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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 *gyrA* and *parC* 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 *gyrA* and *parC* 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 *gyrA* and *parC* genes, specimens from 221 patients were investigated for macrolide resistance, and specimens from 168 patients were examined for 23S rRNA, *gyrA*, and *parC* 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 in the 23S rRNA gene in *Mycoplasma genitalium*, France, 2013–2014\*

Patient no.	Date of collection	Patient		Mutation in the 23S rRNA gene	Amino acid changes in	
		sex	Specimen type		GyrA	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 *parC* or *gyrA* 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, *gyrA*, and *parC* 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