



## Acute Otitis Media

### What proportion of AOM is caused by *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*?

The most common bacterial pathogens causing AOM are:

- *Nontypeable Haemophilus influenzae*: 34–60%
- *Streptococcus pneumoniae*: 15–25%
- *Moraxella catarrhalis*: 12–15%

A 2017 study by Kaur et al. using tympanocentesis showed a decline in *S. pneumoniae* and an increase in *M. catarrhalis* following the introduction of the PCV13 vaccine. The authors also noted rising antibiotic resistance among *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*, particularly in children with multiple antibiotic exposures.

More recent data (Frost et al., 2024) from children seen for AOM between 2018 and 2022 in Denver, Colorado, using nasopharyngeal culture and PCR testing, identified the following pathogens:

- *M. catarrhalis*: 52%
- *S. pneumoniae*: 34%
- *H. influenzae*: 20%
- *S. aureus*: 14%

Treatment failure was uncommon and did not differ by pathogen or beta-lactamase production, supporting amoxicillin as first-line therapy for uncomplicated AOM.

Because tympanocentesis and nasopharyngeal cultures are not routinely performed in clinical practice, local pathogen prevalence data are limited, and national estimates remain the best guide for empiric management.

### There is data that AOM due to *H. influenzae* and *M. catarrhalis* will often resolve without antibiotics. How often does AOM due to *S. pneumoniae* resolve without antibiotics?

Examination of sequential middle ear fluid aspirates has shown that spontaneous clearance occurs in approximately 50% of AOM due to *H. influenzae* and approximately 19% of AOM due to *S. pneumoniae* (Klein, 1994). More contemporary studies (Tahtinen et al., 2017) did not show any difference in spontaneous resolution of AOM based on bacteria detected by nasopharyngeal swab. The study did not evaluate the risk of treatment failure by specific organisms within different age groups, although it did report higher placebo treatment failure rates in children 6–23 months old (49.2%) compared to children 24–35 months old (29.4%).

### Why does the choice of whether to treat or observe differ depending on whether it is unilateral vs. bilateral AOM?

The [2013 AAP Clinical Practice Guideline](#) recommends antibiotic treatment for bilateral AOM in children 6–23 months of age without severe symptoms. *Immediate antibiotics are recommended for all children younger than 6 months and for those with severe AOM, regardless of laterality.*

Bilateral AOM is common and tends to have a more severe clinical course than unilateral infection (Leibovitz et al., 2007). A 2006 meta-analysis by Rovers et al. found that children with otorrhea and those younger than 2 years with bilateral AOM derived the greatest benefit from immediate antibiotics. Among children under 2 years with bilateral AOM, 55% of untreated children and 30% of those on antibiotics still had pain, fever, or both at 3–7 days.

These findings support the recommendation to treat bilateral AOM in young children to promote faster recovery and reduce complications, while observation remains reasonable for most mild, unilateral cases.

## Antibiotics

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### How common are rash and other side effects for amoxicillin vs. cefdinir vs. azithromycin?

Rash and other side effects are relatively uncommon, with diarrhea being the most common adverse event for all three antibiotics.

- Amoxicillin: Rash occurs in approximately 5–10% of children, and diarrhea in 2–20%, depending on dose, duration, and study population. Most rashes are benign and nonallergic, often representing viral-induced exanthemas rather than true drug hypersensitivity.
- Cefdinir: Rash is reported in 1–3% of pediatric patients but may reach up to 8% in children younger than 2 years, often appearing as diaper rash.
- Azithromycin: Rash occurs in 0.4–2% of patients, and diarrhea in 7–14%, depending on dosing regimen.

A 2017 study by Gerber et al. comparing broad-spectrum and narrow-spectrum antibiotic therapy for pediatric respiratory tract infections found that children receiving broad-spectrum agents (e.g., cefdinir, azithromycin) experienced more clinician-diagnosed and patient-reported adverse events, including diarrhea, vomiting, rash, and allergic reactions, than those prescribed narrow-spectrum antibiotics such as amoxicillin.

### What is the recommended maximum dose for high-dose amoxicillin? Is it reasonable to divide the total daily dose TID if the volume of medication is large?

