FOODBORNE PATHOGENS AND DISEASE
Volume 14, Number 2, 2017

DOI: 10.1089/fpd.2016.2180

Original Articles

Ceftriaxone-Resistant Nontyphoidal *Salmonella* from Humans, Retail Meats, and Food Animals in the United States, 1996–2013

Martha Iwamoto,[1] Jared Reynolds,[1] Beth E. Karp,[1] Heather Tate,[2] Paula J. Fedorka-Cray,[3,4] Jodie R. Plumblee,[3] Robert M. Hoekstra,[1] Jean M. Whichard,[1] and Barbara E. Mahon[1]

Abstract

Background: Ceftriaxone resistance in *Salmonella* is a serious public health threat. Ceftriaxone is commonly used to treat severe *Salmonella* infections, especially in children. Identifying the sources and drivers of ceftriaxone resistance among nontyphoidal *Salmonella* is crucial.

Materials and Methods: The National Antimicrobial Resistance Monitoring System (NARMS) tracks antimicrobial resistance in foodborne and other enteric bacteria from humans, retail meats, and food animals. We examined NARMS data reported during 1996–2013 to characterize ceftriaxone-resistant *Salmonella* infections in humans. We used Spearman rank correlation to examine the relationships between the annual percentage of ceftriaxone resistance among *Salmonella* isolates from humans with isolates from retail meats and food animals.

Results: A total of 978 (2.9%) of 34,100 nontyphoidal *Salmonella* isolates from humans were resistant to ceftriaxone. Many (40%) ceftriaxone-resistant isolates were from children younger than 18 years. Most ceftriaxone-resistant isolates were one of three serotypes: Newport (40%), Typhimurium (26%), or Heidelberg (12%). All were resistant to other antimicrobials, and resistance varied by serotype. We found statistically significant correlations in ceftriaxone resistance between human and ground beef Newport isolates ($r = 0.83$), between human and cattle Typhimurium isolates ($r = 0.57$), between human and chicken Heidelberg isolates ($r = 0.65$), and between human and turkey Heidelberg isolates ($r = 0.67$).

Conclusions: Ceftriaxone resistance among *Salmonella* Newport, Typhimurium, and Heidelberg isolates from humans strongly correlates with ceftriaxone resistance in isolates from ground beef, cattle, and poultry, respectively. These findings support other lines of evidence that food animals are important reservoirs of ceftriaxone-resistant *Salmonella* that cause human illness in the United States.

Keywords: *Salmonella*, antimicrobial resistance, foodborne disease, cephalosporin

Introduction

Antimicrobial resistance in *Salmonella* is a serious public health threat. Although antimicrobial agents are not indicated for most infections, they can be life-saving for severe infections. Antimicrobial resistance in *Salmonella* causing human infections can result in increased morbidity and mortality and limit treatment options (Helms *et al.*, 2002; Varma *et al.*, 2005, 2005; Crump *et al.*, 2011; Krueger *et al.*, 2014). Extended-spectrum cephalosporins, such as ceftriaxone, are particularly important because they are commonly recommended for the management of invasive *Salmonella* infections in humans and are the drugs of choice for treating pediatric infections (Geme *et al.*, 1988; Pegues and Miller, 2009; American Academy of Pediatrics, 2015). Reports indicate increasing resistance to ceftriaxone in *Salmonella*

[1]Division of Foodborne, Waterborne, and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia.
[2]Division of Animal and Food Microbiology, Office of Research, Center for Veterinary Medicine, U.S. Food and Drug Administration, Laurel, Maryland.
[3]Bacterial Epidemiology and Antimicrobial Resistance Research Unit, Agricultural Research Service, U.S. Department of Agriculture, Athens, Georgia.
[4]Department of Population Health and Pathobiology, North Carolina State University, College of Veterinary Medicine, Raleigh, North Carolina.
Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention, the U.S. Food and Drug Administration, or the U.S. Department of Agriculture.

strains causing human infections in the United States, where ceftriaxone-resistant strains cause an estimated 36,000 illnesses annually (Centers for Disease Control and Prevention, 2013; Medalla *et al.*, 2013). Therefore, understanding the sources of these resistant strains and the factors that propagate ceftriaxone resistance among *Salmonella* is vital.

Antimicrobials select for resistance wherever they are used—whether in human or veterinary medicine. Many antimicrobials used in food animals are identical or similar to those used in human medicine, and their inappropriate use can create a selective pressure for the development of resistant strains that may be transferred to people via food or through direct contact with animals. The National Antimicrobial Resistance Monitoring System (NARMS), a collaboration among the U.S. Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), and the U.S. Department of Agriculture (USDA), was launched to monitor antimicrobial resistance in foodborne and other enteric bacteria.

Antimicrobial use in animal agriculture is a suspected contributor of ceftriaxone-resistant nontyphoidal *Salmonella* in humans; however, it is difficult to establish a definitive link between a specific use and a specific infection. We used NARMS data to further examine this association, by assessing correlations between the annual percentage of ceftriaxone resistance among nontyphoidal *Salmonella* isolates from humans, retail meats, and food animals. Correlations, while not proving causation, can help us understand the potential contribution of animal sources to human infections with ceftriaxone-resistant *Salmonella*.

Materials and Methods

Surveillance of human infections

We examined data on *Salmonella* infections in humans from two CDC surveillance systems: NARMS and the Foodborne Diseases Active Surveillance Network (FoodNet). We looked at NARMS data from 1996 to 2013. Clinical laboratories routinely send all *Salmonella* isolates to their state or local public health department for serotype determination. Public health laboratories forward isolates from sporadic cases and outbreaks of illness to the NARMS laboratory at CDC for antimicrobial susceptibility testing. In 1996, 13 states participated in NARMS, and by 2003 all 50 states participated. During 1996–2002, participating state public health laboratories forwarded every 10th isolate of nontyphoidal *Salmonella* to CDC; during 2003–2013, they forwarded every 20th isolate. Information including patient demographics, specimen source (e.g., blood, stool), and specimen collection date was submitted with isolates.

We also examined FoodNet data to collect more detailed information about patient demographics, clinical outcomes including hospitalization status and death, and history of recent international travel. FoodNet conducts active, population-based surveillance for laboratory-confirmed human infections with *Salmonella* and other pathogens commonly transmitted through food. FoodNet operates in 10 surveillance areas, which include ~15% of the U.S. population (estimated 48 million). For the subset of NARMS isolates from FoodNet surveillance areas during 2004–2013, we linked FoodNet patient information with NARMS testing results by state laboratory identification number. From this point on, we refer to nontyphoidal *Salmonella* isolates included in the analysis as *Salmonella*.

Surveillance of retail meats

NARMS began retail meat sampling in 2002 in selected sites in Connecticut, Georgia, Maryland, Minnesota, Oregon, and Tennessee. By 2004, California, Colorado, New Mexico, and New York were added and Pennsylvania joined in 2008. Each month, personnel at each site purchased ~40 packages of meat from grocery stores, 10 each of chicken (chicken breasts, wings, or thighs), ground turkey, ground beef, and pork chops. During 2002–2004, NARMS used convenience sampling of grocery stores but changed to a random selection of grocery stores beginning in 2005. Sites cultured the retail meats for *Salmonella* and forwarded isolates to the Center for Veterinary Medicine at FDA for serotype confirmation and antimicrobial susceptibility testing. Maryland did not collect retail meat samples in 2007.

