the extra charges and prolongation of hospitalization due to nosocomial infections: a comparison of methods. *J Infect Dis* 1980; 141:248-257.
5. Kim T, Oh PI, Simor AE. The economic impact of methicillin-resistant *Staphylococcus aureus* in Canadian hospitals. *Infect Control Hosp Epidemiol* 2001; 22:99-104.

Polymyxins: A Word of Caution for Prudent Use of Valuable "Old Antibiotics"

TO THE EDITOR—Infections due to gram-negative bacteria, such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii,* that are resistant to most classes of the available antimicrobial agents are a rapidly growing, worldwide clinical problem that has a serious impact on mortality, morbidity, and healthcare-related costs. The lack of development of new antimicrobial agents to combat these infections, have made the medical community reevaluate the use of polymyxins that are old, almost abandoned antibiotics.

Both polymyxin B and polymyxin E (colistin) have recently been used for the treatment of patients with multidrug-resistant gram-negative bacterial infections. The isolation of colistin from *Bacillus colistinus* was accomplished about 50 years ago. During the ensuing decades, colistin has been used in the treatment of several types of infections, including infectious diarrhea and urinary tract infection, as well as for bowel decontamination. Early clinical experience with polymyxins showed a high incidence of toxicity, mainly nephrotoxicity and neurotoxicity, including neuromuscular blockade.[1] For example, in a large study of 288 patients, the incidences of nephrotoxicity and neurotoxicity after intramuscular administration of colistin were 20.2% and 7%, respectively.[1] Such data led to significant reduction in the systemic administration of polymyxins. During the past 2 decades, the use of polymyxins has mainly been restricted to topical ophthalmic and otic therapy, as well as treatment of pulmonary infections due to multidrug-resistant *P. aeruginosa* in patients with cystic fibrosis.

However, recent experience, including ours, with patients who have nosocomial infections due to multidrug-resistant gram-negative bacteria and who have been given intravenous polymyxins as a salvage therapy, suggests that polymyxins are valuable antimicrobial agents.[2,3] Of note, the observed rates of nephrotoxicity among critically ill patients with infections caused by multidrug-resistant gram-negative bacteria who received intravenous colistin therapy were 8% and 14.3% in 2 recently published studies. Moreover, the comparison of the effectiveness and safety of intravenous colistin versus intravenous meropenem for the treatment of patients with ventilator-associated *A. baumannii* pneumonia revealed that the 2 therapeutic regimens yielded similar clinical responses; however, the rate of nephrotoxicity was considerably lower with colistin treatment. It is noteworthy that the incidence of aminoglycoside-induced nephrotoxicity has been reported to be 5%-25%, which is not that different from the incidence observed in recent studies with intravenous colistin.[4]

We believe that polymyxins are life-saving antibiotics for patients with infections due to gram-negative bacteria resistant to all other available antimicrobial agents. However, the uncontrolled reintroduction of polymyxin therapy in several countries has led to the appearance of bacteria, mainly *P. aeruginosa* strains, that have developed mechanisms of resistance even to these agents.[5] There is an urgent need for restriction of polymyxin use, to decrease the rate of emergence of really pandrug-resistant gram-negative bacteria—that is, bacteria with in vitro resistance to β-lactams, quinolones, aminoglycosides, tetracyclines, and polymyxins. Thus, polymyxins should be reserved for the treatment of patients with infections due to multidrug-resistant gram-negative bacteria when all other available antibiotic regimens have failed or patients with infections caused by microorganisms susceptible only to polymyxins.

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REFERENCES

1. Koch-Weser J, Sidel VW, Federman EB, Kanarek P, Finer DC, Eaton AE. Adverse effects of sodium colistimethate: manifestations and specific reaction rates during 317 courses of therapy. *Ann Intern Med* 1970; 72:857-868.
2. Falagas ME, Kasiakou SK. Colistin: the revival of polymyxins for the management of multidrug-resistant gram-negative bacterial infections. *Clin Infect Dis* 2005; 40:1333-1341.
3. Michalopoulos AS, Tsiodras S, Rellos K, Mentzelopoulos S, Falagas ME. Colistin treatment in patients with ICU-acquired infections caused by multiresistant gram-negative bacteria: the renaissance of an old antibiotic. *Clin Microbiol Infect* 2005; 11:115-121.
4. Smith CR, Lipsky JJ, Laskin OL, et al. Double-blind comparison of the nephrotoxicity and auditory toxicity of gentamicin and tobramycin. *N Engl J Med* 1980; 302:1106-1109.
5. Falagas ME, Bliziotis IA, Kasiakou SK, Samonis G, Athanassopoulou P, Michalopoulos A. Outcome of infections due to pandrug-resistant (PDR) gram-negative bacteria. *BMC Infect Dis* 2005; 5:24.