Optimal antimicrobial duration for common bacterial infections

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Published in:
Australian Prescriber

DOI:
10.18773/austprescr.2019.001

Published: 01/02/2019

Document Version:
Publisher's PDF, also known as Version of record

ARTICLE

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SUMMARY

Most antibiotic use in Australia arises from prescriptions in the community.

The risk of antibiotic-related adverse events, including resistance, increases with longer treatment courses.

When antibiotics are indicated for treatment, short courses are as effective as standard ones for most common infections.

Therapeutic Guidelines: Antibiotic is a key reference for antimicrobial prescribing in Australia.

General practitioners play a key role in reducing antibiotic use.

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Keywords
antibiotic, antimicrobial stewardship, bacterial infections

Aust Prescr 2019;42:5–9
https://doi.org/10.18773/austprescr.2019.001

Introduction

Optimising prescribing of antibiotics in the community is important because it is where most antibiotics are prescribed. In 2015, 30% of all patients attending a general practice received an antibiotic prescription.[1] Most are for acute respiratory infections, and in quantities several-fold more than recommended by Australian guidelines.[2] Repeat prescriptions have been highlighted as a cause for over-use in this setting.[1]

Yet antibiotics are not entirely benign. Their use can be associated with adverse events such as toxicity, allergy (including anaphylaxis), candidiasis, *Clostridium difficile* infection, and antimicrobial resistance – both at community and individual levels.[3-6] The more they are used, the greater the likelihood of adverse events, including resistance.[4-7]

It is important for prescribers to be up to date with best-practice antibiotic prescribing for common infections (Box), particularly the duration of treatment. In Australia, antibiotic prescribing is ideally concordant with the Therapeutic Guidelines: Antibiotic.[8] While other resources are commonly used, such as the Australian Medicines Handbook and MIMS, it is Therapeutic Guidelines that offers comprehensive information on the clinical indications for antibiotic prescription and advice on antibiotic choice, dose and duration. It is also the guideline currently endorsed by the Australian Commission on Safety and Quality in Health Care as the preferred reference for prescribing in the absence of local guidelines.

Antimicrobials are not always needed

Antibiotics are not necessary for most acute respiratory infections including acute rhinosinusitis, acute sore throat and acute otitis media. This is not just because so many of these infections are viral, but because even when the infection is bacterial, the benefits of antibiotic therapy for most patients are modest and outweighed by the harm from adverse effects.[9-12] Australian and local guidelines provide recommendations on when antimicrobial therapy should be used for these conditions.[8,13]

Box Best-practice antimicrobial prescribing in general practice

Do:

- consider microbiological testing to direct therapy (e.g. urinary tract infection, abscess), especially when the causative organism is difficult to predict (e.g. recurrent or unresponsive infection, or overseas travel)
- use the current version of Therapeutic Guidelines: Antibiotic, or available local guidelines
- know *why* you are prescribing the antibiotic (document indication and duration in the medical record)
- prescribe the shortest duration of therapy (or total number of tablets), even if this means the pharmacist breaking the pack.

Don't:

- culture every infection, or potential infection (especially urine in residential aged-care facilities)
- prescribe an antimicrobial without an appropriate indication
- routinely provide a repeat prescription.

Practice points on optimising antibiotic prescribing

It can be difficult to clinically differentiate a patient with a trivial acute respiratory infection from one at an early stage of serious bacterial infection, particularly in children.[14] One option is to 'watch and wait' and ask patients to return if there is clinical deterioration. An alternative is to prescribe an antibiotic but advise the patient to not have it dispensed unless specific symptoms occur. In the setting of acute respiratory infection, this has been shown to reduce antibiotic use by 50% with no significant decrease in patient satisfaction, and importantly no increase in complication rates.[15]

When antibiotics are prescribed, the duration (or number of tablets) should be written on the prescription. This should enable the pharmacist to supply only the number of tablets or capsules required (even if it means breaking the antibiotic pack) which avoids excessive antibiotic use. Repeat scripts are almost never required and we recommend changing the default setting to 'no repeats' in electronic prescribing software when technically feasible.

Antibiotic duration for common infections

Historically, the recommendations for duration of antibiotic treatment have been largely arbitrary. The theoretical principles have been to use enough antibiotic to eliminate the infecting organism and prevent the development of resistance. However, empirical evidence does not support this – shorter courses are nearly always as effective as standard ones.[16] Also, the longer the antibiotic exposure, the greater the pressure to select for antibiotic resistance in commensal bacteria that may cause serious infection in the future.[6,17]

Currently recommended antibiotic durations for the most common bacterial infections managed in general practice are shown in the Table. The total tablet quantity for the suggested duration in adults is included.

