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Erica K. Susky, MSc; Camille Lemieux, MD

Affiliations: Department of Infection Prevention and Control, University Health Network, Toronto, Ontario, Canada.

Address all correspondence to Erica Susky, BSc, MSc, CIC, Infection Prevention and Control, University Health Network, 580 University Avenue, Toronto ON, Canada, M5G 2C4, 9th floor Peter Munk Building, 8PMB 100 (Erica.Susky@uhn.ca).

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Resistant Superbugs: Race against Time

To the Editor—Pseudomonas aeruginosa is one of the most notorious bacteria isolated from nosocomial infections. The growing threat of antimicrobial resistance in *P. aeruginosa* relies on its intrinsic resistance as well as on the transferable resistance determinants that further reduce their spectrum of susceptibility. Surveillance by hospitals to track the emergence of newer strains of *P. aeruginosa* is important to prevent its outbreak. In the present study, a total of 207 nonduplicate *Pseudomonas* isolates were collected over a period of 2 years (2013–2015) from various clinical samples of admitted patients (eg, pus, urine, wounds, and burns). The susceptibility of these isolates was tested against antimicrobial agents according to the Clinical and Laboratory Standards Institute (CLSI) broth microdilution procedure and interpretation criteria.[1] Among these isolates, 26 showed resistance to the following antibiotics: cefepime (89%), ceftriaxone (54%) gentamicin (79%), netillin (39%), ciprofloxacin (59%), and olfloxacin (34%). Based on the restriction pattern of 16S rRNA gene (Msp1 and Hha1), these 26 isolates were divided into 9 strains of *P. aeruginosa*. Among these 9 strains, 67% showed elevated minimum inhibitory concentrations (MICs) for imipenem (MIC, $\geq$10 μg/ml) and meropenem (MIC, $\geq$30 μg/ml). In a few studies from India, the rate of carbapenem resistance in *P. aeruginosa* isolates has been reported to vary from 12% to 43%.[2,3] PCR amplification with NDM-1 primers (forward: CTCGCACC GAATGTCTGGC and reverse: GCGGCGTAGTGCTC AGTGTC) showed amplification in all the carbapenemase producers. The high prevalence rate of carbapenemase producers could be linked to poor control of antibiotic usage in India.[4] Tigecycline, which was approved by the Food and Drug Administration in 2005, and the "old" antibiotic colistin are among the remaining treatment options for these difficult-to-treat infections.[5] Among the carbapenem-resistant *P. aeruginosa* strains, 42% and 35% showed resistance to tigecycline (16–50 mg/L) and colistin (16–500 mg/L), respectively (Figure 1). Among these isolates, 2 (M-30 and R-32) showed resistance to all the last-resort antibiotics tested (ie, imipenem, meropenem, colistin, and tigecycline). This is the first study from India that has reported the emergence of a 'superbug' *P. aeruginosa* that is resistant to last-resort antibiotics.

Due to lack of stringent measures, almost all antimicrobial agents are available to both public and private-sector outpatients in India. Decades of overuse and misuse of antibiotics by both the public and clinicians has led to the evolution of these superbugs. A decline in the development of new antimicrobial agents and the simultaneous increase in resistance to available treatment options pose a threat to the successful treatment of infections caused by these

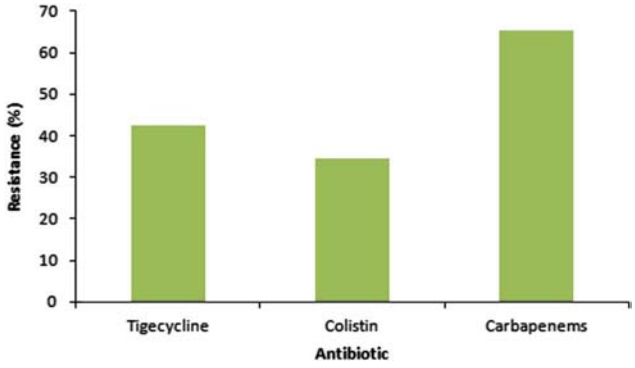

FIGURE 1. Resistance pattern of *P. aeruginosa* to last-resort antibiotics.

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.

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Mohit Kumar, PhD

Affiliations: Biotechnology and Bioinformatics, NIIT University, Neemrana, Rajasthan, India.

Address correspondence to Dr. Mohit Kumar, Biotechnology and Bio informatics, NIIT University, Neemrana, Rajasthan 301705, India (kumarmohit@yahoo.com).

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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,