University of Saskatchewan

Ear You Go: Navigate Through Acute Otitis Media

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FMF
Family Medicine Forum
Forum en médecine familiale

THE COLLEGE OF FAMILY PHYSICIANS OF CANADA
LE COLLÈGE DES MÉDECINS DE FAMILLE DU CANADA

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RBC CONVENTION CENTRE WINNIPEG, MB

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Presenter: Marlys LeBras

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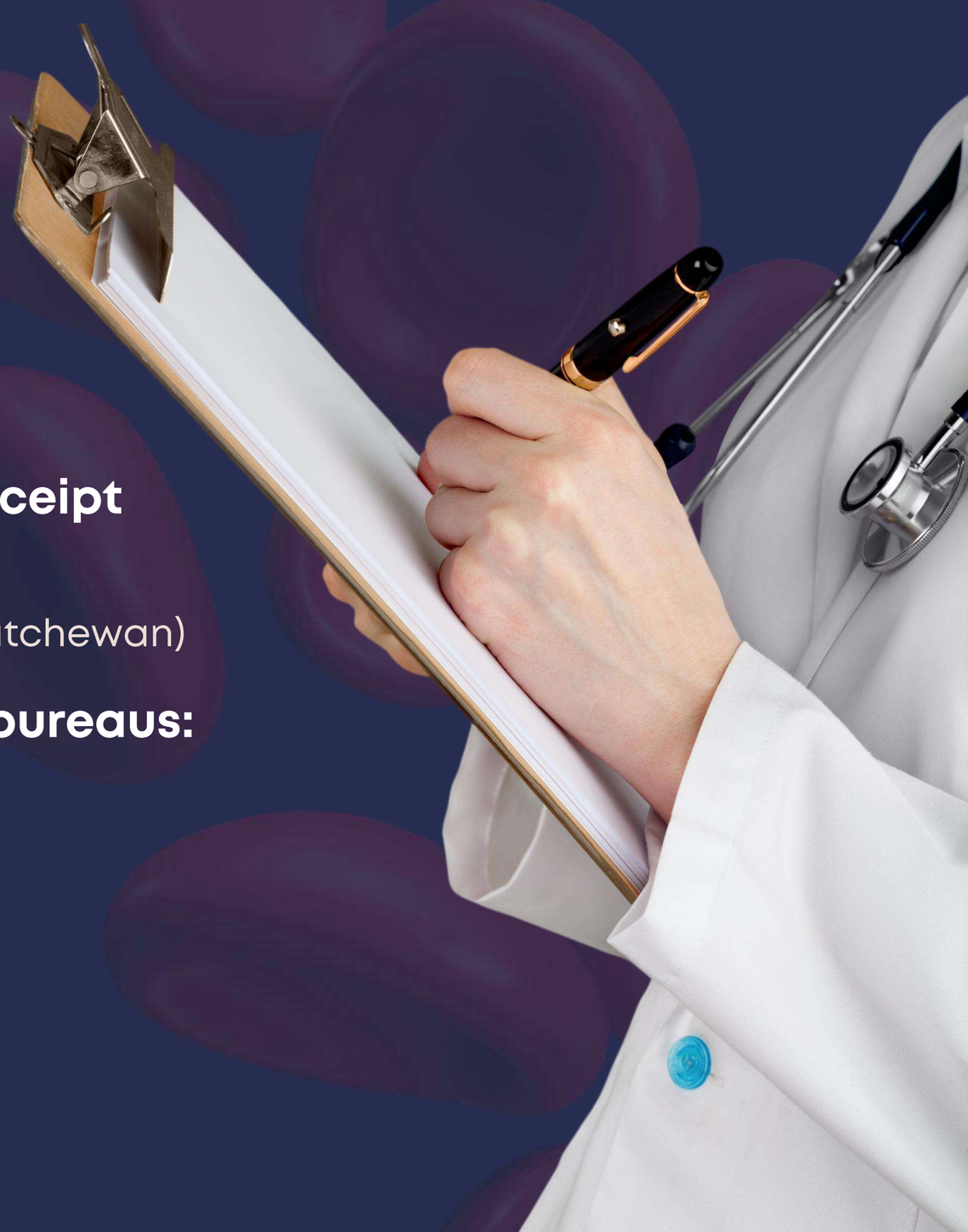

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Presenter: Alesha Bloor

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- RxFiles **does not** receive funding from the pharmaceutical industry.

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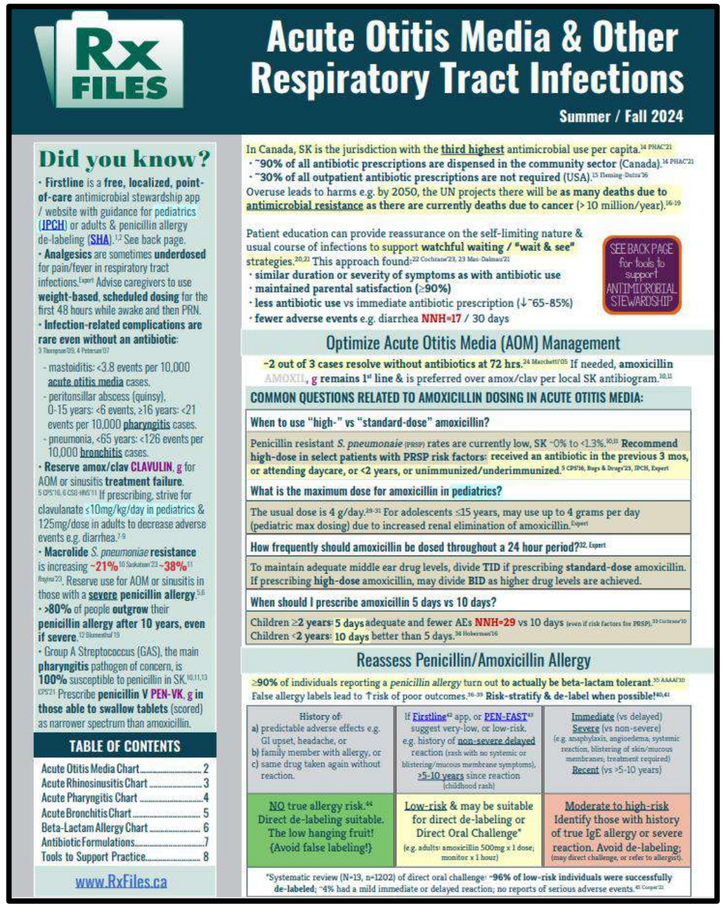
Sharing Perspectives on AOM Management



RX FILES

Acute Otitis Media & Other Respiratory Tract Infections

Summer / Fall 2024

Did you know?

- **Firstline** is a **free, localized, point-of-care** antimicrobial stewardship app / website with guidance for pediatrics (JPCH) or adults & penicillin allergy de-labeling (SHA).[1,2] See back page.
- **Analgesics** are sometimes **underdosed** for pain/fever in respiratory tract infections.[Expert] Advise caregivers to use **weight-based**, **scheduled dosing** for the first 48 hours while awake and then PRN.
- **Infection-related complications are rare even without an antibiotic**: [3 Thompson'09, 4 Petersen'07]
  - mastoiditis: <3.8 events per 10,000 acute otitis media cases.
  - peritonsillar abscess (quinsy), 0-15 years: <6 events, ≥16 years: <21 events per 10,000 pharyngitis cases.
  - pneumonia, <65 years: <126 events per 10,000 bronchitis cases.
- **Reserve amox/clav CLAVULIN**, g for AOM or sinusitis **treatment failure**. [5 CPS'16, 6 CSID-HNS'11] If prescribing, strive for clavulanate <10mg/kg/day in pediatrics & 125mg/dose in adults to decrease adverse events e.g. diarrhea.[7-9]
- **Macrolide** *S. pneumoniae* **resistance** is increasing ~**21%**[10 Saskatoon'21] - ~**38%**[11 Regina'23]. Reserve use for AOM or sinusitis in those with a **severe penicillin allergy**.[5,6]
- **>80%** of people **outgrow** their **penicillin allergy after 10 years, even if severe**.[12 Blumenthal'19]
- Group A Streptococcus (GAS), the main **pharyngitis** pathogen of concern, is **100%** susceptible to penicillin in SK.[10,11,13 CPS'21] Prescribe **penicillin V PEN-VK**, g **in those able to swallow tablets** (scored) as narrower spectrum than amoxicillin.

TABLE OF CONTENTS

www.RxFiles.ca

In Canada, SK is the jurisdiction with the **third highest** antimicrobial use per capita.[14 PHAC'21]
- ~**90% of all antibiotic prescriptions are dispensed in the community sector** (Canada).[14 PHAC'21]
- ~**30% of all outpatient antibiotic prescriptions are not required** (USA).[15 Fleming-Dutra'16]

Overuse leads to harms e.g. by 2050, the UN projects there will be **as many deaths due to antimicrobial resistance as there are currently deaths due to cancer** (> 10 million/year).[16-19]

Patient education can provide reassurance on the self-limiting nature & usual course of infections to support **watchful waiting / "wait & see"** strategies.[20,21] This approach found:[22 Cochrane'23, 23 Mac-Dalmas'21]
- **similar duration or severity of symptoms as with antibiotic use**
- **maintained parental satisfaction (≥90%)**
- **less antibiotic use** vs immediate antibiotic prescription (↓~65-85%)
- **fewer adverse events** e.g. diarrhea **NNH=17** / 30 days

SEE BACK PAGE for tools to support ANTIMICROBIAL STEWARDSHIP

Optimize Acute Otitis Media (AOM) Management

~**2 out of 3 cases resolve without antibiotics at 72 hrs.**[24 Marchetti'05] If needed, **amoxicillin** AMOXIL, g **remains 1st line** & is preferred over amox/clav per local SK antibiogram.[10,11]

COMMON QUESTIONS RELATED TO AMOXICILLIN DOSING IN ACUTE OTITIS MEDIA:

When to use "high-" vs "standard-dose" amoxicillin?

Penicillin resistant *S. pneumonaie* (PRSP) rates are currently low, SK ~0% to <1.3%.[10,11] **Recommend high-dose in select patients with PRSP risk factors: received an antibiotic in the previous 3 mos, or attending daycare, or <2 years, or unimmunized/underimmunized.**[5 CPS'16, Bugs & Drugs'23, IDCK, Expert]

What is the maximum dose for amoxicillin in pediatrics?

The usual dose is 4 g/day.[25-31] For adolescents ≤15 years, may use up to 4 grams per day (pediatric max dosing) due to increased renal elimination of amoxicillin.[Expert]

How frequently should amoxicillin be dosed throughout a 24 hour period?[32, Expert]

To maintain adequate middle ear drug levels, divide **TID** if prescribing **standard-dose** amoxicillin. If prescribing **high-dose** amoxicillin, may divide **BID** as higher drug levels are achieved.

When should I prescribe amoxicillin 5 days vs 10 days?

