Human *Salmonella* and Concurrent Decreased Susceptibility to Quinolones and Extended-Spectrum Cephalosporins

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The National Antimicrobial Resistance Monitoring System monitors susceptibility among Enterobacteriaceae in humans in the United States. We studied isolates exhibiting decreased susceptibility to quinolones (nalidixic acid MIC $\geq 32 \mu g/mL$ or ciprofloxacin MIC $\geq 0.12 \mu g/mL$) and extended-spectrum cephalosporins (ceftiofur or ceftriaxone MIC $\geq 2 \mu g/mL$) during 1996–2004. Of non-Typhi *Salmonella*, 0.19% (27/14,043) met these criteria: 11 Senftenberg; 6 Typhimurium; 3 Newport; 2 Enteridis; and 1 each Agona, Haifa, Mbandaka, Saintpaul, and Uganda. Twenty-six isolates had *gyrA* mutations (11 at codon 83 only, 3 at codon 87 only, 12 at both). All Senftenberg isolates had *parC* mutations (S80I and T57S); 6 others had the T57S mutation. The Mbandaka isolate contained *qnrB2*. Eight isolates contained *bla*<sub>CMY-2</sub>; 1 Senftenberg contained *bla*<sub>CMX-23</sub>. One Senftenberg and 1 Typhimurium isolate contained *bla*<sub>ampC</sub>; the Mbandaka isolate contained *bla*<sub>ampC</sub>. Nine Senftenberg isolates contained *bla*<sub>OXA-30</sub>; 1 contained *bla*<sub>OXA-9</sub>. Further studies should address patient outcomes, risk factors, and resistance dissemination prevention strategies.

Although antimicrobial agents are not indicated for uncomplicated *Salmonella* infections, fluoroquinolones and extended-spectrum cephalosporins are potentially life-saving treatments for extraintestinal infections (1). The National Antimicrobial Resistance Monitoring System (NARMS) has monitored antimicrobial drug resistance among enteric pathogens since 1996. NARMS has documented decreased susceptibility to each of these drug classes, in most instances among separate serotypes (2). Historically, decreased susceptibility to fluoroquinolones, which can be monitored by tracking resistance to nalidixic acid, has been noted among *Salmonella* serotypes (ser.) Typhi, Senftenberg, and Virchow (2,3). More recently, decreased susceptibility to fluoroquinolones has been noted among *Salmonella* ser. Enteritidis (4). Decreased fluoroquinolone susceptibility has also been seen among nalidixic acid–susceptible isolates (5). Extended-spectrum cephalosporin resistance was noted among 15 non-Typhi *Salmonella* NARMS isolates (including 12 ser. Typhimurium) during 1996–1998 (6). In all instances, extended-spectrum cephalosporin resistance was the result of *bla*<sub>CMY-2</sub>, a class C plasmid-encoded *ampC* gene (7). In addition to conferring resistance or decreased susceptibility to extended-spectrum cephalosporins such as ceftiofur and ceftriaxone, this gene also confers resistance to ampicillin (AMP), amoxicillin-clavulanate, cephalexin, and cefoxitin. This AmpC resistance phenotype has been seen in strains of *Salmonella* ser. Newport along with resistance to other drugs including chloramphenicol, streptomycin, sulfamethoxazole, and tetracycline. This MDRAmpC strain rose from 1% (1/77) of *Salmonella* ser. Newport submissions in 1998 to 25% (31/124) in 2001 (4). CMY-2 β-lactamases are largely re-

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sponsible for extended-spectrum cephalosporin resistance among *Salmonella* ser. Newport, Typhimurium, and others isolated in North America (6,8).

