Antimicrobial stewardship
in general practice

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Almost half of the Australian population are supplied at least one antibiotic through the PBS each year. Antimicrobial stewardship – a systematic approach to ensure appropriate antimicrobial prescribing – is essential in general practice to reduce the emergence of antimicrobial resistance locally and globally, as well as to minimise cost and reduce patient-specific adverse effects associated with inappropriate prescribing of antibiotics.

Deaths attributed to infectious diseases have declined dramatically since the mass use of penicillin in the 1940s for treating sick and injured allied troops during World War II, after its development for medical use by the British and Americans and its mass production in the USA. This ushered in a golden era of medicine, when previously incurable diseases such as infective endocarditis and syphilis were now treatable.[1]

Despite the climate of optimism at the discovery and use of penicillin, there were early warnings that antimicrobial resistance would emerge as a result of selective pressure on the bacterial ecology.[2] This ominous prophecy has been fulfilled, with ensuing antimicrobial resistance towards the various classes of antimicrobials emerging, culminating in the worldwide dissemination of methicillin-resistant *Staphylococcus aureus* (MRSA) in the 1990s, and the near pandrug-resistant *Klebsiella pneumoniae* carbapenemase (KPC)-producing *K. pneumoniae* in the early 2000s. Australia is no exception, with the recent Victorian outbreak of KPC-producing *K. pneumoniae* highlighting the need for new antimicrobials to combat these infections.[3]

The vast majority of today's antimicrobial classes were discovered within 30 years from the development of mass production of penicillin, with no new classes of antibiotics introduced into clinical practice since 1987. A so-called 'post-antibiotic era' is now a real possibility, where minor infections and injuries may result in significant morbidity and mortality. At the 68th World Health Assembly in 2015, the WHO endorsed a global action plan to address antimicrobial resistance. Optimising the use of antimicrobials was identified as a strategic objective to achieve sustainable continuity of therapy in the treatment of infectious diseases with effective antimicrobials that are used responsibly and are accessible to all for as long as possible.[4]

Although levels of antimicrobial resistance in Australia are comparatively low, the country's rate of antibiotic prescribing is concerning. Approximately 30% of hospital inpatients are prescribed at least one antimicrobial at any time and, in 2014, 46% of people in Australia were dispensed at least one antimicrobial through the PBS.[5,6] Community patients are prescribed antimicrobials most frequently if they are younger than 4 years of age (57%) or older than 65 years (60%). Prescribing is also generally higher in areas with lower socioeconomic status, which is associated with poorer health and higher infection rates.[6]

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This article provides an introductory discussion to strategies for appropriate antimicrobial prescribing in general practice.

What is antimicrobial stewardship?

Antimicrobial stewardship (AMS) is a systematic approach in the healthcare setting to ensure appropriate antimicrobial prescribing. The intention is to reduce the emergence of antimicrobial resistance, minimise cost and reduce patient-specific adverse effects associated with inappropriate prescribing of antimicrobial therapy.[7]

The basic principles of AMS listed below are included in the antimicrobial creed MIND ME in Box 1:[8]

- prescribe only when indicated
- only use broad-spectrum agents until bacterial antibiotic sensitivities or the results of investigations are known
- use microbiological results to guide therapy whenever possible
- ensure an appropriate duration of treatment.

AMS programs are now commonplace in Australian hospitals. The National Safety and Quality Health Service Standards (NSQHS) produced by the Australian Commission on Safety and Quality in Health Care set out the recommendations for AMS programs at various healthcare institutions. As a minimum requirement, antimicrobial restriction policies are required, clinicians must have access to the current endorsed therapeutic guidelines on antibiotic use, and a practitioner is designated responsible for AMS.[9]

AMS programs in the general practice setting are not as concisely defined and are often under-resourced. Although various community-based AMS strategies are reported, GPs are expected to independently stay abreast of current local antimicrobial resistance patterns and ever-changing prescribing guidelines.[10] Some AMS issues unique to general practice are problems with patient follow up, access to timely microbiological testing and results (especially in more remote GP clinic settings) and managing patient expectations within the confines of the consulting room.[11]

The various roles in an AMS team

The general practice environment requires a champion who will rise to the challenges associated with implementing an AMS program. Any member of the practice may successfully undertake this role, with co-operation from the doctors, nurses, allied health staff, microbiology staff and patients.

The roles of the AMS team members are as follows:

- the AMS champion – to provide leadership and promotion of the AMS program to patients and staff
- GPs – to initiate discussions about the suitability of a particular antimicrobial and the appropriateness of long-term therapy for particular conditions
- practice nurses and pharmacists – to highlight appropriate circumstances for prescribing antimicrobials and reassure patients and their families that antimicrobials are not indicated for minor conditions or when results of microbial culture or urine dipstick analysis are negative
- the local affiliated medical microbiology team or pathology service – to advise medical staff about the local resistance patterns to promote appropriate prescribing of antimicrobials based on the isolated organisms, with concise durations of treatment.

