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## Plasmid-mediated Quinolone Resistance in *Salmonella enterica*, United Kingdom

**To the Editor:** Fluoroquinolones are broad-spectrum antimicrobial drugs used to treat many clinical infections. Salmonellosis is treated with fluoroquinolones only in elderly or immunocompromised patients, but these drugs are also used for treating patients with enteric fever, invasive disease, or long-term salmonellae carriage. High-level fluoroquinolone resistance is uncommon, but reduced susceptibility is increasing.

Since 1998, plasmid-mediated quinolone resistance encoded by *qnr* genes A, B, and S that confer low-level resistance to nalidixic acid and reduced susceptibility to ciprofloxacin has been identified in several enterobacterial species, including *Salmonella*. Their clinical importance is in facilitating resistance to potentially lethal levels of quinolone. Additionally, *qnr* genes are often associated with strains that produce extended-spectrum  $\beta$ -lactamases.

We recently reported identification of *qnr* genes in *Salmonella* in the United Kingdom (1). Most isolates were associated with the Far East. Two isolates of *S. Virchow* were part of an outbreak associated with imported cooked chicken from Thailand. During October 2006–April 2007, we monitored *qnr* genes in nontyphoidal salmonellae isolated in the United Kingdom that expressed reduced susceptibility to ciprofloxacin (MIC 0.125–1.0  $\mu\text{g}/\text{mL}$ ) with concomitant susceptibility to nalidixic acid (MIC <16  $\mu\text{g}/\text{mL}$ ). This resistance phenotype is a useful marker for the *qnr* gene as the sole quinolone resistance determinant (1).

Recent studies showed that isolates of *Salmonella* spp. and *Escherichia coli* with decreased susceptibility to ciprofloxacin (MICs >0.06  $\mu\text{g}/\text{mL}$  and 0.5  $\mu\text{g}/\text{mL}$ , respectively), but with susceptibility or intermediate resistance to nalidixic acid (MIC 8–16  $\mu\text{g}/\text{mL}$  and 4–8  $\mu\text{g}/\text{mL}$ , respectively), all had *qnrA* or *qnrS* genes but lacked mutations in the topoisomerase genes (2,3). Strains with ciprofloxacin MICs >1  $\mu\text{g}/\text{mL}$  were also included to monitor involvement of *qnr* genes in development of high-level ciprofloxacin resistance. Breakpoint concentrations used are based on long-term studies within the Health Protection Agency Laboratory of Enteric Pathogens. Ciprofloxacin Etest (AB Biodisk, Solna, Sweden) results were interpreted according to manufacturer's procedures. A total of 45 *Salmonella* spp. strains were tested. Screening for *qnr* genes by multiplex PCR identified 37 isolates with *qnrS* and 2 carrying *qnrB* variants (Table) (4). However, the *qnrB* primer pair in this multiplex did not fully match all *qnrB* gene variants. PCR and sequencing using primers FQ1 and FQ2 (5) and *qnrS-F* and *qnrS-R* (1), were used to identify specific *qnrB* and *qnrS* gene variants.

The *qnrS1*-positive salmonellae belong to serotypes Typhimurium

Table. Isolates of *Salmonella enterica* with plasmid-mediated *qnr* genes, United Kingdom, October 2006–April 2007

