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# Fluoroquinolone-Resistant *Mycoplasma genitalium*, Southwestern France

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**To the Editor:** *Mycoplasma genitalium* is a sexually transmitted bacterium involved in nongonococcal urethritis in men and associated with cervicitis and pelvic inflammatory disease in women. Azithromycin regimens have been commonly used as a first-line treatment of these conditions, but a recent increase in *M. genitalium* with azithromycin resistance has been described worldwide; in 2012, resistance in the organism was detected in France at a prevalence of 14% (*1*). In case of azithromycin failure, moxifloxacin is a second-line treatment; however, moxifloxacin treatment failures have also been reported and are associated with mutations in ParC or GyrA (*2*).

Prevalence of *M. genitalium* infection was ≈4% in 2013–2014 at Bordeaux University Hospital (Bordeaux, France). To evaluate the prevalence of fluoroquinolone resistance in *M. genitalium* in southwestern France, we examined the quinolone resistance–determining regions (QRDRs) of the *gyr*A and *par*C genes in *M. genitalium*–positive specimens obtained during 2013–2014. We retrospectively collected (from the Department of Bacteriology, Bordeaux University Hospital) 369 *M. genitalium*–positive urogenital specimens and DNA extracts from 344 patients. The *gyr*A and *par*C QRDRs were amplified and sequenced as described (*3,4*). We also assayed macrolide resistance–associated mutations using real-time PCR and melting curve analysis (*1*). To determine resistant genotypes A2058G or A2059G, we sequenced PCR products. Nucleotide positions in the 23S rRNA and amino acid positions in GyrA and ParC were identified according to *Escherichia coli* numbering.

From the 344 *M. genitalium*–positive patients, 200 specimens underwent complete analysis for the *gyr*A and *par*C genes, specimens from 221 patients were investigated for macrolide resistance, and specimens from 168 patients were examined for 23S rRNA, *gyr*A, and *par*C genes. Unsuccessful amplifications could be attributed to low bacterial loads of *M. genitalium* or to the degradation of frozen DNA during storage. Strains from 12/200 patients (6%; 95% CI 3.47%–10.19%) had QRDR mutations, with rates of 6.4% (6/93) for 2013 and 5.6% (6/107) for 2014. This prevalence is in accordance with the 4.5% moxifloxacin resistance described in the United Kingdom in 2011 (*3*) but lower than prevalences found in small numbers of strains in Japan and Australia during 2006–2014, which ranged from 10% to 47% (*4–8*).

Strains from 11 patients (patient nos. 6, 8, 12, 20, 23, 28–31, 46, 47) harbored alterations in the ParC QRDR (Table) at positions 80 (Ser→Asn or Ile) or 84 (Asp-84→Tyr or Asn). These mutations have been previously described for *M. genitalium* (*4,6–8*). In addition, 1 new amino acid alteration, Asn-96→Ser (strain from patient 20), was found in ParC. We detected a GyrA modification with the Ala-93→Thr transition in a strain from 1 patient (patient 3). These 2 amino acid changes were not

**Table.** Fluoroquinolone resistance–associated amino acid changes in GyrA and ParC and macrolide resistance–associated mutations n the 23S rRNA gene in *Mycoplasma genitalium,* France, 2013–2014*

