

Embracing ecology to limit antimicrobial resistance

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See related review paper by Mulvey and Simor, page 408, and related analysis paper by Patrick and Hutchinson, page 416

Headlines declaring “the end of the antimicrobial era” and “superbugs kill patients” are becoming commonplace. Such headlines engender anxiety, anguish and questions among the public. Is there a crisis? Does “something need to be done”? What are the facts about antimicrobial resistance and health risk? In this issue, Patrick and Hutchinson¹ introduce a series about antimicrobial resistance and infection control. Also in this issue, Mulvey and Simor² review the mechanisms of resistance. This series will also include 3 articles about infection control and management of antimicrobial-resistant microbes in 3 different settings — the hospital, clinic and home.

Colonization or infection with 1 of the current “big 3” microbes (methicillin-resistant *Staphylococcus aureus* [MRSA], vancomycin-resistant *Enterococcus*, and *Clostridium difficile*) not only creates anxiety among patients and their families but also often leaves the patient ostracized in health care settings, confined in isolation and approached by health care workers and visitors only through a barrier of gowns, gloves and masks.

Patrick and Hutchinson¹ emphasize that the emergence and evolution of antimicrobial resistance is neither exceptional nor calamitous but is the norm. Antimicrobial resistance predates the use of antimicrobials; resistance is intrinsic to microorganisms. A predictable result of antimicrobial use is the increased isolation of antimicrobial-resistant organisms. Furthermore, the greater the intensity of antimicrobial use, the more rapidly resistant strains will emerge and the higher the proportion of resistant strains. This concept was introduced by Dubos in 1942, soon after the introduction of penicillin.³

Given that increased antimicrobial use leads to increased antimicrobial resistance, appropriate use of antimicrobials is the pre-eminent strategy for limiting resistance. Progress toward the more rational use of antimicrobials has been achieved in the decade since the 1997 publication of *Controlling Antimicrobial Resistance: An Integrated Action Plan for Canadians*.^{4,5} However, the misuse and excessive use of antimicrobials continues to be a problem both in the community and health care institutions.⁵ These agents are still prescribed in cases where no benefits are anticipated. In addition, antibiotics are often continued for too long, and broad spectrum agents are given when targeted therapy is appropriate. The time has come to acknowledge that some strategies, consistently promoted to improve antimicrobial use — in particular, education — have had only limited impact.⁶ Based on the evidence, the most effective interventions appear to be restrictive administrative methods,⁷ including formulary control, which may be applied at either the level of the institution or the province.

Despite the substantial literature addressing the question of adverse clinical consequences of antimicrobial resistance, the topic remains controversial. Several reviews of antimicrobial resistance have suggested both a clinical and economic burden

Key points

- Antimicrobial resistance is a predictable outcome associated with antimicrobial use.
- Appropriate antimicrobial use is the most important strategy to limit antimicrobial resistance.
- The most effective interventions to improve antimicrobial use are restrictive administrative practices, such as formulary restriction.
- Basic infection-control strategies, such as proper hand hygiene and appropriate cleaning of the environment and shared equipment, reduce the transmission of antimicrobial-resistant organisms in health care settings.

with increased morbidity and mortality, and increased costs for patients infected or colonized with resistant organisms.^{8,9} However, significant methodological issues in design and assessment make these analyses subject to bias.¹⁰ Patients colonized or infected with resistant organisms have a greater burden of illness and greater exposure to the health care system (e.g., hospital admissions, interventions, antimicrobial therapy) and are thus at increased risk of infections caused by resistant organisms. Definitive randomized studies to estimate impact are clearly not feasible. However, a delay in the institution of effective therapy and the use of more expensive antimicrobials to treat resistant organisms are unquestionably negative outcomes.

Strategies to limit the spread of resistant microbes in health care settings must also address the prevention of transmission among patients and of infection in patients colonized with resistant organisms.¹¹ Foremost in achieving these goals is adherence to fundamental, overarching strategies for infection control. Optimal hand hygiene, and appropriate cleaning of the environment and shared equipment are essential. The central tenet of these fundamental hygiene practices to prevent health care–acquired infections is applicable for all organisms, irrespective of their resistance profile. Thus, the imperative is not to introduce programs focused on specific resistant organisms, but to strengthen infection-control practices in all health care settings, including acute care settings and office settings, as well as the home. Despite the lessons learned from the SARS outbreak, many institutional infection-control programs in Canada remain underfunded, and there are too few practitioners with expertise in this area.

The additional practices that specifically address resistant organisms — the use of certain barrier precautions, screening cultures and decolonization — remain controversial. However, it is incumbent on all health care professionals to know

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and execute fundamental hygienic practices in all health care settings, and to follow the guidelines in their jurisdiction.

Antimicrobial resistance will continue to interact at the human–microorganism interface, and resistance will ultimately limit the effectiveness of specific antimicrobials. Fortunately, there are only rare organisms currently isolated for which there are no therapeutic options. Minimizing the risk of selection of more multiresistant microorganisms through the appropriate use of antimicrobials, including judicious use when treating infections with presumed resistant organisms, is crucial. Balancing harm from antimicrobial-resistant organisms and optimal antimicrobial use requires knowledge of local antimicrobial resistance patterns, thoughtful prescribing in conjunction with the effective use of basic infection control practices and a firm understanding of the delicate ecological balance in which we co-exist with the microbial world. If we do not work to preserve this balance, we are failing as physicians and as a society.

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REFERENCES

1. Patrick DM, Hutchinson J. Antibiotic use and population ecology: How you can reduce your “resistance footprint.” *CMAJ* 2009;180:416-21.
2. Mulvey MR, Simor AE. Antimicrobial resistance in hospitals: How concerned should we be? *CMAJ* 2009;180:408-15.
3. Moberg CL, René Dubos: A harbinger of antimicrobial resistance to antibiotics. *Microb Drug Resist* 1996;2:287-97.
4. Controlling antimicrobial resistance: An integrated action plan for Canadians. *Can Comm Dis Report* 1997; 23S7:1-32.
5. Conly J. Antimicrobial resistance in Canada. *CMAJ* 2002;167:885-91.
6. Parrino TA. Controlled trials to improve antibiotic utilization; 1984–2004. *Pharmacotherapy* 2005;25:289-98.
7. Davey P, Brown E, Fenlon L, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev* 2005;(4): CD003543.
8. Public Health Agency of Canada. *Antimicrobial resistance: A deadly burden no country can afford to ignore*. Ottawa (ON): The Agency; 2003. Available: www.phac-aspc.gc.ca/publicat/cdr-rmtc/03vol29/dr2918eb.html (accessed 2009 Jan. 12).
9. Maragakis LL, Perencevich EN, Cosgrove SE. Clinical and economic burden of antimicrobial resistance. *Expert Rev Anti Infect Ther* 2008;6:751-63.
10. Cosgrove SE, Carmeli Y. The impact of antimicrobial resistance on health and economic outcomes. *Clin Infect Dis* 2003;36:1433-7.
11. Routine practices and additional precautions for preventing the transmission of infection in health care. *Can Comm Dis Rep* 1999; 25S4.

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