

Controlling Antibiotic Use and Resistance

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(See the article by Apisarnthanarak et al. on pages 768–75)

In this issue of *Clinical Infectious Diseases*, Apisarnthanarak et al. [1] tackle an issue that is of major importance to all persons involved in infectious diseases. The message that a relatively simple and inexpensive, although laborious, intervention program can have a major impact on antibiotic use, as well as on antimicrobial resistance, should prompt all health care providers (not only those in developing countries!) to put even more effort into controlling antibiotic use and resistance.

Antibiotic resistance is on the rise globally [2], and it is mainly driven by the selective pressure imposed by (inappropriate) antibiotic use. Antibiotics are among the most commonly prescribed drugs in hospitals, and infections with drug-resistant microorganisms increase the cost of health care, length of hospital stay, and mortality [3, 4]. Even in a country such as The Netherlands, with its low rates of antibiotic use and resistance rates [5], antibiotic use is often not appropriate [6, 7]. The major reason that antibiotics are prescribed inappropriately is that there is a lack of knowledge about infectious

diseases and antimicrobial therapy; health care providers are afraid *not* to prescribe antibiotics.

Since the 1990s, concern about antibiotic resistance has spread from the medical arena to the public and political arenas, generating numerous agency-based and governmental reports [8]. Basically, these reports advocate the development and implementation of programs for monitoring antibiotic use and resistance, and they advocate promoting appropriate antibiotic use and effective infection control. However, these programs too often stop at the surveillance side and do not cross the bridge to the implementation and evaluation side, to reduce inappropriate antibiotic use and resistance. Too often, these programs are looking at the problem without doing something about it. Much more attention should be paid to the interpretation of antibiotic use and resistance data, to educate and provide relevant feedback to physicians as well as to policy makers.

Various determinants of antibiotic use can be discerned at different levels (e.g., country [developed or developing], hospital [tertiary care or other], department [medicine or surgery], and the relative number of infectious diseases physicians). Reliable data on the quantitative use of antibiotics are essential, and it is therefore important that these data are collected, analyzed, and presented in a standardized manner [9–13]. There is also a clear need for standardization of how to evaluate

qualitative antibiotic use and how to define appropriate antibiotic use. For this, the original criteria of Kunin et al. [14] are often applied to local settings, as in the study by Apisarnthanarak et al. [1]. On the basis of Kunin and colleagues' criteria, Gyssens et al. [15] developed a flow chart that allowed for the evaluation of all aspects of antibiotic prescription: justification for the treatment, alternative treatments, and duration, dosing, and timing of therapy. Not only can this flow chart be used for evaluation purposes, but it is also well suited as a training instrument.

In line with the present study by Apisarnthanarak et al. [1], earlier studies demonstrated that an intervention program combining surveillance, education and feedback, and prescribing controls can be successful in reducing the number of antibiotic prescriptions, inappropriate antibiotic use [16–18], and antibiotic resistance [19, 20]. Some might argue that, in the study by Apisarnthanarak and colleagues, the fact that the infectious diseases physician responsible for implementation of the program was also responsible for evaluation of antibiotic prescription appropriateness could have introduced a bias. If any such bias would have occurred, it would certainly not have any impact on the “hard” data on quantitative antibiotic use and antibiotic resistance and would thus not change the major conclusions of this study. Another issue for discussion could be that the bacterial species selected

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to measure changes in antibiotic resistance are all bacteria that are often involved in outbreaks of infection. No specific data regarding clonality of these bacteria are given; however, it is reassuring that no outbreaks of infection due to these bacteria occurred during the study period.

The study by Apisarnthanarak et al. [1] demonstrates that a combined hospital-wide effort of surveillance, education and feedback, and prescription controls can and will lead to a significant reduction in the number of antibiotic prescriptions, inappropriate antibiotic use, costs, and antibiotic resistance in a tertiary care hospital in a developing country. They looked at the problem and did something about it. To sustain or even further improve these results, lasting and repeated efforts will be needed. Integrating infection-control efforts into this education and antibiotic-control program is warranted. Although this study was performed in a developing country, the results certainly are applicable to the developed world as well. Controlling and improving antibiotic use quantitatively and qualitatively requires long-lasting concerted efforts at local, regional, national, and international levels. Often underestimated, such efforts will be shown to be vital for control of infectious diseases in the future. Or, to quote a Scottish bank commercial, "Less talk...make it happen!"

