

Antibiotic Therapy: When Are Shorter Courses Better?



Updated October 2025

To determine the appropriate duration of antibiotic therapy, consider infection type, source control, severity of infection, antibiotic choice, symptom resolution, potential for relapse, comorbidities, and immune status.¹⁻³ See our toolbox, *Antimicrobial Stewardship*, for more on using antibiotics effectively.



What are the benefits of shorter courses of antibiotics?

- minimized risk of antibiotic resistance.4
- reduced **adverse effects** from the antibiotic and/or superinfections from eliminating normal flora (e.g., *Clostridium difficile*). lower **cost** and improved **adherence** with fewer antibiotic doses. ³

What duration of antibiotic therapy is appropriate for common infections?

Common Infection	Duration of Antibiotic Therapy
Acute sinusitis	 Antibiotics are not usually necessary, as most cases are viral or self-limiting bacterial infections.⁵ For acute uncomplicated bacterial sinusitis in adults, recommend 5 to 7 days of antibiotics.⁵ Longer durations (e.g., 10 to 14 days) may be necessary for more complicated infections and in children.⁵
Acute bronchitis	 Antibiotics are not routinely recommended for acute uncomplicated bronchitis.⁶ Rule out pneumonia and treat acute exacerbations of chronic bronchitis and <u>COPD</u> appropriately.⁶
Community acquired pneumonia	 Recommend 3 to 5 days (5 days in Canada) of antibiotics, provided patient becomes clinically stable.^{7,8} Recommend longer therapy for CAP due to suspected or proven MRSA, <i>Pseudomonas aeruginosa</i>, <i>Staphylococcus aureus</i>, suspected <i>Legionella pneumophila</i>, or other intracellular microorganisms.⁷ Longer courses may also be necessary in certain patients (e.g., recent hospitalization, long-term care resident, underlying lung disease, high burden of disease on x-ray).⁷
<u>Cellulitis</u>	 Recommend 5 days (5 to 7 days in Canada) for most patients with uncomplicated cellulitis that show improvement.^{4,9} Longer courses may be needed if there is insufficient improvement, or in more complicated/severe cases (e.g., purulent/skin abscess, when debridement is necessary, deep soft tissue infections).⁹
Hospital- and ventilator-associated pneumonia	 Recommend 7 days of antibiotics for both HAP and VAP.¹⁰ Use clinical criteria (e.g., cultures, fever) and consider using procalcitonin (PCT) levels to determine duration.¹⁰ Longer courses may be necessary in some patients (e.g., known Pseudomonas or Acinetobacter).¹⁰
Intra-abdominal infections	 Recommend 4 days of antibiotics if the source of the infection is controlled. 11,12 If using medical management only (i.e., no surgical intervention), longer courses of antibiotic therapy are needed. 11,12
<u>Osteomyelitis</u>	 Generally, recommend 6 weeks of antibiotic therapy for uncomplicated cases of osteomyelitis.⁴ Shorter courses may be used in some cases (e.g., post-surgical drainage when organism known, pediatric acute osteomyelitis).⁴ Longer durations are often necessary in complicated cases (e.g., implants, prosthetic joints, undrained abscesses).⁴
Otitis media, acute	 Antibiotics are not always necessary, as many cases are viral or self-limiting bacterial infections.⁴ Recommend oral pain relievers for less severe cases (symptoms <48 hours, temperature <102.2°F [39°C], mild ear pain, no drainage from the ear) and observation/"watchful waiting" (antibiotic treatment is recommended for bilateral AOM in ages 6 months to 23 months). ^{13,14} Recommend 10 days of therapy for children younger than 2 years, recurrent otitis media, or a ruptured eardrum. ^{13,14} Recommend 5 to 7 days (5 days in Canada) of antibiotic therapy for children 2 years and older. ^{13,14}
UTI, pediatric	 Recommend 7 to 10 days (7 to 14 days in Canada) of antibiotics for most children with an UTI. 15,16 Consider a shorter course of antibiotics (e.g., 2 to 4 days) for older, school-aged children without fever. 4,16
UTI, uncomplicated adult	 Recommend short courses of antibiotics for uncomplicated UTI (e.g., 3 days with trimethoprim/sulfamethoxazole, 5 days with nitrofurantoin).^{4,17} Longer durations of therapy are necessary for complicated UTIs (e.g., during pregnancy, catheter-associated).^{4,18}
<u>Pyelonephritis</u>	 Recommend a short course (5 to 7 days of a fluoroquinolone OR 7 days with a non-fluoroquinolone) for uncomplicated pyelonephritis. Longer courses (e.g., 10 to 14 days) may be necessary if treating with trimethoprim/sulfamethoxazole, males, some hospitalized patients (e.g., bacteremia and hypotension), those with urogenital abnormalities.
Uncomplicated gram- negative bacteremia	Recommend 7 days of antibiotics for most patients. ²⁰
Confirmed strep throat	 Treat effectively to eradicate from the pharynx and to prevent complications (e.g., rheumatic fever).²¹ Recommend 10 days of amoxicillin or penicillin for most patients with acute group A streptococcal pharyngitis.^{4,21} Consider a one-time intramuscular injection of benzathine penicillin G for patients unlikely to be adherent for 10 days.²¹
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When are prescribed antibiotics **required** to be completed?

- Patients should not stop antibiotics (even if symptoms resolve) for active tuberculosis, endocarditis, osteomyelitis, or strep throat. 4
- Patients should complete the prescribed duration of therapy for these potentially asymptomatic conditions:

 o asymptomatic bacteriuria during pregnancy

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Abbreviations

AOM = acute otitis media; CAP = community-acquired pneumonia; COPD = chronic obstructive pulmonary disease; HAP = hospital-acquired pneumonia; MRSA = methicillin-resistant Staphylococcus aureus; UTI = urinary tract infection; VAP = ventilator-associated pneumonia.

