 mg BID
Levofloxacin	500-750 mg daily
TMP/SMX	2 DS BID

Retrospective observational multicenter study, 3 community teaching hospitals

194 adult inpatients receiving empiric IV antibiotics transitioned to oral cephalexin, amoxicillin, fluoroquinolone, or TMP/SMX

Primarily *E. coli* or *Klebsiella* infections

Similar 30-day mortality/recurrent bacteremia (1.3% beta-lactam vs 1.7%) FQ or TMP/SMX

Geyer AC et al. Antimicrob Steward Healthc Epidemiol. 2023, 3, e148, 1-6.

Truth

- Although the optimal time to step-down therapy has not been clearly defined, successful step-down therapy has been achieved as early as day 3 of IV therapy.
- Consider the following: clinical stability, absence of fever, and resolving leukocytosis.
- Doses of oral antibiotics in this setting should be optimized
- IV therapy is still recommended for infections where drug levels at the site of infection may be limited, or the host response is severely compromised (ie, meningitis, high-risk neutropenia).

Duke Center for Antimicrobial Stewardship and Infection Prevention

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

Duke University School of Medicine

Duke Center for Antimicrobial Stewardship and Infection Prevention

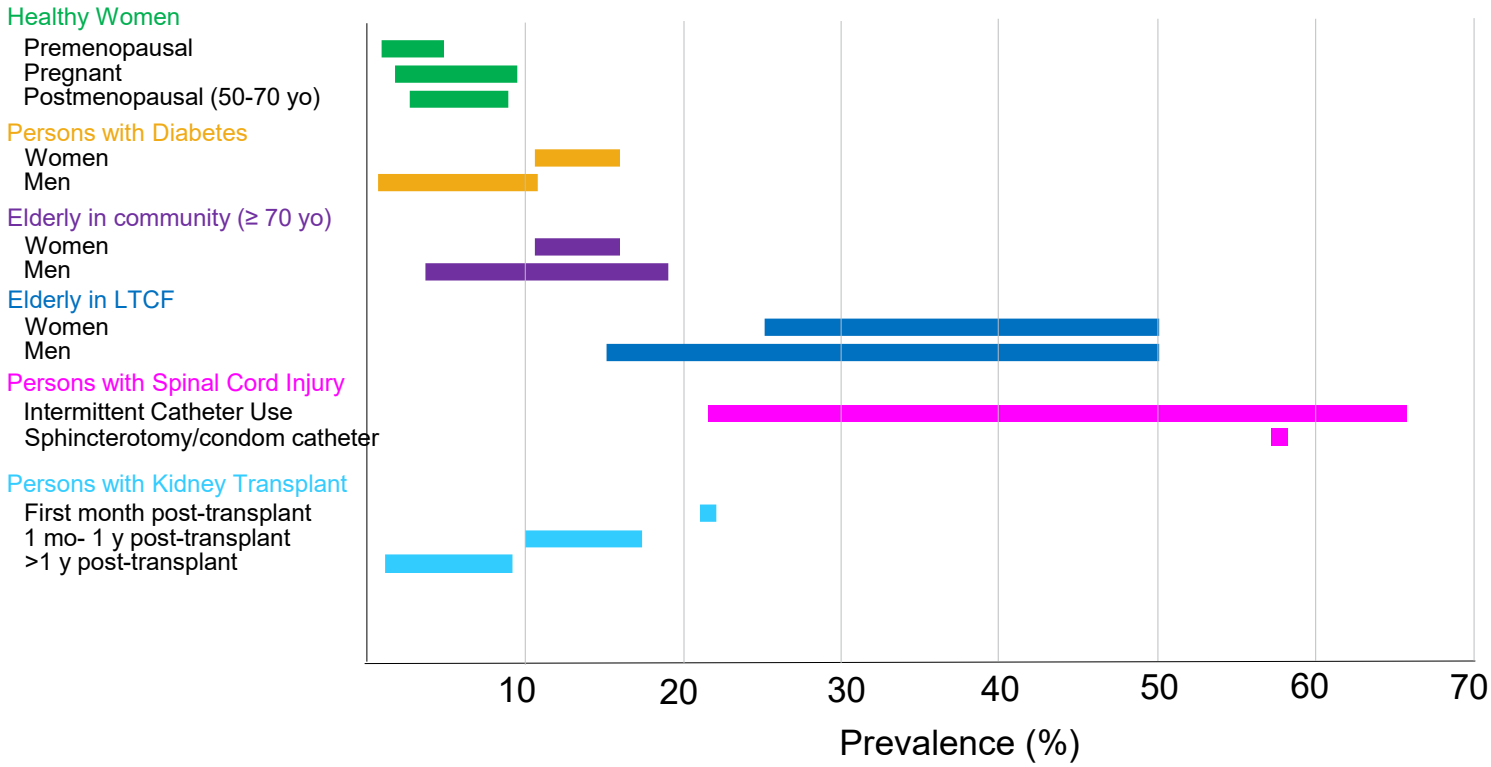
dason DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK

dason.medicine.duke.edu

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%** !

dason DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK

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

- 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

SHOULD BE SCREENED/TREATED

- 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.

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 Osterholz
Mariam Younas, MD; Steven J. Bernstein, MD, MPH; Stephanie Burdick, MD; David Ratz, MS; Julia E. Szymczak, P
Tawny Czilok, MHI, RN; Tanima Basu, MA, MS; Jennifer K. Horowitz, MA; Scott A. Flanders, MD; Tejal N. Gandhi, M

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%

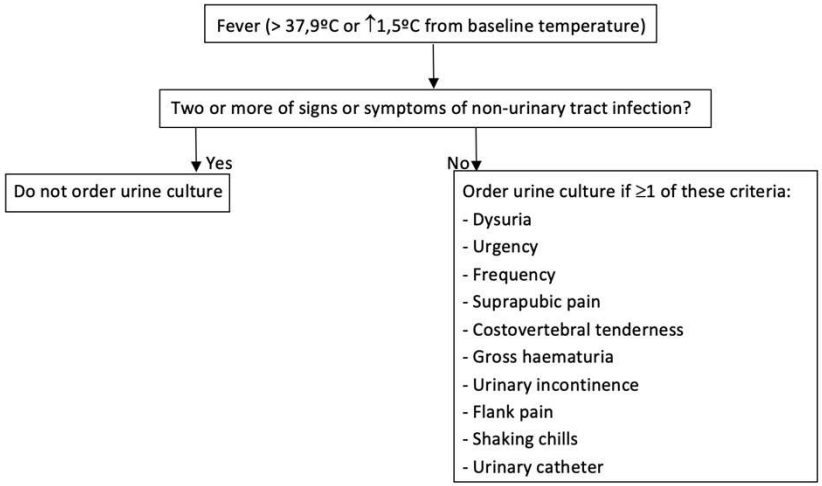
- Antimicrobial Stewardship outcome
- percent of patients with ASB that got antibiotics was not significantly changed over the study period (82% to 76.3%) & mean duration was similar (6.38 days to 5.93 days)

