# Quinolone-Resistant *Salmonella enterica* Serotype Enteritidis Infections Associated With International Travel

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**We found a strong association between nalidixic acid–resistant *Salmonella enterica* serotype Enteritidis infections in the United States and recent international travel by linking *Salmonella* Enteritidis data from the National Antimicrobial Resistance Monitoring System and the Foodborne Diseases Active Surveillance Network.**

***Keywords.*** drug resistance; foodborne diseases; quinolones; *Salmonella*; travel.

An estimated 1.2 million nontyphoidal *Salmonella* infections occur in the United States every year, and 84% of these are estimated to be domestically acquired from foodborne transmission [1]. *Salmonella enterica* serotype Enteritidis (SE) is the most frequently reported serotype [2]. Eggs and broiler chickens are likely the main food sources of SE illness in the United States [3].

The National Antimicrobial Resistance Monitoring System (NARMS) is a joint effort among the Centers for Disease Control and Prevention (CDC), the US Food and Drug Administration (FDA), the US Department of Agriculture (USDA), and participating health departments. NARMS conducts surveillance for antimicrobial resistance among enteric bacteria from humans, retail meat, and food animals. SE accounted for 21% (522/2474) of human nontyphoidal *Salmonella* isolates in NARMS in 2010 [4]. Overall, SE isolates from humans demonstrate relatively little resistance. In 2010, resistance was <2.5% for all agents tested except for the quinolone nalidixic acid. Nalidixic acid resistance among SE isolates from humans rose from 0.9% in 1996 when NARMS testing began to 5.2% in 2010 [4, 5]. Among all nontyphoidal *Salmonella* isolates from humans, nalidixic acid resistance was 2.0% (49/2474) in 2010, and 55% (27/49) of the nalidixic acid-resistant isolates were SE [4]. Resistance to nalidixic acid is correlated with reduced susceptibility to the fluoroquinolone ciprofloxacin and may be associated with treatment failure, so identifying sources of resistant infections is important [6, 7].

Among *Salmonella* isolates from food animals and retail meats submitted to NARMS in 2010, SE was found almost exclusively in chicken carcass rinsate and retail chicken breasts, with 27% (152/564) and 16% (28/171) of *Salmonella* isolates, respectively, identified as SE [8]. However, none of the animal or retail meat SE isolates in 2010 were resistant to nalidixic acid. From the beginning of NARMS testing through 2010, there was only 1 nalidixic acid–resistant isolate among the 1152 SE isolates from chicken carcass rinsate samples and 1 nalidixic acid–resistant SE isolate among the 141 SE isolates from retail chicken breast samples [5, 8]. The near absence of nalidixic acid resistance among poultry SE isolates in NARMS raises questions about the source(s) of nalidixic acid–resistant SE infections in humans in the United States. This study used information collected by both NARMS and the Foodborne Diseases Active Surveillance Network (FoodNet) to evaluate whether nalidixic acid resistance among human SE isolates was associated with a recent history of international travel.

## METHODS AND RESULTS

The NARMS program at the CDC is a national isolate-based surveillance system that systematically collects isolates of nontyphoidal *Salmonella* and other enteric pathogens from humans and tests them for susceptibility to a panel of antimicrobial agents. For this study, interpretive criteria from the CDC NARMS Annual Report were applied to the minimum inhibitory concentrations for 15 antimicrobial agents: amikacin, ampicillin, amoxicillin–clavulanic acid, cefoxitin, ceftiofur, ceftriaxone, chloramphenicol, ciprofloxacin, gentamicin, kanamycin, nalidixic acid, streptomycin, sulfisoxazole, tetracycline, and trimethoprim-sulfamethoxazole [4]. The resistance breakpoints for nalidixic acid and ciprofloxacin were minimum inhibitory concentration (MIC) ≥32 μg/mL and MIC ≥1 μg/mL, respectively. Isolates with ciprofloxacin MICs ranging from 0.12 to 0.5 μg/mL were classified as intermediate.