References

- 1. Spellberg B. The New Antibiotic Mantra-"Shorter Is Better". JAMA Intern Med. 2016 Sep 1;176(9):1254-5.
- 2. Uranga A, España PP, Bilbao A, et al. Duration of Antibiotic Treatment in Community-Acquired Pneumonia: A Multicenter Randomized Clinical Trial. JAMA Intern Med. 2016 Sep 1;176(9):1257-65.
- 3. File TM Jr. Duration and cessation of antimicrobial treatment. J Hosp Med. 2012;7 Suppl 1:S22-33.
- 4. Grant J, Saux NL; members of the Antimicrobial Stewardship and Resistance Committee (ASRC) of the Association of Medical Microbiology and Infectious Disease (AMMI) Canada. Duration of antibiotic therapy for common infections. J Assoc Med Microbiol Infect Dis Can. 2021 Sep 30;6(3):181-197.
- 5. Payne SC, McKenna M, Buckley J, et al. Clinical Practice Guideline: Adult Sinusitis Update. Otolaryngol Head Neck Surg. 2025 Aug;173 Suppl 1:S1-S56.
- 6. CDC. Antibiotic prescribing and use: adult outpatient treatment recommendations. April 16, 2024. https://www.cdc.gov/antibiotic-use/hcp/clinical-care/adult-outpatient.html?CDC_AAref_Val=https://www.cdc.gov/antibiotic-use/clinicians/adult-treatment-rec.html. (Accessed October 21, 2025).
- 7. Jones BE, Ramirez JA, Oren E, et al. Diagnosis and Management of Community-acquired Pneumonia. An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med. 2025 Jul 18.
- 8. Choosing Wisely Canada. The cold standard: a toolkit for using antibiotics wisely for the management of respiratory tract infaections in primary care, 5th edition. 2023. https://choosingwiselycanada.org/download/17352. (Accessed October 21, 2025).
- 9. Yadav K, Ohle R, Yan JW, et al. Canadian Emergency Department Best Practices Checklist for Skin and Soft Tissue Infections Part 1: Cellulitis. CJEM. 2024 Sep;26(9):593-
- 10. Kalil AC, Metersky M, Klompas M, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016 Sep 1;63(5):e61-e111. Erratum in: Clin Infect Dis. 2017 Oct 15;65(8):1435. Erratum in: Clin Infect Dis. 2017 Nov 29;65(12):2161.
- 11. Huston JM, Barie PS, Dellinger EP, et al. Therapeutics and Guidelines Committee. The Surgical Infection Society Guidelines on the Management of Intra-Abdominal Infection: 2024 Update. Surg Infect (Larchmt). 2024 Aug;25(6):419-435.
- 12. Sunnybrook Health Sciences Centre. Treatment guidelines: intra-abdominal infection. https://sunnybrook.ca/content/?page=antimicrobial-stewardship-treatment-quidelines. (Accessed October 21, 2025).
- 13. Lieberthal AS, Carroll AE, Chonmaitree T, et al. The diagnosis and management of acute otitis media. Pediatrics. 2013 Mar;131(3):e964-99. Erratum in: Pediatrics. 2014 Feb;133(2):346.
- 14. Le Saux N, Robinson JL; Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Management of acute otitis media in children six months of age and older. Paediatr Child Health. 2016 Jan-Feb;21(1):39-50.
- 15. Mattoo TK, Shaikh N, Nelson CP. Contemporary Management of Urinary Tract Infection in Children. Pediatrics. 2021 Feb;147(2):e2020012138. Erratum in: Pediatrics. 2022 Oct 1;150(4):e2022059259.
- 16. Canadian Paediatric Society. Urinary tract infections in infants and children: diagnosis and management. Reaffirmed January 1, 2020. https://www.cps.ca/en/documents/position/urinary-tract-infections-in-children. (Accessed October 20, 2025).
- 17. Lee RA, Centor RM, Humphrey LL, et al. Appropriate Use of Short-Course Antibiotics in Common Infections: Best Practice Advice From the American College of Physicians. Ann Intern Med. 2021 Jun;174(6):822-827.
- 18. Mo Y. Tan WC. Cooper BS. Antibiotic duration for common bacterial infections-a systematic review. JAC Antimicrob Resist. 2025 Jan 29:7(1):dlae215.
- 19. Trautner BW, Cortes-Penfield NW, Gupta K, et al. Complicated urinary tract infections (cUTI): clinical guidelines for treatment and management. July 17, 2025. https://www.idsociety.org/practice-guideline/complicated-urinary-tract-infections/. (Accessed October 20, 2025).
- 20. Sheppard D. Short-course antibiotic therapy: The next frontier in antimicrobial stewardship. Can Commun Dis Rep. 2022 Nov 3;48(11-12):496-501.
- 21. Shulman ST, Bisno AL, Clegg HW, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. Clin Infect Dis. 2012 Nov 15;55(10):e86-102. Erratum in: Clin Infect Dis. 2014 May;58(10):1496.

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Managing Beta-Lactam Allergies

modified October 2024

Approximately 10% of the population reports having an allergy to a penicillin or other beta-lactam antibiotic.¹ However, about 90% of these patients are able to safely tolerate penicillins when re-exposed.²-7 Guidelines recommend taking steps to proactively delabel penicillin allergy.⁸ This can help avoid the use of second-line antibiotics, which may be less effective, more expensive, more toxic, or have a broader spectrum of activity than necessary (which may contribute to antibiotic resistance).³,4,9,10 Conducting a thorough allergy history is sometimes enough to determine a falsely labeled allergy. It can also help determine which patients can complete desensitization or challenge, or who should undergo skin testing to rule out IgE-mediated antibiotic allergies.⁵⁻⁷ In patients with a proven penicillin allergy, it is important to know which antibiotics can be safe alternatives. The chart below answers common questions about beta-lactam allergies, cross-reactivity, treatment options, and offers tips for evaluating allergy history with a review of desensitization and challenge protocols.