For high-dose amoxicillin (e.g., treatment of acute otitis media, sinusitis, or pneumonia when *S. pneumoniae* with reduced susceptibility is a concern), the recommended maximum dose of amoxicillin on our algorithms is 2 g BID (total daily dose 4 g/day). It is reasonable to use amoxicillin divided TID if the medication volume is difficult for the patient to tolerate, or if adherence may improve with smaller per-dose volumes. A dose of 1 g TID provides comparable total daily exposure and maintains adequate time above MIC to achieve similar pharmacodynamic effects as 2 g BID (Bradley et al., 2011; Metlay et al., 2019). Lower doses such as 500 mg TID do not achieve equivalent 'high-dose' exposure and should not be considered as a substitute for high-dose therapy.

### Why do the AOM and sinusitis Express Lanes recommend high-dose Augmentin XR® (2,000 mg BID) for larger children and adolescents? Is this safe?

High-dose Augmentin XR® is used to achieve effective amoxicillin exposure for resistant *S. pneumoniae* while maintaining safe clavulanate levels for the treatment of beta-lactamase producing bacteria (e.g., *H. influenzae*, *M. catarrhalis*). Although the dose appears higher than typical adult regimens, it is aligned with pediatric data and national children's hospital practices.

The risk of GI side effects is driven by the clavulanate, not the amoxicillin dose:

- Augmentin 875/125 (1 tab BID) → 125 mg clavulanate per dose
- Augmentin XR® 1,000/62.5 (2 tabs BID) → 125 mg clavulanate per dose
- These regimens provide the same total clavulanate exposure, so GI risk is similar. For a 40 kg patient, this results in ~6.25 mg/kg/day of clavulanate, which is well below the typical safety threshold (10 mg/kg/day).

Why use the XR formulation?

- It allows delivery of adequate high-dose amoxicillin (~2 g per dose).
- It keeps clavulanate exposure low, minimizing GI side effects.
- Standard 875 mg tablets do not provide sufficient amoxicillin for adult-sized patients and increasing the number of 875/125 tablets would increase clavulanate exposure unnecessarily.

## Is it safe to re-challenge a patient who develops a morbilliform rash towards the end of a prior course of amoxicillin?

Yes, in most cases, it is safe to re-challenge.

Both the [British Society for Allergy and Clinical Immunology \(2015\)](#) and the [American Academy of Allergy, Asthma, and Immunology \(2022\)](#) recommend that children with a history of non-immediate or delayed mild rash (such as a morbilliform or maculopapular eruption) after penicillin exposure can safely undergo an oral amoxicillin challenge if the medication is needed again.

The [Canadian Paediatric Society \(2020\)](#) advises that children at low risk for true penicillin allergy [can be prescribed amoxicillin again](#), as mild delayed rashes do not contraindicate future use. When additional reassurance is desired, a single test dose of amoxicillin (15 mg/kg) with 1 hour of observation can confirm tolerance.

These individuals can also safely receive cephalosporins, regardless of side chain similarity, as well as carbapenems and monobactams, without the need for special monitoring.

## Community-acquired pneumonia

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### What is “atypical” pneumonia?

“Atypical” pneumonia refers to pneumonia caused by organisms that differ from the usual bacterial pathogens such as *S. pneumoniae*, *H. influenzae*, or *S. aureus*. Atypical pathogens include *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, and *Legionella* species, which require non-beta-lactam antibiotics such as azithromycin, doxycycline, or a fluoroquinolone. Atypical pneumonia often develops gradually with milder, more nonspecific symptoms such as malaise, sore throat, headache, low-grade fever, and cough that progresses over several days. *M. pneumoniae* is the most common cause of atypical pneumonia in children. While certain features can suggest an atypical pathogen, no clinical findings reliably distinguish it from typical bacterial pneumonia.

