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Antimicrobial stewardship: concepts and strategies in the 21st century

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Abstract

Large worldwide surveillance studies report that resistance to nearly all classes of antimicrobial is increasing, as is the emergence of what have been termed *pan-drug–resistant* and *extremely drug-resistant* pathogens. Concomitantly, bacterial binding sites have been exploited by available antimicrobials, and there has been a decline in the development of antimicrobials using novel mechanisms of action. These trends have prompted healthcare facilities to adopt antimicrobial stewardship programs (ASPs) and infection control programs (ICPs) to monitor antimicrobial use while simultaneously optimizing treatment, outcome, and cost. This article outlines the development of an effective ASP and the key components and operating principles, and also provides insight into the production of materials that will facilitate the execution of these programs at healthcare facilities. In this discussion, education of healthcare providers is emphasized, and a rationale is provided with regard to the health, safety, and financial benefits that can be obtained from an ASP. A brief history of antimicrobial stewardship is included, providing the context for several studies of antimicrobial stewardship practice, which are also reviewed. Programs for optimal use are illustrated, including a prospective audit and feedback strategy and preauthorization procedure. The components of an effective ASP are described in depth, drawing examples from the literature, as well as from the author's personal experience at the Maine Medical Center, Portland, ME.

Keywords: Antimicrobial resistance; Education; Antimicrobial stewardship program; Infection control program; Prospective audit; Drug resistant; Cost

1. Introduction

An epic struggle for survival between single-celled bacteria and developing mammalian species has existed from time immemorial. For pathogenic bacteria, day-to-day skirmishes on the microscopic battlefield against mammals and other living things occurred naturally for millions of years. The only means for mammalian defense was the host's evolving immune system. In many cases, this was just not enough to prevent death from certain types of infection. Seventy years ago, drugs that could be taken by mouth or parenterally joined the battle, providing a shift in our favor and thus beginning the "antibiotic era". Yet, as soon as these drugs were used, clinicians were greeted not only with great success but also with the 1st evidence of antimicrobial resistance.

During the 1940s and 1950s, clinicians recognized that resistance was emerging and that our current arsenal of antimicrobial agents lacked activity against many increasingly recognized strains of bacteria. Antimicrobial development was in high gear, and by 1957, new chemical entities had been discovered from the tetracycline, macrolide, aminoglycoside, glycopeptide, polyene, and polymyxin classes—as well as semisynthetic derivatives of penicillin, such as penicillinase-stable penicillin or "methicillin". However, we have reached a new crossroad in antimicrobial development. Large worldwide surveillance studies report that resistance to nearly all antimicrobial classes is increasing, as is the emergence of what have been termed *pan-drug–resistant* and *extremely drug-resistant* pathogens. In addition, because all of the so-called easily exploitable bacterial binding sites have been exploited, drug development has become more complex than it was decades ago.

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In fact, only 2 antimicrobial agents with genuinely novel mechanisms of action (linezolid and daptomycin) have been released during the last 2 decades.

One thing we must do, as antimicrobial resistance increases and antimicrobial development declines, is use our current cadre of antimicrobials more wisely. Administering antimicrobials judiciously to extend their useful lifetime is but one of the things we can offer immediately to address this public health crisis. This means optimizing antimicrobial use in humans via the development of a prospective, formalized, strategy to ensure that antimicrobials are used appropriately. Programs developed from this strategy are called antimicrobial stewardship programs (ASPs). *Good antimicrobial stewardship* is a practice that ensures the optimal selection, dose, and duration of an antimicrobial therapy that leads to the best clinical outcome for the treatment or prevention of infection while producing the fewest toxic effects and the lowest risk for subsequent resistance (Gerding, 2001). It should be noted that the unregulated use of these drugs does not only induce resistance, but also directly harm patients by increasing their risk of developing side effects such as life-threatening *Clostridium difficile* infection (CDI) (Fraser et al., 1997, 2005; Owens et al., 2004), as well as lead to excessive-drug–related expenditures.

