

Antimicrobial Stewardship: The Next Big Thing?

Sin Yew Wong,¹ *MBBS (Singapore), MMed(Internal Medicine), FAMS (Infectious Diseases)*, David Michael Allen,² *MD, ABIM, FAMS (Infectious Diseases)*

Antimicrobial drug resistance is recognized as a global problem; as such, The World Health Organization dedicated World Health Day on April 7 2011 to highlight this pressing issue.¹ It is widely accepted that there is a direct correlation between antibiotic use and the development of antimicrobial resistance. Sadly, the pace of bacterial antimicrobial resistance development worldwide has surpassed the rate of newer antibiotic discovery to replace those rendered ineffective by resistance. Antimicrobial resistance is relevant to Singapore. In a surveillance study at 4 restructured hospitals in Singapore spanning 2006 to 2008, the prevalence of resistant Gram negative bacteria was high and the prescription volume of broad spectrum antibiotics was correspondingly high.² When studies also report that 25% to 68% of hospital antibiotic prescribing had been suboptimal, we as members of the medical community need to sit up and do better.³

Whilst antimicrobials are often life saving, they have not always been prescribed appropriately. Antibiotic use can result in serious harm to patients, such as life threatening hypersensitivity reactions, drug interactions, nephrotoxicity, QT prolongation, etc as “direct effects”. The “indirect effects” include antimicrobial drug resistance as noted above, *Candida* superinfection, *Clostridium difficile* associated diarrhea (CDAD) and unnecessary costs to name a few. A recent study reported that 20% of patients admitted to the ICU with CDAD were receiving antibiotics without any obvious evidence of infection.⁴

Clinicians have long been aware of the risks of inappropriate antimicrobial use and its effect on antimicrobial resistance and toxicity. Efforts to promote appropriate antibiotic prescribing have recently evolved into antimicrobial stewardship programmes (ASP). Broadly defined, ASP is a multi-disciplinary initiative that ensures the optimal selection, dose and duration of antimicrobials that leads to the best clinical outcome for the treatment or prevention of infection while producing the fewest possible side effects and the lowest risk for subsequent resistance.⁵ The intervention strategies in ASP may be persuasive, restrictive or structural and often, a combination

of these. The need for action is accepted as so urgent and necessary that the California state senate passed a bill which mandated general acute care hospitals to assemble Quality Improvement committees to specifically monitor, evaluate and oversee the judicious use of these medications.⁶

The Infectious Diseases Society of America (IDSA)/ Society of Healthcare Epidemiology of America (SHEA) guidelines published in 2007 have identified formulary restriction/pre-authorization and prospective audit with intervention and feedback as the key evidence based strategies for ASP.⁷ Briefly, an antimicrobial committee develops guidelines for the approved use of selected agents. The first strategy leads to direct control over antimicrobial use at an institution as well as educational opportunities from the ASP staff to the prescribers. In the second strategy, daily audits of targeted agents are undertaken and if necessary, intervention in the form of education and offering alternative agents to the prescribers are provided. Additional strategies that ASP offer include “streamlining”, de-escalation (when cultures are available), dose optimization and IV to PO switch. In a recent Cochrane systematic review of 66 studies, 51 (77%) showed a significant improvement in at least one of the following outcomes: number of hospital acquired infections, decrease in infection related deaths, and decreased length of hospital stay. Restrictive methods of antimicrobial stewardship had a larger impact on judicious antibiotic prescribing than persuasive methods in their analysis.⁸

Implementation of ASP is not for the faint hearted. Two years after the publication of the IDSA/SHEA antibiotic stewardship guidelines, only 48% of the survey respondents stated that their hospital had such a programme.⁹ Why the reluctance? Implementation problems and barriers that have been cited include prescribing etiquette, cultural issues etc.¹⁰⁻¹²

Where are we in Singapore? In the past few years, the Ministry of Health has provided financial support through various grants to restructured hospitals to fund staffing costs (pharmacists and infectious disease physicians) and development of IT systems to manage the ASPs. National

¹Infectious Disease Partners Pte Ltd

²ID Specialists, P.A. Dallas, Texas, USA

Address for Correspondence: Dr Wong Sin Yew, Infectious Disease Partners Pte Ltd, 6 Napier Road #05-13, Singapore 258499.