The importance of good antimicrobial selection and use

Despite the availability of several practical references for the selection of appropriate antimicrobials in general practice in Australia (as listed in Box 2), many antibiotic prescriptions are inappropriate because of incorrect antibiotic selection or excessive treatment duration.

Acute respiratory tract infections are experienced by more than half of the adult population during any six-month period, with approximately one-fifth consulting their GP.[12] Amoxicillin or amoxicillin plus clavulanic acid are the most frequently prescribed antimicrobials for this indication, but have no benefit. Antibiotics are not indicated or therapeutic for viral infections but continue to be prescribed for such infections.

Timely microbiological testing

Both positive and negative microbiological culture results are relevant to clinical decisions about antibiotic use. Appropriate testing before initiating antimicrobial therapy reduces unnecessary use of broad-spectrum antimicrobials and overtreatment. Similarly, early detection of resistant organisms (such as extended-spectrum beta-lactamase (ESBL)-producing bacteria) improves patient outcomes as inappropriate empirical antimicrobials can be ceased early. Microbiological investigations include blood cultures and cultures from other appropriate sites depending on clinical presentation. Gram stains, antigen detection tests and/or nucleic acid amplification tests (e.g. multiplex polymerase chain reaction [PCR] testing of nasal or

throat swabs for respiratory virus detection and identification) may also benefit clinical evaluation.

Review of empirical therapy at 48 to 72 hours may exclude the need for ongoing treatment (the patient is advised to discontinue treatment) or, where a causative organism is identified, prompt the rationalisation of therapy to a narrower-spectrum antimicrobial for a defined duration ('directed therapy').[8,13]

Adequate equipment for microbiological testing (e.g. point-of-care testing such as influenza and respiratory viral DNA rapid tests) should be available in the general practice rooms, and timely results provided to clinicians, which may require a change of practice for staff.[14]

Managing patient demand and expectation
Clear communication
The success of any AMS program depends on clear communication and stakeholder collaboration. In general practice, patient engagement is key to the success of the program. Despite unanimous acknowledgement of this, many GPs do not practically engage patients to discuss their responsibilities to reduce the development of antibiotic resistance, or do it in a way that only alludes to the general social context.[15] In the absence of patient engagement and education regarding infections and their appropriate treatment, when symptom improvement with illnesses such as the common cold coincides with starting antibiotic treatment then patients will be led to believe that the antibiotics are responsible for their clinical improvement.

Patient engagement must address the main barrier to prescribing appropriate antimicrobials of perceived patient demand and patient expectations. GPs often assume that patients presenting with a particular ailment, such as an acute respiratory tract illness, are seeking antibiotic therapy and are not satisfied without a prescription. In reality, patient satisfaction is associated with time taken to reassure them and educate them about their symptoms and other

treatment options, not necessarily with an antibiotic prescription.[16,17]

It is essential that patients support the prescriber's decision to avoid antimicrobials and understand the rationale. When an antimicrobial is prescribed, appropriate discussions regarding compliance, timing of doses (to optimise pharmacokinetics) and duration treatment (particularly if it does not equate to pack size) are necessary. If a repeat prescription is issued then the appropriateness of ongoing administration versus future usage must be discussed to dissuade patients from inappropriate usage.

Practical strategies
Creating a 'symptom action plan'
The handover of a prescription to a patient is traditionally considered a successful method to finalise a medical consultation. An alternative transaction when an antimicrobial is not indicated is to provide a prescription for symptomatic management, such as a decongestant, antiseptic wash or eye drop. A written symptom action plan is another tool that can be provided to patients to convey the most appropriate symptom relief strategies for respiratory tract infections, without suggesting benefits of antimicrobials. An example of such an action plan has been produced by NPS MedicineWise (available online at www.nps.org.au/__data/assets/pdf_file/0007/316285/NPS-MedicineWise-RTI-Action-Plan.pdf).

'Safe netting'
Another strategy to overcome patients' expectations of prescription of an antimicrobial in the absence of positive microbiological results is 'safe netting'. This concept requires the GP to clearly establish actions to take if the course of illness deviates from the expected self-resolution.

Delayed antibiotic prescribing is a form of safe netting used by some practitioners. In this method, the prescriber may give the patient the prescription with instructions to have the medication dispensed only if symptom progression occurs or may retain the antimicrobial prescription

at the surgery reception to be collected by the patient if required. In a recent Cochrane review, delayed antibiotic use has achieved a lower rate of antibiotic consumption compared with immediate supply of antibiotics, with no difference in the clinical outcomes.[18]

Conveying a commitment to AMS
It is essential that GPs are upfront with their patients about their commitment to judicious antimicrobial prescribing. As well as communicating this clearly to patients during the consultation, an approved and signed practice commitment about the prescribing of antimicrobials may be displayed in patient waiting areas, to further educate and inform patients about the importance of AMS.[19]

Antimicrobial dispensing
Reducing the pill burden is not always conducive to AMS
GPs are mindful that large pill burdens for any duration are a potential source of noncompliance with therapy. The optimal antibiotic and the shortest duration necessary should prescribed, as per the recommended national guidelines.[8]

The ideal antibiotic would have only once-daily dosing. Such antibiotics

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3. ANTIBIOTICS SUPPLIED THROUGH THE PBS IN 2013: KEY FINDINGS[23]

- 45% of people in Australia (10,441,015 patients) were supplied at least one antibiotic.