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

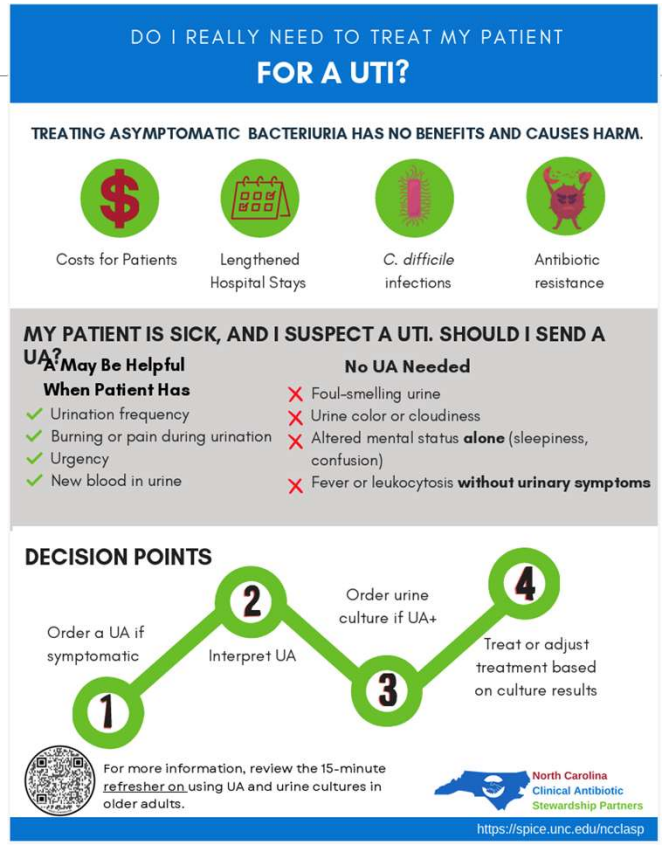
Vaughn VM et al. JAMA Intern Med. 2023;183(9):933-941. doi:10.1001/jamainternmed.2023.2749

Algorithms/tools to guide UTI workup in Nursing Home Residents

- Example: Revised Loeb Criteria



Llor C et al. Clinical Microbiol and Infection. 2024: 30(12): 1523-1528. https://doi.org/10.1016/j.cmi.2024.08.020



https://spice.unc.edu/resource_topics/uti/

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

Duke University School of Medicine

Duke Center for Antimicrobial Stewardship and Infection Prevention

dason DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK

dason.medicine.duke.edu

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

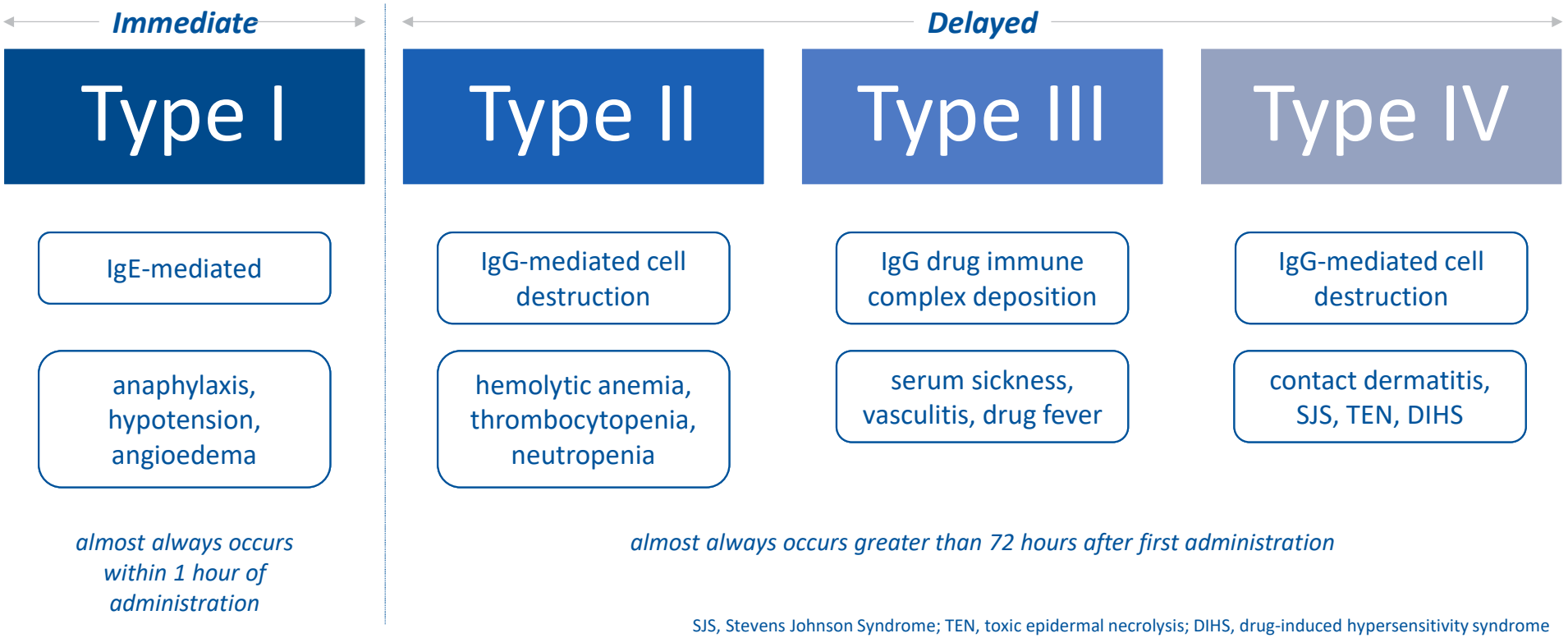
Figure adapted from www.cdc/gov/getsmart.