Clinical Question	Suggested Approach/Pertinent Information
What are the different	Type I Hypersensitivity Reactions: mediated by IgE antibodies. ⁴
types of hypersensitivity	• Immediate: typically occur within one hour (but could be up to six hours) of medication dose. ¹
reactions?	• Accelerated: typically occur within one to 72 hours of medication dose. ¹
	• Signs and symptoms could include anaphylaxis, angioedema, drop in blood pressure, itchy rash, hives, swelling of
	the larynx, and wheezing. Patients may also have GI symptoms (e.g., nausea, vomiting, diarrhea) when the med
	was administered orally. 1,4
	Non-IgE-mediated Hypersensitivity Reactions:
	• Type II (cytotoxic): mediated by IgG or IgM antibodies; onset is hours to days. ^{4,12}
	 Signs and symptoms include hemolytic anemia, interstitial nephritis, and thrombocytopenia.¹
	• Type III (immune complex) : mediated by IgG and IgM immune complexes, onset is 7 to 21 days. ^{4,12}
	 Typically presents as serum sickness (rash, joint pain, itching, swollen lymph nodes).⁴
	• Type IV (cell-mediated): delayed reaction with an onset of days to weeks. ^{4,12}
	o Can present as contact dermatitis, Stevens-Johnson syndrome. 1,12
	• Idiopathic Hypersensitivity Reactions: mediated through unknown mechanisms. 13
	 Most common reaction is a maculopapular or morbilliform rash.¹³
	 Example is the rash after use of ampicillin or amoxicillin in patients with a viral infection (e.g., Epstein-
	Barr, cytomegalovirus). ¹³ Risk appears to be highest in patients who receive ampicillin. ^{13,14}
	 Patients who develop this rash are likely to be able to tolerate penicillins in the future.¹³⁻¹⁵
	o Drug-induced enterocolitis syndrome (DIES) is a rare non-IgE-mediated hypersensitivity reaction, reported
	with amoxicillin (primarily in children). Characterized by protracted vomiting one to four hours after drug
	administration without skin or respiratory symptoms. ⁵⁹

Clinical Question	Suggested Approach/Pertinent Information
Clinical Question How should a penicillin allergy be assessed?	 Suggested Approach/Pertinent Information Obtain a thorough allergy history to assess likelihood of a true allergy and to gauge severity.³⁵ See our resource for more tips on <i>Investigating Possible Drug Allergy or Sensitivity</i>. Consider using a validated clinical decision rule (e.g., PEN-FAST) to identify low-risk penicillin allergies.³⁶ Examples of questions to ask the patient include:^{13,15} Please describe the reaction. How was the reaction managed? How old were you when the reaction occurred? When did the reaction occur? After the first dose? After the tenth dose? How was the penicillin administered? Orally? Intravenously? When the penicillin was stopped, what happened? Have you since taken a penicillin (e.g., amoxicillin), cephalosporin (e.g., cephalexin), carbapenem, or monobactam? If yes, what happened? Document the antibiotic given and its indication, reaction symptoms and their onset, treatment of the reaction, and how long ago the reaction occurred.^{45,17} IgE-mediated reaction risk diminishes over time. After ten years, at least 80% do not react and risk may be as low as 1% to 2%.^{5,18} Guidelines recommend delabeling patients with histories that are not consistent with a penicillin allergy (e.g., headache, family history of a penicillin allergy), without the need for allergy testing.⁸ Single treatment-dose challenge with observation can be used for patients who are reluctant (even after counseling) to remove their penicillin allergy from their medical record.⁸ Reactions can occur in patients with viral infections who are on antibiotics (e.g., a rash in a patient with mononucleosis taking amoxicillin). Be careful that these are not mislabeled as allergic reactions. In general, patients with a penicillin allergy are three t

Clinical Question	Suggested Approach/Pertinent Information
How can antibiotic	Guidelines place an emphasis on risk stratification based on reaction phenotype. ⁸
allergic reaction risk be stratified?	• Consider the reaction symptoms and their severity to help determine the likelihood of true allergy and the risk for subsequent reactions: ⁵
	o High risk : anaphylaxis, within minutes to hours of exposure, is IgE-mediated (type I). ^{5,17,21}
	 signs and symptoms of anaphylaxis typically affect two or more organ systems and may involve:^{5,17} skin and/or mucosa (angioedema, flushing, and/or hives).
	 respiratory tract (shortness of breath, stridor, and/or wheezing).
	• gastrointestinal tract (persistent diarrhea and/or vomiting).
	 circulatory (hypotension and/or syncope); note isolated hypotension may also indicate anaphylaxis. positive skin testing, recurrent and/or recent reactions (less than one year ago), or reaction to two or more meds in the same class.^{5,21} These reactions are more likely to be IgE-mediated (type 1).²¹ Patients with reactions within the previous three months have a 20% to 50% chance of reacting again
	upon re-exposure to the med. ³
	Severe, delayed reactions: organ involvement (e.g., hepatitis), serum sickness, Stevens-Johnson syndrome, and other reactions occurring several days into therapy. ^{4,5}
	• Re-exposure to the med is contraindicated with these reactions. ^{4,22,23}
	• These late-onset reactions are not IgE-mediated. ^{3,4}
	 Moderate risk: isolated hives or an IgE-mediated feature (e.g., abdominal pain, or wheezing. Low risk: isolated GI symptoms, headache, mild rash, or itching.
Which beta-lactams	Cross-reactivity among beta-lactams is primarily driven by R-group side chains.
have similar R-group side chains?	• Reported cross-reactivity rates vary and range from about 16% to 40% between penicillins and cephalosporins with identical R-group side chains . ³⁶
	 Cephalosporins with low R-group side chain similarity to penicillins (e.g., cefazolin, cefuroxime, and the third-, fourth-, and fifth-generation cephalosporins) have a low risk of cross reactivity with penicillins.³⁶ Beta-lactams with identical R-group side chains include:^{8,33,36} amoxicillin, cefadroxil, and cefprozil. ampicillin, cefaclor, and cephalexin. aztreonam, ceftazidime, and cefiderocol. The following cephalosporins share similar R-group side chains:^{8,33,41}
	 cefuroxime and cefoxitin. ceftriaxone, cefotaxime, cefpodoxime, cefditoren, and cefepime. cephalexin, cefaclor, and cefadroxil. Many charts are available online with more information on R-group cross-reactivity (e.g., https://adsp.nm.org/allergy-resources.html).