Children ≥**2 years**: **5 days** adequate and fewer AEs **NNH=29** vs 10 days [even if risk factors for PRSP].[33 Cochrane'10]
Children <**2 years**: **10 days** better than 5 days.[34 Hoberman'16]

Reassess Penicillin/Amoxicillin Allergy

≥**90%** of individuals reporting a *penicillin allergy* turn out **to actually be beta-lactam tolerant.**[35 AAAAI'20]
False allergy labels lead to ↑risk of poor outcomes.[36-39] **Risk-stratify & de-label when possible!**[40,41]

History of: a) predictable adverse effects e.g. GI upset, headache, or b) family member with allergy, or c) same drug taken again without reaction.	If Firstline[42] app, or PEN-FAST[43] suggest very-low, or low-risk. e.g. history of non-severe delayed reaction (rash with no systemic or blistering/mucous membrane symptoms), >5-10 years since reaction (childhood rash)	Immediate (vs delayed) Severe (vs non-severe) (e.g. anaphylaxis, angioedema, systemic reaction, blistering of skin/mucous membranes, treatment required) Recent (vs >5-10 years)
NO true allergy risk.[44] Direct de-labeling suitable. The low hanging fruit! {Avoid false labeling!}	Low-risk & may be suitable for direct de-labeling or Direct Oral Challenge* (e.g. adults: amoxicillin 500mg x 1 dose; monitor x 1 hour)	Moderate to high-risk Identify those with history of true IgE allergy or severe reaction. Avoid de-labeling; (may direct challenge, or refer to allergist).

*Systematic review (N=13, n=1202) of direct oral challenge: ~**96% of low-risk individuals were successfully de-labeled**; ~4% had a mild immediate or delayed reaction; no reports of serious adverse events.[45 Gaspari'21]

Newsletter & references online at: www.RxFiles.ca/antibiotics

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AOM Academic Detailing Visits

Photo credit:
https://en.wikipedia.org/wiki/Flag_of_Saskatchewan

SK Health Care Providers Detailed (n=891)	
Family Physicians	410
Medical Residents	81
Nurse Practitioners	140
Pharmacists	181
Nurses	24
Other (e.g. students)	55

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Learning Objectives

- Confirm and refine approaches for the management of AOM by addressing practical, case-based considerations, such as:
  - Discussing evidence and tools to support **watchful waiting strategies**.
  - **Individualizing an antibiotic prescription** based on patient factors (e.g. age, resistance patterns), when indicated.
  - Using **penicillin allergy risk stratification tools** (e.g. PENFAST) to identify low-risk candidates for possible delabeling.

Consulting RxFiles: Case 1

Photo credit: Canva.com

History of Current Illness

- Aubrey, 3-year-old patient
- Presents with a 1-day history of lest ear pain and fever
  - Maximum temperature of 38.5◦C
  - Responsive to acetaminophen, allowing comfortable sleep
- Symptoms consistent with a viral upper respiratory tract infection (URTI) in the preceding days
  - nasal congestion, rhinorrhea and mild cough

Consulting RxFiles: Case 1

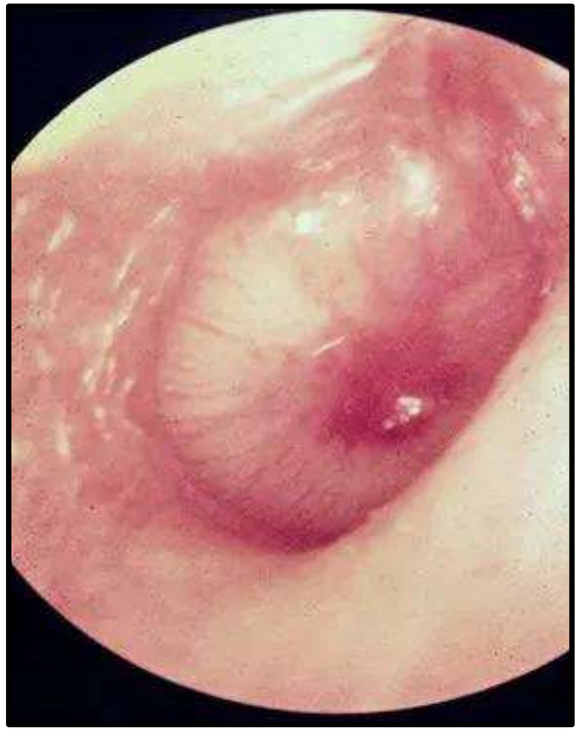

Photo credit: https://media.dynamed.com/image/authenticated/t_thumb_large/q_auto,f_auto/EBSCOHealth/CCMS/Dynamed/images/I504662

Examination

- Aubrey is alert, responsive and in acute distress
- Otoscopic examination reveals a bulging, erythematous left tympanic membrane
- Shotty cervical lymphadenopathy is present, and more prominent on the left side

Consulting RxFiles: Case 1

Photo credit: Canva.com

Review of Medical History

- Immunizations: up to date (including pneumococcal conjugate, H. influenzae type b, influenza, and COVID-19)
- No antibiotics in the past three months
- No allergies
- Weight – 14kg
- Does not attend daycare

How would you manage this case?

Consulting RxFiles: 1

What we will review

- Watchful Waiting / Delayed Antibiotic Prescription
- Individualization of Antibiotic Regimen

Next:

- *Treatment failure*
- *Recurrence*
- *Perforation*
- *Penicillin Allergy*

Newsletter & references online at:
www.RxFiles.ca/antibiotics

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AOM Overview

- Bacterial or viral infection - distinguishing between the two can be difficult - and **BOTH may be present in up to 50% of cases**.

- Commonly develops as a **complication of a viral URTI**.
  - URTI impairs eustachian tube function and leads to middle ear effusion and inflammation.

Did you know?

~**50%** of children with AOM experience symptom resolution by day 3 and up to ~**90%** by days 7 to 8, without antibiotic treatment.*

**total symptom duration may be prolonged when preceded by viral URTI (non-specific RTI resolves in ~15 days)*

Sawada S, Okutani F, Kobayashi T. Comprehensive Detection of Respiratory Bacterial and Viral Pathogens in the Middle Ear Fluid and Nasopharynx of Pediatric Patients With Acute Otitis Media. Pediatr Infect Dis J. 2019 Dec;38(12):1199-1203.
Thompson M, Vodicka TA, Blair PS, Buckley DI, Heneghan C, Hay AD; TARGET Programme Team. Duration of symptoms of respiratory tract infections in children: systematic review. BMJ. 2013 Dec 11;347:f7027.

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Watchful Waiting

Since AOM is often self-limiting, most guidelines recommend a watchful waiting approach for otherwise **healthy children aged 6 months or older**.

- This strategy focuses on **symptomatic relief** and **close caregiver observation** for up to 48 hours (or 72 hours) before initiating antibiotics, unless symptoms worsen or fail to improve.

Table 1. Watchful Waiting is NOT appropriate in the Following Patients[1-6]

• <6 months • Perforated tympanic membrane • Otorrhea i.e. ear discharge (any age) • Moderate to severe presentation - Severe otalgia, poor response to antipyretics OR - Symptoms do not improve after ≥48 hours OR - Temperature ≥39°C (with or without antipyretic use)	• Tympanostomy tubes, cochlear implants • Recurrent AOM (see below) • <2 years with bilateral AOM • Medical co-morbidities (e.g. craniofacial abnormalities, immunodeficiency) • Complex social circumstances e.g. caregiver unable to support child or follow-up

RxFiles AOM Drug Chart:
Acute Otitis Media- Pediatric Management Considerations

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.
Choosing Wisely Canada. "Using Antibiotics Wisely in Primary Care." Last modified 2024. Accessed August 7, 2025. https://choosingwiselycanada.org/primary-care/antibiotics/.

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Watchful Waiting Evidence

- **Infection-related complications are rare even without an antibiotic:**

3 Thompson'09, 4 Peterson'07

- mastoiditis: <3.8 events per 10,000 **acute otitis media** cases.
- peritonsillar abscess (quinsy), 0-15 years: <6 events, ≥16 years: <21 events per 10,000 **pharyngitis** cases.
- pneumonia, <65 years: <126 events per 10,000 **bronchitis** cases.

Patient education can provide reassurance on the self-limiting nature & usual course of infections to support **watchful waiting / "wait & see"** strategies.[20,21] This approach found:[22 Cochrane'23, 23 Mas-Dalmau'21]

- **similar duration or severity of symptoms as with antibiotic use**
- **maintained parental satisfaction (≥90%)**
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- **fewer adverse events** e.g. diarrhea **NNH=17** / 30 days

RxFiles Trial Summary:
Delayed-Antibiotic-Prescription-for-Children-with-Respiratory-Infections.pdf

Spurling GKP, Dooley L, Clark J, Askew DA. Immediate versus delayed versus no antibiotics for respiratory infections. Cochrane Database of Systematic Reviews 2023, Issue 10. Art. No.: CD004417.
Mas-Dalmau 2021 Mas-Dalmau G, Villanueva López C, Gorrotxategi Gorrotxategi P, et al. Delayed Antibiotic Prescription for Children With Respiratory Infections: A Randomized Trial. Pediatrics. 2021;147(3):e20201323.

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Did you know?

Antibiotic exposure in early childhood has been associated with the development of following in later childhood / adolescence:

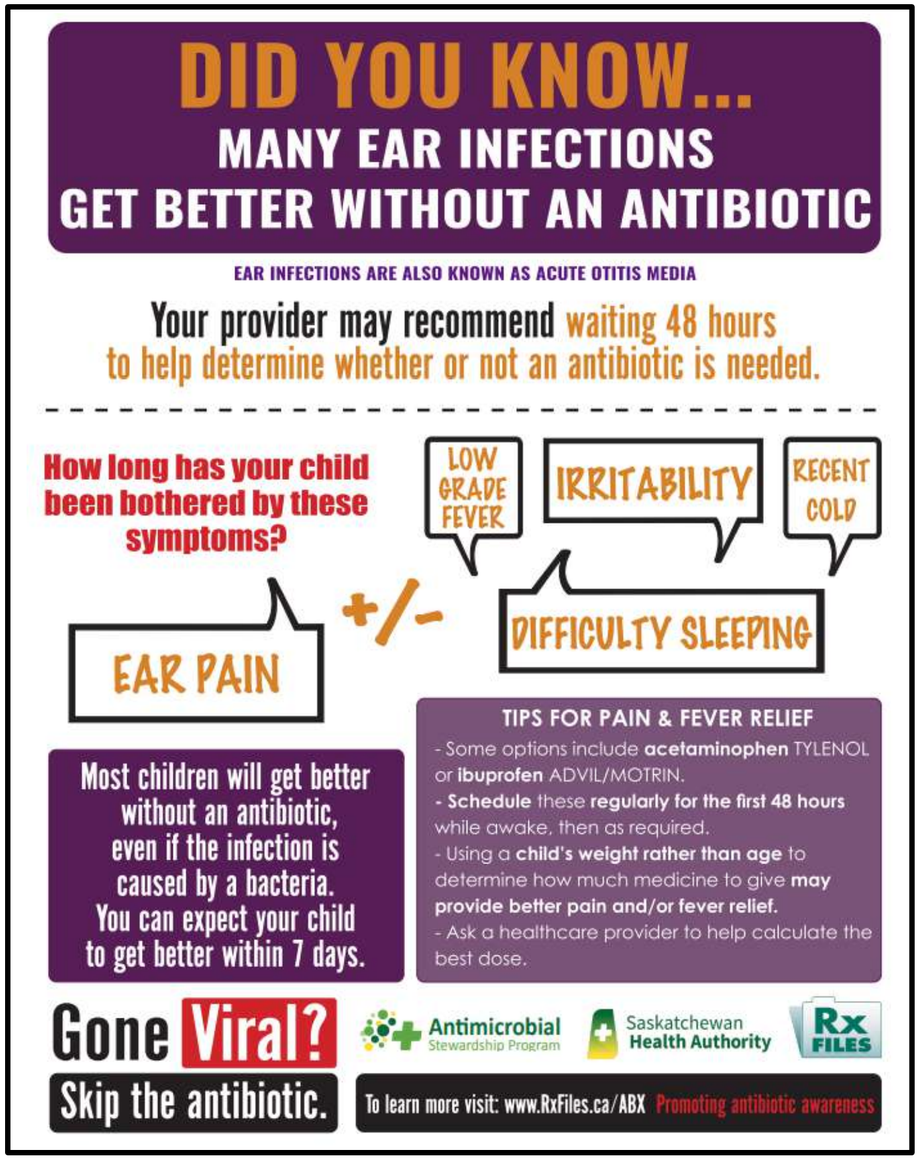
- asthma
- allergic rhinitis
- atopic dermatitis
- celiac disease

Photo credit: Canva.com

Theory? Disruption of early life gut microbiome → development of multiple illnesses

Aversa Z, Atkinson EJ, Schafer MJ, et al. Association of infant antibiotic exposure with childhood health outcomes. Mayo Clin Proc 2021:96(1):66-77.

