References

- Gilbert GL. Knowing when to stop antibiotic therapy. Med J Aust 2015;202:121–2.
- Adembri C, Novelli A. Pharmacokinetic and pharmacodynamic parameters of antimicrobials: potential for providing dosing regimens that are less vulnerable to resistance. Clin Pharmacokinet 2009;48:517–28.
- bpacnz. Antibiotics: choices for common infections. bpacnz, 2013. Available from: www.bpac.org.nz (Accessed Jun, 2015).
- Auckland District Health Board (ADHB). Adult empirical antimicrobial treatment guidelines. ADHB, 2014. Available from: www.adhb.govt.nz/HealthProfessionals/Antimicrobial_ Stewardship.htm#Adult (Accessed Jun, 2015).
- Lutters M, Vogt-Ferrier NB. Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women. Cochrane Database Syst Rev 2008;(3):CD001535.
- 6. Crofts M, Horner P. Chlamydia (uncomplicated, genital). BMJ Clin Evid 2015;2015:1607.
- Havey TC, Fowler RA, Daneman N. Duration of antibiotic therapy for bacteremia: a systematic review and meta-analysis. Crit Care 2011;15:R267.
- Pinzone MR, Cacopardo B, Abbo L, et al. Duration of antimicrobial therapy in community acquired pneumonia: less is more. Sci World J 2014;2014:759138.
- Hepburn M, Dooley D, Skidmore P, et al. Comparison of short-course (5 days) and standard (10 days) treatment for uncomplicated cellulitis. Arch Intern Med 2004;164:1669–74.
- 10. Pakistan Multicentre Amoxycillin Short Course Therapy (MASCOT) pneumonia study group. Clinical efficacy of 3 days versus 5 days of oral amoxicillin for treatment of childhood pneumonia: a multicentre double-blind trial. Lancet 2002;360:835–41.
- 11. Michael M, Hodson E, Craig J, et al. Short compared with standard duration of antibiotic treatment for urinary tract infection: a systematic review of randomised controlled trials. Arch Dis Child 2002;87:118–23.
- 12. Michael M, Hodson E, Craig J, et al. Short versus standard duration oral antibiotic therapy for acute urinary tract infection in children. Cochrane Database of Syst Rev 2003;(1):CD003966.
- 13. El Moussaoui R, de Borgie CAJM, van den Broek P, et al. Effectiveness of discontinuing antibiotic treatment after three days versus eight days in mild to moderate-severe community acquired pneumonia: randomised, double blind study. BMJ 2006;332:1355–8.
- 14. Bell BG, Schellevis F, Stobberingh E, et al. A systematic review and meta-analysis of the effects of antibiotic consumption on antibiotic resistance. BMC Infect Dis 2014;14:13.
- Guillemot D, Carbon C, Balkau B, et al. Low dosage and long treatment duration of beta-lactam: risk factors for carriage of penicillin-resistant Streptococcus pneumoniae. JAMA 1998;279:365–70.
- Schrag SJ, Peña C, Fernández J, et al. Effect of short-course, highdose amoxicillin therapy on resistant pneumococcal carriage: a randomized trial. JAMA 2001;286:49–56.



Delayed antibiotic prescriptions for respiratory tract infections: does the strategy work?

Delayed antibiotic prescribing, also known as a "back pocket prescription", is a strategy of providing a patient with a prescription for an antibiotic, but advising them not to fill it unless their symptoms persist or worsen, or if laboratory results (if requested) subsequently indicate a bacterial infection. Delayed antibiotic prescriptions are most often considered for patients with acute respiratory tract infections (RTIs), which is the focus of the following article.