- 26,436,021 prescriptions were supplied for systemic antibiotics.

- The most common antibiotics were amoxicillin (n=5,665,810), cefalexin (n=5,413,046) and amoxicillin with clavulanic acid (n=4,512,149).

- Repeats were ordered on most prescriptions for cefalexin, amoxicillin with clavulanic acid and roxithromycin. 40% of amoxicillin prescriptions included a repeat.

(e.g. trimethoprim) exist but have limited indications or, in the case of quinolones and macrolides, pose considerable concerns regarding drug interactions and serious adverse effects. Twice-daily amoxicillin plus clavulanic acid is commonly prescribed for community-acquired pneumonia, as opposed to the recommended dual therapy of amoxicillin and doxycycline.[8] Although amoxicillin plus clavulanic acid is an ideal solution for poor compliance, the trade-off is the unnecessarily broad antimicrobial spectrum for directed therapy, which drives the emergence of antibiotic resistant isolates in the local community.[20]

Prescribing the appropriate amount of antibiotics

The disparity between recommended duration of therapy and commercial antimicrobial pack sizes provides the potential for misuse of leftover doses.[21] Leftover doses and repeat prescriptions are easily used to 'self-medicate' either the originally intended patient or a family member or friend.[22] Also, the traditional instructions of 'until all finished' may cause confusion when the pack sizes (and therefore duration of treatment) do not align with current treatment guidelines.

PBS data for 2013 showed that 40% of amoxicillin prescriptions included a repeat, as did most prescriptions for cefalexin, for amoxicillin with clavulanic acid and for roxithromycin (Box 3).[23] It is not uncommon for a repeat prescription to be dispensed at a later time than originally prescribed, raising the question of appropriateness of the antibiotic for the later situation.[23] Diligent pharmacists will query the delayed dispensing, with many recommending medical advice prior to supply. However, it is often difficult to convince a patient to return to their medical practitioner in a timely manner for review.

Some solutions to this issue have been proposed. Simply not issuing repeat prescriptions is only one solution to this challenge and may not always be appropriate, particularly in situations where GP follow up is difficult, such as in a remote setting. Prescribers may choose to set an 'expiry date' on an antimicrobial prescription that is sooner than the legislated 12-month expiry. Annotating 'not to be dispensed after x date' on a prescription allows the patient to utilise the antibiotic if symptoms persist longer than the duration of the original prescription but prevents future usage for on self-diagnosis.

Other initiatives

Instances of local health service collaboration have shown positive improvements in antimicrobial prescribing. Interested AMS practitioners in South-West Victoria have conducted audits and feedback for GPs involved with medical care at several long-term care facilities and hospitals since 2012.[24] Educational events for medical and nursing staff covered up-to-date prescribing patterns and common errors and provided quick prescribing guides.

The National Centre for Antimicrobial Stewardship has developed a national antimicrobial prescribing survey tailored to the aged care setting, the Aged Care National Antimicrobial Prescribing Survey. This auditing tool assists antimicrobial prescribing at long-term aged-care facilities and helps prescribers assess and improve antimicrobial prescribing. The reports of the pilot Aged Care National Antimicrobial Prescribing Survey have shown high rates of inappropriate usage of long-term prophylactic antibiotics.[25]

The government-funded NPS Medicine-Wise MedicineInsight program uses clinical and prescribing data from Australian general practices to review common antimicrobial prescribing and improve quality of prescribing.[26] Reports of antimicrobial usage and indication data, benchmarked against other practices, are provided to individual practitioners and practices. Clinicians can use this information as a self-improvement tool to recognise trends in their prescribing habits.

Conclusion

GPs play a crucial role in safeguarding our ever-dwindling antibiotic arsenal. Healthcare providers need to work together to avoid a potential apocalyptic post-antibiotic era, with increasing antimicrobial resistance both locally and globally. Effective AMS programs involve appropriately prescribing empirical antibiotics, timely microbiological testing and rationalising therapy quickly, as well as educating and empowering patients to make sensible decisions about preventing the inappropriate use of antimicrobials in the community. GPs should be familiar with the concepts of AMS and have their own practice program.

Regardless of time pressures, patient expectations, medicolegal concerns and diagnostic uncertainties, antimicrobial prescribing must be improved. The doctor–patient conversations may potentially last longer, and GPs may expend more effort in educating themselves about the latest emerging infections, local resistance patterns and new emerging antimicrobial therapies. However, the educated patient is our best weapon in the war against antimicrobial resistance and inappropriate antimicrobial prescribing.   MT

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A list of references is included in the website version of this article (www.medicinetoday.com.au).

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