Watchful Waiting / "Wait and See"



RxFiles Clinic Poster:
[AOM Did You Know.pdf]

PRACTICE POINT

Natural progression of infection
~ 7 days

Analgesics are sometimes underdosed for pain/fever in URTIs

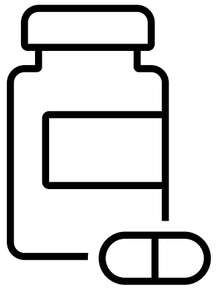
Tips for Pain and Fever Relief:

- **Weight-based** optimal vs age-based
- Use **upper end of dosing range** (may be higher than dose on label)
- **Schedule for 48 hours** while awake, then PRN

Analgesia Evidence

- 2023 Cochrane review found that either **acetaminophen or NSAID (with or without an antibiotic) provided pain relief in 90% of children with AOM** compared to 75% in the placebo group (NNT=7/48 hours).
    - There was **no difference in outcomes between acetaminophen and NSAID (n=411)**

- **Few children (n=71) received combination acetaminophen and NSAID therapy**, resulting in very low-certainty evidence.
    - Some experts recommend combination analgesia…
    - Some experts recommend focusing on a single analgesic…
    - Regardless, ensure appropriate weight-based dosing and give regularly while the child is awake



Paracetamol (acetaminophen) or non-steroidal anti-inflammatory drugs, alone or combined, for pain relief in acute otitis media in children. Cochrane Database Syst Rev. 2023 Aug 18;8(8):CD011534.

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Symptomatic Care: Other Agents?

Other agents for symptomatic management of AOM are **usually not recommended** as they have either **failed to demonstrate a clinically important benefit or are unstudied**.

<table>
<tr><th>Possible Benefit</th><th>Anecdotal Benefit</th><th>Not Recommended</th></tr>
<tr><td>Topical Anaesthetics

• Cochrane review found limited evidence for benefit
• NICE: consider use during watchful waiting</td><td>Hot or Cold Compress
Oil instillation
(e.g. mineral/olive)

• Some recommend against</td><td rowspan="2">Antihistamines or Decongestants

• Cochrane review found no benefit when compared to placebo
• Potential for increased adverse effects

Nasal or Systemic Corticosteroids
• Largely unstudied, low-quality evidence</td></tr>
<tr><td colspan="2">Give in addition to oral analgesics
Only if no eardrum perforation</td></tr>
</table>

Topical analgesia for acute otitis media. Cochrane Database Syst Rev. 2006 Jul 19;(3):CD005657.
Decongestants and antihistamines for acute otitis media in children. Cochrane Database Syst Rev. 2011;(3):CD001727.
Systemic corticosteroids for acute otitis media in children. Cochrane Database Syst Rev. 2018 Mar 15;3:CD012289.

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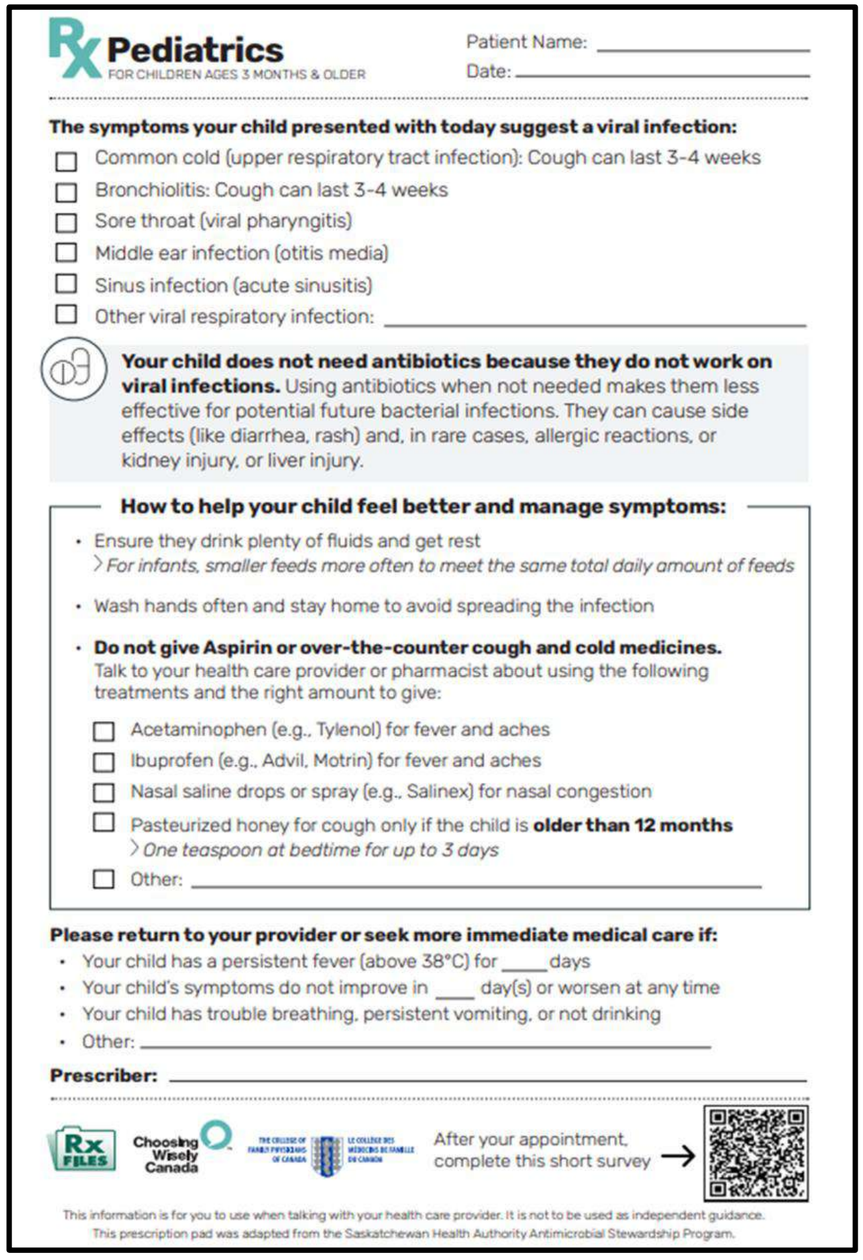

Rx Pediatrics
FOR CHILDREN AGES 3 MONTHS & OLDER

Patient Name: _____
Date: _____

The symptoms your child presented with today suggest a viral infection:

- ☐ Common cold (upper respiratory tract infection): Cough can last 3-4 weeks
- ☐ Bronchiolitis: Cough can last 3-4 weeks
- ☐ Sore throat (viral pharyngitis)
- ☐ Middle ear infection (otitis media)
- ☐ Sinus infection (acute sinusitis)
- ☐ Other viral respiratory infection: _____

Your child does not need antibiotics because they do not work on viral infections. Using antibiotics when not needed makes them less effective for potential future bacterial infections. They can cause side effects (like diarrhea, rash) and, in rare cases, allergic reactions, or kidney injury, or liver injury.

How to help your child feel better and manage symptoms:

- Ensure they drink plenty of fluids and get rest
  - *For infants, smaller feeds more often to meet the same total daily amount of feeds*
- Wash hands often and stay home to avoid spreading the infection
- **Do not give Aspirin or over-the-counter cough and cold medicines.** Talk to your health care provider or pharmacist about using the following treatments and the right amount to give:
  - ☐ Acetaminophen (e.g., Tylenol) for fever and aches
  - ☐ Ibuprofen (e.g., Advil, Motrin) for fever and aches
  - ☐ Nasal saline drops or spray (e.g., Salinex) for nasal congestion
  - ☐ Pasteurized honey for cough only if the child is **older than 12 months**
    - *One teaspoon at bedtime for up to 3 days*
  - ☐ Other: _____

Please return to your provider or seek more immediate medical care if:

- Your child has a persistent fever (above 38°C) for ____ days
- Your child's symptoms do not improve in ____ day(s) or worsen at any time
- Your child has trouble breathing, persistent vomiting, or not drinking
- Other: _____

Prescriber: _____

Rx FILES · Choosing Wisely Canada · The College of Family Physicians of Canada · Le Collège des médecins de famille du Canada

After your appointment, complete this short survey →

This information is for you to use when talking with your health care provider. It is not to be used as independent guidance.
This prescription pad was adapted from the Saskatchewan Health Authority Antimicrobial Stewardship Program.

Viral Prescription Pad

PRACTICE POINT

- Use as a checklist or to help guide the conversation with patients
- Available:
  - Adult and pediatric versions
  - English, French, other languages e.g. Farsi, Ukrainian, Hindi, Arabic, etc

RxFiles/Choosing Wisely/CFPC:
Pediatric_Viral_Prescription.pdf

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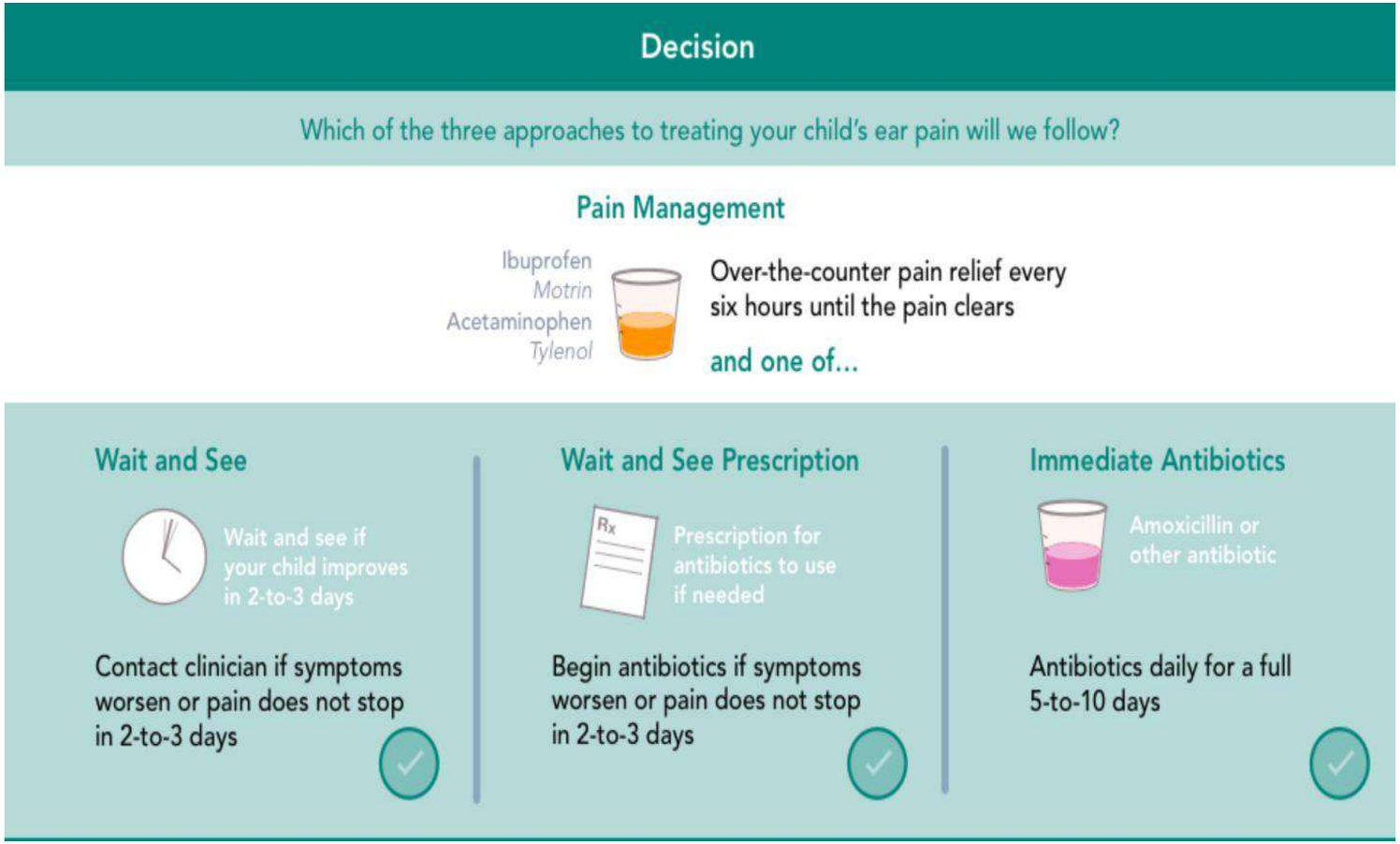
Online Decision Aid



