



FIGURE 1. Resistance pattern of *P. aeruginosa* to last-resort antibiotics.

notorious superbugs. Unless we continue to search fervently for solutions to this problem, we will soon face a time when mortality is caused by common infections.

ACKNOWLEDGMENTS

The author is thankful to Dr. E. Subudhi, Siksha 'O' Anusandhan University, Bhubaneswar, Odisha, India and Dr. Dinesh Goyal, Shiv Astha Clinic, Haryana, India for kindly providing the samples. Ethical approval was not required.

Financial support. This research was partly supported by SERB, Department of Science & Technology, New Delhi, India.

Potential conflicts of interest. The author reports no conflicts of interest relevant to this article.

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Infect. Control Hosp. Epidemiol. 2016;37(3):365–366

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Encouraging Antibiotic Development and Endorsing Conservation: Tandem Approaches to Our Declining Antibiotic Reserves

To the Editor—We are currently facing a crisis in healthcare: an increase in antibiotic-resistant infections coincident with a decrease in antimicrobials available to effectively and safely treat these pathogens.¹ Over the past decade, antibiotic development has lagged, failing to keep pace with growing bacterial resistance.² There are both economic and scientific reasons for this slowdown in antibiotic development.³ From the economic perspective, it is difficult for pharmaceutical companies to generate a substantial profit from antibiotics.^{1,2} Unlike agents that are administered for chronic conditions, antibiotics are prescribed to treat acute conditions and thus used for a limited period. Furthermore, newer agents are generally targeted to antimicrobial-resistant organisms and thus have limited applications. From a scientific perspective, new antimicrobial targets of action have been elusive and agents that have tried to exploit new targets have had unacceptable toxicity.

In an attempt to spur antibiotic development, recent legislative efforts have focused on economic incentives for antibiotic research and development, including legislation to reduce pharmaceutical research and development costs through tax incentives.^{4,5} The current legislative efforts tackle only one part of the problem: the current financial disincentives that restrict development of antibiotics for resistant organisms. A complementary approach emphasizing the judicious use of our existing antibiotic supply is also needed. Creating more antibiotics will provide an immediate benefit to patients infected with highly resistant organisms. With fewer antibiotics available to these patients, this is an absolute necessity. However, focusing only on new antibiotic development has the potential to distract us from complementary approaches essential for a long-term solution to this problem. In addition to increasing antibiotic development, we also need to preserve our existing antimicrobial agents and control antibiotic overuse. Strengthening antimicrobial stewardship program (ASP) initiatives will provide this much needed oversight.

For medications other than antibiotics, treatment decisions impact a single patient. Although nonantibiotic medications can produce adverse effects or be ineffective in that patient, the agents remain effective and available for other patients. In contrast, antibiotic prescribing for one patient can induce resistance and thus limit the effectiveness of that agent in other patients. In recognition of both individual patient and societal paradigms, ASPs have been developed to provide oversight of antibiotic prescribing by individual providers.⁶ Antimicrobial stewardship, at its core, emphasizes the judicious use of antibiotics. Stewardship involves a coordinated, interdisciplinary approach to optimize antibiotic selection, dose, duration, and route of administration.⁶ ASPs improve patient outcomes,

reduce costs, and can reduce antimicrobial resistance.^{6–8} For individual patients, the goal of stewardship is to achieve the best possible clinical outcome while minimizing adverse drug events and antibiotic toxicity. On the societal level, ASPs seek to reduce the emergence of antimicrobial-resistant organisms and reduce healthcare costs.⁹ Thus, ASPs balance the needs of individual patients with the long-term viability of existing antimicrobial agents.

Fortunately, there is a growing awareness among the healthcare community and the public about antibiotic resistance and antibiotic overuse in both healthcare and agricultural settings. The White House Commission emphasized that judicious antibiotic use is essential to combat the rise in antibiotic resistance. Two recent legislative efforts, the Preventing Antibiotic Resistance Act of 2013 (S1256) and the Preservation of Antibiotics for Medical Treatment Act of 2013 (HR 1150), attempt to limit antibiotic use in the livestock industry and direct the US Food and Drug Administration to restrict antibiotics important for human health from being used in livestock without a clear medical reason to use such antibiotics in specific animals. The human healthcare community applauds these efforts.

Less attention has been paid to the financial burden of antibiotics on patients, which is not addressed by efforts to subsidize drug development. A new antibiotic will be expensive. The cost of development, the limited use of new agents, and the short patent period make it difficult for a pharmaceutical company to recoup their research and development costs on new antibiotics. This cost may be necessary as an incentive for driving innovation.¹⁰ Off-label prescribing could occur and would be profitable but it would also accelerate the emergence of resistance. As stated in McKellar and Fendrick's economic analysis on antibiotic development, drug development therefore "must be coupled with antimicrobial stewardship to protect against overutilization and reduce selective pressure for resistance."^{10(pS106)} We applaud that the recent legislation anticipates the potential for off-target use of new agents and monitors antibiotic use to ensure that taxpayer-subsidized drug development is reserved for highly resistant organisms. New drugs will be expensive, but we owe our patients an open and informed discussion of the potential impact of recent legislative efforts on healthcare costs.

In summary, although recent drug development efforts are necessary and an important step in the treatment of patients with antibiotic-resistant infections, simultaneous efforts should focus on improving and strengthening antibiotic stewardship. Using both approaches will provide a longer-term solution to the dilemma of antibiotic resistance in healthcare. We suggest that additional legislative or regulatory approaches are needed to support and fund implementation of ASPs and to monitor antimicrobial use across the continuum of healthcare. We further suggest that incentivizing providers to use antibiotics appropriately and furthering educational efforts for the public regarding judicious antibiotic use will preserve the activity of both existing and new antibiotics while reducing antimicrobial

resistance and costs. The "build more antibiotics approach," while clearly necessary for highly resistant infections, if used alone, will not provide a sustainable solution.

ACKNOWLEDGMENTS

Financial support. None reported.

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article.

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Infect. Control Hosp. Epidemiol. 2016;37(3):366–367

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