Coreistance to fluoroquinolones and extended-spectrum cephalosporins would limit therapeutic options for *Salmonella* infections. Decreased susceptibility to both drug classes was identified in Thailand in 1993 (ser. Anatum, Derby, Enteritidis, Typhimurium, Weltevreden, and I 4,5,12::i::-) (9), the United Kingdom in 1998 (ser. Senftenberg, Typhimurium, and Vibrioch) (10), Belgium as early as 2001 (ser. Virchow) (11), India in 2002 (ser. Typhi) (12), the United States in 2002 (ser. Mbandaka) (13), France in 2003 (11), and Taiwan in 2004 (ser. Choleraesuis, Cairo, and Kaduna) (14). In the United States, 27 (4.6%) of 588 *Salmonella* ser. Typhimurium isolates (clinical and slaughter) obtained from food animals in 1999 were resistant to cefotiorf and nalidixic acid: 22 (81%) from turkeys, 4 (15%) from horses, and 1 (4%) from cattle (15).

To understand coreistance to both antimicrobial classes among *Salmonella* isolates obtained from humans in the United States, we studied the NARMS human collection from 1996 through 2004, looking for decreased susceptibility to quinolones and extended-spectrum cephalosporins. Information for some of the isolates has been presented elsewhere (3,13,16–18). We present the molecular epidemiology of this phenotype and mechanisms responsible for its decreased susceptibility.

**Materials and Methods**

**Isolates and Antimicrobial Drug Susceptibility Testing**

NARMS-participating state and local public health laboratories submitted non-Typhi *Salmonella* isolates to the Centers for Disease Control and Prevention (CDC) for antimicrobial susceptibility testing: every 10th isolate from the Centers for Disease Control and Prevention (CDC) for 1682 Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 13, No. 11, November 2007

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...was performed according to manufacturer's instructions by using control strains *Escherichia coli* ATCC25922 and ATCC35218, and *Klebsiella pneumoniae* ATCC700603 (for extended-spectrum β-lactamase [ESBL] confirmation only). When available, Clinical Laboratory Standards Institute (CLSI) guidelines were used for interpretation (20).**

**Isoelectric Focusing for β-Lactamases**

The methods of Rasheed et al. were used with modification (21). Three-hour tryptophan soy broth cultures (grown at 37°C with shaking at 300 rpm) were pelleted, resuspended in 0.2% sodium acetate to 5% of original culture volume, and freeze-thawed 4 times (dry ice/ethanol bath and 37°C water bath). Preparations were diluted 2-fold with distilled water and swirled occasionally on ice for 30 min. Supernatants were collected after centrifugation (30 min at 20,200× g), and 3–5-μL aliquots were resolved for 1.5 h on Amphotoline PAGplate polyacrylamide gels, pH 3.5–9.5 (APBiotech, Piscataway, NJ, USA). Gels were stained with nitrocefin (500 μg/mL; Becton Dickinson, Franklin Lakes, NJ, USA). Isoelectric points (pIs) were estimated by comparison with the following standard β-lactamases: TEM-12 (pI 5.25), KPC-2 (pI 6.7), SHV-3 (pI 7.0), SHV-18 (pI 7.8), and MIR-1 (pI 8.4).

**PCR Detection of Antimicrobial Drug Resistance Genes**

Presence of *qnr* genes was determined by using PCR with primers QP1 and QP2 for *qnrA* (22), FQ1 and FQ2 for *qnrB* (23), and 5′-ATGGAAACCTCAAATCATAC-3′ and 5′-AAAAACACCTCGACATTAGT-3′ for *qnrS*. The *qnrB* allele was determined by amplification and sequencing with primers FQ1 and FQ2. Screening for *aac(6′)-Ib-cr* was performed as described (24). Primer pairs used for amplification of β-lactamase genes were: *bla*CMY (5′-ATGATGAAAAATCGTATAGC-3′) and 5′-TTGCAAGCTTTTCAAGAATGGC-3′ (25); *bla*OXA-1 (5′-AATGGCACCAGATTCAAATC-3′) and 5′-CTTGGCTTTTATGCTTGATG-3′ (26); *bla*TEM (5′-TTC TTGAAGCAAGAGGC-3′) and 5′-ACGCCTAGTG GAACGAAAAC-3′ (27); and *bla*SHV (5′-GGTTATGCGT TATATCCGAC-3′) and 5′-TTAGCTTGCAACGGTC-3′ (28) or at Lahey (5′-GCCGCGGTATATTCTTATGGC-3′) and 5′-TCTTTCGATGCGGCCGAGC-3′ (29). *bla*CTX-M genes were screened by using a multiplex PCR assay (30).