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References

1. Apisarnthanarak A, Danchaivijitr S, Khawcharoenporn T, et al. Effectiveness of education and an antibiotic-control program in a tertiary care hospital in Thailand. *Clin Infect Dis* **2006**;42:768–75 (in this issue).
2. Livermore DM. Bacterial resistance: origins, epidemiology, and impact. *Clin Infect Dis* **2003**;36(Suppl 1):S11–23.
3. Ibrahim EH, Sherman G, Ward S, Fraser VJ, Kollef MH. The influence of inadequate antimicrobial treatment of bloodstream infections on patient outcomes in the ICU setting. *Chest* **2000**;118:146–55.
4. Cosgrove SE, Carmeli Y. The impact of antimicrobial resistance on health and economic outcomes. *Clin Infect Dis* **2003**;36:1433–7.
5. Cars O, Molstad S, Melander A. Variation in antibiotic use in the European Union. *Lancet* **2001**;357:1851–3.
6. van Kasteren ME, Kullberg BJ, de Boer AS, Mintjes-de Groot J, Gyssens IC. Adherence to local hospital guidelines for surgical antimicrobial prophylaxis: a multicentre audit in Dutch hospitals. *J Antimicrob Chemother* **2003**;51:1389–96.
7. Schouten JA, Hulscher ME, Kullberg BJ, et al. Understanding variation in quality of antibiotic use for community-acquired pneumonia: effect of patient, professional and hospital factors. *J Antimicrob Chemother* **2005**;56:575–82.
8. Livermore DM. Minimising antibiotic resistance. *Lancet Infect Dis* **2005**;5:450–9.
9. Mackenzie F, Gould IM. Quantitative measurement of antibiotic use. In: Gould IM, van der Meer JW, eds. *Antibiotic policies: theory and practice*. New York: Kluwer Academic/Plenum Publishers, **2005**:105–18.
10. Natsch S. Collecting, converting, and making sense of hospital antimicrobial consumption data. In: Gould IM, van der Meer JW, eds. *Antibiotic policies: theory and practice*. New York: Kluwer Academic/Plenum Publishers, **2005**:67–74.
11. World Health Organization (WHO). Guidelines for ATC classification and DDD assignment. Oslo: WHO Collaborating Centre for Drug Statistics Methodology, Norwegian Institute of Public Health, **2005**.
12. Monnet DL, Lopez-Lozano JM, Campillos P, Burgos A, Yague A, Gonzalo N. Making sense of antimicrobial use and resistance surveillance data: application of ARIMA and transfer function models. *Clin Microbiol Infect* **2001**;7(Suppl 5):29–36.
13. Filius PM, Liem TB, van der Linden PD, et al. An additional measure for quantifying antibiotic use in hospitals. *J Antimicrob Chemother* **2005**;55:805–8.
14. Kunin CM, Tupasi T, Craig WA. Use of antibiotics: a brief exposition of the problem and some tentative solutions. *Ann Intern Med* **1973**;79:555–60.
15. Gyssens IC, van den Broek PJ, Kullberg BJ, Hekster Y, van der Meer JW. Optimizing antimicrobial therapy: a method for antimicrobial drug use evaluation. *J Antimicrob Chemother* **1992**;30:724–7.
16. Thamlikitkul V, Danchaivijitr S, Kongpattanakul S, Ckokloikaew S. Impact of an educational program on antibiotic use in a tertiary care hospital in a developing country. *J Clin Epidemiol* **1998**;51:773–8.
17. Thuong M, Shortgen F, Zazemba V, Girou E, Soussy CJ, Brun-Buisson C. Appropriate use of restricted antimicrobial agents in hospitals: the importance of empirical therapy and assisted re-evaluation. *J Antimicrob Chemother* **2000**;46:501–8.
18. van Kasteren ME, Mannien J, Kullberg BJ, et al. Quality improvement of surgical prophylaxis in Dutch hospitals: evaluation of a multi-site intervention by time series analysis. *J Antimicrob Chemother* **2005**;56:1094–102.
19. Bantar C, Sartori B, Vesco E, et al. A hospitalwide intervention program to optimize the quality of antibiotic use: impact on prescribing practice, antibiotic consumption, cost savings, and bacterial resistance. *Clin Infect Dis* **2003**;37:180–6.
20. White AC Jr, Atmar RL, Wilson J, Cate TR, Stager CE, Greenberg SB. Effects of requiring prior authorization for selected antimicrobials: expenditures, susceptibilities, and clinical outcomes. *Clin Infect Dis* **1997**;25:230–9.