Evidence for short-course antimicrobial therapy

There is evidence to support recommendations for shorter antibiotic courses.

Acute rhinosinusitis

A systematic review of 12 studies found no significant difference in clinical cure rate, microbiological efficacy and relapse when 3–7 days versus 6–10 days of antibiotics were given for acute bacterial sinusitis.[16]

Acute tonsillopharyngitis

Short-course antibiotic treatment (5–7 days vs standard 10 days) is associated with equivalent rates of clinical cure in acute tonsillopharyngitis.[18] There is inferior bacteriological eradication, but this is of unknown clinical significance. It also is not known whether short-course therapy reduces the risk of non-suppurative complications (acute rheumatic fever and glomerulonephritis). A full 10-day course is still currently recommended to prevent these complications, especially in high-risk populations (previous history, remote indigenous populations).

Acute otitis media

A systematic review of short-course (<7 days) versus longer duration therapy in children with acute otitis media found that short-course therapy is non-inferior for clinical cure measured at one month and is associated with a significant reduction in gastrointestinal adverse events.[19]

Mild community-acquired pneumonia

Australian studies show that a penicillin and doxycycline (or a macrolide) is effective and safe for most patients with community-acquired pneumonia.[20] Monotherapy is recommended for mild infections providing the patient's progress can be reviewed after 48 hours.[8] A duration of 5–7 days of antibiotics is recommended in adults. This is supported by a systematic review showing no significant difference in outcomes between 3–7 days of antibiotics compared to 7 days or longer.[16] For children with non-severe pneumonia there is no difference between 3 versus 5 days of antibiotics.[21] Therapeutic Guidelines: Antibiotic currently recommends 5 days of oral antibiotics.[8] However, 3 days is endorsed by other Australian expert groups such as the Australian and New Zealand Paediatric Infectious Diseases group.[22]

Acute uncomplicated urinary tract infection

The evidence for antibiotic duration in urinary tract infections is sparser than for acute respiratory infections. For uncomplicated urinary tract infections in women there is no significant difference in clinical cure rates, and fewer adverse events in those given 3 days of antibiotics versus 5 days or longer.[23] However, the risk of bacteriological failure is higher in women given a shorter course. Bacterial elimination from the urine is likely to be relevant for women who are pregnant, experience recurrent and painful urinary tract infections or who have urinary tract prosthetic material in situ (e.g. stent or catheter).

Table **Recommended antibiotic prescribing for common bacterial infections** *

Diagnosis	Indications for antibiotic therapy	First-line antimicrobial (if indicated)	Duration	Tablets (for maximum adult dose)
Acute tonsillopharyngitis	2–25 years, high risk of acute rheumatic fever, or rheumatic heart disease, or scarlet fever	Phenoxymethylpenicillin 12-hourly	10 days †	20 x 500 mg
Acute rhinosinusitis	Symptoms >7 days, or high fever >3 days, or biphasic illness	Amoxicillin 8-hourly	5 days †	15 x 500 mg
Acute otitis media	<6 months old, or systemic symptoms, or indigenous community	Non-indigenous: amoxicillin 12-hourly	5 days †	20 x 500 mg
		Indigenous: amoxicillin 12-hourly	7 days †	28 x 500 mg
Community-acquired pneumonia (mild, can review progress in 48 hours)		Adults: amoxicillin 8-hourly, or doxycycline 12-hourly	5–7 days#	30 x 500 mg / 10 x 100 mg
		Children:		
		• 1 month to <3 months: azithromycin daily ‡	3–5 days	–
		• 3 months to <5 years: amoxicillin 8-hourly	3–5 days †	–
		• 5 years or older: amoxicillin 8-hourly §	3–5 days †	–
Uncomplicated urinary tract infection		Non-pregnant women: trimethoprim daily	3 days	3 x 300 mg
		Pregnant women: cefalexin or nitrofurantoin 12-hourly	5 days	10 x 500 mg / 10 x 100 mg
		Men: trimethoprim daily	7 days	7 x 300 mg
		Children ≥1 month: trimethoprim/sulfamethoxazole 12-hourly	3–5 days ¶	–
Cellulitis (mild, low risk for methicillin-resistant *Staphylococcus aureus*)		Dicloxacillin or flucloxacillin 6-hourly, or	5 days ††	20 x 500 mg
		phenoxymethylpenicillin 6-hourly **	5 days †, ††	20 x 500 mg
Impetigo		Non-remote setting:		
		• Localised lesion: topical mupirocin	7 days	–
		• Multiple lesions/recurrent: dicloxacillin or flucloxacillin 6-hourly	3–10 days ‡‡	40 x 500 mg
		Remote setting:		
		• trimethoprim/sulfamethoxazole 12-hourly, or	5 days	10 x 160/800 mg
		• benzathine penicillin intramuscular	single dose	–
Abscess (low risk for methicillin-resistant *Staphylococcus aureus*)	Spreading cellulitis, or systemic symptoms, or large lesion/critical area	Dicloxacillin or flucloxacillin 6-hourly, as an adjunct to incision and drainage	5 days	20 x 500 mg