It should be stressed that antimicrobial stewardship is only 1 strategy for minimizing the development of resistance. To be successful, there must be a collaboration

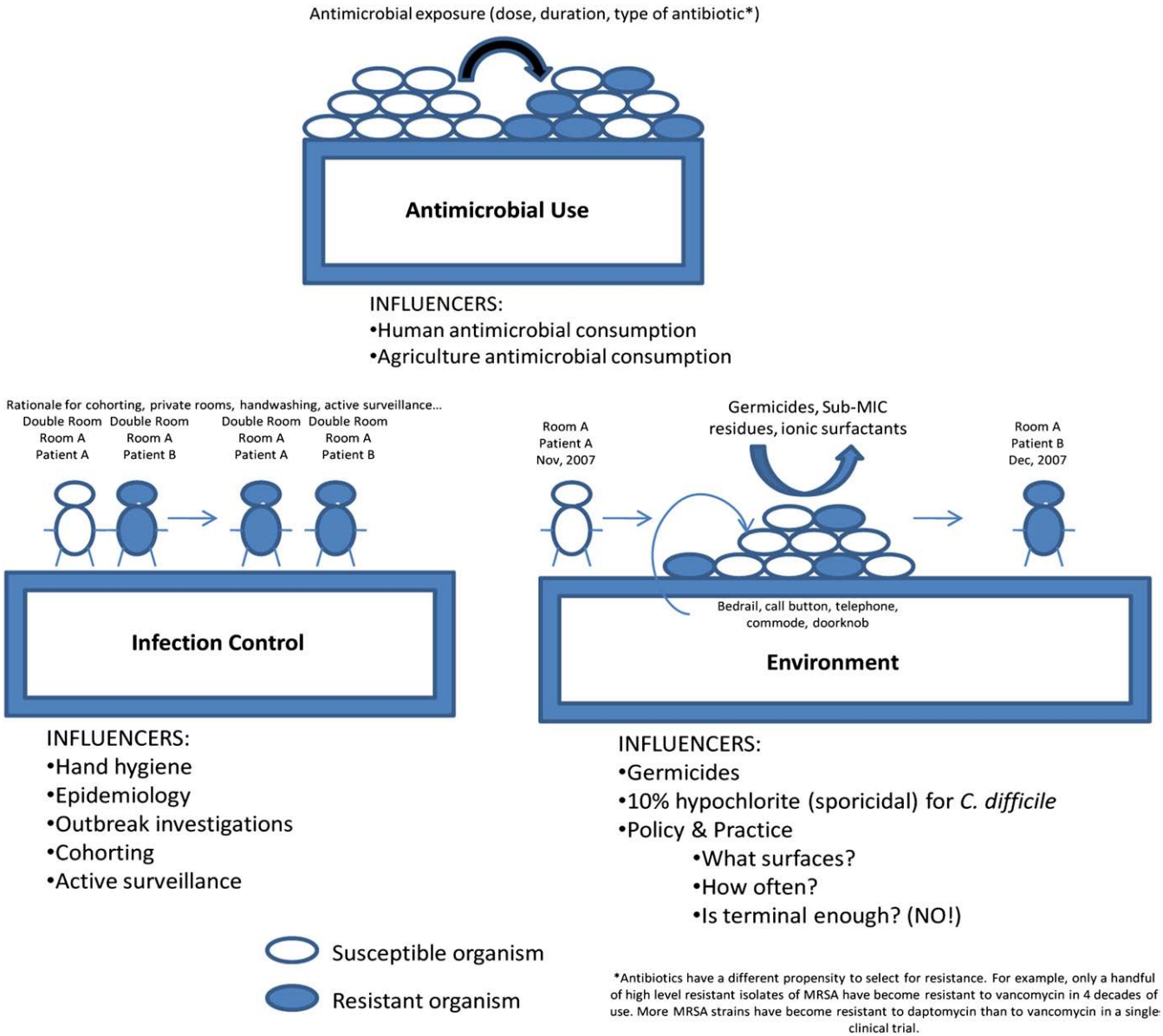

Fig. 1. Why antimicrobial resistance cannot be solved with single intervention alone. All 3 aspects of the "holy trinity" of resistance development and spread must be addressed.