Most patients with acute upper or lower RTI symptoms do not benefit from antibiotics and prescribing antibiotics inappropriately for these patients leads to unnecessary cost, adverse effects and the development of antibiotic resistance. Decades of observational and interventional studies involving thousands of patients have, however, identified subgroups of patients with conjunctivitis, sinusitis, sore throat and acute cough for whom antibiotics should be considered, based on the presence of key features in their history, examination or laboratory test results (see: "Antibiotics: choices for common infections", reference over page). These features may not be evident when the patient first presents to the general practice clinic, but may develop in the subsequent days to weeks. Options to capture this group of patients include immediate prescription of antibiotics to all patients, a delayed prescription that can be used later if it becomes necessary, scheduling a follow-up consultation or phone call, and no prescription of antibiotics (the patient may return for reassessment later if new symptoms develop).

There are many factors that may contribute to the decision to offer a delayed prescription for a patient with a RTI, including concerns about the potential for symptoms to worsen significantly in a patient with co-morbidities, previous history of complications with RTIs, patient expectations and socioeconomic aspects such as the likelihood of the patient being able to return for a consultation if their condition deteriorates. Examples of the pros and cons of the delayed prescription strategy are listed in the box below.

The goals of delayed antibiotic prescription are to minimise antibiotic use for conditions in which an antibiotic has little or no benefit, to have no negative effect on symptom duration or rate of serious complications, to provide patient satisfaction and to positively influence patients' future expectations around antibiotic treatments. A number of studies have now evaluated delayed antibiotic strategy with these goals in mind.

For further information, see: "Antibiotics: choices for common infections", bpac^{nz} 2013, available from: www.bpac. org.nz/Supplement/2013/July/antibiotics-guide.aspx

What percentage of patients fill delayed antibiotic prescriptions?

It is estimated that up to 50% of patients given a delayed prescription for an antibiotic will collect their prescription.

A 2013 Cochrane systematic review compared delayed antibiotic prescribing versus immediate or no antibiotics in patients with a RTI.² Patients who were managed with a delayed prescribing strategy took fewer antibiotics (32%) than patients who were prescribed an antibiotic immediately (93%).² Patients who were not initially prescribed an antibiotic had the lowest level of subsequent antibiotic use (14%).²

Pros	Cons
May reduce antibiotic use and therefore reduce adverse effects and antibiotic resistance (compared with receiving an immediate prescription)	May increase antibiotic use and therefore increase adverse effects and antibiotic resistance (if the antibiotic is used)
Safety net if more severe symptoms and signs develop	Risk that patient may fill the prescription regardless of their symptoms or for the wrong reasons
Fulfils expectations for some patients and maintains the clinician-patient relationship	Risk that patient may use the prescription inappropriately at a later date or for another family member
Empowers the patient to be actively involved in their treatment	May confuse messages about antibiotic stewardship
Reduces costs and time for the patient of having to re-consult	Instructions on using a delayed prescription may not be correctly understood or remembered by the patient if not communicated effectively by the prescriber
Allows control of factors such as the "Friday consultation", upcoming travel or important events	May result in negative perception of the clinician's competence
Reserves the use of antibiotics for more severe RTIs	Serious illness or complications may be missed at the first consultation, or patients who later develop serious illness or complications will collect the antibiotic prescription but might have been better re-consulting a doctor and receiving more comprehensive treatment, e.g. hospitalisation

Pros and cons of delayed antibiotic prescribing¹

A randomised controlled trial published after the Cochrane review found that 33 - 39% of patients given a delayed antibiotic prescription subsequently filled their prescription.³ The study involved 889 patients who presented to primary care in the United Kingdom with an acute RTI. The 556 patients not judged to require immediate antibiotics were randomised to one of four delayed prescribing strategies ("re-contact" the practice by phone to request a prescription, "post-dated" prescription, placement of prescription at reception for "collection" and giving the patient a prescription with advice to delay – "patient led") or a "no prescribing" strategy. It is not clear what criteria the patients were advised for filling their prescription. No significant differences were found between the four delayed strategies in the percentage of patients who filled their prescription; 26% of patients who were not offered a prescription subsequently returned for re-consultation and filled an antibiotic prescription.³