Surveillance of food animals at slaughter

In 1997, NARMS began antimicrobial susceptibility testing of *Salmonella* isolates from chicken, turkeys, cattle, and swine. As part of the Pathogen Reduction/Hazard Analysis and Critical Control Point (HACCP) *Salmonella* verification testing program, the USDA Food Safety and Inspection Service (FSIS) cultured carcass rinsates (chicken), carcass swabs (turkeys, cattle, and swine), and raw ground products (chicken, turkey, and beef) collected from federally inspected slaughter and processing plants (U.S. Department of Agriculture *et al.*, 2008).

From 1997 through June 2006, FSIS collected most of the samples at establishments selected at random, with additional samples collected from establishments that did not meet HACCP compliance standards. In mid-2006, the sampling of establishments changed to risk-based criteria, to focus resources on establishments with the most samples yielding *Salmonella* and the greatest number of samples with serotypes most frequently associated with human salmonellosis (U.S. Food and Drug Administration, 2014). FSIS forwarded isolates to the USDA Agricultural Research Service for antimicrobial susceptibility testing (U.S. Food and Drug Administration, 2014).

Laboratory methods

The NARMS laboratories at CDC, FDA, and USDA tested the *Salmonella* isolates for susceptibility to the following antimicrobials: amikacin, ampicillin, amoxicillin-clavulanic acid, cefoxitin (beginning in 2000), ceftiofur, ceftriaxone, chloramphenicol, ciprofloxacin, gentamicin, kanamycin, nalidixic acid, streptomycin, sulfonamides (sulfamethoxazole or sulfisoxazole), tetracycline, and trimethoprim-sulfamethoxazole. In 2011, azithromycin replaced amikacin on the test panel. Minimal inhibitory concentrations (MIC) were determined by broth microdilution (Sensititre®; Trek Diagnostic Systems, Oakwood Village, Ohio). The results were interpreted according to standards from the Clinical and Laboratory Standards Institute (CLSI), where established, including the current interpretive criterion for ceftriaxone resistance, defined as MIC $\geq 4\ \mu$g/mL (CLSI, 2014). CLSI does not have ceftiofur, streptomycin, or azithromycin interpretive criteria for *Salmonella* isolated from humans, so resistance breakpoints developed by NARMS were used (MIC ≥ 8, ≥ 64, and $\geq 32\ \mu$g/mL, respectively) (Centers for Disease Control and Prevention, 2013).

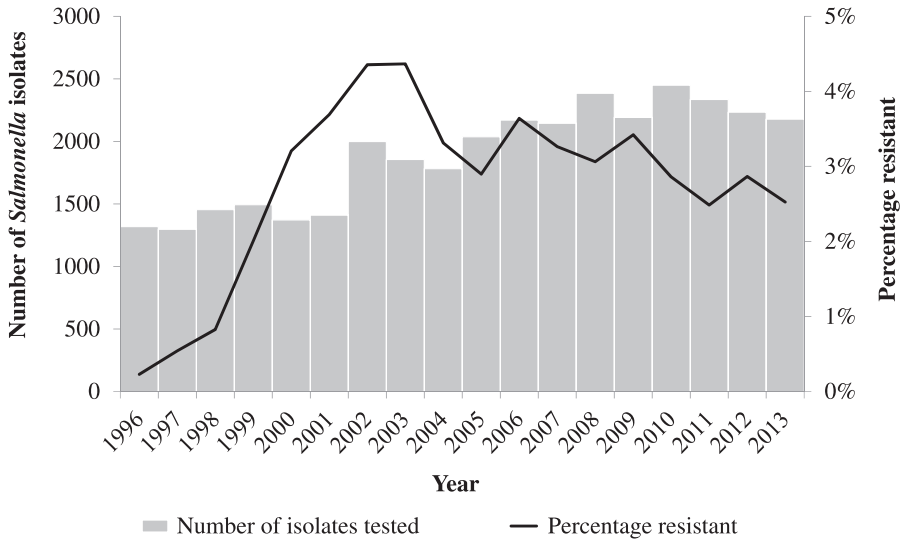

FIG. 1. Number of nontyphoidal *Salmonella* isolates from humans tested and percentage resistant to ceftriaxone, by year, 1996–2013.

Statistical analysis

We categorized *Salmonella* isolates as ceftriaxone-resistant or nonresistant to ceftriaxone. The nonresistant group included ceftriaxone-susceptible isolates and those with an intermediate interpretation for ceftriaxone. We calculated odds ratios and 95% exact confidence intervals (CI) for categorical variables comparing infections caused by *Salmonella* resistant to ceftriaxone and nonresistant to ceftriaxone. We calculated CI around point estimates of annual percentage resistance by serotype and source, using methods described by Agresti and Coull (1998).

We used Spearman rank correlation (*r)* to examine the relationships between the annual percentage of ceftriaxone resistance among *Salmonella* isolates from humans and that among isolates from retail meats and food animals. We calculated exact *p*-values to determine statistical significance. Correlation analyses were performed for each of the three most common serotypes causing ceftriaxone-resistant *Salmonella* infections in humans and the specific food animals and animal-derived foods with which those serotypes have been linked through outbreak investigations or epidemiological studies–Newport in ground beef and cattle (Gupta *et al.*, 2003; Varma *et al.*, 2006), Typhimurium in retail chicken, ground beef, chicken, and cattle (Fey *et al.*, 2000; White *et al.*, 2001; Folster *et al.*, 2014; Grass *et al.*, 2014), and Heidelberg in retail chicken, ground turkey, chicken, and turkeys (Dutil *et al.*, 2010; Folster *et al.*, 2010, 2012; Centers for Disease Control and Prevention, 2013). Statistical analyses were conducted using SAS software, version 9.3 (SAS Institute, Cary, NC).

Results

Characteristics of human infections caused by ceftriaxone-resistant nontyphoidal Salmonella

During 1996–2013, the NARMS laboratory at CDC tested 34,100 *Salmonella* clinical isolates from NARMS-participating public health laboratories for antimicrobial

Table 1. Number of Isolates and Percentage Resistant Among the Most Common Ceftriaxone-Resistant Nontyphoidal *Salmonella* Serotypes Isolated from Humans, NARMS, 1996–2013

Salmonella *serotype*	*No. (%) isolates resistant to ceftriaxone*	*Total no. isolates tested*
Newport	393 (11.6)	3388
Typhimurium	253 (3.9)	6512
Heidelberg	120 (7.8)	1531
Agona	34 (6.9)	490
Dublin	32 (31.4)	102
I 4,[5],12:i:-	25 (2.7)	919
Infantis	18 (2.7)	679
Enteritidis	15 (0.2)	6308
Saintpaul	8 (1.1)	761
Concord	7 (70.0)	10
Senftenberg	6 (4.1)	148
Reading	5 (9.3)	54
Berta	4 (1.8)	222
Javiana	4 (0.3)	1599
Kentucky	4 (5.7)	70
Schwarzengrund	4 (1.9)	207
Other serotypes[a]	42 (0.4)	10,093
Partially serotyped or unknown	4 (0.4)	1007
Total	978 (2.9)	34,100

[a]Other nontyphoidal *Salmonella* serotypes with isolates resistant to ceftriaxone were Mbandaka (3), Montevideo (3), Uganda (3), Albert (2), Bredeney (2), Cubana (2), Derby (2), Ealing (2), Ohio (2), Paratyphi B. var. L (+) tartrate + (2), Thompson (2), I 4,[5],12:-:1,2 (1), IV 44:z4,z23:- (1), Adelaide (1), Albany (1), Anatum (1), Blockley (1), Chester (1), Choleraesuis (1), Edinburg (1), Haifa (1), Hato (1), Lindenburg (1), Matopeni (1), Muenster (1), Poona (1), Stanley (1), Worthington (1).