**Given how challenging it is to discern “typical” vs. “atypical” CAP, when should we be using amoxicillin vs. azithromycin vs. both? What about a 10-year-old with persistent cough, fatigue, and diffuse wheezing on exam, not responsive to inhaled steroids and albuterol, clearly consistent with a *Mycoplasma pneumoniae*. Will this child still need to take amoxicillin for 3 days before switching to azithromycin?**

Amoxicillin remains the first-line treatment for most children with community-acquired pneumonia. If the child does not improve after 48–72 hours of appropriate therapy, azithromycin can be added to cover the possibility of *M. pneumoniae* or other atypical pathogens. This approach reflects the stronger evidence supporting amoxicillin for typical bacterial pneumonia, where omitting it increases the risk of treatment failure. In contrast, the benefit of azithromycin for atypical pneumonia is less clear, and delayed initiation is unlikely to worsen outcomes.

Due to high resistance rates among typical respiratory pathogens, including *S. pneumoniae*, azithromycin monotherapy is generally not recommended except in specific circumstances where atypical infection is strongly suspected:

1. Confirmed or highly-suspected *M. pneumoniae* infection. For example, when the patient has a positive PCR test or when there is a known school-based outbreak of *M. pneumoniae* or a sibling or close contact was recently diagnosed with *M. pneumoniae* pneumonia.
2. Classic presentation. For example, a school-aged child with prolonged cough, fatigue, and diffuse bilateral infiltrates on chest radiograph, with minimal response to bronchodilators or steroids.

In such cases, azithromycin monotherapy may be appropriate. Otherwise, starting with amoxicillin and reassessing at 48–72 hours remains the preferred strategy.

### Is cefprozil (Cefzil®) a reasonable alternative for the treatment of CAP?

Cefprozil has an antimicrobial spectrum that includes common CAP pathogens (e.g., *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*) and has demonstrated efficacy in related lower respiratory infections such as acute bacterial exacerbations of chronic bronchitis. However, its role as an alternative to amoxicillin is not well supported by current guidelines. Unfortunately, cefprozil also shares an identical R1 side chain as amoxicillin, meaning the chance of allergy cross-reactivity is very high. This makes it an unacceptable alternative for patient with amoxicillin allergy. While the [IDSA/ATS pediatric CAP guidelines](#) specifically mention cefuroxime and cefprozil as alternative oral step-down therapy in the setting when amoxicillin cannot be used, the available clinical data for cefprozil in CAP is limited, particularly regarding optimal dosing and duration, and much of the evidence predates current pneumococcal resistance patterns. Additionally, as cefprozil is infrequently prescribed in practice, availability (especially suspension) may be inconsistent across retail pharmacies, which may be a practical barrier for outpatient treatment.

### Why is cefdinir (Omnicef®) not recommended for the treatment of CAP?

Cefdinir may seem like an appealing alternative to amoxicillin as it is considered palatable by most children and has convenient dosing options; however, there are several limitations to cefdinir that providers should be aware of to limit inappropriate use:

- **It has poor absorption, a short half-life, and high protein-binding.** As a result, it is difficult to achieve appropriate drug concentrations at the desired site (including the middle ear), *especially if using only once-daily dosing*. This can lead to treatment failure.
- **It has activity against *H. influenzae* and *Moraxella*, but can have reduced activity against *Streptococcus pneumoniae*** especially for penicillin-intermediate or penicillin-resistant strains. Amoxicillin is still preferred to oral cephalosporins for *Streptococcus pneumoniae* infections, and the high-dose amoxicillin strategy can overcome *S. pneumoniae*'s altered penicillin-binding protein.
- **It has an unnecessarily broad spectrum of activity for pediatric ARTIs**, which can lead to antibiotic resistance.
- **It is more expensive than first line agents.**
- **Its safety has not been established in infants under 6 months of age**

Additionally, cefdinir should not be used for:

- Recurrent or refractory AOM *after* failure of high-dose amoxicillin/clavulanate.
- CAP with concern for amoxicillin or amoxicillin/clavulanate failure.
- Infections with known or suspected penicillin non-susceptible strains of *S. pneumoniae*.

Taken together, these factors increase the risk that cefdinir will not achieve reliable treatment for CAP, particularly when pneumococcal resistance is present. For this reason, we prioritize agents with more predictable pneumococcal coverage and lung exposure in the CAP algorithm and Express Lane.