| <i>Salmonella</i> serotype | Phage type* | No. isolates | VNTR profile† | Ciprofloxacin MIC (μg/mL)‡ | Additional resistance to antimicrobial drugs§                | <i>qnr</i> identified |
|----------------------------|-------------|--------------|---------------|----------------------------|--|-----------------------|
| Corvallis                  | –           | 1            | –             | 0.25                       | S, Su, T   | <i>qnrS1</i>          |
| Corvallis                  | –           | 2            | –             | 0.38                       | S, Su, T   | <i>qnrS1</i>          |
| Corvallis                  | –           | 1            | –             | 1.0                        | S, Su, T, Cf   | <i>qnrS1</i>          |
| Corvallis                  | –           | 1            | –             | 0.25                       | None   | <i>qnrS1</i>          |
| Corvallis                  | –           | 1            | –             | 0.38                       | None   | <i>qnrS1</i>          |
| Schwarzengrund             | –           | 1            | –             | 0.25                       | T  | <i>qnrB5</i>          |
| Typhimurium                | DT120       | 4            | 1–6–0–0–3     | 0.38                       | S, Su, T   | <i>qnrS1</i>          |
| Typhimurium                | DT120       | 3            | 1–6–0–0–3     | 0.50                       | S, Su, T   | <i>qnrS1</i>          |
| Typhimurium                | DT120       | 3            | 1–4–0–0–3     | 0.38                       | S, Su, T   | <i>qnrS1</i>          |
| Typhimurium                | DT120       | 1            | 1–4–0–0–3     | 0.50                       | S, Su, T   | <i>qnrS1</i>          |
| Typhimurium                | DT120       | 1            | 1–4–0–0–3     | 0.38                       | None   | <i>qnrS1</i>          |
| Typhimurium                | DT120       | 1            | 1–5–0–0–3     | 0.38                       | S, Su, T   | <i>qnrS1</i>          |
| Typhimurium                | DT193       | 1            | 1–6–0–0–3     | 0.50                       | S, Su, T   | <i>qnrS1</i>          |
| Typhimurium                | DT193       | 1            | 1–4–0–0–3     | 0.38                       | C, S, Su, Sp, T, Tm  | <i>qnrS1</i>          |
| Typhimurium                | DT193       | 1            | 1–4–0–0–3     | 0.38                       | S, Su, T   | <i>qnrS1</i>          |
| Typhimurium                | DT193       | 2            | 1–5–0–0–3     | 0.38                       | S, Su, T   | <i>qnrS1</i>          |
| Typhimurium                | DT193       | 1            | 1–4–0–0–3     | 0.50                       | A, Su  | <i>qnrS1</i>          |
| Typhimurium                | 49b         | 1            | 1–4–19–1–3    | 0.25                       | A, G, Ne, K, S, Su, Sp, T, Tm, Ak, Cx, Cr, Cf, Cn, Ct        | <i>qnrB2</i>          |
| Typhimurium                | NC          | 1            | 1–4–0–0–3     | 0.25                       | S, Su, T   | <i>qnrS1</i>          |
| Typhimurium                | UT          | 1            | 3–8–19–1–2    | >32                        | A, C, G, S, Su, Sp, T, Tm, Fu, Nx                            | <i>qnrS1</i>          |
| Virchow                    | 43          | 5            | –             | 1.0                        | A, Fu, Nx  | <i>qnrS1</i>          |
| Virchow                    | 43          | 2            | –             | 1.5                        | A, Fu, Nx  | <i>qnrS1</i>          |
| Virchow                    | 25a         | 1            | –             | 0.75                       | Tm   | <i>qnrS1</i>          |
| Virchow                    | 11          | 1            | –             | 1.0                        | A, Fu, Nx  | <i>qnrS1</i>          |
| Virchow                    | NC          | 1            | –             | 1.5                        | A, C, G, Ne, K, S, Su, Sp, T, Tm, Fu, Nx, Cx, Cr, Cf, Cn, Ct | <i>qnrS1</i>          |

\*DT, definitive type; NC, does not conform to a recognized pattern; UT, untypeable.

†VNTR, variable number tandem repeat. Loci of the VNTR profiles are presented in the following order: STTR9-STTR5-STTR6-STTR10pl-STTR3. The number 0 in the VNTR profile represents cases with no amplification of PCR product.

‡Determined by Etest.

§Antimicrobial drugs (breakpoint final concentrations): S, streptomycin (16 mg/L); Su, sulfonamide (64 mg/L); T, tetracycline (8 mg/L); Cf, cefuroxime (16 mg/L); C, chloramphenicol (8 mg/L); Sp, spectinomycin (64 mg/L); Tm, trimethoprim (2 mg/L); A, ampicillin (8 mg/L); G, gentamicin (4 mg/L); Ne, neomycin (8 mg/L); K, kanamycin (8 mg/L); Ak, amikacin (4 mg/L); Cx, cefalexin (16 mg/L); Cr, cefradine (16 mg/L); Cn, ceftriaxone (1 mg/L); Ct, cefotaxime (1 mg/L); Fu, furazolidone (8 mg/L); Nx, nalidixic acid (16 mg/L).

(21 isolates), Virchow (10), and Corvallis (6). Most *S. Typhimurium* isolates were either definitive phage type 120 or 193, and most *S. Virchow* isolates were phage type 43 (Table). Thirteen *qnrS1*-positive isolates were from patients who reported recent travel to Egypt, India, Malaysia, Morocco, Thailand, or an undisclosed destination.