**DNA Sequencing**

Full-length sequences were obtained for β-lactamase genes. A 255-bp region covering the quinolone-resistant determining region (QRDR) of *gyrA* (Met52 to Leu137) was amplified by using primers *gyrA1*: 5′-CATGAAAGCTATTGGGCAATG-3′ and *gyrA2*: 5′-AGATCGGGCCAT CAGTTCGTTG-3′. QRDRs of *gyrB*, *parC*, and *parE* were amplified and sequenced by using previously described primers (31), except primers *parCF* (5′-ATCGTGGTTT GCCGTTAT-3′) and *parCR* (5′-GCCGCTTGGCCACATC-3′) were used to enhance coverage of *parC*. Amplicons were sequenced by using ABI Big-Dye 3.1 chemistry and ABI 3730XL automated DNA sequencers (PE Bio-
systems, Foster City, CA, USA). Analysis was performed by using BioEdit (www.mbio.ncsu.edu/BioEdit/bioedit.htm) or SeqMan software (DNASTar, Madison, WI, USA). QRDR sequences of gyrA, gyrB, parC, and parE were compared with those of Salmonella ser. Typhimurium LT2 (GenBank accession nos. AE008801, AE008878, AE008846, and AE008846, respectively).

Pulsed-Field Gel Electrophoresis (PFGE)

PFGE was performed as previously described (32). Isolates that produced indistinguishable patterns with XbaI (Roche Molecular Biochemicals, Indianapolis, IN, USA) were restricted with BlnI. Patterns were analyzed by using the BioNumerics version 4.0 software (Applied Maths, Sint-Martens-Latem, Belgium) and compared by unweighted pair group method with averages by using the Dice coefficient with a 1.5% band position tolerance window. The DNA sequence and deduced amino acid sequence for the Salmonella ser. Senftenberg bla_CMY-23 gene were assigned GenBank accession no. DQ463751.

Results

Decreased susceptibility to quinolones and extended-spectrum cephalosporins was first noted in NARMS data in 1997 and represented 0.19% (27/14,043) of non-Typhi Salmonella from 1996 through 2004 (Table 1). Salmonella ser. Senftenberg was the most frequent serotype (n = 11), followed by Typhimurium (n = 6), Newport (n = 3), and Enteritidis (n = 2). The phenotype was found in 9 different serotypes in 13 states (Table 2).

PFGE comparison by XbaI and, if applicable, BlnI restriction showed that 15/27 Salmonella isolates differed by ≥1 band. No indistinguishable patterns among different Salmonella serotypes were identified. Of the 3 ser. Newport isolates tested, 2 (AM15201 and AM21465) had indistinguishable XbaI patterns but different BlnI patterns (87.51% similarity). The 2 Enteritidis isolates (AM09124 and AM15266) were indistinguishable by both enzymes.

Of the 11 ser. Senftenberg isolates, 5 exhibited unique XbaI PFGE patterns, while the remaining 6 were separated into 2 groups with indistinguishable XbaI PFGE patterns (group 1: AM06960, AM08081, AM16094, and AM19422; group 2: AM20227 and AM20256). BlnI restriction demonstrated that AM19422 differed from the other group 1 isolates by a single band difference (97.44% similarity). PFGE results for some of the Senftenberg isolates are described elsewhere (16,18). All Typhimurium isolates exhibited unique XbaI PFGE patterns (77%–93% similarity).

Antimicrobial drug susceptibility results are presented in Table 3. For nalidixic acid, 25 isolates exhibited an MIC >32 μg/mL, and 2 (Mbandaka and Newport) had an MIC of 16 μg/mL. For ciprofloxacin, MICs of 0.12–0.5 μg/mL were found for all isolates except the 11 Senftenberg, for which the MIC was >4 μg/mL. For ceftriaxone, 14 isolates exhibited resistance (MIC ≥8 μg/mL). For cefotaxime, 2 isolates exhibited resistance according to the current CLSI breakpoint (64 μg/mL), and 7 exhibited intermediate resistance (MIC 16 or 32 μg/mL). Three isolates (Mbandaka, Senftenberg, and Typhimurium) exhibited an ESBL phenotype according to ceftazidime and cefotaxime MIC alone and with clavulanate. Seven isolates exhibited the MDRAmpC phenotype, including 1 Agona, 2 Newport, 3 Typhimurium, and 1 Uganda. According to current CLSI guidelines, 1 isolate (ser. Senftenberg) was fully resistant to ciprofloxacin, ceftriaxone, ceftazidime, and cefotaxime.