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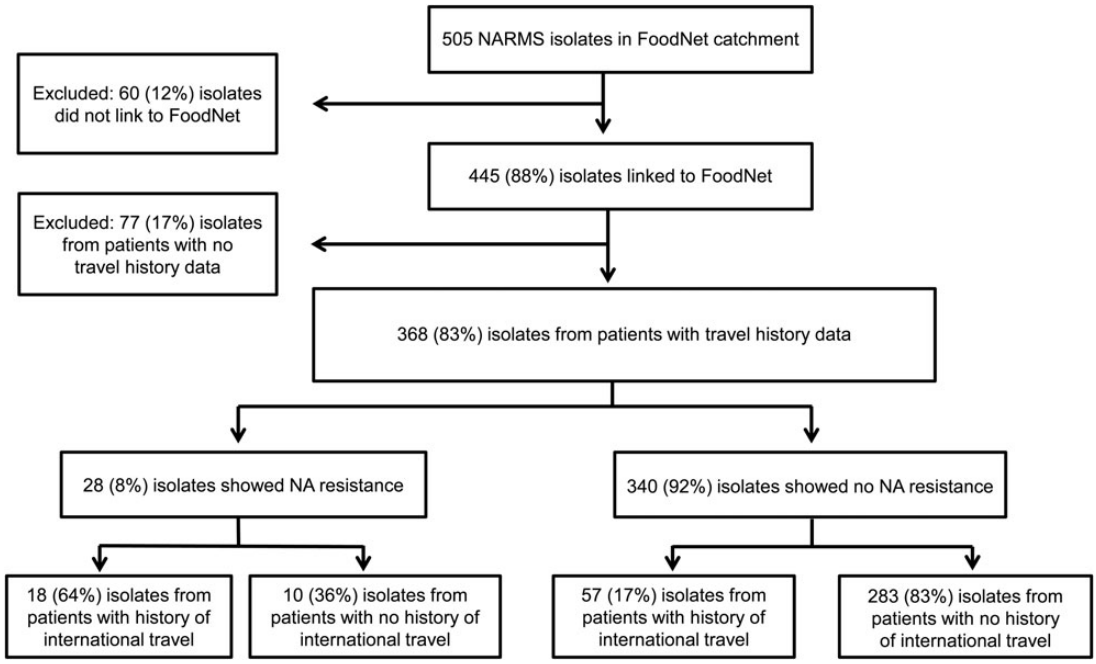


**Figure 1.** National Antimicrobial Resistance Monitoring System *Salmonella enterica* serotype Enteritidis isolates included in the study and the number and percentage of isolates from persons with a reported history of international travel within 7 days before illness onset. Abbreviations: FoodNet, Foodborne Diseases Active Surveillance Network; NA, nalidixic acid; NARMS, National Antimicrobial Resistance Monitoring System.

FoodNet is a collaboration of the CDC, 10 state health departments, the USDA's Food Safety and Inspection Service, and the FDA [2]. FoodNet conducts active surveillance for laboratory-confirmed infections with 9 pathogens transmitted commonly through food. Data collected include history of international travel in the 7 days before illness onset. If a patient traveled abroad during this period, the infection is considered travel-associated [9].

We linked NARMS and FoodNet data for SE isolates with specimen collection dates from 1 January 2004 through 31 December 2010 by using the state laboratory identification number, specimen collection date, patient age, county of residence, sex, and specimen source. Eighty-eight percent (445/505) of NARMS SE isolates from FoodNet catchment sites were linked to FoodNet data, and 368 (83%) of these were from patients with travel history information (Figure 1). Patients with nalidixic acid–resistant isolates (n = 28) were compared with patients with nalidixic acid–susceptible isolates (n = 340) with respect to reported history of international travel. For both groups, we calculated the proportion of isolates from persons with a history of international travel within 7 days before illness and compared results using Fisher exact test.