Email: drwong@infection.com.sg

University Hospital, Tan Tock Seng Hospital and Singapore General Hospital have had ASPs in various forms for the past few years and have published their experience. The ASP at Singapore General Hospital has reported their experience with 3 clinical departments.¹³ Similarly, a prospective audit and feedback intervention in the adult Haematology-Oncology Division was reported by the ASP at National University Hospital.¹⁴ These 2 recent publications indicate the success of ASP in selected departments at restructured hospitals in Singapore. In June 2011, the Ministry of Health has committed a further S\$21 million over the next 5 years to fund the development of ASP in all the restructured hospitals in Singapore. No doubt we will see more publications in the future on the implementation of ASP in Singapore.

In this issue of the *Annals*, Teng CB et al describe the key training components that are required for the staff managing the ASP.¹⁵ This is important as it provides the critical framework to replicate ASPs in other hospitals.

What are the other features that ensure the success of an ASP? Medical staff education is the cornerstone for any successful programme to improve and change prescribing behaviour. There must be updated guidelines, rapid microbiological results to ensure that the decision support system will move prescribing to the “appropriate choice” as the “default choice”. In the past this involved lectures, production of educational flyers, posters, continued campaigns, antibiotic order forms, restricted antimicrobial formulary, pre-authorization, etc. These earlier methods were relatively inefficient, logistically challenging and vulnerable to the commercial bias of sponsors.

In the 21st century, we believe a successful ASP will have technology as the “enabler” and should have the following fundamental components. Antimicrobial prescribing guidelines will be “localized” to a specific hospital and will take into account the patient’s co-morbid and allergy status. With computerized physician order entry for a particular patient in a specific location having a defined or probable infection, pre-determined rules in the background kick in to support the decision process. Clearly, guidelines for antimicrobial prescribing must be different for a bone marrow transplant recipient experiencing neutropenic sepsis in the intensive care unit from a previously healthy 30-year old man with appendicitis. The capacity of pre-determined rules to distinguish distinct clinical scenarios and generate recommendations accordingly is critical as much of the antimicrobial prescribing in restructured hospitals is by junior medical staff. The presence of a computerized decision support system will augment the educational component provided by the staff responsible for the ASP. Just as important is the component of “choice” (albeit reduced) in the selection of antimicrobial agents. No computer decision support system can incorporate all

the rules that cater to the varied and complicated clinical considerations that a physician/surgeon must take into account when prescribing therapy. Such a system will allow “choice”, utilising a non-restrictive policy and continue to have prescriber autonomy. The human touch must not be forgotten and the ASP pharmacists will provide a “human face” during their daily utilization audit reviews and the infectious disease physician will add further clinical expertise when consultations are initiated.

ASPs have the potential to reduce antimicrobial costs by limiting the use of and inappropriate use of these agents and by promoting active intravenous to oral switch therapy. The IDSA/SHEA guidelines report that comprehensive programs can lead to a reduction in antimicrobial use by 22% to 36%, resulting in significant cost savings. These cost savings have usually “paid for” the staff salaries and support systems needed to run such a program. Reducing the upward trajectory of a healthcare institution’s antimicrobial drug costs has also been used to justify the need for an ASP. What is critical is the emphasis on patient safety that ASPs provide and this must over-ride the financial focus. By improving and oftentimes, reducing overall antimicrobial usage, ASPs will also have the potential to reduce drug related adverse effects and unintended consequences such as antimicrobial resistance, adverse drug effects and CDAD. Interestingly, at the SGH ASP, Teo et al reported an acquisition cost reduction of almost S\$200,000 during the study period but the total volume of antibiotic consumption did not decrease significantly.¹³ This was explained by the fact that a substantial number of their ASP interventions involved “increased consumption” including broadening antibiotic coverage and/or correcting underdosing.