NARMS, National Antimicrobial Resistance Monitoring System.

susceptibility. Of these, 978 (2.9%) were resistant to ceftriaxone. The annual percentage of ceftriaxone resistance among *Salmonella* isolates from humans increased from 0.2% in 1996 to 2.5% in 2013, peaking at 4.4% in 2002–2003 (Fig. 1). Ceftriaxone resistance was detected in 44 *Salmonella* serotypes; most (78%) of ceftriaxone-resistant *Salmonella* isolates were one of 3 serotypes: Newport (393, 40%), Typhimurium (253, 26%), or Heidelberg (102, 12%). No other serotype comprised more than 4% of ceftriaxone-resistant isolates. The number and proportion of isolates resistant to ceftriaxone varied by serotype; for example, Newport was the serotype with the largest number of ceftriaxone-resistant isolates, 393 of 3388 (11.6%), while Concord was the serotype with the highest percentage of isolates resistant to ceftriaxone, 7 of 10 (70%) (Table 1).

The 978 ceftriaxone-resistant isolates all harbored resistance to other antimicrobial agents. Resistance to other antimicrobial agents among the ceftriaxone-resistant isolates varied among serotypes (Table 2). Among Newport isolates, resistance to ampicillin, chloramphenicol streptomycin, sulfonamides, tetracycline, amoxicillin-clavulanic acid, and ceftriaxone (resistance-type ACSSuTAuCx) was high (377 of 393 ceftriaxone-resistant isolates, 95.9%). This resistance pattern was less common in ceftriaxone-resistant Typhimurium isolates (138 of 253, 54.5%), and much less common (6 of 120 isolates, 5.0%) in ceftriaxone-resistant Heidelberg isolates. Altogether, 57 (5.8%) ceftriaxone-resistant *Salmonella* isolates showed decreased susceptibility or resistance to ciprofloxacin (MIC ≥0.12 μg/mL).

Table 3 shows characteristics of patients with infections caused by ceftriaxone-resistant strains compared with those among patients having infections caused by strains not resistant to ceftriaxone. Among patients whose age was reported, 40% (367/922) of those with ceftriaxone-resistant *Salmonella* and 44% (13,407/30,386) of those with *Salmonella* not resistant to ceftriaxone were <18 years old. A lower proportion of infections in children 1–4 years, and conversely, a higher proportion of *Salmonella* infections in older adults were caused by resistant strains compared with adults 18–64 years, approaching statistical significance (Table 3). There was no statistical association between specimen source and ceftriaxone resistance (Table 3).

During 2004–2013, 94 (2.9%) ceftriaxone-resistant *Salmonella* isolates were submitted among 3254 NARMS *Salmonella* isolates linked to FoodNet case reports. The proportion of patients hospitalized and the case fatality rate were higher in patients with ceftriaxone-resistant *Salmonella* than in patients with *Salmonella* not resistant to ceftriaxone, although these findings were not statistically significant (Table 3). Among patients with information on international travel before illness onset, 7 (9.2%) of 76 with ceftriaxone-resistant *Salmonella* reported international travel, compared with 224 (9.4%) of 2389 with *Salmonella* not resistant to ceftriaxone (Table 3). Patients with infection caused by ceftriaxone-resistant *Salmonella* were diagnosed in the United States after reported travel in China, Egypt, Ethiopia, Mexico, and Peru.

Table 2. Number and Percentage of Ceftriaxone-Resistant Nontyphoidal *Salmonella* Isolates from Humans Resistant to Other Selected Antimicrobial Agents, by Serotype 1996–2013

	All serotypes (N = *978*)		*Newport* (N = *393*)		*Typhimurium* (N = *253*)		*Heidelberg* (N = *120*)		*Other serotypes*[a] (N = *212*)	
	n	%	N	%	n	%	n	%	N	%
Antimicrobial agent										
Amoxicillin-clavulanic acid	940	96.1	392	99.7	245	96.8	118	98.3	185	87.3
Ampicillin	975	99.7	393	100	253	100	120	100	209	98.6
Ceftiofur	974	99.6	393	100	253	100	119	99.2	209	98.6
Chloramphenicol	639	65.3	379	96.4	145	57.3	8	6.7	107	50.5
Ciprofloxacin	8	0.8	0	0	2	0.8	0	0	6	2.8
Gentamicin	74	7.6	21	5.3	16	6.3	10	8.3	27	12.7
Nalidixic acid	42	4.3	3	0.8	11	4.3	0	0	28	13.2
Streptomycin	699	71.5	384	97.7	161	63.6	37	30.8	117	55.2
Sulfamethoxazole/sulfisoxazole[b]	722	73.8	384	97.7	188	74.3	17	14.2	133	62.7
Tetracycline	731	74.7	384	97.7	186	73.5	35	29.2	126	59.4
Trimethoprim-sulfamethoxazole	117	12.0	50	12.7	27	10.7	3	2.5	37	17.5
Resistance pattern										
Resistance to β-lactam agents only[c]	212	21.7	8	2.0	58	22.9	80	66.7	66	31.1
Resistance to *at least* AAuCx[d]	940	96.1	392	99.7	245	96.8	118	98.3	185	87.3
Resistance to *at least* ACSSuTAuCx[e]	610	62.4	377	95.9	138	54.5	6	5.0	89	42.0
Decreased susceptibility or resistance to ciprofloxacin (MIC ≥0.12 μg/mL)	57	5.8	11	2.8	11	4.3	0	0	35	16.5

[a]Includes four isolates with partial or unknown serotype.
[b]Sulfamethoxazole was replaced by sulfisoxazole in 2004.
[c]β-lactam agents include amoxicillin-clavulanic acid, ampicillin, ceftiofur, and cefoxitin, in addition to ceftriaxone.
[d]AAuCx: ampicillin, amoxicillin-clavulanic acid, ceftriaxone.
[e]ACSSuTAuCx: ampicillin, chloramphenicol, streptomycin, sulfamethoxazole/sulfisoxazole, tetracycline, amoxicillin-clavulanic acid, ceftriaxone.
MIC, minimal inhibitory concentration.