Clinical Question	Suggested Approach/Pertinent Information
How/when can a patient reporting a penicillin allergy be treated with a penicillin?	 Low-risk patients^a may be appropriate for a direct challenge.^{3,5,8} Moderate-risk patients^a may be appropriate for skin testing if available, or can consider a drug challenge.^{3,5} High-risk patients,^a when the culprit med is required therapy: use desensitization (note that if a patient has a negative skin test, desensitization is not needed).^{3,5,24} Avoid penicillins, including penicillin skin testing, in patients who have a history of severe NON-IgE-mediated reactions to penicillin, such as type II, III, or IV reactions (e.g., Stevens-Johnson syndrome, interstitial nephritis, hemolytic anemia).^{5,26,31,32} Patients who have allergic reactions to piperacillin/tazobactam may tolerate other penicillins.⁸ Specific piperacillin/tazobactam skin testing may be helpful in these patients when amoxicillin and penicillin skin testing is negative.⁸
What is the likelihood that a penicillin-allergic patient will react to a cephalosporin?	 Data show that between 1% and 4% of patients with a penicillin allergy will have a true allergy to a cephalosporin, much lower than previously suggested.^{5,33} More specifically, cross-reactivity with cephalosporins is: about 0.1% if penicillin reaction was mild or without skin test-confirmed penicillin allergy. about 2% for patients with a positive penicillin skin test. Cross-reactivity is primarily driven by R1-group side chains, rather than to the beta-lactam structure itself.^{2,8,20} Historically, cephalosporins were contraindicated in patients with a penicillin allergy. Older studies suggested cross-reactivity between penicillins and cephalosporins was as high as 50%.³⁵ Some experts hypothesize that early cephalosporins (pre-1980) may have been contaminated with trace amounts of benzylpenicillin.³³
Can a patient reporting a penicillin allergy be treated with a cephalosporin?	 Generally, any cephalosporin can be given to patients with a nonanaphylactic history.^{3,31,32,37} For patients with an anaphylactic reaction to penicillin, a non-cross-reactive cephalosporin can be given without prior testing (see above section on similar R-group side chains).⁸ Avoid cephalosporins in patients who have a history of severe NON-IgE-mediated reactions to penicillin (e.g., serum sickness, Stevens-Johnson, interstitial nephritis, hemolytic anemia).^{31,32}
Can a patient reporting a penicillin or cephalosporin allergy be treated with a carbapenem?	 Cross-reactivity of type I IgE-mediated reactions between penicillins and carbapenems is very low.^{36,38-40} Guidelines suggest that patients with either a penicillin or cephalosporin allergy (even if it was anaphylactic) can be given a carbapenem without testing or precautions.⁸ As with all beta-lactams, carbapenems must be avoided in patients who have a history of severe NON-IgE-mediated reactions to penicillin (e.g., serum sickness, Stevens-Johnson, interstitial nephritis, hemolytic anemia).^{31,32}

Clinical Question	Suggested Approach/Pertinent Information
Can a patient allergic to penicillin or cephalosporins be treated with aztreonam?	 Aztreonam (a monocyclic beta-lactam) can be administered to patients with allergies to penicillin or cephalosporins (except ceftazidime or cefiderocol) without prior testing.^{8,43} There is potential cross-reactivity with aztreonam and ceftazidime or cefiderocol, due to an identical R-group side chain.^{8,33,40,44} Use caution with aztreonam in cystic fibrosis when patients have hypersensitivities to beta-lactam antibiotics.^{40,45} Potentially due to exposure to high-dose repetitive antibiotics, these patients can have high rates of beta-lactam hypersensitivity and may have higher rates of cross-reactivity with aztreonam.⁴⁵
What treatment considerations are important for patients reporting a CEPHALOSPORIN allergy?	 Treatments for patients reporting a cephalosporin allergy may be chosen based on R-group side-chain similarities.⁸ Patients with an immediate or accelerated allergy to a cephalosporin should not receive a cephalosporin (or aztreonam) with the same R-group side chain without cephalosporin skin testing and desensitization to that drug.⁸ A cephalosporin with a different R-group side chain may be able to be used safely. Direct challenge is suggested with cephalosporins with dissimilar side chains in patients with non-anaphylactic cephalosporin allergy.⁸ The use of cephalosporin skin testing, following by either desensitization or drug challenge, is suggested before a parenteral cephalosporin is administered if there is a history of anaphylaxis.⁸
What treatment considerations are important for patients who report a CARBAPENEM allergy?	 Patients with type I reactions to one carbapenem should avoid the use of other carbapenems due to lack of data on cross-reactivity. 46 Can consider desensitization, if a carbapenem is truly needed (e.g., extended spectrum beta-lactamase producing organisms). 32 Low-risk^a patients can usually be given a penicillin or cephalosporin. 32 Moderate-risk patients can be given a penicillin or cephalosporin after a direct or graded challenge. 32 High-risk^a patients can be given a penicillin or a cephalosporin after desensitization. 32
When are desensitization or drug challenges considered?	 Desensitization and drug challenge are contraindicated for types II, III, IV, and idiopathic reactions (those with organ involvement). 4,20,47 A graded drug challenge may be favored over skin testing in patients with a higher risk for true allergy (e.g., a severe reaction within the previous five years). 4,5,22,24 Graded or direct drug challenge are used for patients with a history of non-life-threatening reactions, when there is a low clinical probability of a true drug allergy. 8,49 direct challenge (also called one-step) may be preferred for most patients. 3,8 patients with multiple drug allergies or significant anxiety may prefer a graded challenge. 8 Be aware that allergists can differ on when to use graded vs direct challenge. 6,7,29,34,37,50-52