A New Zealand study, which was included in the 2013 Cochrane review, found that just under half of patients given a delayed prescription took an antibiotic. The study randomised patients with an upper RTI presenting to a general practice clinic in Auckland, who requested antibiotics or were perceived to want antibiotics, to receive either an immediate prescription for an antibiotic or a delayed prescription with instructions to fill it after three days if their symptoms did not improve. It was found that 89% of the 62 patients who were given an immediate prescription used the antibiotic, compared to 48% of the 67 patients given a delayed prescription.⁴

Does delayed antibiotic prescribing lead to good clinical outcomes for patients?

Patients who take an antibiotic for a RTI are unlikely to shorten the duration of their symptoms, but they may be less likely to experience suppurative complications; however, the development of complications in a patient with an acute RTI, regardless of antibiotic use, is relatively uncommon.

It is probably not possible to demonstrate a difference in clinical outcome for antibiotic strategies in patient populations who are unlikely to benefit from antibiotics in the first place. It is not surprising, therefore, that there was no difference in symptom duration between patients randomised to delayed antibiotic prescribing versus no antibiotic in a population of patients with mostly upper respiratory tract infections and sore throats,³ and in a population of patients with uncomplicated lower respiratory tract infections.⁵ At least two studies, however, have detected a possible reduction in complications in patients assigned to delayed antibiotic prescription versus no antibiotic. In the primary care trial where patients were randomised to different antibiotic prescribing strategies, complications of RTI

were experienced by 1.5% of patients who received a delayed prescription compared to 2.5% of patients who were given an antibiotic immediately and 2.5% of patients not given an antibiotic (not statistically significant).³ In a non-randomised cohort study of 12677 patients with sore throat, the risk of complications was 0.58-fold in patients who used an antibiotic compared to those who did not (adjusted risk ratio 0.34-0.98).⁶ The overall rate of suppurative complications observed among the patients in this study was 1.4%; otitis media (0.6%) quinsy (0.4%), sinusitis (0.3%), impetigo or cellulitis (0.2%).⁶ Although the supportive evidence for this is not strong, prevention of late complications is a key goal of providing a delayed prescription to low-risk patients.

There was no measureable difference in adverse effects reported between patients using delayed and no antibiotic strategies.^{3, 5} Antibiotic resistance rates were not measured.

Does delayed antibiotic prescribing help meet patient expectations and improve the clinician-patient relationship?

Patients who do not receive an antibiotic for a RTI are just as satisfied as those who do, provided that the reasons for not prescribing an antibiotic are effectively explained.

There is evidence that patients expect antibiotic prescriptions less often than physicians believe they do, and patient satisfaction is not reduced when the reasons for not prescribing an antibiotic are effectively communicated, including reassurance that an antibiotic is not always appropriate or effective.⁷ It has also been reported that a patient's satisfaction scores are more strongly associated with receiving understandable information and reassurance than actually receiving an antibiotic prescription.⁸

This is supported by the findings of the Cochrane review. Overall, patient satisfaction was high with immediate (92%), delayed (87%) and no prescription (83%) strategies, with no significant differences in satisfaction between patients managed using the delayed or no antibiotic prescribing strategies.² In the primary care trial of antibiotic prescribing strategies, there were also no significant differences found in satisfaction between patients who did not receive an antibiotic (79% very satisfied) versus patients who were managed using the delayed antibiotic strategies (74 – 89%).³

In a New Zealand study of perceptions about delayed antibiotic prescriptions, it was found that patients were not as concerned about being involved in decision-making about their health care as their clinicians perceived them to be.¹ Most patients preferred their clinician to decide whether they needed an

antibiotic.¹ Some clinicians believed that offering a delayed antibiotic prescription would help the clinician to cope with the pressure to prescribe an antibiotic for a RTI and be favourably received by the patient, act to reassure the patient and prevent them from visiting another clinician for a prescription. However, the converse view was that by not making a decision about whether the patient needed an antibiotic, the patient may perceive the doctor to be incompetent.¹