Table 3. Characteristics of Patients with Infection Caused by Nontyphoidal *Salmonella* Resistant to Ceftriaxone Compared with Patients with Nontyphoidal *Salmonella* not Resistant to Ceftriaxone

	Patients with Salmonella *resistant to ceftriaxone No. (%)*	*Patients with* Salmonella *not resistant to ceftriaxone No. (%)*	*Odds ratio (95% CI)*[a]
Age of patient[b]			
0–11 months	76 (2.6)	2839 (97.4)	0.8 (0.7–1.1)
1–4 years	136 (2.4)	5519 (97.6)	0.8 (0.6–1.0)
5–17 years	155 (3.0)	5049 (97.0)	1.0 (0.8–1.2)
18–64 years	421 (3.1)	13,353 (96.9)	Referent
65 years and older	134 (3.6)	3626 (96.4)	1.2 (1.0–1.4)
Missing data	56 (2.0)	2736 (98.0)	
Sex of patient[b]			
Female	492 (3.0)	16,032 (97.0)	Referent
Male	430 (2.8)	14,693 (97.2)	1.0 (0.8–1.1)
Missing data	56 (2.3)	2397 (97.7)	
Specimen source[b]			
Stool	828 (2.8)	28,273 (97.2)	Referent
Blood	63 (3.5)	1730 (96.5)	1.2 (0.9–1.6)
Urine	37 (2.3)	1563 (97.7)	0.8 (0.6–1.1)
Other	22 (2.7)	805 (97.3)	0.9 (0.6–1.4)
Missing data	28 (3.6)	751 (96.4)	
Patient race[c]			
American Indian or Alaska Native	1 (3.3)	29 (96.7)	1.1 (0.03–6.9)
Asian	5 (3.7)	130 (96.3)	1.2 (0.4–3.1)
Black	7 (1.5)	459 (98.5)	0.5 (0.2–1.1)
Multiple races or other race	7 (7.2)	90 (92.8)	2.5 (0.9–5.7)
White	63 (3.0)	2026 (97.0)	Referent
Missing data	11 (2.5)	426 (97.5)	
Patient ethnic group[c]			
Hispanic or Latino	16 (5.3)	288 (94.7)	1.9 (1.0–3.4)
Not Hispanic or Latino	64 (2.9)	2181 (97.1)	Referent
Missing data	14 (2.0)	691 (98.0)	
Patient outcomes[c]			
Hospitalization	34 (3.7)	888 (96.3)	1.5 (0.9–2.3)
Death within 7 days of culture	1 (5.0)	19 (95.0)	1.7 (0.04–11.2)
Patient travel history[c]			
International travel within 7 days of illness onset	7 (3.0)	224 (97.0)	1.0 (0.4–2.2)
No international travel	69 (3.1)	2165 (96.9)	Referent
Missing data	18 (2.3)	771 (97.7)	

[a]Odds ratio and Fisher's exact confidence intervals. Missing data were not used in computing odds ratios.
[b]NARMS clinical isolates, 1996–2013, ($n = 34,100$).
[c]Isolates in NARMS that were linked to FoodNet case reports, 2004–2013 ($n = 3254$).
CI, confidence interval.

Correlations in resistance proportions among isolates from humans, retail meats, and food animals

During 2002–2013, the NARMS laboratory at FDA detected ceftriaxone resistance in 509 (26.2%) of 1940 *Salmonella* isolates from retail chicken, 167(9.0%) of 1862 isolates from ground turkey, and 21 (13.5%) of 155 isolates from ground beef. During 1997–2013, ceftriaxone resistance was detected in 1576 (9.5%) of 16,608 isolates from chicken at slaughter, 248 (5.6%) of 4457 isolates from turkeys, and 1192 (12.6%) of 9461 isolates from cattle. Estimates and CI of annual percentages of resistance to ceftriaxone in *Salmonella* serotypes Newport, Typhimurium, and Heidelberg isolated from humans, retail meats, and food animals are shown in Figure 2, while Table 4 shows the observed number of *Salmonella* isolates recovered by serotype and source and the number and percentage of isolates resistant to ceftriaxone. Supplementary Figure S1(Supplementary Data are available online at www.liebertpub.com/fpd) includes Spearman rank correlation coefficients, CI, *p*-values, and scatter plots, which compare the relationship between annual percentage of ceftriaxone resistance among *Salmonella* from different isolate sources.

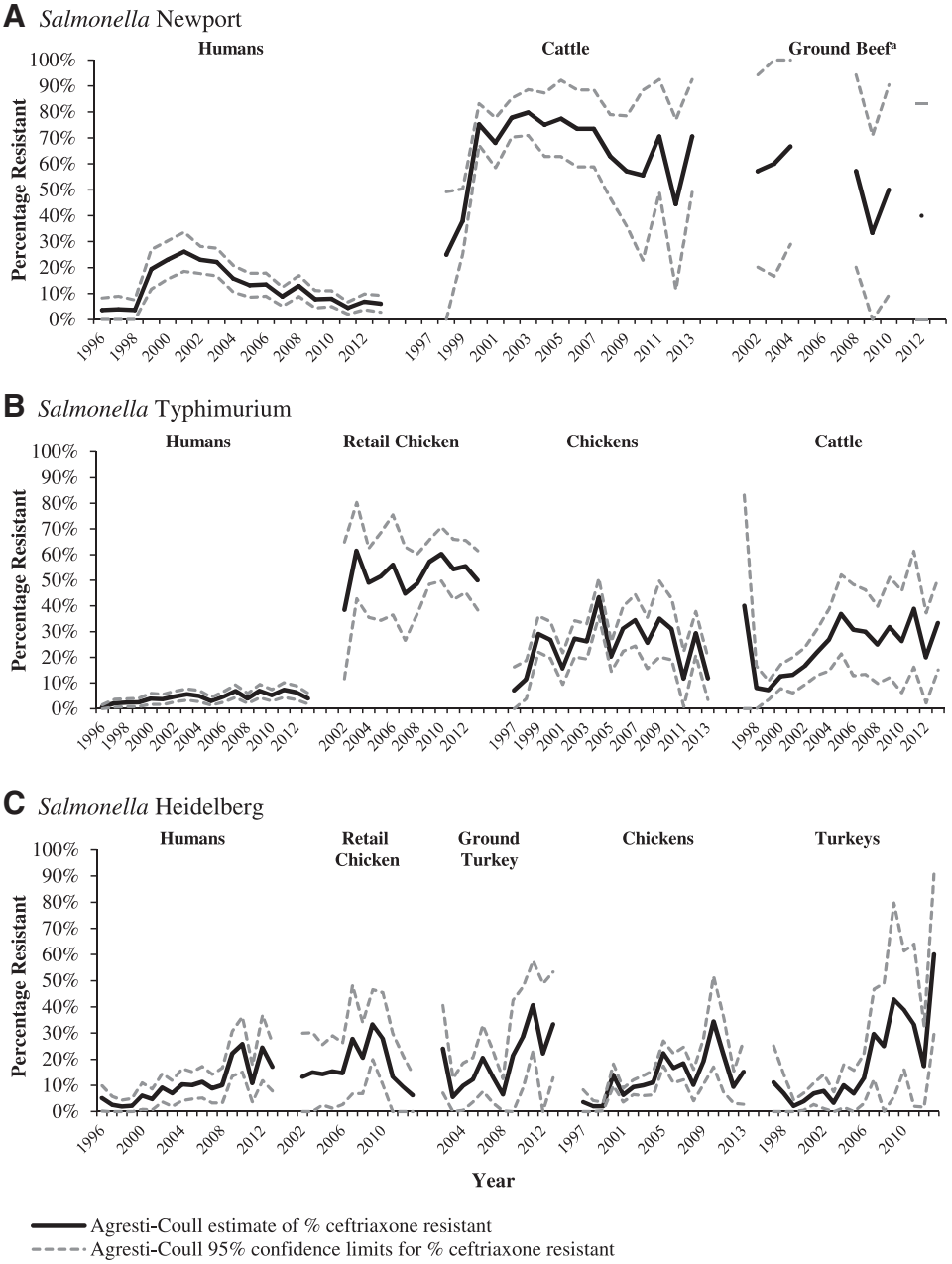

FIG. 2. Agresti-Coull estimates and 95% confidence intervals for percentage resistant to ceftriaxone among *Salmonella* ser. Newport **(A)**, Typhimurium **(B)**, and Heidelberg **(C)**, by source, 1996–2013. No ground beef samples yielded *Salmonella* Newport during 2005–2007, 2011, and 2013.

