Antibiotic Use in the Elderly: Issues and Nonissues

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Despite the well-recognized increase in mortality and morbidity due to infections in the elderly, antibiotics may, in most cases, be used in a manner similar to that in younger patients. The decreased lean body weight and reduced renal function typical of elderly patients, however, require consideration of reduced doses and longer dosing intervals, especially for renally excreted antibiotics. Length of therapy should be conservative because underlying anatomic or functional predispositions to infections tend to complicate treatment. Oral antibiotics are equally well absorbed in the elderly and younger patients and may be used for the same indications as for younger patients. A notable, important difference in the choice of antibiotics for serious infections in older versus younger patients is that empirical therapy should be broader in spectrum for elderly patients, and especially for elderly long-term residents, since the variety of infecting bacteria tends to be greater and polymicrobial infections tend to be common.

Antibiotic Dosing in the Elderly: A Nonissue?

Many classes of drugs require special attention to dosing and dose intervals to avoid adverse events in elderly patients that are rarely encountered in younger patients. Important examples include cardiovascular agents such as antihypertensives or antiarrhythmics, neuromusculars such as sedatives and antipsychotics, and anticonvulsants. Such drugs may or may not have different pharmacokinetic characteristics in elderly patients, but many of them have significantly different, clinically important pharmacodynamic properties in elderly patients. These changes in pharmacodynamic properties result from the increased prevalence of chronic diseases in the elderly, as well as changes in functioning of cardiovascular, neurological, and other organ systems that are thought to be caused by aging itself; examples include the increased risk of upper gastrointestinal hemorrhage with nonsteroidal antiinflammatory drugs or serious arrhythmias from theophylline, risks in the elderly that are independent of doses.

This is not the case with antibiotics. Antibiotic dosing is relatively unaffected by age-related changes, per se. If the basic rules for antibiotic dosing in all patients, regardless of age, are followed, taking into account the reduced total weight and usually reduced renal function of elderly patients, antibiotic doses and dose intervals will be appropriately chosen [1–4]. The important corollary to this assumption is that antibiotic dosing in elderly patients should usually be based on lean body weight and calculated creatinine clearance, not on total body weight and serum creatinine level. The equations for calculating creatinine clearance, such as the traditionally employed Cockcroft-Gault calculation (creatinine clearance = \( \frac{(140 – \text{age}) \times \text{lean body weight}}{72 \times \text{serum creatinine level}} \)), are inferior to measurements of serum antibiotic concentrations or actual creatinine clearance but superior to estimation of serum creatinine alone [5].

Oral Antibiotic Use: A Nonissue

The elderly absorb oral medications reliably. Although the peak antibiotic concentration may be blunted, probably from atrophy of gastrointestinal mucosa and decreased blood supply, total absorption, as measured by the area under the curve, is comparable to that in younger patients. Slowed or decreased excretion and metabolism of drugs, moreover, may result in higher serum trough concentrations and a longer duration of action of oral antibiotics. There are no indications that oral therapy, when appropriately prescribed, is less effective in the elderly or that parenteral therapy is safer when appropriate oral therapy is available.

Antibiotic Choice: An Issue

One of the safest generalizations that may be drawn from decades of research and commentary on the treatment of infections in the elderly is that empirical therapy should be broader in the spectrum of antibacterial activity because the variety of infecting pathogens in community-acquired infections is more diverse. Colonization with bacteria that are not ordinarily present in the oropharynx or on the skin in younger, healthier persons is presumably at least partially responsible for the wider range of pathogens found in community- and nursing home–acquired infections in the elderly. Aging has been asso-
associated with colonization with gram-negative bacilli, a well-recognized risk factor for subsequent upper and lower respiratory infection with gram-negative bacilli [6–9]. The elderly, in addition, are more likely to have other risk factors for colonization with gram-negative bacilli: recent antibiotic use, diabetes, incontinence, immobility, and general debility from multiple chronic diseases. Residence in a nursing home increases exposure to and colonization with gram-negative bacilli and other antibiotic-resistant bacteria, perhaps independently of other risk factors [10, 11].