Clinical Question	Suggested Approach/Pertinent Information
Clinical Question What are direct and graded drug challenges?	 Suggested Approach/Pertinent Information For a direct (one-step) challenge the antibiotic is given, then the patient is monitored for 30 to 60 minutes. 45.47 o For example, for a penicillin allergy, give amoxicillin 250 to 500 mg and observe for one hour. 45.47 o For example, for a penicillin allergy, give amoxicillin 250 to 500 mg and observe for one hour. 45.47 o For example, for a penicillin allergy, give amoxicillin 250 to 500 mg and observe for one hour. 45.47 o can be performed by trained clinicians. Close vital sign monitoring and quick access to meds for treating anaphylactic reactions are required. 5 typically, involves two to three escalating doses, starting with a small percentage of the total dose and building up to the full dose. 5.482 IV: 1% of the dose is given, then 10%, then the full dose. Doses are given 30 to 60 minutes apart. Use of a smaller initial dose may help offset the potentially higher allergic reaction risk associated with IV administration. Orally: 10% to 25% of the dose is followed by the full dose 20 to 30 minutes later. 5 Patient should be monitored for signs of reaction after each dose and have rescue meds readily available. 4.51 Graded challenge procedures vary but generally involve giving two to three rapidly escalating stepwise doses. 5.48 For example, for an oral graded challenge for cephalexin. 48 Prepare doses using cephalexin oral suspension 250 mg/5 mL. Give 1/10th of the therapeutic dose (e.g., 50 mg [1 mL] for a target dose of 500 mg). Observe the patient for 30 minutes. If there are no signs of an allergic reaction, give the full dose (e.g., 500 mg [10 mL]). Observe the patient for signs of a reaction for an additional 60 minutes. Patients who don't react during a drug challenge are deemed non-allergic to the med and their medical records should be updated accordingly. 3.15<!--</th-->

Clinical Question	Suggested Approach/Pertinent Information
What is desensitization?	 Desensitization temporarily induces tolerance to the culprit antibiotic for a needed treatment course. 15,23,24 It is reserved for patients at high risk of life-threatening reactions (e.g., history of anaphylaxis). Desensitization is preferred for patients with compromised cardiac or respiratory status and during pregnancy. Due to the risk of serious allergic reaction, desensitization should be performed under supervision of an allergist or specialist, in an ICU or other specialized care area with continuous vital sign monitoring, including rescue meds. 5,15,17,23 Informed consent must be completed prior to initiation of desensitization. Continuous dose escalations (often 12 or more) are given to increase blood levels of the med without triggering an immune response. 4,15,23,47 Institutions should develop desensitization protocols which standardize the dose escalations given to achieve tolerance of the full dose. 3,5 Published desensitization protocols are available for beta-lactams, carbapenems, sulfonamides, tobramycin, and vancomycin. 3,17,26,47,53-57
How often does desensitization or graded challenge need to be repeated?	 Desensitization induces temporary tolerance that lasts only as long as the med is taken continuously.^{3,8,21,23} When the antibiotic treatment is held or discontinued, tolerance is lost and the desensitization procedure must be repeated/restarted if the patient requires further therapy.^{3,21} Educate patients to contact the prescriber for advice on how to proceed if one or more doses are missed. Tolerance is generally maintained through two to five half-lives of the antibiotic.³ Lack of allergic response following desensitization does NOT indicate a change in the patient's allergy status.¹⁵ Ensure patients understand that they are still allergic to the med and that desensitization will likely need to be repeated for future treatment courses.⁵ Patients who don't have a reaction during direct or graded challenge should be considered nonallergic.⁵ Be sure to update allergy info in the patient's medical records to reflect their true allergy status.⁵ Tell patients that they are no longer allergic to the med and that it is safe for them to receive if needed.^{5,48}