Ceftriaxone resistance in *Salmonella* serotype Newport isolates from humans increased from 0% in 1996 to a peak of 25.4% in 2001 and then declined to 5.3% in 2013 (Fig. 2). Similarly, there was a sharp rise in ceftriaxone resistance among Newport isolates from cattle, with a peak of 81% during 2005. However, the annual percentage of ceftriaxone resistance in isolates from humans did not correlate with resistance in cattle ($r = 0.34$, CI = –0.14–0.81, $p = 0.20$). Newport was detected infrequently in retail ground beef samples, but resistance correlated strongly with that in isolates from humans ($r = 0.83$, CI = 0.47–1.0, $p = 0.03$) and from cattle ($r = 0.90$, CI = 0.69–1.0, $p = 0.01$).

Ceftriaxone resistance among *Salmonella* Typhimurium isolates from humans increased from 0% in 1996 to a high of 6.8% in 2011. The annual percentages of resistance were higher in cattle and chicken isolates than in human isolates. Ceftriaxone resistance in human isolates correlated strongly with that in cattle isolates ($r = 0.57$, CI = 0.11–1.0, $p = 0.02$). The correlation between resistance in human and chicken isolates was lower and was not statistically significant ($r = 0.48$, CI = –0.03–0.99, $p = 0.05$). For *Salmonella* Typhimurium, we found no correlations in resistance between retail meat (retail chicken or ground beef) and human isolates, or between retail meat and animal isolates.

Among Heidelberg isolates from humans, chicken, turkeys and retail poultry, ceftriaxone resistance has increased in recent years. We found significant correlations in resistance between human and chicken isolates ($r = 0.65$, CI = 0.60–1.0,

Table 4. Number and Percentage of *Salmonella* Newport, Typhimurium, and Heidelberg Isolates Resistant to Ceftriaxone, by Selected Source and Year, 1996–2013[a]

Serotype source	*1996*	*1997*	*1998*	*1999*	*2000*	*2001*	*2002*	*2003*	*2004*	*2005*	*2006*	*2007*	*2008*	*2009*	*2010*	*2011*	*2012*	*2013*
Newport																		
Humans	0, 0% (51)	0, 0% (47)	1, 1.3% (78)	18, 18.2% (99)	27, 22.1% (122)	32, 25.4% (126)	55, 22.5% (244)	49, 21.7% (226)	29, 15.1% (192)	26, 12.6% (207)	28, 12.8% (218)	18, 8.1% (222)	32, 12.4% (258)	17, 7.1% (239)	23, 7.5% (306)	11, 3.8% (286)	16, 6.2% (258)	11, 5.3% (209)
Ground beef							2, 66.7% (3)	1, 100% (1)	2, 100% (2)	N/A[b] (0)	N/A[b] (0)	N/A[b] (0)	2, 66.7% (3)	0, 0% (2)	1, 50.0% (2)	N/A[b] (0)	0, 0% (1)	N/A[b] (0)
Cattle		N/A[b] (0)	1, 12.5% (8)	20, 37.0% (54)	83, 76.1% (109)	60, 69.0% (87)	89, 78.8% (113)	61, 81.3% (75)	34, 77.3% (44)	22, 81.5% (27)	23, 76.7% (30)	23, 76.7% (30)	20, 64.5% (31)	10, 58.8% (17)	3, 60.0% (5)	10, 76.9% (13)	2, 40.0% (5)	10, 76.9% (13)
Typhimurium																		
Humans	0, 0% (307)	5, 1.5% (328)	7, 1.8% (380)	7, 1.9% (363)	10, 3.3% (304)	10, 3.1% (325)	17, 4.3% (394)	21, 5.1% (409)	17, 4.5% (382)	11, 2.5% (438)	17, 4.2% (408)	26, 6.4% (405)	14, 3.5% (396)	24, 6.5% (370)	17, 4.7% (359)	22, 6.8% (323)	17, 5.7% (296)	11, 3.4% (325)
Retail Chicken							3, 33.3% (9)	14, 63.6% (22)	24, 49.0% (49)	15, 51.7% (29)	12, 57.1% (21)	11, 44.0% (25)	33, 48.5% (68)	70, 57.4% (122)	48, 60.8% (79)	36, 54.5% (66)	49, 55.7% (88)	34, 50.0% (68)
Ground beef							0, 0% (2)	0, 0% (1)	N/A[b] (0)	N/A[b] (0)	0, 0% (1)	0, 0% (3)	0, 0% (2)	N/A[b] (0)	N/A[b] (0)	N/A[b] (0)	0, 0% (1)	N/A[b] (0)
Chicken		0, 0% (24)	6, 9.1% (66)	44, 28.6% (154)	38, 26.2% (145)	19, 14.6% (130)	40, 26.7% (150)	40, 25.6% (156)	74, 43.3% (171)	36, 19.7% (183)	32, 30.5% (105)	28, 33.7% (83)	17, 24.3% (70)	12, 33.3% (36)	16, 29.6% (54)	2, 6.7% (30)	30, 28.6% (105)	5, 9.1% (55)
Cattle		0, 0% (1)	1, 3.0% (33)	12, 6.3% (189)	22, 11.8% (187)	10, 11.5% (87)	15, 15.3% (98)	16, 20.5% (78)	12, 25.0% (48)	12, 35.3% (34)	6, 27.3% (22)	7, 26.9% (26)	6, 21.4% (28)	5, 27.8% (18)	3, 20.0% (15)	5, 35.7% (14)	2, 12.5% (16)	7, 30.4% (23)
Heidelberg																		
Humans	2, 2.7% (74)	0, 0% (75)	0, 0% (101)	0, 0% (88)	3, 3.8% (79)	3, 2.9% (102)	8, 7.6% (105)	5, 5.2% (96)	8, 8.7% (92)	11, 8.8% (125)	10, 9.8% (102)	7, 7.1% (98)	6, 8.0% (75)	18, 20.9% (86)	15, 24.2% (62)	6, 8.6% (70)	9, 22.0%	9, 15.0% (60)
Retail chicken							0, 0% (11)	1, 6.3% (16)	3, 9.7% (31)	2, 9.1% (22)	3, 10.0% (30)	3, 21.4% (14)	5, 16.7% (30)	14, 31.8% (44)	5, 23.8% (21)	0, 0% (11)	0, 0% (17)	0, 0% (28)
Ground turkey							4, 19.0% (21)	0, 0% (32)	2, 5.4% (37)	5, 9.4% (53)	6, 17.1% (35)	4, 9.8% (41)	2, 3.5% (57)	1, 10.0% (10)	4, 23.5% (17)	11, 39.3% (28)	0, 0% (5)	5, 29.4% (17)
Chicken		0, 0% (51)	1, 0.7% (143)	4, 1.3% (297)	35, 13.5% (259)	19, 5.8% (329)	36, 8.9% (403)	21, 9.3% (226)	17, 10.2% (167)	62, 21.9% (283)	26, 15.9% (164)	25, 17.6% (142)	8, 8.5% (94)	13, 17.6% (74)	8, 32.0% (25)	5, 17.9% (28)	6, 7.4% (81)	3, 10.3% (29)
Turkeys		0, 0% (14)	1, 2.6% (39)	1, 0.7% (139)	3, 2.4% (125)	8, 5.6% (142)	3, 5.0% (60)	0, 0% (57)	3, 6.5% (46)	0, 0% (25)	4, 9.3% (43)	6, 26.1% (23)	1, 12.5% (8)	1, 33.3% (3)	5, 35.7% (14)	1, 20.0% (5)	2, 10.5% (19)	4, 66.7% (6)