Thus, we believe that the focus of ASP should be patient safety, reduction of antimicrobial resistance and cost savings in this order. Clearly, ASP don’t operate in a vacuum. The local medical environment is impacted by a complex interplay of critical factors in addition to ASP such as the large quantities of antimicrobials prescribed in the outpatient setting and the important role that infection control programmes have in integrating with ASP to reduce antimicrobial resistance. The ASP initiative is but one component of the larger goal of comprehensive healthcare quality improvement.

Antibiotics have probably saved more lives than any other group of drugs. They constitute a critical and finite resource that the medical community needs to reserve for use when there is evidence that significant benefit to health is likely. ASP in institutional practice is an important next step.

REFERENCES

1. WHO press statement 2011. www.who.int/mediacentre/news/releases/2011/whd_20110406/en/index.html
 2. Hsu LY, Tan TY, Tam VH, Kwa A, Fisher DA, Koh TH. Surveillance and correlation of antibiotic prescription and resistance of Gram negative bacteria in Singaporean hospitals. *Antimicrob Agents Chemother* 2010;54:1173-8.
 3. House of Lords Select Committee on Science and Technology. Resistance to antibiotics and other antimicrobial agents. Session 1997-1998. 7th report. London: The Stationary Office, 1998;1-108.
 4. Marra AR, Edmond MB, Wenzel RP, Bearman GM. Hospital acquired *Clostridium difficile* associated disease in the intensive care unit setting: Epidemiology, clinical course and outcome. *BMC Infect Dis* 2007;7:42.
 5. MacDougall C, Polk RE. Antimicrobial stewardship programs in health care systems. *Clin Microbiol Rev* 2005;18:638-56.
 6. http://www.tufts.edu/med/apua/news/newsletter_5_2041403174.pdf
 7. Dellit TH, Owens RC, McGowan JE Jr, Gerding DN, Weinstein RA, Burke JP, et al. Infectious Diseases Society of America and the Society of Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* 2007;44:159-77.
 8. Davey P, Brown E, Fenelon L, Finch R, Gould I, Hartman G, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev* 2005;19:CD003543.
 9. Pope SD, Dellit TH, Owens RC, Hooton TM. Results of survey on implementation of Infectious Diseases Society of America and Society of Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antibiotic stewardship. *Infect Control Hosp Epidemiol* 2009;30:97-8.
 10. Charani E, Cooke J, Holmes A. Antibiotic stewardship programmes – what’s missing? *J Antimicrob Chemother* 2010; 65:2275-7.
 11. Drew RH. Antimicrobial Stewardship Programs: How to start and steer a successful program. *J Manag Care Pharm* 2009;15(suppl): S18-23.
 12. Hulscher ME, Grol RP, van der Meer JW. Antibiotic Prescribing in Hospitals: a social and behavioural scientific approach. *Lancet Infect Dis* 2010;10:167-75.
 13. Teo J, Kwa AL, Loh J, Chlebicki MP, Lee W. The effect of a whole system approach in an antimicrobial stewardship programme at Singapore General Hospital. *Eur J Clin Microbiol Infect Dis* 2011; epub.
 14. Yeo CL, Chan SG, Earnest A, Wu TS, Yeoh SF, Lim R, et al. Prospective audit and feedback on antibiotic prescription in an adult hematology-oncology unit in Singapore. *Eur J Clin Microbiol Infect Dis* 2011; epub.
 15. Teng CB, Lee W, Yeo CL, Lee SY, Ng TM, Yeoh SF, et al. Guidelines for Antimicrobial Stewardship Training and Practice. *Ann Acad Med* 2012;1:29-34.
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