Mayo Clinic: [Your Child's Ear Pain Decision Aid]

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Back to Case 1

You sit down with her parent to discuss the findings and next steps:

- Explain watchful waiting, review current acetaminophen use and recommend a **target dose of 15mg/kg per dose** (weight of 14kg equates to ~200mg of acetaminophen per dose)

Photo credit: Canva.com

*"Use this higher dose of acetaminophen every 4 to 6 hours while Aubrey is awake to a **maximum of 5 doses in 24 hours** to keep her comfortable during this illness. **Don't wait until Aubrey is uncomfortable to give the dose.***

*Most children improve quickly, and antibiotics often aren't needed. In fact, **studies show that up to 90% of children recover fully by day 7 or 8 without antibiotics**.*

Using antibiotics only when necessary helps avoid side effects like diarrhea or rash, and it also helps prevent antibiotic resistance."

Back to Case 1

Knowing that it can be challenging for your patients to book follow-up appointments within a tight timeframe, you offer a **delayed antibiotic prescription**.

Photo credit: Canva.com

*"Just in case Aubrey **doesn't improve or gets worse after 48 hours, I'll give you a prescription for an antibiotic today**.*

You don't need to fill it right away.

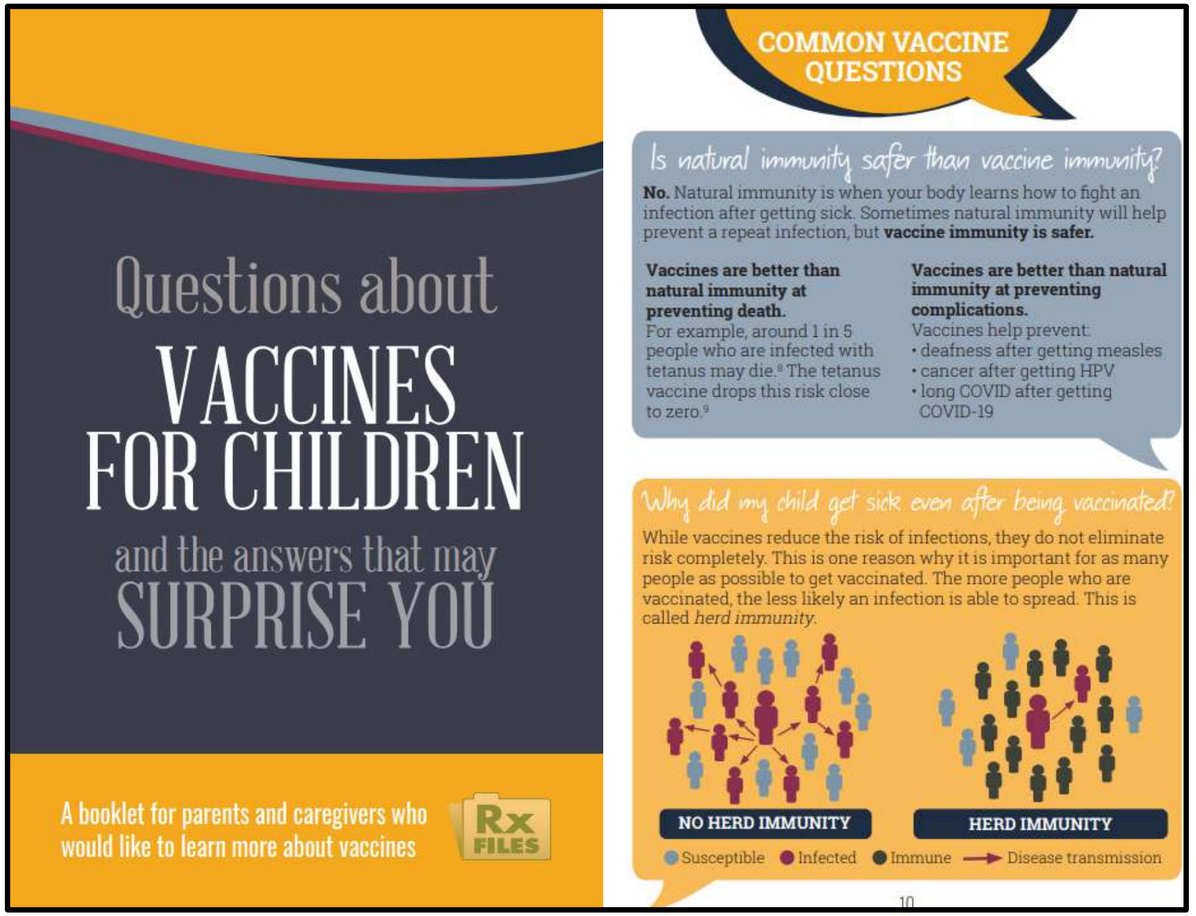
If her fever or pain continues beyond two days, or if she seems more unwell - like not eating, very sleepy or hard to console – you can fill the antibiotic prescription and start the medication.

***Otherwise, don't use the antibiotics and continue with the acetaminophen**."*

AOM Etiology – Informing Antibiotic Choice

- If the cause of AOM is bacterial, ***Streptococcus pneumoniae*** remains the most common pathogen.

- Other bacterial pathogens, such as *Moraxella catarrhalis* or *nontypeable Haemophilus influenzae*, may be involved but are typically **less virulent and more likely to spontaneously resolve** without antibiotics.



Casey JR, Adlowitz DG, Pichichero ME. New patterns in the otopathogens causing acute otitis media six to eight years after introduction of pneumococcal conjugate vaccine. Pediatr Infect Dis J. 2010 Apr;29(4):304-9.
UpToDate. Acute Otitis Meida in Children: Epidemiology, Microbiology, and Complications. Wolters Kluwer Heath. Accessed August 7, 2025.

RxFiles: vaccine-patient-booklet.pdf

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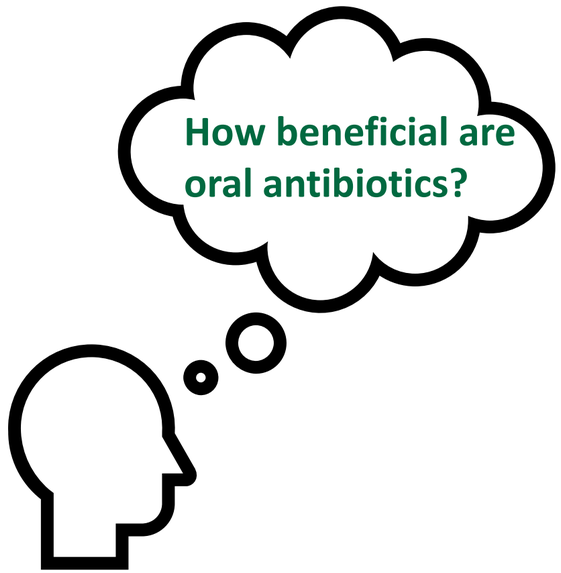
Antibiotic Evidence



2023 Cochrane Review (13 RCTs, 3401 children)	Antibiotic	Placebo	NNT / NNH
Ear pain at 24 hours	60%	60%	--
Ear pain resolution at 48-72 hours (analgesia allowed in both arms)	Resolved in ~ 90%	Resolved in ~85%	**NNT≈20**
Tympanic membrane perforation	2%	5%	**NNT≈34**
Bilateral otitis in unilateral cases	11%	19%	**NNT≈12**
Hearing loss at 3 months	23%	24%	--
Adverse events (vomiting, diarrhea, rash)	27%	20%	**NNH≈14**

Venekamp RP, Sanders SL, Glasziou PP, Rovers MM. Antibiotics for acute otitis media in children. Cochrane Database Syst Rev. 2023 Nov 15;11(11):CD000219.

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Antibiotic Choice

If an antibiotic is indicated, **amoxicillin** remains the first-line treatment for uncomplicated AOM:

- high efficacy against *S. pneumoniae*
- narrow spectrum of activity
- generic available and low cost
- good tolerability

PRACTICE POINT

Other antibiotic alternative are generally not preferred

The role of macrolides e.g. azithromycin **ZITHROMAX**, clarithromycin **BIAXIN** is limited due to the **higher prevalence of S. Pneumoniae resistance** in comparison to other antibiotics

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.
Anti-infective Guidelines for Community-acquired Infections (MUMs). 2024 edition. Anti-infective Review Panel.
Blondel-Hill E, Fryters S. Bugs & Drugs 2.0. Alberta Health Services. App Accessed March 2025.
Gilbert N et al. The Sanford Guide to Antimicrobial Therapy. 55th edition. 2025.

Amoxicillin Dosing

When to use "high-" vs "standard-dose" amoxicillin?

Penicillin resistant *S. pneumonaie* (PRSP) rates are currently low, SK ~0% to <1.3%.[10,11] **Recommend high-dose in select patients with PRSP risk factors:** received an antibiotic in the previous 3 mos, or attending daycare, or <2 years, or unimmunized/underimmunized.[5 CPS'16, Bugs & Drugs'23, JPCH, Expert]

PRACTICE POINT

S. Pneumoniae penicillin resistance can be overcome with high-dose amoxicillin **80-90mg/kg/day**

Children without these risk factors can be prescribed standard-dose amoxicillin **40-50mg/kg/day**

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.
Anti-infective Guidelines for Community-acquired Infections (MUMs). 2024 edition. Anti-infective Review Panel.
Blondel-Hill E, Fryters S. Bugs & Drugs 2.0. Alberta Health Services. App Accessed March 2025.
Gilbert N et al. The Sanford Guide to Antimicrobial Therapy. 55th edition. 2025.
Firstline. Jim Pattison Children's Hospital. Firstline - Clinical Decisions

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Is Clavulanate Effective Against PRSP?

Did you know?