A history of international travel before illness began was reported by 75 of the 368 (20%) SE patients with travel history data. Among the 368 patients, 28 had isolates that exhibited resistance to nalidixic acid, of which 18 (64%) came from patients with international travel before illness began. Twenty-four (86%) of the 28 nalidixic acid–resistant isolates exhibited reduced susceptibility to ciprofloxacin (MIC ≥0.12 μg/mL); 1 isolate was resistant to ciprofloxacin (MIC ≥1 μg/mL) and 23 had intermediate ciprofloxacin MICs (0.12–0.5 μg/mL). All 18 nalidixic acid–resistant isolates from patients with travel had intermediate ciprofloxacin MICs. Among patients with a reported history of international travel, 24% (18/75) had nalidixic acid–resistant SE infections, compared with 3% (10/293) of patients who reported no travel. Information on countries visited was available for 14 of the 18 patients with nalidixic acid–resistant SE infections. Patients traveled to the Dominican Republic (4), Mexico (3), China (1), India (1), the Philippines (1), Poland (1), Russia (1), and Spain (1); 1 patient traveled to England, France, Poland, Greece, and Germany.

The proportion of patients with recent international travel was significantly higher ($P < .05$) among those with nalidixic acid–resistant SE than those with nalidixic acid–susceptible SE (18/28 [64%] vs 57/340 [17%]). Five nalidixic acid–resistant isolates had co-resistance to other antimicrobial agents (4 were resistant to 1 other agent and 1 was resistant to 2 other agents). Three of the 5 nalidixic acid–resistant isolates with co-resistance came from patients with a history of international travel. None of the isolates with co-resistance exhibited resistance to the

extended-spectrum cephalosporin ceftriaxone. When the 5 co-resistant isolates were excluded, there was no appreciable change in the proportion of patients with a history of international travel (15/23 [65%]).

To investigate whether international travel was associated specifically with nalidixic acid resistance and not with resistance to any agent, a subanalysis was performed on the nalidixic acid–susceptible group. Isolates with resistance to at least 1 of the 14 antimicrobial agents other than nalidixic acid (n = 19) were compared with isolates with no resistance (n = 321; includes pansusceptible and intermediate resistance isolates). There was no significant difference in the proportion of patients with a history of international travel between these 2 subgroups (4/19 [21%] vs 53/321 [17%]).

## CONCLUSIONS

We found that a high proportion of nalidixic acid–resistant SE infections were associated with travel outside the United States. Studies in other countries including Denmark, England, and Wales have also found quinolone-resistant SE infections to be related to foreign travel [10, 11]. Most nontyphoidal *Salmonella* infections in the United States are domestically acquired. However, SE is more common among patients with a history of travel, accounting for 40% of nontyphoidal *Salmonella* infections associated with international travel, compared with 17% of infections acquired in the United States [9].

Our findings suggest that the majority of nalidixic acid–resistant SE infections in the United States are associated with foreign travel, but the source of nalidixic acid–resistant infections among people who did not have a history of international travel in the 7 days before illness began is not known. Some may have acquired antimicrobial-resistant SE abroad but remained asymptomatic until they took an antimicrobial agent for another reason [12]. NARMS animal and retail meat data suggest that chicken is not an important source of nalidixic acid–resistant SE infections acquired in the United States [5, 8]. Eggs are a major source of domestic SE infections [3], but we are not aware of recent nalidixic acid susceptibility data for SE isolated from US eggs. Imported foods are another possible source. The FDA has found nalidixic acid–resistant SE in samples of several different seafood products offered for import into the United States (unpublished data).

This analysis provides important information regarding sources of nalidixic acid–resistant SE that may provide a better understanding of the diversity of sources and transmission pathways of salmonellosis. Additional research is needed to ascertain travel destinations and exposure sources associated with nalidixic acid–resistant SE infections acquired during international travel, to identify sources of domestically acquired nalidixic acid–resistant SE infections, and to examine clinical outcomes of nalidixic acid–resistant infections.

## Notes

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