| Patient no. | Date of collection | Patient sex | Specimen type | Mutation in the 23S rRNA gene | Amino acid changes in GyrA | Amino acid changes in ParC |
|---|---|---|---|---|---|---|
| 1 | 2013 Jan 9 | F | Vaginal swab | A2058G/A2059G | NA | NA |
| 2 | 2013 Feb 1 | F | Vaginal swab | A2058G | – | – |
| 3 | 2013 Feb 1 | M | Urethral swab | A2058G/A2059G | Ala-93→Thr | – |
| 4 | 2013 Feb 18 | M | Urethral swab | A2058G/A2059G | – | – |
| 5 | 2013 Feb 20 | M | Urine | A2058G/A2059G | – | – |
| 6 | 2013 Mar 11 | M | Urine | A2058G/A2059G | – | Asp-84→Tyr |
| 7 | 2013 Mar 28 | F | Vaginal swab | A2058G/A2059G | NA | – |
| 8 | 2013 Apr 3 | M | Urine | Wild-type | – | Asp-84→Tyr |
| 9 | 2013 Apr 8 | F | Vaginal swab | A2058G/A2059G | – | – |
| 10 | 2013 Apr 11 | F | Vaginal swab | A2058G/A2059G | NA | NA |
| 11 | 2013 Apr 16 | F | Vaginal swab | A2058G | – | NA |
| 12 | 2013 Apr 19 | F | Vaginal swab | Wild-type | – | Ser-80→Asn |
| 13 | 2013 May 21 | M | Urethral swab | A2059G | – | – |
| 14 | 2013 Jul 4 | M | Urine | A2059G | – | – |
| 15 | 2013 Jul 4 | M | Urethral swab | A2059G | – | – |
| | 2013 Jul 19 | M | Urine | A2059G | – | – |
| 16 | 2013 Jul 19 | M | Urine | A2058G | – | – |
| 17 | 2013 Aug 9 | F | Vaginal swab | A2059G | NA | – |
| 18 | 2013 Sep 30 | F | Vaginal swab | A2058G/A2059G | – | – |
| 19 | 2013 Sep 30 | F | Vaginal swab | A2058G/A2059G | – | – |
| 20 | 2013 Oct 29 | F | Vaginal swab | Wild-type | – | Asn-96→Ser |
| 21 | 2013 Nov 22 | F | Vaginal swab | A2058G/A2059G | NA | NA |
| 22 | 2013 Nov 29 | F | Vaginal swab | A2062T | – | – |
| 23 | 2013 Dec 1 | F | Vaginal swab | Wild-type | – | Asp-84→Tyr |
| 24 | 2014 Jan 21 | F | Vaginal swab | A2059G | – | – |
| 25 | 2014 Jan 29 | F | Vaginal swab | A2059G | – | – |
| 26 | 2014 Jan 30 | F | Vaginal swab | A2058G/A2059G | NA | – |
| 27 | 2014 Feb 13 | F | Vaginal swab | A2059G | – | – |
| 28 | 2014 Feb 18 | M | Urine | Wild-type | – | Ser-80→Ile |
| 29 | 2014 Feb 24 | F | Vaginal swab | Wild-type | – | Asp-84→Asn |
| 30 | 2014 Mar 5 | F | Vaginal swab | Wild-type | – | Asp-84→Asn |
| 31 | 2014 Mar 14 | M | Urine | NA | – | Ser-80→Asn |
| 32 | 2014 Apr 3 | F | Endocervical swab | A2058G | – | – |
| 33 | 2014 Apr 7 | M | Urethral swab | A2059G | – | – |
| 34 | 2014 Jun 24 | F | Vaginal swab | A2059C | – | – |
| 35 | 2014 Jul 9 | F | Endocervical swab | A2059G | NA | – |
| 36 | 2014 Jul 25 | F | Urine | A2058G/A2059G | NA | NA |
| 37 | 2014 Jul 25 | F | Vaginal swab | A2058G | – | – |
| 38 | 2014 Aug 19 | F | Endocervical swab | A2062T | – | NA |
| 39 | 2014 Aug 28 | F | Vaginal swab | A2058G/A2059G | – | – |
| 40 | 2014 Sep 24 | F | Vaginal swab | A2059G | – | – |
| 41 | 2014 Oct 7 | F | Vaginal swab | A2059G | – | – |
| 42 | 2014 Oct 15 | F | Vaginal swab | A2058G/A2059G | – | – |
| 43 | 2014 Oct 31 | M | Urine | A2058G | – | – |
| 44 | 2014 Nov 5 | F | Vaginal swab | A2058G/A2059G | NA | – |
| 45 | 2014 Nov 28 | F | Vaginal swab | A2058G | – | – |
| 46 | 2014 Dec 3 | F | Vaginal swab | Wild-type | – | Asp-84→Asn |
| 47 | 2014 Dec 3 | M | Urethral swab | Wild-type | – | Asp-84→Asn |
| 48 | 2014 Dec 4 | M | Urine | A2059G | – | – |

*A2058/A2059G indicates a macrolide–resistant (A2058G or A2059G) genotype. Positions in the 23S rRNA and in GyrA and ParC are identified according to *Escherichia coli* numbering. NA, not available; –, no amino acid change.

previously reported; however, mutations at the next positions (97 in ParC and 95 in GyrA) have been described for *M. genitalium* (*4,7*), and these positions are within the QRDRs, suggesting their involvement in fluoroquinolone resistance. As previously described, *M. genitalium* ParC alterations predominate over GyrA alterations.

None of the 12 patients with strain *par*C or *gyr*A mutations had a history of fluoroquinolone treatment. Six patients received no treatment; 4 patients received azithromycin (1 g); 2 patients received extended azithromycin (1.5 g), 1 patient after azithromycin (1 g) failure, and 1 after receiving doxycycline for 7 days. Therapeutic outcomes were not available except for 1 patient, who experienced clinical failure after 2 azithromycin treatments.

Regarding macrolide resistance, 38 of 221 patients (17.20%; 95% CI 12.79%–22.72%) had *M. genitalium* with macrolide resistance–associated 23S rRNA mutations; prevalence was 17% (19/112) for 2013 and 17.4% (19/109)

for 2014. This prevalence is increasing compared to that described in France in 2012 (14%). We found 35 A→G substitutions at position 2058 or 2059, two A2062T mutations and one A2059C mutation (Table) (*1*,*9*). Notably, in patients 15 and 33, who were infected with strains with macrolide resistance–associated mutations, *M. genitalium* infection was unsuccessfully treated with azithromycin, with treatment failures after azithromycin (1 g) and extended azithromycin (1.5 g for 5 d), but moxifloxacin treatment was effective. Patient 15 had been treated 1 year earlier with azithromycin (1 g) for nongonococcal urethritis.

Among the 168 patients whose isolates were examined for the 23S rRNA, *gyr*A, and *par*C genes, strains from 2 patients (patients 3 and 6) had both macrolide- and fluoroquinolone-associated mutations (1.2%; 95% CI 0.33%–4.24%). Both patients received azithromycin (1 g), and patient 6 received additional azithromycin (1.5 g) after failure of azithromycin (1 g). Patient 6 experienced azithromycin failure again after the extended regimen. *M. genitalium* multidrug resistance is described in France at a prevalence of 1.2%, lower than prevalence described in Australia (7.5%) (*7*) and Japan (30.8%) (*10*).

In conclusion, *M. genitalium* fluoroquinolone resistance is emerging in France, with a prevalence of 6% in 2013–2014. Further, macrolide resistance also increased during this period, to a rate of 17.2%. Patients infected with *M. genitalium* strains containing both macrolide and fluoroquinolone resistance mutations associated with therapeutic failure raise concerns about untreatable *M. genitalium* infections.

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# Possible Transmission of *mcr-1*–Harboring *Escherichia coli* between Companion Animals and Human

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**To the Editor:** Plasmid-mediated, colistin-resistance mechanism gene *mcr-1* was first identified in *Escherichia coli* isolates from food, food animals, and human patients in November 2015 (*1*). Reports on detection of *mcr-1* in *Enterobacteriaceae* from humans and food animals