- Adding clavulanate to amoxicillin **CLAVULIN** broadens the antimicrobial spectrum to include **coverage for beta-lactamase–producing organisms** such as:
  - *Haemophilus influenzae*
  - *Moraxella catarrhalis*
- **Clavulanate does not improve activity against penicillin-resistant Streptococcus pneumoniae.**
- Amoxicillin-clavulanate **CLAVULIN** has higher rates of AEs (GI symptoms RR 1.15, yeast infection RR 1.33) vs amoxicillin.
- Up to ~ $10-20 more expensive than amoxicillin.

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.
Savage TJ, Kronman MP, Sreedhara SK, Lee SB, Oduol T, Huybrechts KF. Treatment Failure and Adverse Events After Amoxicillin-Clavulanate vs Amoxicillin for Pediatric Acute Sinusitis. JAMA. 2023 Sep 19;330(11):1064-1073.

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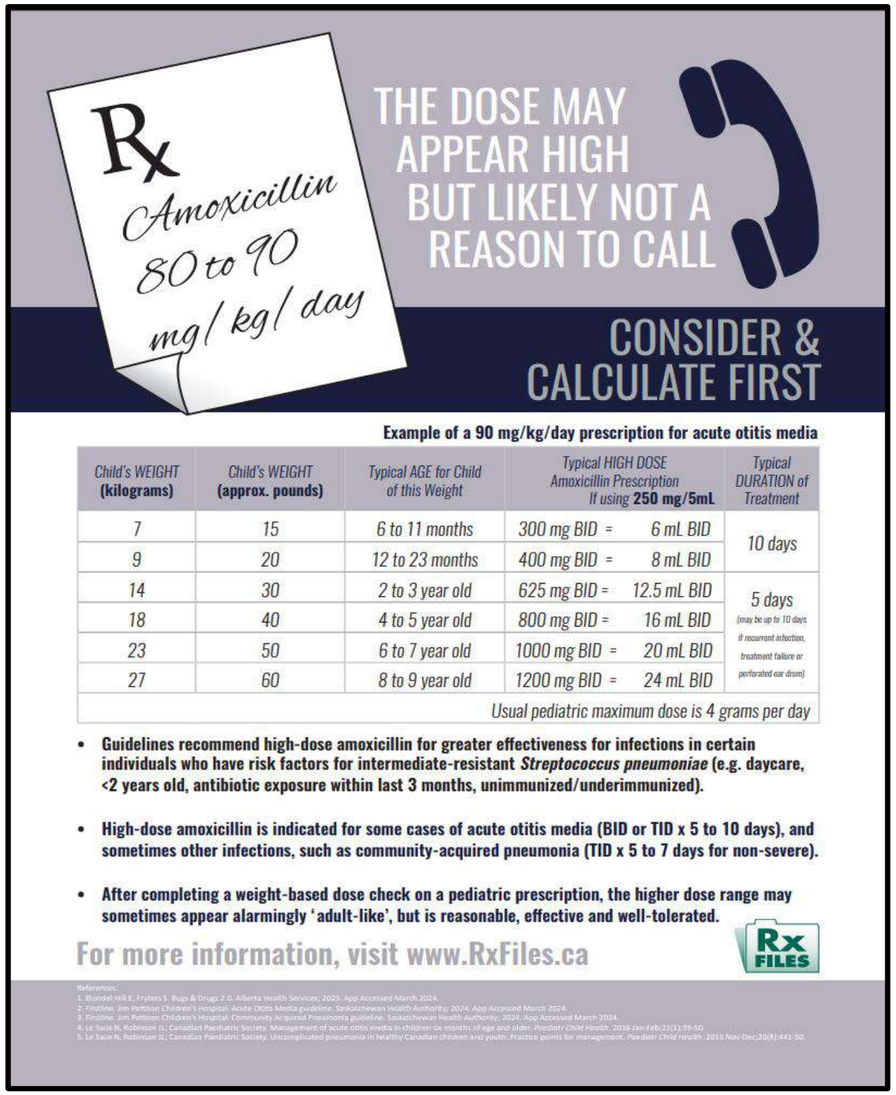
Amoxicillin Dosing



Did you know?

The usual maximum daily dose of amoxicillin is **higher in children ≤15 years** (4000mg/day) than adults (3000mg/day) due to increased renal elimination

RxFiles Amoxicillin Dosing Poster:
Amoxicillin-HIGH-DOSE-Infographic.pdf

Lexidrug. Amoxicillin.
Firstline. Jim Pattison Children's Hospital. Saskatchewan Health Authority; 2024.
PedMed, Pediatric Online Formulary. BC Children's Hospital. Amoxicillin. https://www.pedmed.org/DrugApp/pedshowdrug.php?drugID=3.

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Amoxicillin Dosing

How frequently should amoxicillin be dosed throughout a 24 hour period?[32, Expert]

To maintain adequate middle ear drug levels, divide **TID** if prescribing **standard-dose** amoxicillin. If prescribing **high-dose** amoxicillin, may divide **BID** as higher drug levels are achieved.

There are no head-to-head trials of standard-dose vs high-dose amoxicillin

Meta-analysis (indirect comparison)	Standard-dose	High-dose	Comments
Diarrhea	~9%	~14%	• Overlapping confidence intervals • High heterogeneity
Rash	~3%	~6.5%	

Hum SW, Shaikh KJ, Musa SS, Shaikh N. Adverse Events of Antibiotics Used to Treat Acute Otitis Media in Children: A Systematic Meta-Analysis. J Pediatr. 2019 Dec;215:139-143.e7.

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Antibiotic Duration

When should I prescribe amoxicillin 5 days vs 10 days?

Children ≥2 years: **5 days** adequate and fewer AEs **NNH=29** vs 10 days (even if risk factors for PRSP).[33 Cochrane'10]

Children <2 years: **10 days** better than 5 days.[34 Hoberman'16]

POINT
PRACTICE

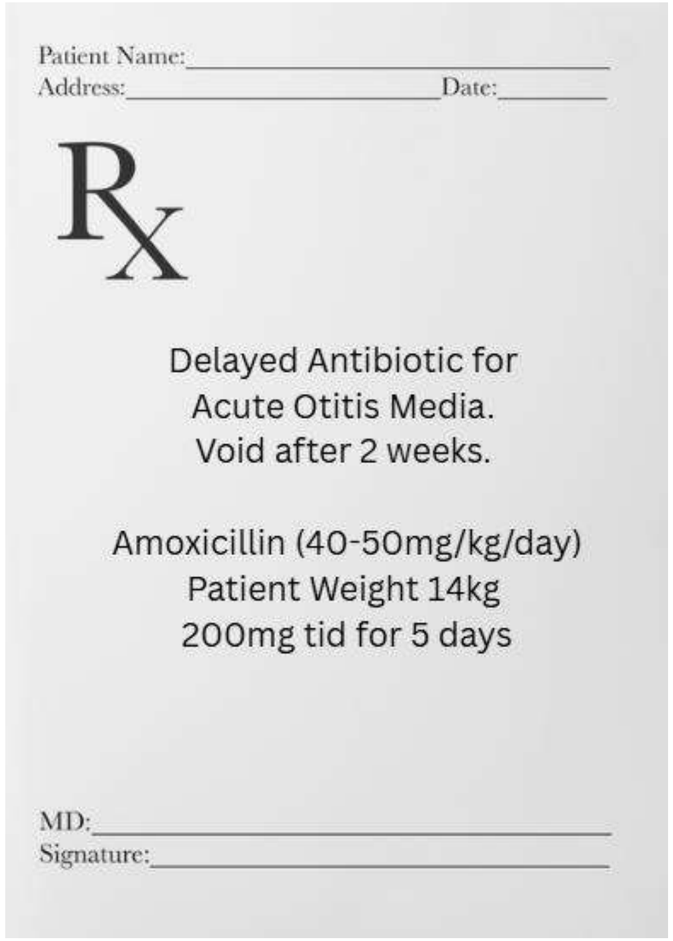
A 10-day antibiotic course is still recommended for children:

- Less than 2 years of age
- AOM with perforation
- Recurrent AOM

RxFiles Trial Summary: Shortened-Antimicrobial-tx-AOM.pdf

Kozyrskyj A, Klassen TP, Moffatt M, Harvey K. Short-course antibiotics for acute otitis media. Cochrane Database Syst Rev. 2010 Sep 8;(9):CD001095.
Hoberman A, Paradise JL, Rockette HE, et al. Shortened Antimicrobial Treatment for Acute Otitis Media in Young Children. N Engl J Med. 2016 Dec 22;375(25):2446-2456.

Back to Case 1


Patient Name:_____
Address:_____Date:_____

Rx

Delayed Antibiotic for
Acute Otitis Media.
Void after 2 weeks.

Amoxicillin (40-50mg/kg/day)
Patient Weight 14kg
200mg tid for 5 days

MD:_____
Signature:_____

Photo credit: Canva.com

After discussing the delayed antibiotic prescription, Aubrey's parent agrees to this plan.

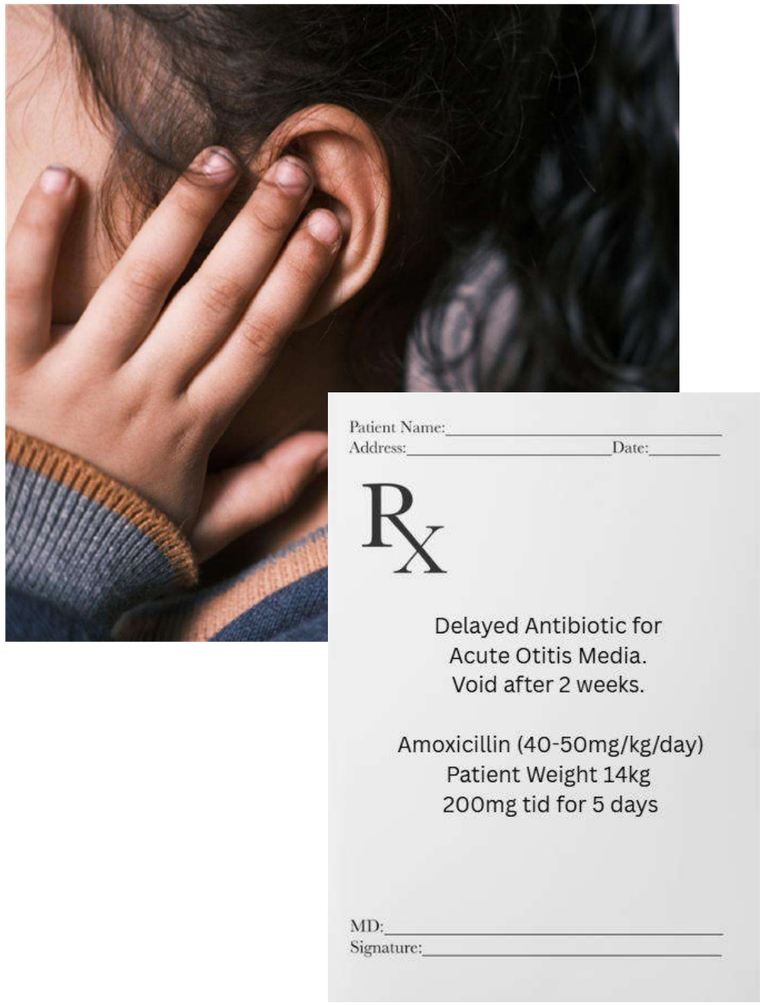
You write a prescription for Amoxicillin:

✓**Standard Dose**
- No risk factors for *Penicillin Resistant S.pneumoniae*

✓**Divided three times daily**
- Recommended to maintain adequate middle ear drug levels with standard-dose amoxicillin (based on PK/PD principles e.g. Tmax > MIC)

✓**5-day course**
- Older than 2 years of age without perforation

Consulting RxFiles – What if Case 1 Returns?