[a]Isolates have been collected and tested since 1996 for humans; since 1997 for cattle, chicken, and turkeys; and since 2002 for ground beef, retail chicken, and ground turkey. Numbers in parentheses indicate total number of isolates obtained for antimicrobial resistance testing.

[b]N/A indicates that no isolates were obtained for antimicrobial resistance testing.

$p = 0.0004$) and between human and turkey isolates ($r = 0.62$, CI = 0.27–1.0, $p = 0.01$). As with Typhimurium and Newport, relatively few Heidelberg isolates were available from retail meats, and correlations in resistance were lower and were not statistically significant between human and retail poultry isolates (retail chicken [$r = 0.17$, CI = –0.47–0.81, $p = 0.59$] and ground turkey [$r = 0.24$, CI = –0.37–0.85, $p = 0.45$]) and between retail poultry and poultry isolates (chicken sources [$r = 0.40$, CI = –0.11–0.91, $p = 20$ and turkey sources [$r = 0.55$, CI = 0.17–0.92, $p = 0.07$]).

Discussion

Ceftriaxone resistance has emerged and persisted among nontyphoidal *Salmonella* recovered from humans, retail meats, and food animals in the United States over the past several years, although resistance to ceftriaxone was relatively infrequent among *Salmonella* isolates from humans overall. NARMS data show ceftriaxone resistance among *Salmonella* in some retail meats and food animals is high and trends in ceftriaxone resistance among isolates from humans generally parallel those seen in food animals. We saw strong correlations between ceftriaxone resistance among *Salmonella* serotype Heidelberg isolates in humans and poultry at slaughter, which is consistent with other studies recognizing the connection between human Heidelberg infection and poultry at slaughter and at retail (Dutil *et al.*, 2010; Folster *et al.*, 2010, 2012; Hoffmann *et al.*, 2012; Centers for Disease Control and Prevention, 2013). Similarly, the correlation we found between ceftriaxone resistance in Typhimurium isolates from humans and cattle supports previous reports of ceftriaxone-resistant Typhimurium infections associated with cattle and foods derived from them (Fey *et al.*, 2000; Jackson *et al.*, 2013; Folster *et al.*, 2014; Grass *et al.*, 2014). These correlations help support, though they do not prove, that food animals are an important source of ceftriaxone-resistant *Salmonella*, which may be transmitted to humans through the foods we eat.

The presence of ceftriaxone-resistant *Salmonella* in food animals may be a consequence of ceftiofur use in agriculture (Dunne *et al.*, 2000; Fey *et al.*, 2000; Zhao *et al.*, 2001; Dutil *et al.*, 2010). Ceftiofur is a third-generation cephalosporin-like ceftriaxone and cross-resistance between the two drugs is common (U.S. Food and Drug Administration, 2014). It is the only extended-spectrum cephalosporin approved for use in food animals in the United States (U.S. Food and Drug Administration, 2012, 2016). It was first approved for use in cattle in 1988, swine and chickens (day-old chicks) in 1992, sheep and turkeys (day-old poults) in 1996, and goats in 2001, with label indications for the treatment and control of certain diseases (U.S. Food and Drug Administration, 2014, 2016). Historically, the same molecular mechanism has been responsible for resistance to both ceftiofur and ceftriaxone in NARMS isolates (Dunne *et al.*, 2000; Fey *et al.*, 2000; Winokur *et al.*, 2000; White *et al.*, 2001; Zhao *et al.*, 2001; Folster *et al.*, 2011, 2012; Sjolund-Karlsson *et al.*, 2013).

Although cattle and beef are known sources of ceftriaxone-resistant Newport infections in humans (Gupta *et al.*, 2003; Varma *et al.*, 2006), we detected a statistically significant correlation between Newport human and ground beef isolates only and not with cattle isolates. Additionally, we did not detect a correlation between Typhimurium human and chicken isolates, while ceftriaxone-resistant Typhimurium is commonly found in poultry (White *et al.*, 2001; Folster *et al.*, 2014; U.S. Food and Drug Administration, 2014).

It is difficult to draw conclusions from the lack of statistically significant correlations, because of several limitations to our data. NARMS surveillance data do not include the specific sources of the infections among humans. The sources of *Salmonella* Newport and Typhimurium infections are diverse and changing, and they include animal- and plant-derived foods and environmental sources (Varma *et al.*, 2006; Greene *et al.*, 2008; Jackson *et al.*, 2013). We based our correlation analyses only on the prevalence of resistance captured by NARMS, that is, percentage of resistance among *Salmonella* isolates tested, not incidence of resistant infections in humans, frequency of isolation of resistant *Salmonella* from food animals and retail meats, or proportion of infections associated with food animal sources. For example, while there continue to be high levels of ceftriaxone resistance in Newport isolates from cattle, the number of Newport isolates from cattle has declined in recent years (U.S. Department of Agriculture and Food Safety Inspection Service 2011; U.S. Food and Drug Administration, 2014), concurrent with an increase in isolate submission rates of pansusceptible Newport in humans (Chai *et al.*, 2012), suggesting that an increasing number and proportion of Newport infections in humans are attributable to non-bovine sources. Additionally, the sample sizes and periods of surveillance differed among sources; this may have resulted in comparisons that lacked power to detect statistical temporal associations, particularly with retail meats. NARMS retail meat sampling is limited to only a few surveillance areas and did not begin until 2002. Consequently, there were relatively few *Salmonella* isolates from retail meats, especially ground beef, available for antimicrobial susceptibility testing, resulting in wide CI around annual percentage estimates of resistance.

Our analysis was subject to limitations beyond those discussed above. NARMS sampling methods may have introduced biases in our study. NARMS monitoring of human infections was not national until 2003. Additionally, human isolates surveillance is passive, with possible biases in sampling because of differences in diagnostic strategies employed by clinicians and state-to-state variations in isolate submission to public health laboratories. NARMS isolates from food animals originated from USDA in-plant HACCP monitoring. When this sampling program was changed in 2006, more samples likely came from establishments that were out of compliance, rather than from a random selection of slaughter establishments. The potential biases that this sampling strategy introduced are unknown.