**Pneumonia.** Clinical prevalence studies indicate that the causes of pneumonia in adults are changing, in part because the population contracting pneumonia now tends to be older than in the past—although other factors, e.g., selective survival of organisms in the presence of widespread antibiotic use, are undoubtedly also responsible [12, 13]. Gram-negative, staphylococcal, and polymicrobial pneumonias occur predominantly in the elderly, and in the elderly nursing home patient in particular [13–25]. Although convincing confirmatory studies are lacking, the seriously ill elderly with pneumonia should be treated with broad-spectrum antibiotics that cover both gram-positive and gram-negative pathogens and, in some circumstances, atypical organisms [26, 27]. Previous empirical-treatment recommendations, such as those of the American Thoracic Society, may have been too narrow in spectrum for safe treatment of the elderly [28, 29].

**Urinary tract infections.** In older women, as in younger women, *Escherichia coli* is the most common cause of urinary tract infection (UTI) [30, 31], but the proportion of infections caused by *E. coli* is much less in older women [32, 33]. One must assume that there is at least an equal chance that a UTI in an older woman is caused by a coliform other than *E. coli*, such as a *Proteus, Klebsiella, Enterobacter, Serratia,* or *Pseudomonas* species. In addition, as many as one-third of older women with UTI have more than one potential pathogen isolated in a urine culture [30, 31, 34]. This means that trimethoprim-sulfamethoxazole, a previously dependable empirical choice for the treatment of UTI, may not have a sufficiently broad spectrum of antimicrobial activity for routine use and that a fluoroquinolone that is concentrated in the urine is preferable [35–37]. A similar situation probably pertains to older men, in whom fluoroquinolones have the additional advantage of excellent penetration into prostatic tissues, but there are no data to guide recommendations.

**Miscellaneous infections.** Gram-negative parotitis, sialadenitis, and septic arthritis are usually infections of the elderly. Diarrheal illness in the elderly resident of a long-term-care facility is more likely to be bacterial than community-acquired. The elderly are at greater risk for *Pseudomonas aeruginosa* otitis externa and *Listeria monocytogenes* meningitis. The epidemiology of endocarditis has changed over the past few decades, with a shift to older age groups, as rheumatic valvular disease has become uncommon. The elderly are more likely to be infected with enterococci and nonenterococcal group D streptococci, requiring consideration of vancomycin/gentamicin for empirical therapy in order to provide coverage for staphylococci, streptococci, and enterococci [38]. Because osteomyelitis in the elderly is more likely to be secondary to infected pressure ulcers or to involve the lumbosacral vertebrae, gram-negative or polymicrobial infection involving anaerobic bacteria and Enterobacteriaceae, in addition to staphylococcal infection (as is typically encountered in younger patients), must be considered when empirical therapy is devised [39].

### Specific Antibiotic-Related Concerns: Sometimes an Issue

A perusal of the most recent edition of *Mandell, Douglas and Bennett’s Principles and Practice of Infectious Diseases* [40] yields a list of possible special concerns about antibiotic use in the elderly, which are included in table 1. Regardless of method of dosing and the care with which serum levels are controlled, aminoglycoside nephrotoxicity and ototoxicity are more common. Cephalothin causes excess nephrotoxicity at high doses, and erythromycin causes more ototoxicity if impaired renal function is present. Higher doses of clarithromycin, such as those used for antitymcobacterial therapy, are poorly tolerated by older patients. It is well recognized that the elderly are at particular risk for isoniazid-related hepatotoxicity. Trimethoprim-sulfamethoxazole is more likely to cause neutropenia in older persons. Blindness may occur from ordinary doses of ethambutol, and amikacin is preferable to streptomycin for treating elderly patients with tuberculosis who have renal or hearing impairment. Rimantadine has a wider therapeutic margin than amantadine for elderly patients with or at risk of contracting influenza A.

### Duration of Therapy: Probably an Issue

Overall, the mortality and morbidity associated with all serious infections tend to be higher in the elderly than in their younger counterparts, a generalization that holds true especially for residents of long-term-care facilities. Cutting corners with therapy in high-risk populations, prima facie, makes little sense.
In addition, infection in the elderly is more likely to be related to underlying anatomic or physiological predispositions to infection, such as malnutrition or vascular insufficiency and cellulitis; incomplete bladder emptying and urinary tract infection; poor cough or recurrent aspiration and pneumonia; or sinusesis or pneumonia and meningitis. Therefore, sufficient duration of therapy to eradicate coinfection or colonization of a poorly functioning organ with a virulent pathogen is probably important to maximize the benefits of therapy.

References