## Are there any studies on placebo vs. high-dose amoxicillin for children with CAP?

The evidence for placebo versus amoxicillin is limited to non-severe community-acquired pneumonia in low-resource outpatient settings (Hazir et al., 2011; Ginsburg et al., 2018; Awasthi et al., 2008). No placebo-controlled comparisons exist from high-income settings or among children with severe pneumonia.

## CORIZA

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### What is the CORIZA Project?

CORIZA, short for “Clinical Optimization of Respiratory Infections: Zeroing in on Antibiotics,” is a PCORI-funded, four-year collaborative implementation project (February 1, 2025–January 31, 2029) focused on supporting clinicians in delivering the best care for children with acute respiratory tract infections (ARTIs). The project aims to make antibiotic prescribing easier, more consistent, and more aligned with evidence, while respecting the realities of busy outpatient and emergency room physicians. It is grounded in partnership among frontline clinicians, local champions, families, and stewardship experts so that every tool and resource is practical, relevant, and co-created with those who use them every day.

CORIZA includes four key interventions designed with clinicians: (1) Provider education, offering concise, role-specific updates and resources on best practices; (2) Patient/Caregiver-facing education, co-developed with families to make antibiotic conversations more effective and efficient; (3) Clinical decision support, embedding tools in the electronic health record to guide diagnosis, prescribing, and follow-up; and, (4) Audit and feedback, using individualized, non-punitive reports to help clinicians see how their prescribing patterns align with peers and evidence. Providers can expect to hear about CORIZA regularly through existing meetings, educational sessions, and data updates. The project is designed with sustainability in mind, so that once the formal funding period ends, the systems and workflows developed through CORIZA will continue to run in the background, ensuring long-term improvements in pediatric antibiotic prescribing.

### Where can I find the antibiotic stewardship educational materials if I was unable to attend one of the live sessions?

The video has been posted to the [Connect Anywhere - PCHA Pediatric Presentation Series Recordings](#).

### What do I need to do to receive ABP MOC Part 4 credit for participation in this project?

Additional information on ABP MOC Part 4 Credit can be found in the [CORIZA MOC Part 4 Credit FAQ](#).

### I don't have an antibiotic commitment poster in my office. Who do I contact?

Please contact your Practice Manager or Tammy Ojeda-Leao, Executive Director-General Pediatrics, PCHA ([TOjedaLeao@stanfordchildrens.org](mailto:TOjedaLeao@stanfordchildrens.org)) for questions related to the antibiotic commitment posters.

### Who can I contact with questions or feedback about acute respiratory tract infections, this document, or the CORIZA project?

We welcome your questions, comments, and feedback!  
Please email [corizaproject@stanford.edu](mailto:corizaproject@stanford.edu) or use the QR code to submit your inquiry directly to our team.



## Sinusitis

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### What is the data to support the use of amoxicillin (rather than amoxicillin/clavulanate) for children with sinusitis?

For most children with uncomplicated acute bacterial rhinosinusitis, amoxicillin and amoxicillin/clavulanate perform similarly, while amoxicillin/clavulanate causes more side effects. The strongest recent evidence comes from a large cohort study of nearly 200,000 children by Savage et al. (2023), which found:

- No difference in treatment failure between amoxicillin and amoxicillin/clavulanate
- Higher rates of GI symptoms and yeast infections with amoxicillin/clavulanate

Earlier randomized trials show a similar pattern with no added clinical benefit from clavulanate when compared directly with amoxicillin. The latest AAP guidelines recommend amoxicillin with or without clavulanate as first-line therapy, while the IDSA favors amoxicillin/clavulanate, largely based on microbiologic considerations. More recent clinical data suggest that this theoretical advantage has not translated into improved outcomes for most children with uncomplicated sinusitis.

Given similar effectiveness and better tolerability, high-dose amoxicillin is the preferred first-line option for most children with sinusitis. Amoxicillin/clavulanate remains appropriate in select situations, such as:

- More severe illness
- Age < 2 years, daycare attendance, or immunocompromised status
- Recent (< 30 days) antibiotic exposure

### For children with acute bacterial rhinosinusitis, what is the role of sinus rinses in reducing the need to treat with antibiotics?