Our findings of correlations in ceftriaxone resistance between *Salmonella* isolates from humans and food animals contribute to the growing body of evidence that food animals are an important source of ceftriaxone-resistant *Salmonella* causing human infections, although they do not establish causality. Nevertheless, to reduce the transmission of resistant nontyphoidal *Salmonella* to humans, it is essential to decrease the prevalence of resistant *Salmonella* in food products and food animals. Our findings underscore the need to reduce unnecessary uses of extended-spectrum cephalosporins in animals and in humans and to find alternatives to their use, which will require multidisciplinary efforts by veterinarians, the agricultural industry, clinicians, and public health agencies. To help address the problem FDA issued an order

prohibiting certain extralabel uses of cephalosporins (excluding cephapirin) in cattle, swine, chicken, and turkeys in 2012 (U.S. Food and Drug Administration, 2012). In Canada, a voluntary withdrawal of ceftiofur for *in ovo* use in hatcheries preceded a marked decline in ceftiofur-resistant *Salmonella* serotype Heidelberg in retail chicken and in humans, demonstrating that the management of ceftiofur use in hatcheries could be an effective control strategy (Dutil *et al.*, 2010). Additionally, FDA issued guidance recommending that antibiotics important for human health be limited to uses in food animals that are necessary to assure animal health and involve veterinary oversight or consultation (U.S. Food and Drug Administration and Center for Veterinary Medicine, 2012, 2012). Continued national surveillance through NARMS will be important to evaluate the impact of regulatory actions and antimicrobial stewardship efforts and to direct additional efforts aimed at preserving the efficacy of extended-spectrum cephalosporins for the treatment of human infections.

Acknowledgments

We are indebted to the local and state health departments and laboratories that participate in the National Antimicrobial Resistance Monitoring System. We thank Jennifer Huang for her assistance in gathering the data, and Patricia Griffin and Patrick McDermott for their helpful review of this report.

Disclosure Statement

No competing financial interests exist.

References

Agresti A, Coull B. ''Approximate is better than 'exact' for interval estimation of binomial proportions.'' Am Stat 1998; 52:119–126.

American Academy of Pediatrics. *Red Book: 2015 Report of the Committee on Infectious Diseases*. Elk Grove Village, IL: American Academy of Pediatrics, 2015.

Centers for Disease Control and Prevention. (2013, June 4, 2014). ''2011 NARMS Annual Human Isolates Report.'' Available at: www.cdc.gov/narms/reports.html, accessed November 11, 2015.

Centers for Disease Control and Prevention. (2013, July 14, 2014). ''Antibiotic Resistance Threats in the United States, 2013.'' Available at: www.cdc.gov/drugresistance/threat-report-2013/, accessed May 12, 2016.

Centers for Disease Control and Prevention. ''Outbreak of *Salmonella* Heidelberg infections linked to a single poultry producer—13 states, 2012–2013.'' Morb Mortal Wkly Rep 2013;62:553–556.

Chai S, Crim S, Nisler A, Reynolds J, Swanson K, Gould L, and Karp B. *The Increasing Problem of* Salmonella enterica *Serotype Newport in Infants and in the South, United States, 2004–2010*. Atlanta, Georgia: International Conference on Emerging Infectious Diseases, 2012.

CLSI. *Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Fourth Informational Supplement*. CLSI document M100-S24. Wayne, PA: Clinical and Laboratory Standards Institute, 2014.

Crump J, Medalla F, Joyce K, Krueger A, Hoekstra R, Whichard J, Barzilay E; Emerging Infections Program NARMS Working Group. Antimicrobial resistance among invasive nontyphoidal *Salmonella enterica* isolates in the United States: National Antimicrobial Resistance Monitoring System, 1996 to 2007. Antimicrob Agents Chemother 2011;55: 1148–1154.

Dunne E, Fey P, Kludt P, Reporter R, Mostashari F, Shillam P, Wicklund J, Miller C, Holland B, Stamey K, Barrett T, Rasheed J, Tenover F, Ribot E, Angulo. F. Emergence of domestically acquired ceftriaxone-resistant *Salmonella* infections associated with AmpC beta-lactamase. JAMA 2000;284:3151–3156.

Dutil L, Irwin R, Finley R, Ng L, Avery B, Boerlin P, Bourgault A, Cole L, Daignault D, Desruisseau A, Demczuk W, Hoang L, Horsman G, Ismail J, Jamieson F, Maki A, Pacagnella A, Pillai D. Ceftiofur resistance in *Salmonella enterica* serovar Heidelberg from chicken meat and humans, Canada. Emerg Infect Dis 2010;16:48–54.

Fey P, Safranek T, Rupp M, Dunne E, Ribot E, Iwen P, Bradford P, Angulo F, Hinrichs S. Ceftriaxone-resistant *Salmonella* infection acquired by a child from cattle. N Engl J Med 2000;342:1242–1249.

Folster J, Pecic G, Bolcen S, Theobald L, Hise K, Carattoli A, Zhao S, McDermott P, Whichard J. Characterization of extended-spectrum cephalosporin-resistant *Salmonella enterica* serovar Heidelberg isolated from humans in the United States. Foodborne Pathog Dis 2010;7:181–187.

Folster J, Pecic G, Rickert R, Taylor J, Zhao S, P. Fedorka-Cray, Whichard J, McDermott P. Characterization of multidrug-resistant *Salmonella enterica* serovar Heidelberg from a ground turkey-associated outbreak in the United States in 2011. Antimicrob Agents Chemother 2012;56:3465–3466.

Folster J, Pecic G, Singh A, Duval B, Rickert R, Ayers S, Abbott J, B. McGlinchey, J. Bauer-Turpin, Haro J, Hise K, Zhao S, P. Fedorka-Cray, Whichard J, McDermott P. Characterization of extended-spectrum cephalosporin-resistant *Salmonella enterica* serovar Heidelberg isolated from food animals, retail meat, and humans in the United States 2009. Foodborne Pathog Dis 2012;9:638–645.

Folster J, Pecic G, McCullough A, Rickert R, Whichard J. Characterization of bla(CMY)-encoding plasmids among *Salmonella* isolated in the United States in 2007. Foodborne Pathog Dis 2011;8:1289–1294.

Folster J, Tolar B, Pecic G, Sheehan D, Rickert R, Hise K, Zhao S, P. Fedorka-Cray, McDermott P, Whichard J. Characterization of blaCMY plasmids and their possible role in source attribution of *Salmonella enterica* serotype Typhimurium infections. Foodborne Pathog Dis 2014;11:301–306.

Geme J, Hodes H, Marcy S, Pickering L, Rodriguez W, McCracken G, Nelson J. Consensus: Management of *Salmonella* infection in the first year of life. Pediatr Infect Dis J 1988;7:615–621.

Grass J, Richardson L, Nisler A, Bicknese A, Hise K, Gould LH, Brown A. *Antimicrobial Resistance Among Foodborne Disease Outbreaks of Non-typhoidal* Salmonella *Infections, United States, 2003–2011*. San Antonio, Texas: InFORM 2013, 2014.

Greene S, Daly E, Talbot E, Demma L, Holzbauer S, Patel N, Hill T, Walderhaug M, Hoekstra R, Lynch MF, Painter J. Recurrent multistate outbreak of *Salmonella* Newport associated with tomatoes from contaminated fields, 2005. Epidemiol Infect 2008;136:157–165.