Aubrey returns to the clinic with her parent, who reports that although the pain initially settled with scheduled acetaminophen, it worsened the following day.

On Day 2 of symptoms, they began the **delayed amoxicillin prescription**.

Despite completing the initial course of Amoxicillin 3 days ago, she continues to experience:

- Intermittent ear pain, particularly at night
- Low-grade fevers (37.8–38.2°C)
- Persistent irritability, poor sleep, and decreased appetite

The parent also notes that Aubrey is "just not herself" and remains clingy and more tired than usual.

Consulting RxFiles - What if Case 1 Returns?

Examination:

- Temperature: 38.1°C
- Otoscopy:
  - Left tympanic membrane **still** erythematous and bulging, with persistent loss of landmarks
  - Right tympanic membrane is normal
  - No otorrhea or perforation
- Cervical lymphadenopathy still noted on the left
- No mastoid tenderness or swelling

What is the preferred approach?

1) Switch to **high dose amoxicillin-clavulanate**
2) Switch to **standard dose amoxicillin-clavulanate**
3) Switch to **high-dose amoxicillin**
4) Continue **supportive care with acetaminophen and/or ibuprofen** as needed for fever/pain
5) **Monitor** for improvement in 48–72 hours

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Treatment Failure

Table 3. Managing Treatment Failure[1-6] (no symptomatic improvement after ~2-3 days of antibiotics)

Middle ear effusion does not equal treatment failure, ~60-70% of individuals will have persistent middle ear effusion after an episode of acute otitis media and ~90% of all cases will self-resolve by 3 months.[49,50]

Amoxicillin	**High-dose** regimen (see left for dosing)	• Use if failure of standard-dose amoxicillin.[Expert, SK]
Amoxicillin/ Clavulanate CLAVULIN, g ≥3mos: do not use **4:1** product ↑volume, AEs Dose listed as amoxicillin component	If failure of **high-dose** amoxicillin: **Standard-dose**: Amox/clav **7:1 ratio** 45 mg/kg/day ÷ **TID** x **10 days** cc • **Standard-dose** amox/clav provides coverage of beta-lactamase positive *H. influenza* & *M. catarrhalis* without excessive clav (associated with ↑diarrhea).[51]	• **Reserve** amox-clav when able (broad spectrum). • Some suggest **high-dose amox/clav** for all failures as high-dose amoxicillin (e.g. 90mg/kg/day) overcomes some PRSP.[1 Sanfords'24, 6 AAP'13] In Canada, requires 2 prescriptions to create 14:1 ratio which limits total clav dose (↑diarrhea >10mg/kg/day clavulanate).[51] (USA: 1 prescription as 14:1 ratio commercially available) - {❶ Amox/clav **7:1 ratio** 45 mg/kg/day **PLUS** ❷ Amoxicillin 45mg/kg/day} ÷ **BID** x **10 days** cc.
Ceftriaxone ROCEPHIN, g ✗▼	50mg/kg IM/IV daily x **3 days**	• Unable to tolerate oral, fail amox/clav, severe penicillin allergy. If IM: follow local policies e.g. dilute/reconstitute with lidocaine 1% (& may buffer) to ↓pain, ≥1 injection if ↑volume.[Expert] • May also consider cefprozil or cefuroxime, see left.

ENT referral: persistent tx failure ?tympanocentesis for culture of middle ear fluid, or middle ear effusion >3 months.

PRACTICE POINT

Amoxicillin/clavulanate **CLAVULIN** should be reserved for:

- Amoxicillin failure
- Amoxicillin in previous 4-6 wks
- Immunocompromised

SK: reserve for treatment failure with standard-dose amoxicillin:

- Step up to high-dose amoxicillin before changing to amoxicillin-clavulanate **CLAVULIN**

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.
Anti-infective Guidelines for Community-acquired Infections (MUMs). 2024 edition. Anti-infective Review Panel.
Blondel-Hill E, Fryters S. Bugs & Drugs 2.0. Alberta Health Services. App Accessed March 2025.
Gilbert N et al. The Sanford Guide to Antimicrobial Therapy. 55th edition. 2025.

Back to Case 1: Treatment Failure

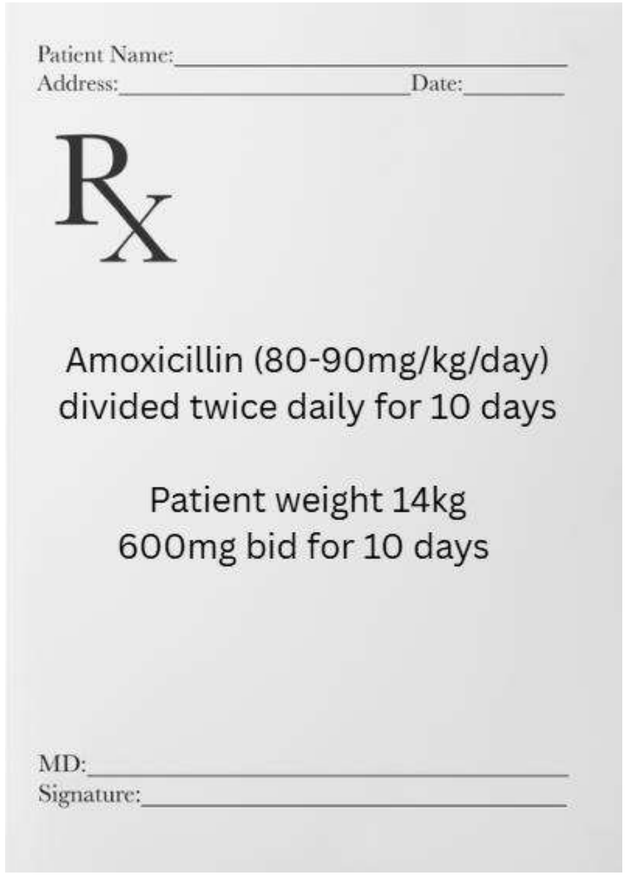

Photo credit: Canva.com

After discussing various options, Aubrey's parent agrees to this plan and you write a prescription for Amoxicillin:

✓**High-Dose**
- Treatment failure with a standard-dose Amoxicillin prescription

✓**Divided twice daily**
- Maintain adequate middle ear drug levels
- Option to discuss with parent:
  - BID (less frequent) vs TID (less liquid)

✓**10-day course**
- Treatment failure

Recurrence

Managing Recurrence *AOM incidence decreases with increasing age*

- Definition: ≥3 AOM episodes within 6 months or ≥4 episodes in 12 months (with ≥ 1 episode in the past 6 months).

2 Bugs & Drugs'23, 5 CPS'16 ('22), 6 AAP'13 No indication for prophylactic antibiotic as not effective & ↑resistance.[1,52,53]

No antibiotic in the past 4-6 weeks	Usually amoxicillin standard or high dose x **10 days** (see left for dosing).
Antibiotic in the past 4-6 weeks	Usually amox/clav x **10 days** (see managing treatment failure above).

- Consider **ENT referral** as tympanostomy tubes may be explored.
- **Prevention strategies**: handwashing, breastfeeding (exclusively for 6 months), smoke avoidance, vaccination (pneumococcal, annual influenza, *H. influenza*e type b), ?xylitol (gum, lozenge available **OTC** ~$10-20/month).[54]

PRACTICE POINT

- Limited evidence and varying recommendations from guidelines
- Typically, <u>not</u> eligible for watchful waiting
- Antibiotic treatment duration x 10 days

Consulting RxFiles – Case 2

History of Current Illness

- Harper, 4-year-old patient
- Presents with sudden onset of **yellowish discharge from the right ear,** first noticed this morning
  - Irritable and tugging at her ear for the past 2 days
  - Intermittent low-grade fevers (maximum temperature of 38.4°C)
- Since the onset of the ear discharge, Harper appears more comfortable, but her mother remains concerned seeks further evaluation

Photo credit: Canva.com

Consulting RxFiles – Case 2

Examination

- Otoscopic examination of the **right ear** reveals perforation of the tympanic membrane, accompanied by mild erythema of the surrounding tissue
- A small amount of purulent discharge is noted in the external auditory canal
- The **left ear** appears normal, with an intact and healthy tympanic membrane

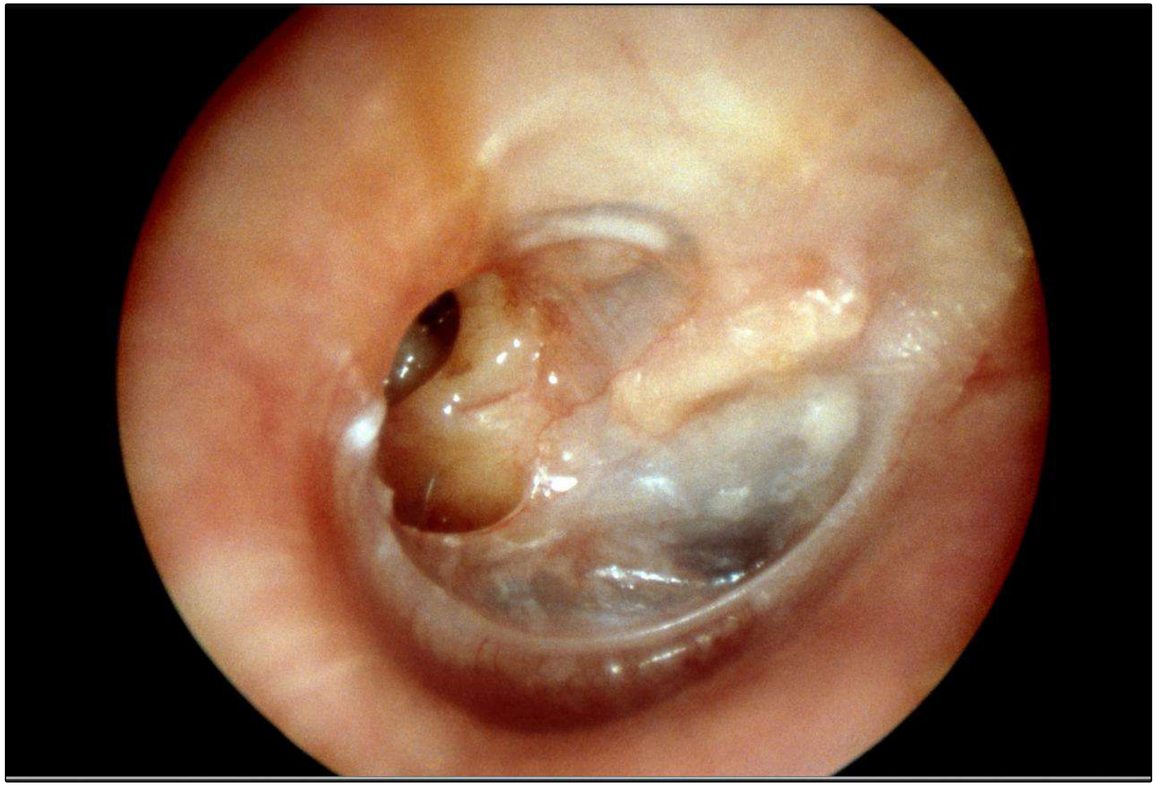

Photo credit: https://www.dynamed.com/condition/acute-otitis-media-aom-in-children#GUID-8947B2BA-3CED-44BA-801E-27D015EFDF64

Consulting RxFiles – Case 2

Review of Medical History

- Immunizations: up to date (including pneumococcal conjugate, H. influenzae type b, influenza, and COVID-19)
- No antibiotics in the past three months
- No allergies to medications
- Weight – 20kg
- Attends daycare

Photo credit: Canva.com

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AOM Perforation Management

Perforation may indicate bacterial etiology and worse prognosis

- Typically, not eligible for watchful waiting
- 2023 Cochrane Review found antibiotics decreased tympanic membrane perforation (1.7% vs placebo 4.8%; NNT≈33)
    - limitation: outcome only assessed in ~30% of the population (n=1075/3401 children with AOM)

PRACTICE POINT

Oral antibiotics preferred over topical antibiotics

- Limited evidence for topical antibiotics in AOM & acute perforation
- Caution as potential for rapid, spontaneous tympanic membrane healing that can prevent adequate topical drug delivery to the middle ear

Duration of treatment **x 10-day oral antibiotic course**

Venekamp RP, Sanders SL, Glasziou PP, Rovers MM. Antibiotics for acute otitis media in children. Cochrane Database Syst Rev. 2023 Nov 15;11(11):CD000219.
Venekamp RP, Prasad V, Hay AD. Are topical antibiotics an alternative to oral antibiotics for children with acute otitis media and ear discharge? BMJ. 2016 Feb 4;352:i308.
Hay AD, et al. Immediate oral versus immediate topical versus delayed oral antibiotics for children with acute otitis media with discharge: the REST three-arm non-inferiority electronic platform-supported RCT. Health Technol Assess. 2021 Nov;25(67):1-76.