Intranasal saline irrigation with either physiologic or hypertonic saline is recommended as an adjunctive therapy for adults with acute bacterial rhinosinusitis (ABRS) based on the [2012 IDSA guideline](#). Evidence in children is more limited but generally supports a modest benefit in symptom relief and quality of life, with few adverse effects. At least two studies suggest that nasal saline irrigation may reduce antibiotic use in children with uncomplicated ABRS. Ragab et al. (2015) reported similar clinical cure rates with amoxicillin plus saline (83.9%) and saline alone (71%,  $p = 0.22$ ). Cabillot et al. (2020) found improvements in symptoms and lower antibiotic prescribing rates among patients using saline irrigation. Overall, saline nasal irrigation is safe, well tolerated, and can provide symptomatic relief comparable to antibiotic therapy in some children with uncomplicated ABRS. The optimal concentration, volume, and frequency of irrigation have not yet been established.

## Streptococcal pharyngitis

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### Is it really ok to use once-daily amoxicillin for strep throat?

Yes. Once-daily amoxicillin is the recommended first-line treatment for group A streptococcal pharyngitis. Major guidelines, including those from the [CDC](#), [IDSA](#), [AHA](#), and [AAP](#) support amoxicillin 50 mg/kg once daily (max 1,000 mg) as an appropriate regimen.

This recommendation is grounded in multiple studies showing that compared to twice-daily dosing, once-daily dosing has:

- Comparable clinical outcomes (symptom resolution)
- Similar or improved microbiologic eradication rates
- Equivalent adverse event profiles

From a practical standpoint, once-daily dosing may be easier for some families and improves the likelihood that the full 10-day course is completed.

### **What is the recommended maximum dose of amoxicillin for streptococcal pharyngitis?**

For children, adolescents, and adults, the recommended maximum dose of amoxicillin for streptococcal pharyngitis is 1 g per day. This can be given as: 1 g once daily or 500 mg BID. Both dosing strategies have been shown to be equally effective in achieving clinical cure and bacterial eradication.

### **For true amoxicillin allergic patients, aren't the cephalosporins (e.g., cephalexin, cefdinir) a reasonable treatment alternative for streptococcal pharyngitis?**

It depends on the cephalosporin and the type of allergic reaction.

For patients with a true IgE-mediated (Type I) allergy to amoxicillin or penicillin, such as anaphylaxis, angioedema, or immediate hives, cephalexin should be avoided. Cephalexin shares an identical R1 side chain with amoxicillin, which carries a high risk of cross-reactivity.

Later-generation cephalosporins, such as cefdinir, do not share this R1 side chain and have a much lower risk of cross-reaction. However, their use for streptococcal pharyngitis is not preferred. Although cefdinir is FDA approved for a 5-day course for streptococcal pharyngitis, the [2012 IDSA guidelines](#) do not recommend it. The clinical trials supporting short-course therapy had significant limitations, including inconsistent diagnostic criteria, poor adherence tracking, and limited ability to distinguish relapse from reinfection.

Because of these limitations and the broader antimicrobial spectrum and higher cost of cefdinir compared with alternative second-line therapies (i.e., clindamycin, azithromycin), routine use of cefdinir for streptococcal pharyngitis is discouraged.

### **Should we treat every non-Group A beta-hemolytic streptococcal pharyngitis?**

It is estimated that 1.5-3% of children and approximately 6% of adults are group C/G *Streptococcus* (GCS/GGS) carriers. Pharyngitis due to GCS/GGS typically resemble group A streptococcal (GAS) pharyngitis and are most commonly diagnosed in adolescents and young adults. It is generally not necessary to confirm non-GAS causes of pharyngitis except in patients who have prolonged symptoms or in those who are very ill. There is no evidence from controlled studies to guide therapy of acute pharyngitis when GCS or GGS are isolated. If a physician elects to treat, the regimen should be similar to that for GAS pharyngitis and penicillin is the antibiotic of choice. GCS/GGS pharyngitis is not known to trigger acute rheumatic fever; therefore, a treatment course of 5 days (rather than 10 days) is reasonable.