* As recommended by Therapeutic Guidelines: Antibiotic. Refer to the complete guideline for further information on indications for antibiotic dosing, second-line antibiotics, and when broader spectrum therapy and specialist involvement may be appropriate. Refer also to local guidelines. Use oral regimen unless indicated otherwise.

† Repeat script required only if using liquid formulation for a large child.

‡ *Chlamydia trachomatis* may be the cause in this age group if afebrile and only mildly unwell.

§ Atypical cover with doxycycline, azithromycin or clarithromycin is recommended if *Mycoplasma pneumoniae* or another atypical pathogen is suspected. Doxycycline should not be used in children younger than 8 years of age.

Repeat prescription required only if using amoxicillin.

¶ 5 days for children <1 year, 3 days for children ≥1 year.

** If *Streptococcus pyogenes* clinically suspected or isolated from culture.

†† Up to 10 days if cellulitis more severe.

‡‡ Stop therapy earlier than 10 days if infection has resolved.

Currently 5 days of therapy is recommended for pregnant women and for second-line drugs in non-pregnant women.[8] The first-line 3-day recommendation of trimethoprim in non-pregnant women has been extrapolated from data for trimethoprim/sulfamethoxazole, a drug that is considered equivalent to trimethoprim for this condition.[24]

Short-course therapy has not been adequately evaluated in men and so it is not recommended at present. A Cochrane review of childhood lower urinary tract infection found no difference in persistent bacteriuria or recurrence when comparing 2–4 days with 7–14 days of oral antibiotics.[25]

Oral fosfomycin has recently been registered for use in Australia as a single-dose treatment for uncomplicated urinary tract infections in females over the age of 12 years. However, this antibiotic should generally be reserved for resistant organisms.

Skin and soft tissue infections

There is a lack of systematic review data to guide short-course therapy for skin and soft tissue infection.

Incision and drainage is the primary therapeutic modality for soft tissue abscesses. A recently published systematic review found that for uncomplicated abscesses, adjunctive antibiotic therapy provides a modest benefit in terms of treatment success and prevention of recurrence,[26] but this needs to be balanced against an increased risk of adverse events. Antibiotic courses ranged from 3–14 days and no recommendation on duration was made.[26]

A randomised controlled trial conducted in the remote Australian setting showed that short-course oral trimethoprim/sulfamethoxazole for 3–5 days is effective for impetigo, and equivalent to intramuscular benzathine penicillin.[27]

Stopping antibiotics earlier than the intended standard duration

Since many common infections are spontaneously remitting, the use of antibiotics is often discretionary. Numerous opinions have been published in support of stopping antibiotics earlier.[28-30]

A practical approach in the community setting is to educate patients and advise them that it is safe to cease the antibiotics early if microbiological results exclude a bacterial cause for their symptoms (e.g. negative urine culture or viral acute respiratory infection), or the patient feels better for conditions where the benefit of antibiotics is small and the infection is not severe (e.g. acute respiratory infections).

Patients should be advised to return any remaining antibiotics to the pharmacy for safe disposal, rather than storing them (which risks future inappropriate use) or disposing of them in general household waste (which risks environmental contamination).

Conclusion

There is good evidence that shorter durations of antimicrobials can reduce adverse effects associated with their use. Furthermore, systematic reviews have found that clinical outcomes are similar between short and long courses for many common infections. Given Australia's relatively high rates of prescribing, we can all play a significant role in reducing the burden of inappropriate antimicrobial use by prescribing short-course therapy when appropriate and limiting prescriptions when they are not indicated. ◀

Christopher Del Mar has been awarded grants by the National Health and Medical Research Council for research into antibiotic resistance in primary care, and for the Cochrane Acute Respiratory Infections Group.

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