Bad Bugs, No Drugs: No ESCAPE Revisited

To the Editor—It was with appreciation that I read your update from the Infectious Diseases Society of America in the January 2009 issue of the journal that highlighted the impact of the ESKEAPE pathogens (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species) as a group of particularly troublesome bacteria having the ability to “escape” the effects of current antimicrobial agents [1]. I would, however, like to offer a “friendly amendment” and suggest that, moving forward, the term “ESKAPE” be changed to “ESCAPE” (E. faecium, S. aureus, Clostridium difficile, A. baumannii, P. aeruginosa, and Enterobacteriaceae).

Including C. difficile as the new “C” acknowledges C. difficile infection (CDI) as one of the problematic diseases, and this inclusion is justified because CDI is one of the most common hospital-associated infections that we face, occurring among patients receiving antibiotics and thus “escaping” the beneficial effects of these antibiotics. Globally, cases of CDI appear to be growing more virulent [2], with CDI causing more frequent illness than in the past [3] and with patients not responding well to metronidazole therapy [4]. This recognition of C. difficile would not only include it in the acronym ESCAPE but would also potentially focus the need for increased funding to understand CDI’s unique relationship as a complication in the treatment of modern infectious diseases.

As to including Enterobacteriaceae in the ESCAPE pathogens as the new final “E,” this new terminology (ESCAPE) would then encompass not only K. pneumoniae (the former “K”) and Enterobacter species (the former final “E”) but also the other critically important pathogens that can express increasing levels of antibiotic resistance (including extended-spectrum β-lactamases and carbapenemases), aminoglycoside resistance, and decreasing levels of fluoroquinolone susceptibility (namely, Escherichia coli and Proteus species) [5]. I suggest this change because drug resistance in isolates of E. coli, K. pneumoniae, Enterobacter species, and other members of Enterobacteriaceae is not only a potential threat but a reality that needs to be stressed. Even though the percentage of drug-resistant isolates may be lower for E. coli, the fact that E. coli is the predominant etiologic pathogen for gram-negative infections indicates that it represents a greater total burden of disease than do K. pneumoniae and Enterobacter species combined [6–7]. Furthermore, Livermore et al [8] point out that E. coli infections currently account for ∼20% of all cases of bacteremia in the United Kingdom. This rivals the incidence of S. aureus infection and is nearly double that associated with any other pathogen. This finding, coupled with the emergence of extended-spectrum β-lactamase–mediated and carbapenemase–mediated resistance in Enterobacteriaceae other than Klebsiella species, speaks to the benefit of focusing on the larger family of Enterobacteriaceae as a global problem in the aggregate burden of infectious diseases.

Boucher et al eloquently reiterate that “the late-stage clinical development pipeline for antibacterials remains unacceptably lean” and that “the United States must make the development of a sustainable antibacterial drug research and development infrastructure a national priority” [1, pp. 9–10]. The ESCAPE concept is a most useful idea to focus attention on the problematic bacterial pathogens that we are all now facing in global health care. I suggest a slight change in the spelling of the acronym, thereby having it encompass more fully all of the current problem pathogens that challenge the safe and efficacious treatment of infectious diseases.

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Reply to Bradley

To the Editor—We thank Dr John S. Bradley [1] for his editorial commentary in which he nicely describes the problems in accomplishing a good treatment study in children. However, he comes to a conclusion [1, p. 1212] which is not quite true: that we had a 10% failure rate in the short-term (10 days of antimicrobial) treatment group. There was not a single failure among those 63 patients.

To some extent, it might be a matter of defining a “failure.” In a treatment study, one may deem any patient whose medication has deviated a bit from the protocol a failure, but here the interpretation is not that straightforward.

In our article [2], the second table showed 5 children in the 10-day treatment group who received antimicrobials longer, but by no means did they all fail the initial treatment. The point is that we kept the preset criterion that the CRP level had to be decreased to ≤20 mg/L before the agent was discontinued. As we explained [2, p. 1207], we currently do not necessarily wait that long if recovery is otherwise likely. It is quite obvious that antimicrobial could have been discontinued after 10 days in most of these 5 cases, because it is not known if, say, a level of 50 mg/L or a 75% decrease from the highest level would serve as well as ≤20 mg/L, which we have used for >25 years [3, 4]. Thus, his statement “knowledge of a 10% [clinical] failure rate (perhaps higher for hip infections)” [1, p. 1212] is not supported by our study [2].

We also do not think that, in septic arthritis, a “treatment failure will certainly impact the quality of life for the rest of the child’s life” [1, p. 1212]. In our study, the child with 2 late reinfections demonstrated that a catastrophe hardly follows a recurring osteoarticular infection if the infection is treated promptly. Septic arthritis is not bacterial meningitis.

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