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

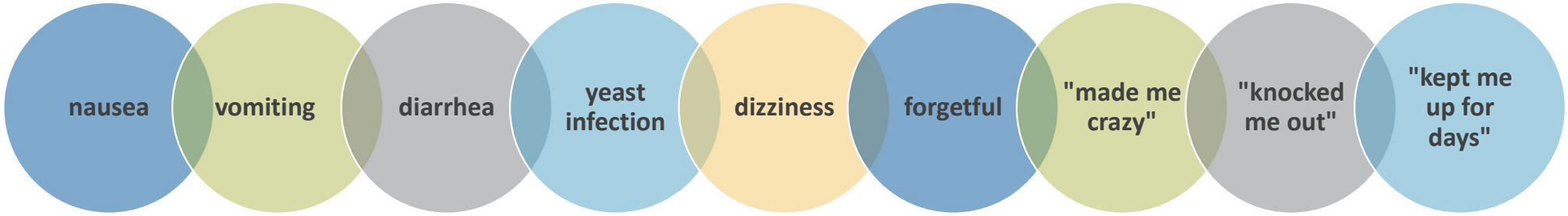
Macy E et al. J Allergy Clin Immunol 2014;133:790-96.

Overview of Hypersensitivity Reactions:

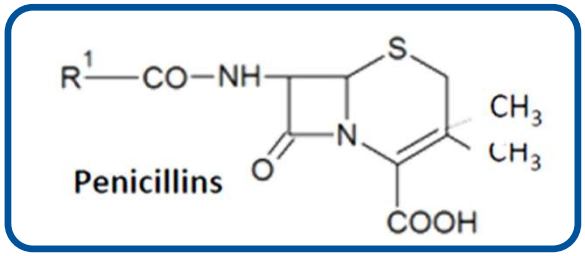


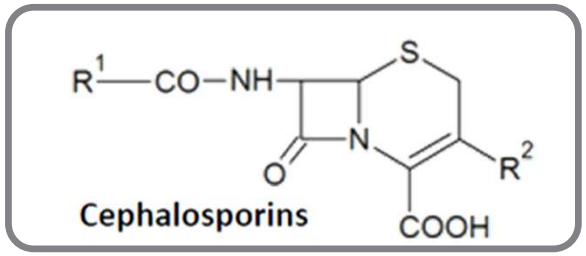
SJS, Stevens Johnson Syndrome; TEN, toxic epidermal necrolysis; DIHS, drug-induced hypersensitivity syndrome