Twelve isolates from patients who had not traveled abroad were assumed to be from UK-acquired infections. *S. Virchow* isolates had been associated with cooked chicken from Thailand (1), and *qnrS1* has recently been described in *S. Corvallis* strains from humans in Denmark or isolated in Thailand from humans, chicken, pork, and beef (3). Comparison of pulsed-field

gel electrophoresis patterns and resistance phenotypes of *qnrS1*-positive *S. Corvallis* strains identified common types, suggesting that some UK patients may have acquired *S. Corvallis* from chicken from Thailand.

Thirteen isolates showed resistance to ceftriaxone, cefotaxime, or ampicillin. Plasmids with *qnr* genes have been found to co-transfer TEM, SHV, and CTX-M genes (1,5,6). Co-transmission of fluoroquinolone and β-lactamase resistance is clinically important because co-selection of resistance by use of either drug may occur.

Twenty-one *qnrS1*-positive *S. Typhimurium* were subtyped by variable number tandem repeat (VNTR) analysis to determine whether the increase

was caused by spread of ≥1 distinct strains (7). Twenty isolates produced 1 of 3 related profiles (loci of VNTR profiles are ordered STTR9-STTR5-STTR6-STTR10pl-STTR3): 1–4–0–0–3, 9 isolates; 1–5–0–0–3, 3 isolates; or 1–6–0–0–3, 8 isolates. Alleles 4 and 5, and 5 and 6 at locus STTR5 only differed by an extra 6-bp repeat, which suggests a clonal relationship between the *qnrS1*-positive *S. Typhimurium* in this study (Table) (8). *S. Typhimurium* isolates with the 1–6–0–0–3 profile have been isolated from tourists returning from Asia (7), which suggests that the UK *qnrS1*-positive *S. Typhimurium* isolates have originated in the Far East.

These findings show increased occurrence of *qnr* genes, particularly

*qnrS1*, in nontyphoidal salmonellae in the United Kingdom. These data are in contrast to those of recent studies in the United States and France, which show low incidences of *qnrS* genes in larger strain collections (9,10). The *qnr* phenotype is in contrast to resistance mediated by mutations in the topoisomerase genes whereby 1 mutation confers low-level resistance to fluoroquinolones and full resistance to nalidixic acid. Our previous study demonstrated that *qnrS1* was sufficient to cause decreased susceptibility to ciprofloxacin in the absence of mutations in *gyrA* (*I*). In this study, a *qnr* gene was sufficient to increase the ciprofloxacin MIC to 0.38–0.75 µg/mL. In addition, a *qnr* gene contributed to high-level ciprofloxacin resistance in 10 isolates, thereby potentially jeopardizing first-line treatment of vulnerable patient groups with ciprofloxacin.

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## *Saksenaea vasiformis* Infection, French Guiana

**To the Editor:** The Zygomycetes are a class of filamentous fungi that are ubiquitous in the environment. Most of the species known to cause human or animal infections belong to a few genera within the order Mucorales. *Saksenaea vasiformis*, isolated from soil in India and described by Saksena in 1953, was reported to cause human infection for the first time by Ajello et al. (*I*). We report a case of a cutaneous lesion caused by *S. vasiformis* in French Guiana.

A nonimmunocompromised 47-year-old woman with a long history of non-type 1 diabetes mellitus, who had lived in French Guiana for many years, was admitted to Cayenne Hospital on November 18, 2005, with a cutaneous lesion of the abdominal wall and a fever that had lasted for 5 days before she was hospitalized. A skin biopsy specimen was obtained, and the first surgical debridement was performed on day 4 of hospitalization. A diagnosis of zygomycosis was made after direct examination and histopathologic examination of the tissue samples. Treatment was initiated on day 8, beginning with liposomal amphotericin B and itraconazole for 10 days, followed by liposomal amphotericin B alone for 12 days. Persistence of necrotic tissues at the infection site required additional surgical debridement on day 10. Histopathologic examination of the resected tissues showed damaged hyphae of zygomycetes. Resolution of clinical signs was excellent. Additional biopsy specimens taken by the end of treatment on day 21 were negative for fungi by direct examination and culture. Finally, a cicatrix was formed.

Histologic examination of the initial excised tissues showed a localized periumbilical cutaneous lesion of