Patient satisfaction is strongly linked to patient expectations.⁸ Patient expectations may be unreasonable, however, such as when a patient expects an antibiotic despite lack of evidence for benefit in that condition and in the face of increasing antibiotic resistance. Patient satisfaction should not be the only goal of the clinician-patient interaction but can hopefully be maintained in those not given an immediate antibiotic prescription by reassurance, positive advice on symptomrelief, and a strategy for identifying if a patient's condition is deteriorating.

Does delayed antibiotic prescribing help educate patients and improve future expectations?

Giving a delayed prescription, which is subsequently not required, can help to educate patients that in most cases, RTIs are self-limiting and can be managed with symptomatic treatment

There is some evidence that delayed prescriptions educate patients about the limitations of using antibiotics for RTIs and have a positive effect on future expectations about antibiotic prescribing for RTIs. A randomised controlled trial involving 807 primary care patients with an acute lower RTI, investigated the effectiveness of three antibiotic prescribing strategies (an immediate prescription for an antibiotic, a delayed prescription with advice to collect the prescription from reception if symptoms did not resolve after 14 days or no offer of antibiotics), with or without an information leaflet about antibiotics. Patients who received a delayed prescription were the least likely to believe in the effectiveness of antibiotics for RTI (40%), compared to those who did not receive a prescription (47%) and those who received an immediate prescription (75%).⁵ Receiving the information leaflet did not have any effect on this outcome, possibly because all patients were also given verbal information about antibiotics.⁵

So, should a delayed antibiotic prescription be given to a patient with a RTI?

Yes...or no. It depends on the individual situation.

Taking all factors into consideration, it appears that patients can be effectively managed using a "no antibiotic" strategy rather than a delayed antibiotic strategy, when the prescriber judges that an immediate antibiotic is not required. The evidence suggests that not prescribing the patient an antibiotic initially, explaining why this decision has been made and ensuring that patients understand

to contact the practice if symptoms do not resolve, is likely to reduce antibiotic use and result in similar clinical outcomes and patient satisfaction than using a delayed prescribing strategy. However, in practice there will always be exceptions to this.

Delayed prescriptions are a good option for many patients who do not need antibiotics at the time of consultation but may need them later. This strategy leads to far fewer prescriptions being filled than immediate prescription of antibiotics and only a few more being filled than for patients not initially offered a prescription. Patients given a delayed antibiotic prescription may have fewer complications of RTI, and satisfaction may be higher, compared with no antibiotic prescription although neither of these has been proven with statistical significance, and satisfaction is largely dependent on effective communication regardless of prescribing strategy. Giving a delayed prescription may have a positive effect on a patient's future expectations for receiving an antibiotic for a RTI, especially if their symptoms resolve without filling the prescription. This may be a good strategy for "weaning" a patient from the idea that they always need an antibiotic.

There are several ways to offer a delayed prescription, e.g. collect from reception, post-dated prescription, phone call – none has yet shown to be a better strategy than another. More research is needed to determine whether patients who fill delayed prescriptions do so for the right reasons and how this might be improved. Delayed prescription strategies will not suit all patients – some will benefit most from a face-to-face or telephone follow up, but combined with careful history and examination, reassurance, symptom-control advice and clear instructions on when to fill the prescription, it can be a good option.

Gever For further discussion on prescribing antibiotics for RTIs, see our GP debate (Page 5).

Acknowledgment: Thank you to Dr Richard Everts, Specialist Physician, Medical Microbiologist and Infectious Disease Specialist, Nelson and Marlborough DHB and Professor Bruce Arroll, Department of General Practice and Primary Healthcare, University of Auckland for expert review of this article.