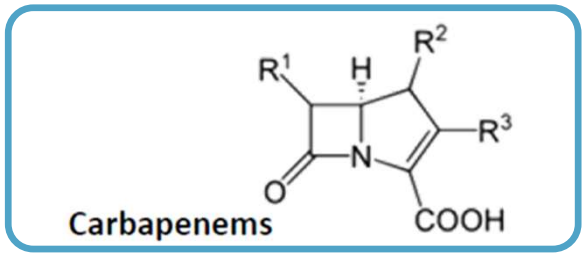
Overview of Intolerances:



Cross-reactivity Among Beta-lactams







Aminopenicillins:

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

Cephalosporins:

0.17% to 8.4%

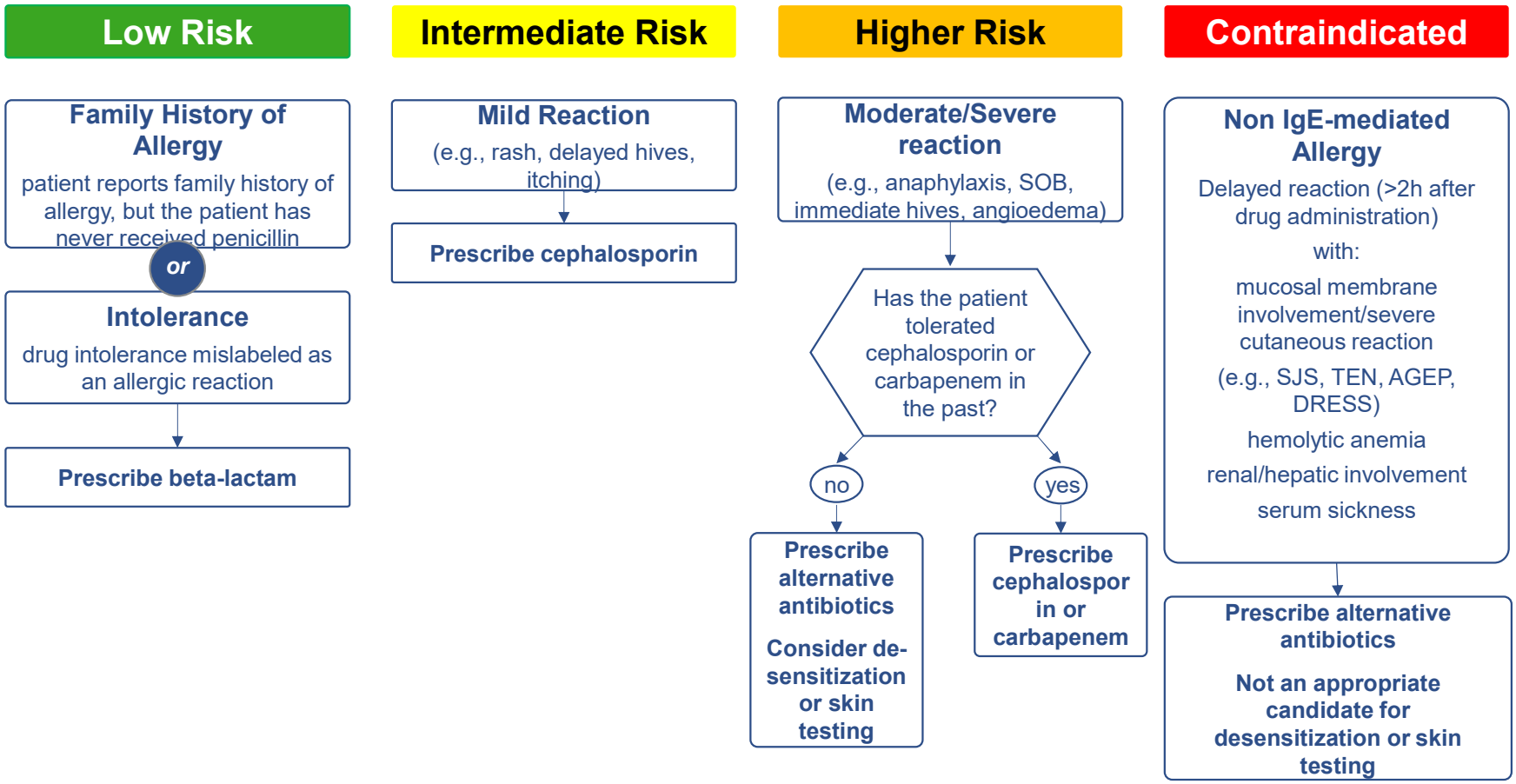
Carbapenems:

< 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

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

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)

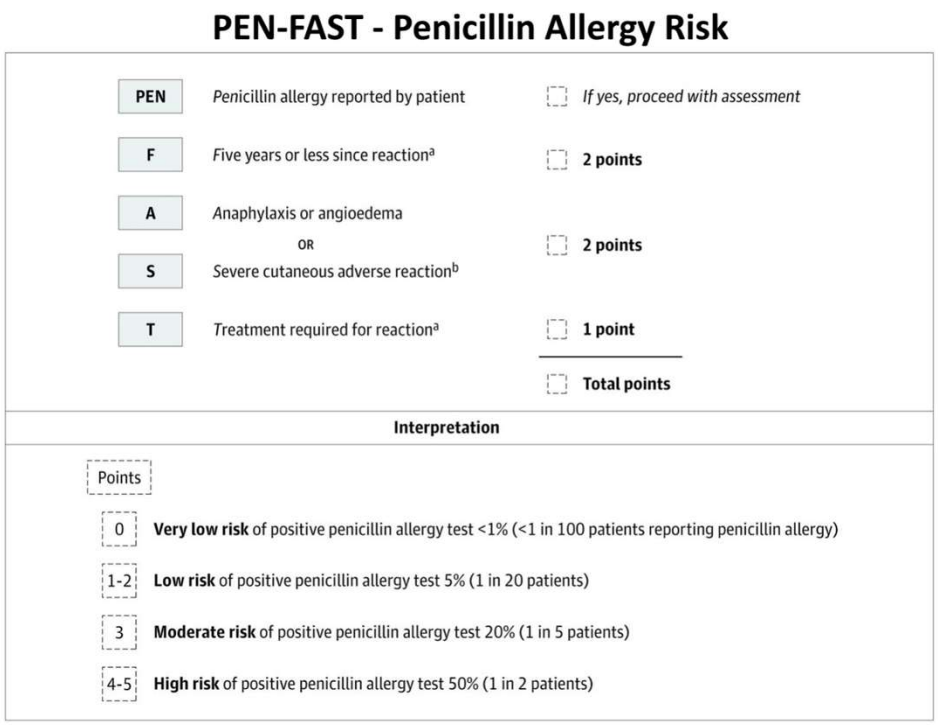
Compared Direct oral challenge vs pinprick testing followed by oral challenge

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	
	OR	☐ **2 points**
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

Cephalosporins for patients with penicillin allergy history?

- Consider if penicillin allergy was childhood reaction, intolerance, rash or IgE mediated reaction
- Drug Allergy Practice Parameters Update, 2022:
  - "*patients with a history of an unverified nonanaphylactic penicillin allergy, any cephalosporin can be administered routinely without testing or additional precautions. For example, patients with a history of urticaria to a penicillin can receive any cephalosporin routinely without prior testing*"
  - "*for those rare patients with a history of anaphylaxis to penicillin, a non–cross-reactive cephalosporin (eg, cefazolin) can be administered routinely without prior testing*"

- 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.