Gupta A, Fontana J, Crowe C, Bolstorff B, Stout A, Van Duyne S, Hoekstra R, Whichard J, Barrett T, Angulo F; National Antimicrobial Resistance Monitoring System PulseNet Working Group. Emergence of multidrug-resistant *Salmonella enterica* serotype Newport infections resistant to expanded-spectrum cephalosporins in the United States. J Infect Dis 2003;188: 1707–1716.

Helms M, Vastrup P, Gerner-Smidt P, Molbak K. Excess mortality associated with antimicrobial drug-resistant *Salmonella* Typhimurium. Emerg Infect Dis 2002;8:490–495.

Hoffmann M, Zhao S, Luo Y, Li C, Folster J, Whichard J, Allard M, Brown EW, McDermott P. Genome sequences of five *Salmonella enterica* serovar Heidelberg isolates associated with a 2011 multistate outbreak in the United States. J Bacteriol 2012;194:3274–3275.

Jackson B, Griffin P, Cole D, Walsh K, Chai S. Outbreak-associated *Salmonella enterica* serotypes and food commodities, United States, 1998–2008. Emerg Infect Dis 2013;19:1239–1244.

Krueger A, Greene S, Barzilay E, Henao O, Vugia D, Hanna S, Meyer S, Smith K, Pecic G, Hoefer D, Griffin P. Clinical outcomes of nalidixic acid, ceftriaxone, and multidrug-resistant nontyphoidal *Salmonella* infections compared with pansusceptible infections in FoodNet Sites, 2006–2008. Foodborne Pathog Dis 2014;11:335–341.

Medalla F, Hoekstra R, Whichard J, Barzilay E, Chiller T, Joyce K, Rickert R, Krueger A, Stuart A, Griffin P. Increase in resistance to ceftriaxone and nonsusceptibility to ciprofloxacin and decrease in multidrug resistance among *Salmonella* strains, United States, 1996–2009. Foodborne Pathog Dis 2013;10:302–309.

Pegues D, Miller S. Salmonella *Species, Including* Salmonella *Typhi. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. Philadelphia, PA: Churchill Livingstone, 2009; 2887–2903.

Sjolund-Karlsson M, Howie R, Blickenstaff K, Boerlin P, Ball T, Chalmers G, Duval B, Haro J, Rickert R, Zhao S, Fedorka-Cray P, Whichard J. Occurrence of beta-lactamase genes among non-Typhi *Salmonella enterica* isolated from humans, food animals, and retail meats in the United States and Canada. Microb Drug Resist 2008;19:191–197.

U.S. Department of Agriculture, Agricultural Research Service and Food Safety Inspection Service. Salmonella *Verification Sampling Program: Response to Comments and New Agency Policies*. Washington, DC: Federal Register, 2008; 4767–4774.

U.S. Department of Agriculture and Food Safety Inspection Service. (2011, March 24, 2015). Serotypes profile of *Salmonella* isolates from meat and poultry products, January 1998 through December 2011. Available at: www.fsis.usda.gov/wps/portal/fsis/topics/data-collection-and-reports/microbiology/annual-serotyping-reports, accessed November 11, 2015.

U.S. Food and Drug Administration. (2012). New animal drugs; Cephalosprin drugs; Extralabel animal drug use; Order of prohibition. Federal Register, Available at: www.gpo.gov/fdsys/pkg/FR-2012-01-06/pdf/2012-35.pdf, accessed November 11, 2015.

U.S. Food and Drug Administration. (2014, September 3, 2014). FOIA Drug Summaries. Available at: www.fda.gov/AnimalVeterinary/Products/ApprovedAnimalDrugProducts/FOIADrugSummaries/default.htm, accessed August 7, 2016.

U.S. Food and Drug Administration. (2014, October 2, 2014). NARMS 2011 executive report. Available at: www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/ucm407957.htm, accessed November 11, 2015.

U.S. Food and Drug Administration. (2016, February 2, 2016). Approved animal drug products (Green Book). Available at: www.fda.gov/AnimalVeterinary/Products/ApprovedAnimalDrugProducts/, accessed August 7, 2016.

U.S. Food and Drug Administration and Center for Veterinary Medicine. (2012, April 13, 2012). Guidance for industry: New animal drugs and new animal drug combination products administered in or on medicated feed or drinking water of food-producing animals: Recommendations for drug sponsors for voluntarily aligning product use conditions with GFI #209. Available at: www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM299624.pdf, accessed November 11, 2015.

U.S. Food and Drug Administration and Center for Veterinary Medicine. (April 13, 2012). Guidance for industry: The judicious use of medically important antimicrobial drugs in food-producing animals. Available at: www.fda.gov/downloads/animalveterinary/guidancecomplianceenforcement/guidanceforindustry/ucm216936.pdf, accessed November 11, 2015.

Varma J, Greene K, Ovitt J, Barrett T, Medalla F, Angulo F. Hospitalization and antimicrobial resistance in *Salmonella* outbreaks, 1984–2002. Emerg Infect Dis 2005;11:943–946.

Varma J, Marcus R, Stenzel S, Hanna S, Gettner S, Anderson B, Hayes T, Shiferaw B, Crume T, Joyce K, Fullerton K, Voetsch A, Angulo F. Highly resistant *Salmonella* Newport-MDRAmpC transmitted through the domestic US food supply: A FoodNet case-control study of sporadic *Salmonella* Newport infections, 2002–2003. J Infect Dis 2006;194:222–230.

Varma J, Molbak K, Barrett T, Beebe J, Jones T, Rabatsky-her T, Smith K, Vugia D, Chang H, Angulo F. Antimicrobial-resistant nontyphoidal *Salmonella* is associated with excess bloodstream infections and hospitalizations. J Infect Dis 2005;191:554–561.

White D, Zhao S, Sudler R, Ayers S, Friedman S, Chen S, McDermott P, McDermott S, Wagner D, Meng J. The isolation of antibiotic-resistant *Salmonella* from retail ground meats. N Engl J Med 2001;345:1147–1154.

Winokur P, Brueggemann A, DeSalvo D, Hoffmann L, Apley M, Uhlenhopp E, Pfaller M, Doern G. Animal and human multidrug-resistant, cephalosporin-resistant *Salmonella* isolates expressing a plasmid-mediated CMY-2 AmpC beta-lactamase. Antimicrob Agents Chemother 2000;44:2777–2783.

Zhao S, White D, McDermott P, Friedman S, English L, Ayers S, Meng J, Maurer J, Holland R, Walker R. Identification and expression of cephamycinase bla(CMY) genes in *Escherichia coli* and *Salmonella* isolates from food animals and ground meat. Antimicrob Agents Chemother 2001;45:3647–3650.

Address correspondence to:
Martha Iwamoto, MD, MPH
Division of Foodborne, Waterborne, and Environmental Diseases
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention
1600 Clifton Road NE, Mailstop C-09
Atlanta, GA 30333

E-mail: miwamoto@cdc.gov

Jared Reynolds, MPH
Division of Foodborne, Waterborne, and Environmental Diseases
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention
1600 Clifton Road NE, Mailstop C-09
Atlanta, GA 30333

E-mail: jreynolds3@cdc.gov