 When is allergy skin testing warranted? Drug challenge is typically preferred over allergy skin testing (especially in patients with non-anaphylar reactions or with a history of non-severe cutaneous reactions).⁸ Skin testing is of most value in patients with a history of anaphylaxis or a recent suspected IgE-mediate (e.g., immediate onset urticaria).⁸ Skin testing is suggested for patients with anaphylactic cephalosporin allergy (rare), in addition to drug prior to administration of penicillin therapy.⁸ Skin testing may permit the preferred beta-lactam antibiotic to be used in a patient who may have had an mediated reaction, when alternatives are less desirable, as when treating.^{5,17,21,24} methicillin-sensitive Staph aureus (MSSA) bacteremia with nafeillin rather than vancomycin.^{5,24} uncomplicated gonorrhea with ceftriaxone instead of broader-spectrum antibiotics.^{5,25} syphilis with penicillin during pregnancy rather than an a less effective alternative.^{5,26} Suggest consideration of delayed intradermal test and/or patch tests to identify culprit drugs when a patihad a delayed reaction and the offending med is uncertain.⁸ Skin testing must be done in a controlled setting with close monitoring, including rescue meds (epineph Medications with antihistamine activity may interfere with skin test interpretation.²² Most of these meds should be stopped for at least two to three days before skin testing, but some reclonger (e.g., loratadine should be held for at least one week prior).²² Skin testing can be performed by specially trained pharmacists, nurses, or physicians.^{19,26} Follow state laws, policies, and procedures for test administration. To locate an allergist for testing, go to: http://acaai.org/locate-an-allergist. Use billing code 95076 (first 120 minutes) and 95079 (for each additional hour) for o	
 Medications with antihistamine activity may interfere with skin test interpretation.²² Most of these meds should be stopped for at least two to three days before skin testing, but some recolonger (e.g., loratadine should be held for at least one week prior).²² Skin testing can be performed by specially trained pharmacists, nurses, or physicians.^{19,26} Follow state laws, policies, and procedures for test administration. To locate an allergist for testing, go to: http://acaai.org/locate-an-allergist. Use billing code 95018 for percutaneous (scratch, puncture, prick) and intracutaneous/intradermal to Use billing code 95076 (first 120 minutes) and 95079 (for each additional hour) for oral challenge to Skin testing may involve the following:^{4,5,22,24} Skin prick test with one or more determinants, a positive control (histamine), and a negative control (saline).²⁷ Penicillin: major and minor determinants are <i>Pre-Pen</i> and a penicillin (e.g., Penicillin G), respectively. Penicillin: major and minor determinants are <i>Pre-Pen</i> and a penicillin (e.g., Penicillin G), respectively.	ted reaction g challenge, an IgE-
 Other antibiotics: determinant is a nonirritating antibiotic concentration (a 10- to 1,000-fold dile full-strength concentration).^{22,28} Nonirritating concentrations have been determined for cephalog clindamycin, levofloxacin, macrolides, sulfamethoxazole/trimethoprim, tobramycin, and vancon The patient is observed for 15 minutes, then results are interpreted by measuring any wheals that of the skin prick results are negative or indeterminant, an intradermal test may be done with the same determinant(s) and controls. The patient is observed for 15 minutes, then results are interpreted as with the skin prick test. 	tests. ¹¹ tests. ¹¹ rol pectively. ²⁷ lilution from losporins, omycin. ^{22,28} hat form.

Clinical Question	Suggested Approach/Pertinent Information
Skin testing, continued	 If the intradermal test is negative, the patient may be given a direct oral challenge of the med (e.g., amoxicillin) and observed for one hour. Note that penicillin skin testing is not recommended prior to a direct oral challenge of amoxicillin in low-risk (e.g., benign cutaneous reactions) pediatric patients.⁸ Negative skin test results may indicate a low chance of a severe allergic reaction, depending on the med tested.^{4,17} Only 3% of patients with negative penicillin skin testing will react upon re-exposure to the med.^{3,4,17} The predictive value of negative skin testing is less clear for other antibiotics.^{3,17,22} Positive skin test results suggest true IgE-mediated allergy to the tested med.^{17,29} However, false positives limit its usefulness, since a positive result reflects only a 50% chance of severe reaction upon re-exposure.²⁴
How should allergy information be updated in patient profiles?	 Ensure accurate documentation of allergies. This helps ensure effective electronic allergy screenings.⁵⁸ Document the exact medication, not a medication class when updating allergies.⁵⁸ Add information about which medications the patient has tolerated or any allergy testing/challenges done. Educate patients about their allergies to help keep inaccuracies from being re-added. Inaccurate allergies could mean exposing patients to less effective, more expensive, more toxic, or unnecessarily broad coverage antibiotics.⁵⁸ False penicillin allergy labels can lead to longer hospital stays and increased risk of serious infections.⁴² Allergy information can be updated at any time, but admission and discharge are perfect opportunities to ensure allergy information is current.

Abbreviations: GI = gastrointestinal; IV = intravenous.

- a. Risk of a true IgE-mediated reaction:5
 - o low-risk: isolated GI symptoms, headache, mild rash, or itching.
 - o moderate-risk: isolated hives, abdominal pain, or wheezing.
 - high-risk: anaphylaxis, positive skin test, recurrent and/or recent reactions (less than one year ago).
- b. Note that product labeling for ceftolozane/tazobactam (*Zerbaxa*), a fifth-generation cephalosporin, lists **serious** beta-lactam allergy as a contraindication to use.^{30,34}