J All Clin Immunol 2022; https://doi.org/10.1016/j.jaci.2022.08.028

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	CPa,b		Nb	Yb	Na,b	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Nb	Yb	Yb	CPb	Nb	CPb
Ampicillin/Amp/sulb [16-21]	N	Cpa,b	Nb		Yb	Na,b	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Nb	Yb	Yb	CPb	Nb	CPb
Aztreonam [17, 19, 21]	Yb	Yb	Yb	Yb		Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Nb	CPb	Yb	Yb	Yb
Cefaclor [16-21]	N	N	Na,b	Na,b	Yb		Yb	Ya,b	Yb	Yb	Yb	Yb	UAa	UAa	Na,b	Yb	Yb	Yb	UAb	CPb
Cefazolin [16-21]	Ya,b	N	Yb	Yb	Yb	Yb		Yb	Yb	Ya,b	Yb	Yb	Ya,b	Ya,b	Yb	Yb	Yb	Yb	Yb	Yb
Cefepime [16-19, 21]	Ya,b	N	Yb	Yb	Yb	Ya,b	Yb		Nb	Yb	UAb	UAb	Na,b	Na,b	Yb	CPb	CPb	Yb	Yb	Yb
Cefotaxime [16-21]	Ya,b	N	Yb	Yb	Yb	Yb	Yb	Nb		UAb	UAb	UAb	Na,b	Na,b	Ya,b	Na,b	CPb	Yb	Yb	Yb
Cefoxitin [16-21]	UAb	N	Yb	Yb	Yb	Yb	Ya,b	Yb	UAb		Yb	Yb	UAb	Nb	Ya,b	Yb	Yb	Yb	Nb	Yb
Cefdinir [16-19, 21]	Yb	N	Yb	Yb	Yb	Yb	Yb	UAb	UAb	Yb		UAb	UAb	Yb	Yb	UAb	UAb	Yb	Yb	Yb
Ceftaroline [17-19, 21]	Yb	N	Yb	Yb	Yb	Yb	Yb	UAb	UAb	Yb	UAb		UAb	UAb	Yb	UAb	UAb	Yb	Yb	Yb
Ceftriaxone [16-21]	Ya,b	N	Yb	Yb	Yb	UAa	Ya,b	Na,b	Na,b	UAb	UAb	UAb		Na,b	UAa,b	Na,b	UAb	Yb	Yb	Yb
Cefuroxime [16-21]	Ya,b	N	Yb	Yb	Yb	UAa	Ya,b	Na,b	Na,b	Nb	Yb	UAb	Na,b		Ya,b	UAa,b	UAb	Yb	Yb	Yb
Cephalexin [16-21]	Na,b	N	Nb	Nb	Yb	Na,b	Yb	Yb	Ya,b	Ya,b	Yb	Yb	UAa,b	Ya,b		UAa	Yb	CPa	Nb	CPb
Ceftazidime/avibactam [16-21]	Ya,b	N	Yb	Yb	Nb	Yb	Yb	CPb	Na,b	Yb	UAb	UAb	Na,b	UAa,b	UAa		Nb	Yb	Yb	Yb
Ceftolozane/tazobactam [17, 19, 21]	Yb	N	Yb	Yb	CPb	Yb	Yb	CPb	CPb	Yb	UAb	UAb	UAb	UAb	Yb	Nb		Yb	Yb	Nc
Ertapenem [18]	Ya,b	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb
Meropenem [18]	Ya,b	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb
Nafcillin [17, 19]	CPb	Yb	CPb	CPb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	CPa	Yb	Yb		CPb	CPb
Penicillin G [16-21]	N	CPb	Nb	Nb	Yb	UAb	Yb	Yb	Yb	Nb	Yb	Yb	Yb	Yb	Nb	Yb	Yb	CPb		CPb
Piperacillin/tazobactam [17-19]	N	UA	CPb	CPb	Yb	CPb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	Yb	CPb	Yb	Nc	CPb	CPb	