The mechanisms responsible for resistance and decreased susceptibility are shown in Table 4. Some mechanisms for some of the isolates are presented elsewhere (3,17,18). At least 1 gyrA mutation was found in 26 of 27 isolates. A gyrA mutation at codon 83 only was found for 11 isolates; a mutation at codon 87 only was found for 3; mutations at both codons were found for 12. No functional mutations were detected in gyrB or parC genes. All Senftenberg isolates had parC mutations (S80I and T57S), and 6 other isolates had the T57S mutation. In addition to the T57S mutation in parC, the Mbandaka isolate contained a

| Year | No. that met MIC criteria/total tested (%) | Senftenberg | Typhimurium | Newport | Enteritidis | Other (no.) |
|------|------------------------------------------|-------------|-------------|---------|-------------|-------------|
| 1996 | 0/1,324 (0)                              | 1           |             |         |             |             |
| 1997 | 1/1,301 (0.08)                           | 1           |             |         |             |             |
| 1998 | 1/1,460 (0.07)                           | 1           |             |         |             |             |
| 1999 | 1/1,497 (0.07)                           | 1           | 1           |         |             |             |
| 2000 | 4/1,377 (0.29)                           | 2           | 1           | 1       |             |             |
| 2001 | 4/1,419 (0.28)                           | 2           | 1           |         |             |             |
| 2002 | 5/2,008 (0.25)                           | 1           | 2           | 1       |             |             |
| 2003 | 4/1,864 (0.21)                           | 2           |             | 1       |             |             |
| 2004 | 7/1,793 (0.39)                           | 3           | 1           | 1       |             |             |
| Total| 27/14,043 (0.19)                         | 11          | 6           | 3       | 2           | 5           |

*NARMS, National Antimicrobial Resistance Monitoring System. Reduced susceptibility to quinolones and extended-spectrum cephalosporins defined as MIC ≥32 μg/mL for nalidixic acid or ≥0.12 μg/mL for ciprofloxacin and ≥2 μg/mL for ceftriaxone.
Table 2. Isolate, year reported, state, and serotype for NARMS non-Typhi Salmonella isolates with decreased susceptibility to quinolones and extended-spectrum cephalosporins, United States, 1996–2004

| Isolate     | Year | State | Serotype |
|-------------|------|-------|----------|
| AM18280     | 2003 | TX    | Agona    |
| AM09124     | 2000 | CA    | Enteritidis |
| AM15266     | 2003 | IL    | Enteritidis |
| AM12389     | 2001 | NJ    | Hafnia   |
| AM15010     | 2002 | NY    | Mbandaka |
| AM03005     | 1998 | NY    | Newport  |
| AM15201     | 2002 | ME    | Newport  |
| AM21465     | 2004 | GA    | Newport  |
| AM20428     | 2004 | GA    | Saintpaul |
| AM06960     | 1999 | FL    | Senftenberg |
| AM08081     | 2000 | FL    | Senftenberg |
| AM08208     | 2000 | GA    | Senftenberg |
| AM09884     | 2001 | FL    | Senftenberg |
| AM11007     | 2001 | MA    | Senftenberg |
| AM14058     | 2002 | TX    | Senftenberg |
| AM16094     | 2003 | FL    | Senftenberg |
| AM18622     | 2003 | FL    | Senftenberg |
| AM19422     | 2004 | FL    | Senftenberg |
| AM20227     | 2004 | GA    | Senftenberg |
| AM20256     | 2004 | FL    | Senftenberg |
| AM02544     | 1997 | MN    | Typhimurium |
| AM08739     | 2000 | KS    | Typhimurium |
| AM11682     | 2001 | NY    | Typhimurium |
| AM14364     | 2002 | WI    | Typhimurium |
| AM14807     | 2002 | NY    | Typhimurium |
| AM20205     | 2004 | PA    | Typhimurium |
| AM19537     | 2004 | CA    | Uganda   |