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

References

- Spacek LA. Johns Hopkins Medicine. Johns Hopkins antibiotic ABX guide: beta-lactam allergy. December 11, 2022.
 - https://www.hopkinsguides.com/hopkins/view/Johns_ Hopkins_ABX_Guide/540622/all/Beta_lactam_allerg y. (Accessed March 29, 2023).
- Ledford DK. Cephalosporin administration with a penicillin allergy history. February 2, 2016. https://www.aaaai.org/allergist-resources/ask-theexpert/answers/old-ask-the-experts/cephalosporinpenicillin. (Accessed March 28, 2023).
- Macy E, Romano A, Khan D. Practical Management of Antibiotic Hypersensitivity in 2017. J Allergy Clin Immunol Pract. 2017 May-Jun;5(3):577-586.
- Gonzalez-Estrada A, Radojicic C. Penicillin allergy: A practical guide for clinicians. Cleve Clin J Med. 2015 May;82(5):295-300.
- Shenoy ES, Macy E, Rowe T, Blumenthal KG. Evaluation and Management of Penicillin Allergy: A Review. JAMA. 2019 Jan 15;321(2):188-199.
- Blumenthal KG, Wickner PG, Hurwitz S, et al. Tackling inpatient penicillin allergies: Assessing tools for antimicrobial stewardship. J Allergy Clin Immunol. 2017 Jul;140(1):154-161.e6.
- Mill C, Primeau MN, Medoff E, et al. Assessing the Diagnostic Properties of a Graded Oral Provocation Challenge for the Diagnosis of Immediate and Nonimmediate Reactions to Amoxicillin in Children. JAMA Pediatr. 2016 Jun 6:170(6):e160033.
- Khan DA, Banerji A, Blumenthal KG, et al. Drug allergy: A 2022 practice parameter update. J Allergy Clin Immunol. 2022 Dec;150(6):1333-1393.
- Jeffres MN, Narayanan PP, Shuster JE, Schramm GE. Consequences of avoiding β-lactams in patients with β-lactam allergies. J Allergy Clin Immunol. 2016 Apr;137(4):1148-1153.
- Rochester Regional Health. Penicillin skin testing. February 2016. https://www.rochesterregional.org//media/files/air/penicillinbrochure.pdf?la=en. (Accessed March 29, 2023).
- American Academy of Allergy, Asthma, & Immunology. Review 2023 CMS values for commonly used allergy/immunology codes. November 2022. https://www.aaaai.org/Aaaai/media/Media-Library-PDFs/About/Advocacy/2023-Allergy-RVU-values-asof-November-2022-Edited.pdf. (Accessed April 21, 2023).
- 12. Marwa K, Kondamudi NP. Type IV hypersensitivity reaction. Updated March 6, 2023. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing: 2023 Jan-.
- Salkind AR, Cuddy PG, Foxworth JW. The rational clinical examination. Is this patient allergic to penicillin? An evidence-based analysis of the likelihood of penicillin allergy. JAMA. 2001 May 16;285(19):2498-505.
- Ikediobi NI, Tyring SK. Cutaneous manifestations of Epstein-Barr virus infection. Dermatol Clin. 2002 Apr;20(2):283-9.

- 15. Joint Task Force on Practice Parameters; American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology. Drug allergy: an updated practice parameter. Ann Allergy Asthma Immunol. 2010 Oct;105(4):259-273.
- Trubiano JA, Vogrin S, Chua KYL, et al. Development and Validation of a Penicillin Allergy Clinical Decision Rule. JAMA Intern Med. 2020 May 1;180(5):745-752.
- 17. Lieberman P, Nicklas RA, Randolph C, et al. Anaphylaxis--a practice parameter update 2015. Ann Allergy Asthma Immunol. 2015 Nov;115(5):341-84.
- CDC. Antibiotic prescribing and use: evaluation and diagnosis of penicillin allergy for healthcare professionals. October 31, 2017. https://www.cdc.gov/antibiotic-use/community/forhcp/Penicillin-Allergy.html. (Accessed March 28, 2023).
- Wall GC, Peters L, Leaders CB, Wille JA. Pharmacistmanaged service providing penicillin allergy skin tests. Am J Health Syst Pharm. 2004 Jun 15;61(12):1271-5.
- Pichichero ME. A review of evidence supporting the American Academy of Pediatrics recommendation for prescribing cephalosporin antibiotics for penicillinallergic patients. Pediatrics. 2005 Apr;115(4):1048-57.
- Wheatley LM, Plaut M, Schwaninger JM, et al. Report from the National Institute of Allergy and Infectious Diseases workshop on drug allergy. J Allergy Clin Immunol. 2015 Aug;136(2):262-71.e2.
- Bernstein IL, Li JT, Bernstein DI, et al. Allergy diagnostic testing: an updated practice parameter. Ann Allergy Asthma Immunol. 2008 Mar;100(3 Suppl 3):S1-148.
- Liu A, Fanning L, Chong H, et al. Desensitization regimens for drug allergy: state of the art in the 21st century. Clin Exp Allergy. 2011 Dec;41(12):1679-89.
- Unger NR, Gauthier TP, Cheung LW. Penicillin skin testing: potential implications for antimicrobial stewardship. Pharmacotherapy. 2013 Aug;33(8):856-67.
- CDC. Gonorrhea treatment and care. December 1, 2022. https://www.cdc.gov/std/gonorrhea/treatment.htm. (Accessed April 13, 2023).
- CDC. Sexually transmitted infections treatment guidelines, 2021: managing persons who have a history of penicillin allergy. September 21,2022. https://www.cdc.gov/std/treatmentguidelines/penicillin-allergy.htm. (Accessed March 28, 2023).
- PRE-PEN. Implementing penicillin allergy skin testing. https://www.penallergytest.com/implementing-penicillin-allergy-skin-testing/. (Accessed April 13, 2023).
- Empedrad R, Darter AL, Earl HS, Gruchalla RS. Nonirritating intradermal skin test concentrations for commonly prescribed antibiotics. J Allergy Clin Immunol. 2003 Sep;112(3):629-30.