Back to Case 2

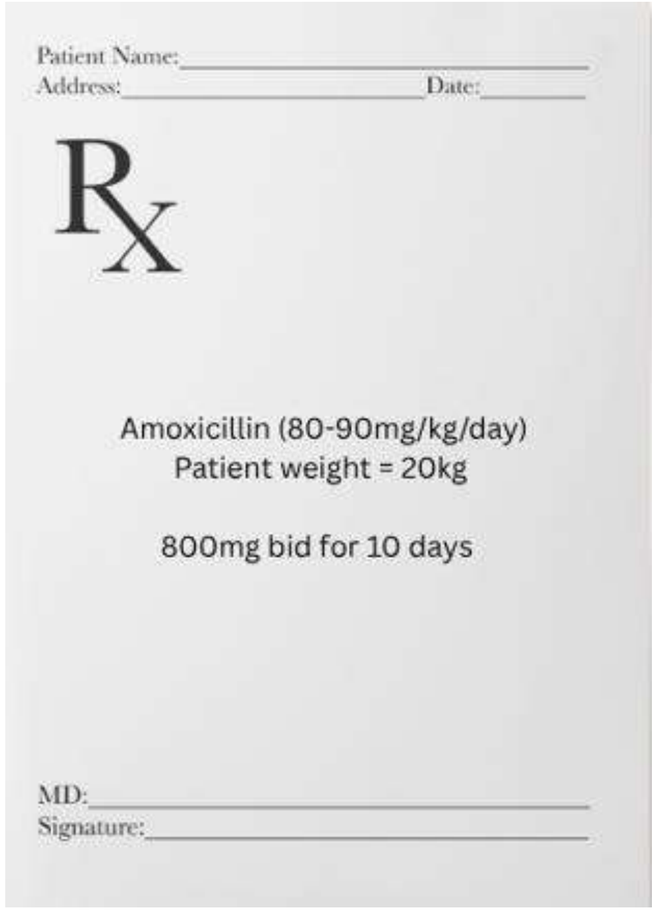

Photo credit: Canva.com

After discussing the available options, you write a prescription for oral Amoxicillin:

- ✓**High-Dose**
  - Risk factors for *Penicillin Resistant S.pneumoniae (PRSP)*
- ✓**Divided twice daily**
  - Maintain adequate middle ear drug levels
  - Option to discuss with parent:
    - BID (less frequent) vs TID (less liquid)
- ✓**10-day course**
  - Perforation
- ✕ No topical antibiotic or antibiotic/corticosteroid required

Consulting RxFiles – Case 3

While accompanying his son in clinic, James shares he was **diagnosed with a penicillin allergy during childhood**.

Photo credit: Canva.com

“I was really young—maybe 5 or 6—when I got a rash after taking amoxicillin for an earache.

I don’t remember much about it.

My parents said it wasn’t itchy, and there were no other symptoms. I haven’t taken amoxicillin since.”

He was unaware of the potential health implications of carrying this label and did not realize that his allergy could be reassessed and possibly de-labelled.

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PENFAST Decision Aid

PEN-FAST: an Allergy Decision Rule (for adults only) [9,22,28] **PALACE**

PEN = **Pen**icillin allergy reported (if yes, continue…)

F = ≤ **F**ive years since reaction or interval unknown (2 points)

A,S = **A**naphylaxis, **A**ngioedema, or **S**evere cutaneous reaction (2 points)

T = **T**reatment was required for the allergy (1 point)

Score: **0**=very low risk (<1%), **1-2**=low risk (5%), **3**=moderate risk (20%), **4-5**=high (50%)

RxFiles Drug Chart:
Beta Lactam Allergies

MDCalc
Medical reference software

Penicillin Allergy Decision Rule (PEN-FAST) (mdcalc.com)

QxMD

Clinical version: PEN-FAST - Penicillin Allergy Risk Tool | QxMD

PALACE RCT

Population	• 6 outpatient clinics (USA, Canada, and Australia) • 382 adult patients with **PENFAST score < 3** (low risk for penicillin allergy) • **96% PENFAST score < 1** (very low risk for penicillin allergy)
Intervention	• Direct oral challenge (amoxicillin 250-500mg)
Comparison	• Stand of care (skin testing, then oral challenge if skin testing negative)
Outcome	• **In each arm, 1 patient** had a positive oral challenge (**mild skin reaction**) within 60 minutes which resolved with a single dose of antihistamine. • **Delayed immune-mediated reaction** occurred in **5%** of participants in **both groups** (antihistamine treatment given, **no hospitalizations or emergency department visits required**) • **Overall: penicillin allergy label was removed for ~98% of patients in both groups**

Copaescu AM, Vogrin S, James F, et al. Efficacy of a clinical decision rule to enable direct oral challenge in patients with low-risk penicillin allergy: the PALACE randomized clinical trial. JAMA Intern Med. 2023;183:944-952.
Thomas BS, Perry D, Moe SS, Turgeon RD, Potter J, Braschi É, Dugré N, Kirkwood JEM, Allan GM. Top studies of 2023 relevant to primary care: From the PEER team. Can Fam Physician. 2024 Apr;70(4):245-248.

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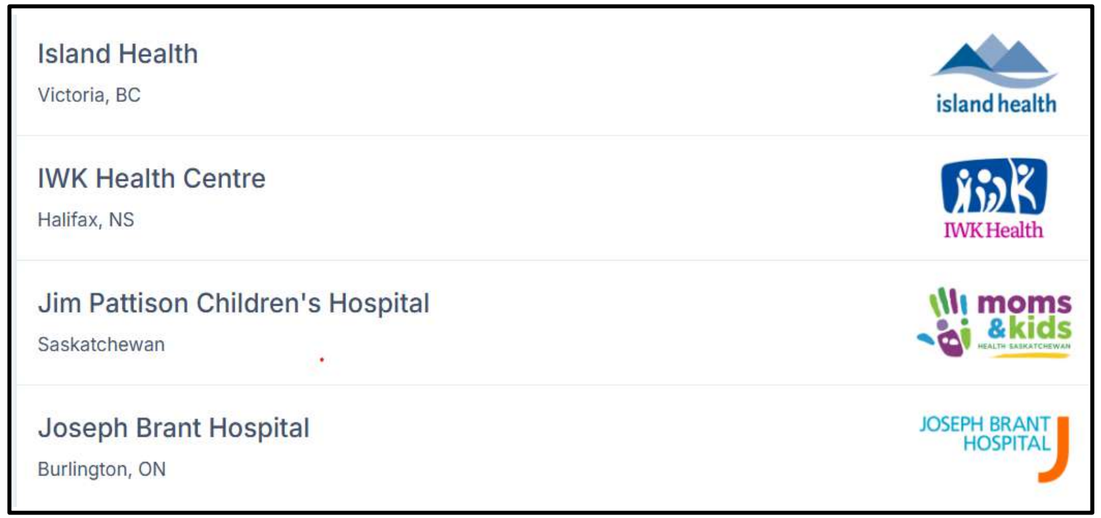
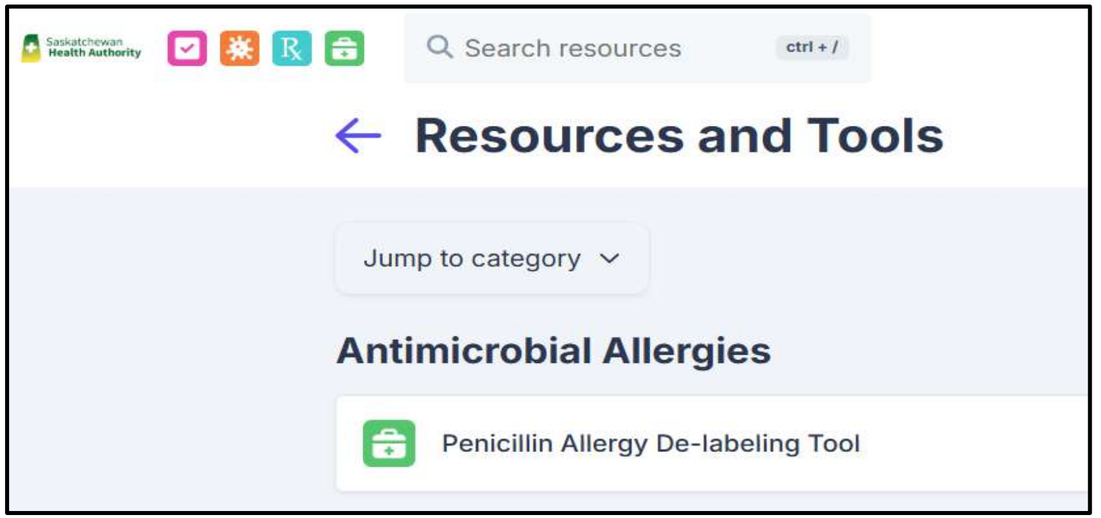
Clinical Guidance

For Healthcare Providers

Designed to help you make informed decisions at the point of care.