- 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

dason DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK

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%

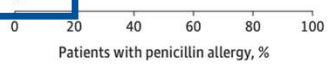
Meta-analysis of 77 studies

6147 patients

Duke Center for Antimicrobial Stewardship and Infection Prevention

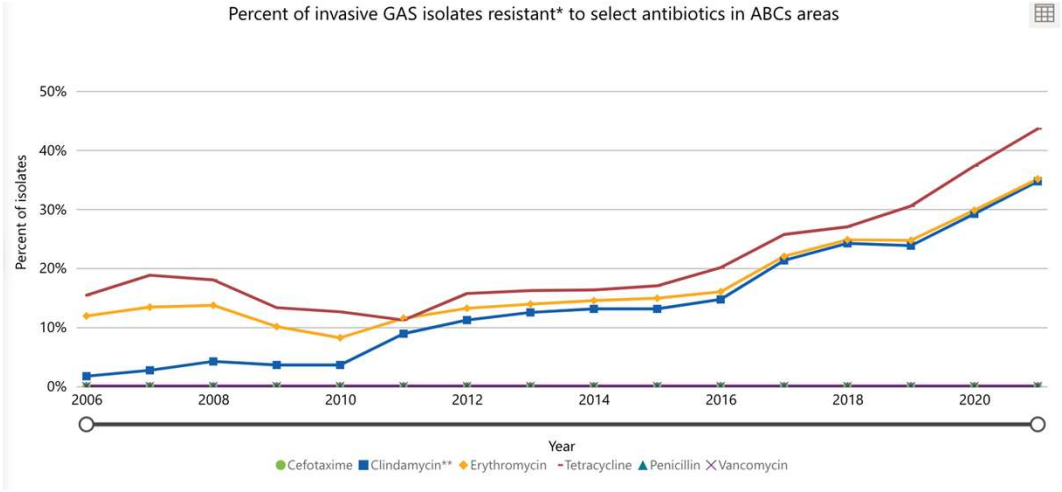
A Cefazolin allergy in patients with allergy to penicillins

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%		



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

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

MYTH: NITROFURANTOIN CAN BE USED FOR UTIS ONLY IF CREATININE CLEARANCE EXCEEDS 60 ML/ MIN

Duke University School of Medicine

Duke Center for Antimicrobial Stewardship and Infection Prevention

dason DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK

dason.medicine.duke.edu

Background

- Nitrofurantoin is an orally administered nitrofuran antibiotic with 40% of the active drug excreted in the urine.
- Nitrofurantoin has retained excellent activity against bacteria, especially Escherichia coli.
- It is recommended by the Infectious Diseases Society of America as a first-line treatment for uncomplicated cystitis in females, and emerging data support its use for cystitis in males.
- However, there have been concerns about both the efficacy and safety of nitrofurantoin in patients with renal impairment.

Where are we now?

PRO

- More recent studies have suggested that the labeled cut-off of 60 mL/min for use of nitrofurantoin when treating cystitis may be unwarranted
- More limited evidence supporting efficacy for those with creatinine clearances of 30 ml/min

CON

- A few retrospective studies have suggested that efficacy may be lower in those with clearances <60 mL/min
- Chronic (>14 days), rather than acute, use of nitrofurantoin was associated with a higher risk of pulmonary toxicity in an elderly population

Truth

CLINICAL INVESTIGATIONS

American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults

*By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel**

See related editorial by Steinman et al. in this issue.

The American Geriatrics Society (AGS) Beers Criteria®

existing criteria should be removed or undergo changes to their recommendation, rationale, level of evidence, or

Anti-infective				
Nitrofurantoin	Potential for pulmonary toxicity, hepatoxicity, and peripheral neuropathy, especially with long-term use; safer alternatives available	Avoid in individuals with creatinine clearance <30 mL/min or for long-term suppression	Low	Strong

under specific situations, such as in certain diseases or conditions. For the 2019 update, an interdisciplinary expert

JAGS 67: 674 – 694, 2019

Duke Center for Antimicrobial Stewardship and Infection Prevention

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

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