References

- 1. Arroll B, Goodyear-Smith F, Thomas DR, et al. Delayed antibiotic prescriptions: what are the experiences and attitudes of physicians and patients? J Fam Pract 2002;51:954–9.
- Spurling GKP, Del Mar CB, Dooley L, et al. Delayed antibiotics for respiratory infections. Cochrane Database Syst Rev 2013;4:CD004417.
- Little P, Moore M, Kelly J, et al. Delayed antibiotic prescribing strategies for respiratory tract infections in primary care: pragmatic, factorial, randomised controlled trial. BMJ 2014;348:g1606.
- 4. Arroll B, Kenealy T, Kerse N. Do delayed prescriptions reduce the use of antibiotics for the common cold? A single-blind controlled trial. J Fam Pract 2002;51(4):324–8.

Should I prescribe a topical antiseptic cream instead of a topical antibiotic for minor skin infections?

Increasing rates of resistance to topical antibiotics continues to change the use of these medicines in primary care. Topical antiseptics have been suggested as an alternative, but at present, there is little evidence to support their effectiveness in the treatment of minor skin infections.

Topical antibiotics are associated with high rates of antibiotic resistance

In October, 2014 we published an article outlining appropriate use of topical antibiotics in response to concerns over increasing rates of bacterial resistance, in particular to fusidic acid (See: "Topical antibiotics: very few indications for use", BPJ 64). In early 2015 we updated our advice on the management of eczema in children (See: "Treating childhood eczema: a topical solution for a topical problem", BPJ 67). It has become increasingly apparent in the intervening months that recommendations regarding the role of topical antibiotics, such as fusidic acid, in superficial skin infections have narrowed

- Little P, Rumsby K, Kelly J, et al. Information leaflet and antibiotic prescribing strategies for acute lower respiratory tract infection. A randomised controlled trial. JAMA 2005;293:3029–35.
- Little P, Stuart B, Hobbs FDR, et al. Antibiotic prescription strategies for acute sore throat: a prospective observational cohort study. Lancet Infect Dis 2014;14:213–9.
- Coenen S, Francis N, Kelly M, et al. Are patient views about antibiotics related to clinician perceptions, management and outcome? A multi-country study in outpatients with acute cough. PLoS ONE 2013;8:e76691.
- 8. Welschen I, Kuyvenhoven M, Hoes A, et al. Antibiotics for acute respiratory tract symptoms: patients' expectations, GPs' management and patient satisfaction. Fam Pract 2004;21:234–7.

further. Expert opinion now suggests that topical fusidic acid should no longer be considered for use in the treatment of children with infected eczema. The preference is for oral antibiotic treatment, chosen based on local resistance patterns, and with appropriate coverage for Staphylococcus aureus and Streptococcus pyogenes (Group A ß haemolytic streptococcus). Fusidic acid may remain an effective treatment option for children with three or less localised areas of impetigo,¹ however, in many cases, as with infected eczema, an oral antibiotic is likely to be more appropriate. Topical mupirocin should only be considered instead of fusidic acid if the infection is known to be resistant to fusidic acid and sensitive to mupirocin. Topical antibiotics (chosen according to culture results) do continue to have a role in the management of patients with recurrent skin infections who require S. aureus nasal decolonisation. The role of combination antimicrobial/corticosteroid products, such as hydrocortisone, natamycin and neomycin cream and ointment (Pimafucort) and betamethasone and fusidic acid cream (Fucicort), is unclear due to a lack of quality research and concerns about increasing resistance rates. Currently is it suggested that they are only used short term for the treatment of small areas of localised skin infection (including fungal infection) in patients with underlying inflammatory skin conditions.²

In the majority of healthy patients, minor skin infections do not require antibiotic treatment at all. Other skin infections, such as furuncles and carbuncles, are usually more appropriately managed by incision and drainage.

Are topical antiseptics an acceptable alternative?

Topical antiseptic agents have been used for centuries in the management of wounds but their role and their effectiveness