

23. Significance and sources of antimicrobial-resistant nontyphoidal *Salmonella* infections in humans in the United States

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I. Clinical significance of antimicrobial-resistant nontyphoidal salmonellae

Salmonellosis results in considerable morbidity in the United States. Although most *Salmonella* infections result in a mild, self-limiting gastrointestinal illness characterized by diarrhea, fever and abdominal cramps, the infection can spread to the bloodstream, bone marrow or meningeal linings of the brain, leading to severe and occasionally fatal illness. Each year, there are an estimated two to four million human *Salmonella* infections in the US, (1, 2) causing an estimated 80,000 to 160,000 persons to seek medical attention (CDC unpublished data). Clinical specimens from persons who have sought medical attention result in approximately 40,000 culture-confirmed cases reported to the Centers for Disease Control and Prevention (CDC) annually (3, 4). An estimated 8,000 to 18,000 persons are hospitalized and up to 500 persons die of *Salmonella* infections each year in the US (5).

Antimicrobials are not indicated for *Salmonella* infections which manifest as uncomplicated gastroenteritis. Such infections are self-limiting and treatment does not reduce the duration or severity of symptoms, may prolong the carrier state, and may result in the emergence of a resistant infection. Nevertheless, antibiotics are commonly prescribed for persons with *Salmonella* infections who seek medical attention. In surveys conducted by CDC, 40% of persons with *Salmonella* infections who sought medical at-

tention were treated with antimicrobial agents (5,6). Ciprofloxacin, a fluoroquinolone antimicrobial agent, is the most commonly prescribed antimicrobial agent for *Salmonella* infections (CDC unpublished data).

In contrast to uncomplicated gastroenteritis, antimicrobials are essential for the treatment of patients with bacteremia, meningitis, or other extraintestinal *Salmonella* infections. Approximately six percent of the culture-confirmed cases reported to CDC are invasive isolates (3, 4). Antimicrobials, therefore, are critical and often life-saving for at least 2,400 persons a year with invasive *Salmonella* infections in the US. The selection of antimicrobials for the treatment of invasive infections has become increasingly restricted, however, due to the increasing resistance among *Salmonella* isolates to antimicrobials, particularly chloramphenicol, ampicillin, and trimethoprim-sulfamethoxazole, antimicrobials which have been frequently used to treat such infections (5,6). Among 1,272 randomly selected *Salmonella* isolates tested at CDC in the National Antimicrobial Resistance Monitoring System in 1996, 21% were resistant to ampicillin, 10% to chloramphenicol, and 4% to trimethoprim-sulfamethoxazole (7). Fortunately, almost all *Salmonella* isolates in the US have been susceptible to fluoroquinolones and third-generation cephalosporins. For this reason, and because of the favorable pharmacodynamic properties of these antimicrobials, fluoroquinolones and third-generation cephalosporins are the drugs-of-choice for the treatment of invasive *Salmonella* infections in adults and children,