*NARMS, National Antimicrobial Resistance Monitoring System.

plasmid-mediated qnrB2 gene and has been described (13). Four isolates contained aac(6)-Ib, but none contained the ciprofloxacin-modifying aac(6)-Ib-cr variant.

Nine AmpC phenotype isolates produced β-lactamase with a pl ≥8.4 (Table 4); 8 contained blaCMY-2 but the Senftenberg strain contained a blaCMY-23 gene (GenBank accession no. DQ463751) identical to that found in an E. coli isolate (GenBank accession no. DQ438952). This gene differs from blaCMY-2 by 1 amino acid. Three of the blaCMY- positive isolates, including the strain positive for blaCMY-23, also contained blatem-Ib. The Mbandaka isolate was positive for blashv-30 with pl 7.0 (33) and also produced an enzyme with a pl 7.6, the nature of which is still under study. Two isolates (1 Senftenberg and 1 Typhimurium) contained blashv-12 and both also contained blaOXA and blatem genes. Of the 11 Senftenberg isolates, 10 contained blaoxa-1 (n = 9) or blaoxa-4 (n = 1). No isolates contained blactxm-2 genes.

Discussion

Fluoroquinolone and extended-spectrum cephalosporin coresistance is rare; however, the appearance of this phenotype in 2 commonly isolated serotypes from humans (Typhimurium and Newport) is concerning. Sporadic infections are alarming, but if clonal expansion of an isolate with this phenotype were to take place, as occurred with Salmonella ser. Typhimurium DT104 and Newport-MDRAmpC, the clinical consequences could be dramatic. Statistically significant increases in resistance to nalidixic acid (odds ratio [OR] 6.7, 95% confidence interval [CI] CI 2.6–17.7) and ceftriaxone (OR 43.2, 95% CI 10.5–177.4) have been documented among non-Typhi Salmonella of human origin submitted to NARMS during 1996–2003 (4). Of 202 nalidixic acid–resistant non-Typhi Salmonella collected by NARMS during 1996–2003, most were ser. Enteritidis (31%) or Typhimurium (10%). Most of the 324 ceftriaxone-resistant non-Typhi Salmonella collected by NARMS during the same period were ser. Newport (56%) or Typhimurium (23%). A slightly broader geographic representation can be found in the SENTRY surveillance project, which analyzed 786 Salmonella isolates (blood and stool) from medical facilities in Latin America and North America (including Canada) during 2001–2003 (8). Of these, 11% were resistant to nalidixic acid, and 2% exhibited decreased susceptibility to ceftriaxone, cefotaxime, or aztreonam.

Extended-spectrum cephalosporin-resistant Newport and Typhimurium isolates are typically obtained from community-acquired infections. Newport-MDRAmpC infections have been associated with consumption of contaminated beef and unpasteurized dairy products (34). Salmonella containing blaCMY genes have been isolated from ground chicken (Typhimurium DT208), turkey (Agona), and beef (Agona) purchased from retail outlets in the Washington DC area (35). In addition, cattle, chickens, turkeys, pigs, horses, and dogs have all been sources of blaCMY-containing Salmonella, including common serotypes such as Typhimurium, Newport, and Heidelberg (26,36,37). Decreased susceptibility to fluoroquinolones among Salmonella serotypes that typically carry blaCMY genes warrants exploration of factors that could select for decreased susceptibility to fluoroquinolones in animal reservoirs and in the human host.

PFGE showed diversity within some serotypes and indistinguishable strains within others. PFGE diversity among 2 serotypes commonly associated with extended-spectrum cephalosporin resistance (Newport and Typhimurium) is not surprising, given that CMY-producing strains have been seen at least since the late 1990s. Isolates of ser. Enteritidis are highly clonal; therefore, PFGE-indistinguishable patterns among isolates with no apparent epidemiologic link are not unusual. All PFGE-indistinguishable Senftenberg isolates from group 1 were isolated in the same state. Results for the Florida Senftenberg isolates are described elsewhere (16,18).