- 29. Kuruvilla M, Thomas J. Direct oral amoxicillin challenge without antecedent penicillin skin testing in low-risk patients. Ann Allergy Asthma Immunol. 2018 Nov:121(5):627-628.
- Product information for Zerbaxa. Merck Sharp & Dohme. Rahway, NJ 07065. May 2022.
- 31. Blumenthal KG, Shenoy ES, Wolfson AR, et al. Addressing Inpatient Beta-Lactam Allergies: A Multihospital Implementation. J Allergy Clin Immunol Pract. 2017 May-Jun;5(3):616-625.e7.
- 32. University of Wisconsin Health. Treatment of patients with reported allergies to beta-lactam antibiotics adult inpatient clinical practice guideline. September 2016. https://www.uwhealth.org/cckm/cpg/infection-and-isolation/Treatment-of-Patients-with-Reported-Allergies-to-Beta-Lactam-Antibiotics---Adult--- Inpatient-16.09.20.pdf. (Accessed March 28, 2023).
- 33. Chaudhry SB, Veve MP, Wagner JL. Cephalosporins: A Focus on Side Chains and β-Lactam Cross-Reactivity. Pharmacy (Basel). 2019 Jul 29;7(3):103.
- 34. Product monograph for Zerbaxa. Merck Canada. Kirkland, QC H9H 4M7. October 2020.
- Daulat S, Solensky R, Earl HS, et al. Safety of cephalosporin administration to patients with histories of penicillin allergy. J Allergy Clin Immunol. 2004 Jun;113(6):1220-2.
- Picard M, Robitaille G, Karam F, et al. Cross-Reactivity to Cephalosporins and Carbapenems in Penicillin-Allergic Patients: Two Systematic Reviews and Meta-Analyses. J Allergy Clin Immunol Pract. 2019 Nov-Dec;7(8):2722-2738.e5.
- Macy E, Blumenthal KG. Are Cephalosporins Safe for Use in Penicillin Allergy without Prior Allergy Evaluation? J Allergy Clin Immunol Pract. 2018 Jan-Feb;6(1):82-89.
- 38. Saxon A, Adelman DC, Patel A, et al. Imipenem cross-reactivity with penicillin in humans. J Allergy Clin Immunol. 1988 Aug;82(2):213-7.
- Romano A, Viola M, Gueant-Rodriguez RM, et al. Imipenem in patients with immediate hypersensitivity to penicillins. N Engl J Med. 2006 Jun 29;354(26):2835-7.
- 40. Frumin J, Gallagher JC. Allergic cross-sensitivity between penicillin, carbapenem, and monobactam antibiotics: what are the chances? Ann Pharmacother. 2009 Feb;43(2):304-15.
- 41. Chaudhry SB, Veve MP, Wagner JL. Cephalosporins: A Focus on Side Chains and β-Lactam Cross-Reactivity. Pharmacy (Basel). 2019 Jul 29;7(3):103.
- Macy E, Contreras R. Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: A cohort study. J Allergy Clin Immunol. 2014 Mar;133(3):790-6.
- Clinical Pharmacology powered by ClinicalKey. Tampa (FL): Elsevier. 2023. http://www.clinicalkey.com. (Accessed April 13, 2023).
- Robinson JL, Hameed T, Carr S. Practical aspects of choosing an antibiotic for patients with a reported allergy to an antibiotic. Clin Infect Dis. 2002 Jul 1;35(1):26-31.

- 45. Moss RB. Sensitization to aztreonam and cross-reactivity with other beta-lactam antibiotics in high-risk patients with cystic fibrosis. J Allergy Clin Immunol. 1991 Jan:87(1 Pt 1):78-88.
- Noguerado-Mellado B, Pinto Fernandez C, Pineda-Pineda R, et al. Cross-reactivity between carbapenems: two case reports. J Allergy Clin Immunol Pract. 2014 Nov-Dec;2(6):816-7.
- Castells M. Rapid desensitization for hypersensitivity reactions to medications. Immunol Allergy Clin North Am. 2009 Aug;29(3):585-606.
- 48. Iammatteo M, Ferastraoaru D, Koransky R, et al. Identifying Allergic Drug Reactions Through Placebo-Controlled Graded Challenges. J Allergy Clin Immunol Pract. 2017 May-Jun;5(3):711-717.e2.
- Iammatteo M, Alvarez Arango S, Ferastraoaru D, et al. Safety and Outcomes of Oral Graded Challenges to Amoxicillin without Prior Skin Testing. J Allergy Clin Immunol Pract. 2019 Jan;7(1):236-243.
- Gaeta F, Valluzzi RL, Alonzi C, et al. Tolerability of aztreonam and carbapenems in patients with IgEmediated hypersensitivity to penicillins. J Allergy Clin Immunol. 2015 Apr;135(4):972-976.
- 51. Kelso JM. Provocation Challenges to Evaluate Amoxicillin Allergy in Children. JAMA Pediatr. 2016 Jun 6;170(6):e160282.
- Wall GC, Nayima VA, Neumeister KM. Assessment of hypersensitivity reactions in patients receiving carbapenem antibiotics who report a history of penicillin allergy. J Chemother. 2014 Jun;26(3):150-3.
- 53. Leoung GS, Stanford JF, Giordano MF, et al. Trimethoprim-sulfamethoxazole (TMP-SMZ) dose escalation versus direct rechallenge for Pneumocystis Carinii pneumonia prophylaxis in human immunodeficiency virus-infected patients with previous adverse reaction to TMP-SMZ. J Infect Dis. 2001 Oct 15;184(8):992-7.
- Gorman SK, Zed PJ, Dhingra VK, Ronco JJ. Rapid imipenem/cilastatin desensitization for multidrugresistant Acinetobacter pneumonia. Ann Pharmacother. 2003 Apr;37(4):513-6.
- Wilson DL, Owens RC Jr, Zuckerman JB. Successful meropenem desensitization in a patient with cystic fibrosis. Ann Pharmacother. 2003 Oct;37(10):1424-8.
- 56. Spigarelli MG, Hurwitz ME, Nasr SZ. Hypersensitivity to inhaled TOBI following reaction to gentamicin. Pediatr Pulmonol. 2002 Apr;33(4):311-4.
- Wazny LD, Daghigh B. Desensitization protocols for vancomycin hypersensitivity. Ann Pharmacother. 2001 Nov;35(11):1458-64.
- Shands at the University of Florida. Drug & Therapy Bulletin: the importance of accurate drug allergy information. May 2010. http://professionals.ufhealth.org/files/2011/11/0510drugs-therapy-bulletin.pdf. (Accessed March 28, 2023).
- 59. Product information for amoxicillin. Micro Labs. Somerset, NJ 08873. January 2024.

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Cite this document as follows: Clinical Resource, Managing Beta-Lactam Allergies. Pharmacist's Letter/Pharmacy Technician's Letter/Prescriber's Letter. May 2023. [390503]

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