- ✓ Risk assessment
- ✓ Oral challenge protocols
- ✓ Documentation tools
- ✓ Pictures (hives vs maculopapular rash)

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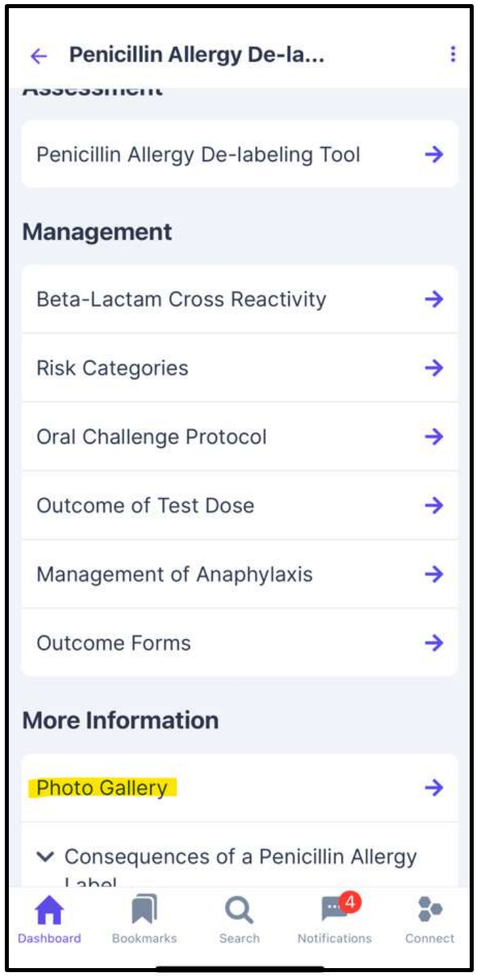
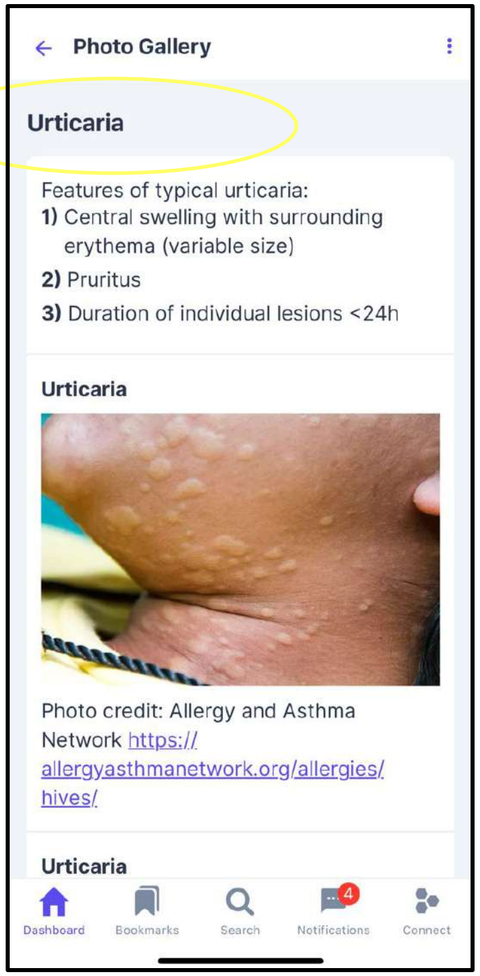
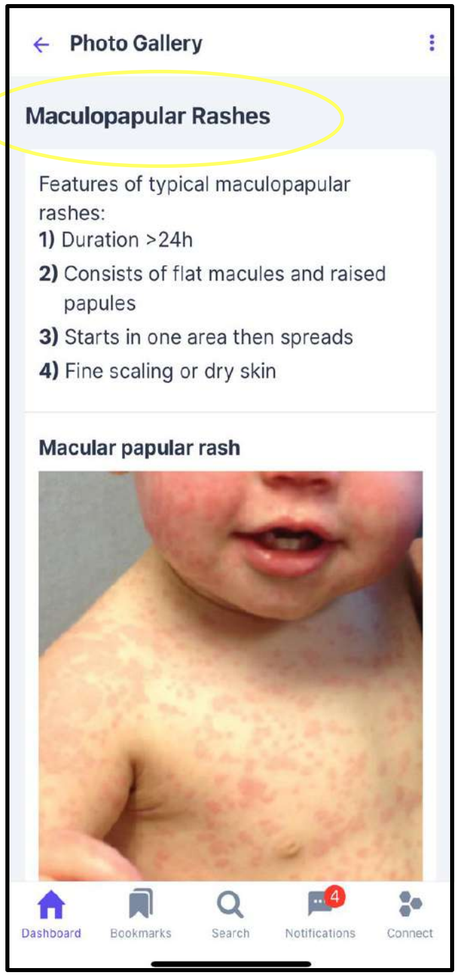
Hives vs Maculopapular Rash







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Back to Case 3

Upon further questioning he does not recall:

- Breathing difficulties or requiring a hospital visit or treatment for the rash

PEN = Penicillin allergy reported ✓

PEN-FAST: an Allergy Decision Rule (for adults only) 9,22,28 PALACE

PEN = **Pen**icillin allergy reported (if yes, continue…)

F = ≤ **F**ive years since reaction or interval unknown (2 points)

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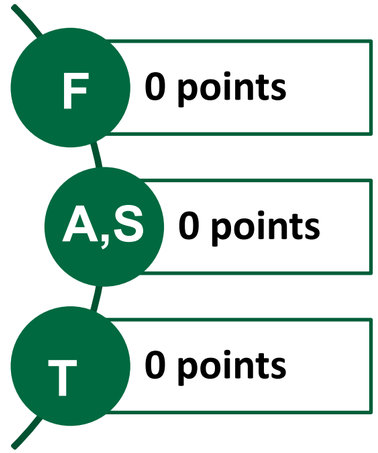

RxFiles Drug Chart:
Beta Lactam Allergies

Total score = 0
Very low risk (<1%)

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Back to Case 3

You explain that the rash he experienced was likely a **non-severe, delayed maculopapular rash**, which is common in children who have a concurrent viral infection, even if they did take amoxicillin.

You reassure James that he has **less 1% risk of having a true penicillin allergy** and offer to book him for an in-clinic oral penicillin challenge.

PRACTICE POINT

- In adults who are low risk (PENFAST score < 2), oral challenge is safe and effective for facilitating the removal of penicillin allergy labels.
- ≥90% of individuals reporting a penicillin allergy turn out to be beta-lactam tolerant.
- >80% of people outgrow their penicillin allergy after 10 years, even if severe .

Joint Task Force on Practice Parameters representing the American Academy of Allergy, Asthma and Immunology **(AAAAI)**. Drug allergy: an updated practice parameter. Ann Allergy Asthma Immunol. 2010Oct;105(4):259-273.
Blumenthal KG, Peter JG, Trubiano JA, Phillips EJ. Antibiotic allergy. Lancet. 2019 Jan 12;393(10167):183-198.

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Consulting RxFiles – What about a “true” penicillin allergy in a patient with AOM *requiring* an antibiotic?

How would you manage?

e.g. anaphylaxis (facial swelling, difficulty breathing, hives) within an hour of the first dose.

1) Prescribe a **macrolide** i.e. clarithromycin, azithromycin
2) Prescribe **doxycycline**
3) Prescribe a **cephalosporin**
4) Prescribe **amoxicillin-clavulanate**

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Weighing The Options

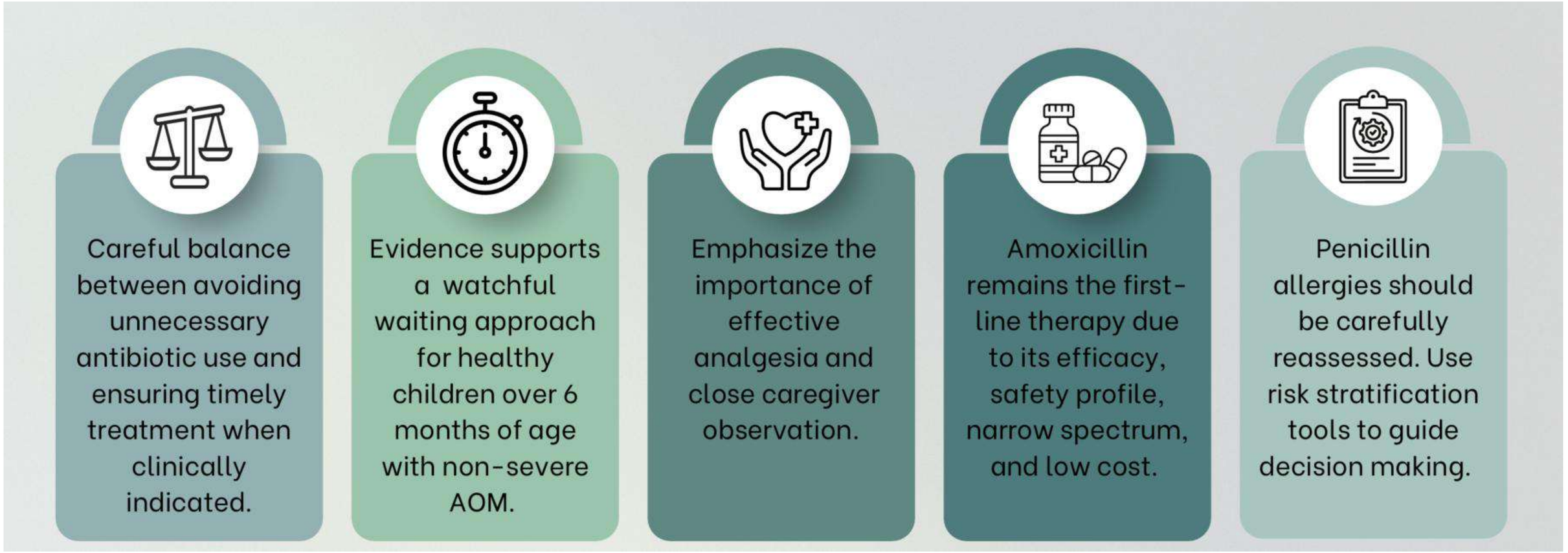
Antibiotic	Pros	Cons

Doxycycline	• Can be considered – **even in children less than 8 years of age**
	• Updated safety data shows lack of dental staining with short-term use (up to 21 days)
		• Only available as capsule or tablet
		• **Not available as a suspension formulation**
		  • May crush tab (off-label)
		  • May open cap & mix with applesauce (off-label)
		  • Compounding pharmacy (full benefit NIHB)
		• Daily or BID administration

Macrolides	• Azithromycin – short duration of therapy (5 days regardless of patient modifiers) • Available as tablets or commercial suspension • Daily administration	• High prevalence of *S. pneumoniae* resistance in comparison to other antibiotics
Note: some guidelines suggest using cephalosporin with a differing side chain from amoxicillin e.g. cefuroxime		

Ravindra D, Huang G, Hallett K, Burgner DP, Gwee A, Silva MJ. Antibiotic Exposure and Dental Health: A Systematic Review. Pediatrics. 2023 Jul 1;152(1):e2023061350.
American Academy of Pediatrics. Committee on Infectious Diseases, American Academy of Pediatrics; Kimberlin D, Barnett E, Lynfield R, Sawyer M. Red Book. 31st edition.
The Society of Hospital Pharmacists of Australia. Australian Don't Rush to Crush Handbook. Therapeutic Options for people unable to swallow solid oral medications. 4th ed. Collingwood, Vic:, 2021.
Public Health Agency of Canada. "Antimicrobial Resistance: Seasonal Update." Canadian Antimicrobial Resistance Surveillance System (CARSS). Last modified November 28, 2024.
Wong T, Atkinson A, t'Jong G, Rieder MJ, Chan ES, Abrams EM. Beta-lactam allergy in the paediatric population. Paediatr Child Health. 2020 Feb;25(1):62-63.

AOM Summary


Careful balance between avoiding unnecessary antibiotic use and ensuring timely treatment when clinically indicated.
Evidence supports a watchful waiting approach for healthy children over 6 months of age with non-severe AOM.
Emphasize the importance of effective analgesia and close caregiver observation.
Amoxicillin remains the first-line therapy due to its efficacy, safety profile, narrow spectrum, and low cost.
Penicillin allergies should be carefully reassessed. Use risk stratification tools to guide decision making.

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Questions??

RxFiles Academic Detailing Team

Front: Julia Bareham, Katherine Neil, Tahirih McAleer, Alesha Bloor; missing: Amy Wiebe

Middle: Zack Dumont, Marc Legge, Brent Jensen, Colette Regier, Debbie Bunka, Andrea Holaday, Loren Regier, Derek Jorgenson

Back: Marlys LeBras, Taisa Trischuk, Jackie Myers, Tanya Nystrom

Other Acknowledgements

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