Salmonella ser. Senftenberg exhibiting decreased susceptibility to fluoroquinolones has been associated with
nosocomial infections in healthcare facilities in the United States (18). All 11 isolates contained identical gyrA mutations (S83Y and D87G) and parC mutations (T57S and S80I). These parC mutations have been identified in several Salmonella serotypes including Senftenberg (38). Ten Senftenberg isolates included in this study contained blaOXA genes; the blaOXA-negative Senftenberg strain contained a blaCMY mechanism of extended-spectrum cephalosporin resistance. Acquisition of a blaCMY gene by a traditionally nalidixic acid–resistant serotype warrants further epidemiologic and laboratory investigation. The blaOXA gene has been identified in Salmonella ser. Typhimurium and is

Table 3. Susceptibility results for NARMS non-Typhi Salmonella isolates with decreased susceptibility to quinolones and extended-spectrum cephalosporins, United States, 1996–2004*  

| Isolate  | NAL | CIP | XNL | CRO | TAZ | TAZ/CLAV | FOT | FOT/CLAV | Other†  |
|----------|-----|-----|-----|-----|-----|----------|-----|----------|---------|
| AM18280  | >32 | 0.25| >8  | 16  | 32  | 16/4     | 16  | 8/4      | AMP, AMC, CHL, FOX, KAN, STR, SUL, SXT, TET |
| AM09124  | >32 | 0.5 | 2   | ≤0.25| 0.5 | 0.25/4   | 0.25| 0.12/4   | ND      |
| AM15266  | >32 | 0.5 | 2   | ≤0.25| 0.5 | 0.25/4   | 0.25| 0.12/4   | (CHL)   |
| AM12389  | >32 | 0.5 | 2   | ≤0.25| 0.25| 0.25/4   | 0.1 | 0.12/4   | (CHL), SUL, SXT, TET |
| AM15010  | 16  | 0.25| 8   | 8   | 64  | 0.5/4    | 4   | 0.25/4   | AMP, (CHL), SUL, SXT |
| AM03005  | 16  | 0.25| 2   | 0.5 | 0.25| 0.12/4   | 0.12| ≤0.06/4  | AMP, AMC, CHL, FOX, (GEN), KAN, STR, SUL, SXT |
| AM15201  | >32 | 0.12| >8  | 8   | 16  | 16/4     | 16  | 8/4      | AMP, AMC, CHL, FOX, STR, SUL, TET |
| AM21465  | >32 | 0.12| >8  | 16  | 16  | 16/4     | 8   | 8/4      | AMP, AMC, CHL, FOX, STR, SUL, TET |
| AM20428  | >32 | 0.5 | 2   | ≤0.25| 0.5 | 0.5/4    | 0.5 | 0.12/4   | (CHL), (FOX) |
| AM09960  | >32 | >4  | 8   | 8   | 0.5 | 0.25/4   | 1   | 0.12/4   | AMP, AMC, (CHL), GEN, KAN, STR, SUL, SXT |
| AM08081  | >32 | >4  | 4   | 0.5 | 0.5 | 0.25/4   | 1   | 0.12/4   | AMP, AMC, CHL, FOX, (GEN), KAN, STR, SUL, SXT |
| AM08208  | >32 | >4  | 2   | ≤0.25| 0.5 | 0.25/4   | 0.5 | 0.25/4   | AMP, (AMC) CHL, GEN, KAN, STR, SUL, SXT, TET |
| AM09964  | >32 | >4  | 8   | 8   | 64  | 0.25/4   | 8   | 0.25/4   | AMP, (CHL), (FOX), GEN |
| AM11007  | >32 | >4  | 4   | 0.5 | 1   | 0.5/4    | 1   | 0.5/4    | AMP, AMC, CHL, FOX, (GEN), KAN, STR, SUL, SXT |
| AM14058  | >32 | >4  | >8  | >64 | 64  | 64/4     | 128 | >64/4    | (AMI), AMP, AMC, CHL, FOX, KAN, STR, SUL |
| AM16094  | >32 | >4  | 4   | ≤0.25| 0.5 | 0.25/4   | 1   | 0.25/4   | AMP, (AMC), CHL, (FOX), (GEN), KAN, STR, SUL, SXT |
| AM18622  | >32 | >4  | 8   | 1   | 2   | 0.5/4    | 4   | 0.5/4    | AMP, AMC, CHL, KAN, STR, SUL, SXT |
| AM19422  | >32 | >4  | 4   | ≤0.25| 0.5 | 0.5/4    | 2   | 0.25/4   | AMP, AMC, (GEN), KAN, STR, SUL, SXT |
| AM20227  | >32 | >4  | 2   | ≤0.25| 1   | 2/4      | 1   | 0.5/4    | AMP, AMC, (CHL), (FOX), GEN, KAN, STR, SUL, SXT |
| AM20256  | >32 | >4  | 4   | ≤0.25| 0.5 | 0.5/4    | 1   | 0.25/4   | AMP, (AMC), (CHL), (GEN), KAN, SUL, TET |
| AM02544  | 256 | 0.25| >16 | 64  | 128 | 0.5/4    | 32  | 0.12/4   | AMP, (AMC), KAN, STR, SUL, TET |
| AM08739  | >32 | 0.25| >8  | 32  | 16  | 16/4     | 16  | 8/4      | AMP, AMC, CHL, FOX, GEN, KAN, STR, SUL, TET |
| AM11682  | >32 | 0.25| >8  | 16  | 16  | 8/4      | 16  | 8/4      | AMP, AMC, FOX |
| AM14364  | >32 | 0.25| >8  | 32  | 32  | 16/4     | 32  | 16/4     | AMP, AMC, CHL, FOX, GEN, KAN, STR, SUL, TET |
| AM14807  | >32 | 0.25| >8  | 16  | 32  | 16/4     | 16  | 32/4     | AMP, AMC, CHL, FOX, STR, SUL, TET |
| AM20205  | >32 | 0.25| 2   | ≤0.25| 0.5 | 0.5/4    | 0.25| 0.25/4   | AMP, KAN, STR, TET |
| AM19537  | >32 | 0.12| >8  | 16  | 16/4 | 8       | 8   | 8/4      | AMP, AMC, CHL, FOX, (GEN), (KAN), STR, SUL, TET |

* NARMS, National Antimicrobial Resistance Monitoring System; NAL, nalidixic acid; CIP, ciprofloxacin; XNL, cefotaxim; CRO, cefotaxime; TAZ, ceftazidime; TAZ/CLAV, ceftazidime/ceftazidime; FOT, cefotaxime; FOT/CLAV, cefotaxime/ceftazidime; AMP, ampicillin; AMC, amoxicillin/ceftaxidime; CHL, chloramphenicol; FOX, cefotaxim; KAN, kanamycin; STR, streptomycin; SUL, sulfoxathazoxole or sulfoisoxazole; SXT, trimethoprim/sulfamethoxazole; TET, tetracycline; AMI, amikacin; GEN, gentamicin.
† Drugs in parentheses had intermediate results.
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reported to be carried by an integron (39); bla_{OXA-9} has been associated with Tn1331 (40).

The epidemiology of Salmonella with decreased susceptibility to fluoroquinolones is relatively well characterized, as is that of Salmonella with bla_{CMY}-mediated extended-spectrum cephalosporin resistance. Conversely, little is known about the events leading to quinolone and extended-spectrum cephalosporin co-resistance and the epidemiology of these infections in humans. Patients with Salmonella infections who exhibit decreased susceptibility to both antimicrobial drug classes should be interviewed to determine risk factors and the effects of antimicrobial drugs and other potential selective factors on this phenomenon.

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Dr Whichard is a researcher with NARMS at CDC. Her interests include \(\beta\)-lactamases, multidrug-resistant Salmonella isolates, bacteriophages, and other mobile genetic elements.

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