

Subject: Detection of ceftriaxone-resistant gonococcal (*Neisseria gonorrhoeae*) infections (MDR and XDR) in France and identification of clusters in 2025–2026, highlighting the risk of spread in Europe

The French national reference Centre for STI and its associated laboratory for *Neisseria gonorrhoeae* (NG) expertise (Saint-Louis Hospital), in collaboration with Santé publique France, notify the STI network of an increasing number of MDR/XDR NG infections detected in France as well as the identification of clusters during 2025-2026.

In France, sporadic cases of ceftriaxone-resistant MDR or XDR gonococcal infections had previously been reported (one in 2019, two in 2022, four in 2023 including a two cases cluster, and one in 2024), but the recent rise in detections suggests a shift towards more sustained circulation.

Since January 2025, 16 ceftriaxone-resistant NG strains, classified as MDR (n=11) or XDR (n=5), have been identified in France (F98, F100 to F114).

Cases involved 10 men, 5 women, and 1 transgender man. When sexual orientation was known, most cases occurred in heterosexual individuals (12/13), indicating spread beyond traditionally higher-risk groups. Infections were predominantly genital (9 urethritis, 6 vaginitis), with one extra-genital manifestation (finger arthritis). Geographical distribution showed a concentration of cases in the Île-de-France region (7 cases), with additional cases across several regions, suggesting multiple introduction events.

All strains showed resistance to ceftriaxone, mainly associated with the mosaic *penA-60.001* allele or related variants, known to confer reduced susceptibility to extended-spectrum cephalosporins [6]. All were also resistant to fluoroquinolones (mutations in *gyrA* and *parC*). XDR strains additionally exhibited high-level resistance to azithromycin (23S rRNA mutations), further limiting treatment options.

Genomic analysis identified three clusters:

- **Cluster 1 (September 2025, Île-de-France):** three cases (ST1903, NG-STAR CC233) with a fourth PCR positive case epidemiologically linked (contact of another case). Investigation identified an index case imported from Asia, followed by secondary local transmission.

- **Cluster 2 (2026, Occitanie / Pyrénées-Orientales):** two closely related XDR strains (MLST 16406) with high-level resistance to azithromycin, tetracycline, and fluoroquinolones.
- **Cluster 3 (2026, Ile de France):** two MDR strains (MLST 7365) with fluoroquinolone resistance.

Investigations for clusters 2 and 3 are ongoing. The identification of multiple independent clusters within a short timeframe suggests that resistant strains are not only being imported, but may also be establishing local transmission networks.

Non-clustered strains were genetically diverse, reflecting multiple acquisition sources. Reported exposures included travel to (or sexual contact with someone who traveled to) Southeast Asia, as well as within Europe (Spain, Germany, England) and North Africa (Tunisia), highlighting the role of international mobility in the spread of resistant NG strains and the risk of dissemination within European sexual networks.

These findings confirm the circulation of ceftriaxone-resistant NG in France, including documented local transmission and the emergence of distinct clusters. Importantly, they underscore a growing risk for Europe: the establishment and spread of MDR/XDR NG clones could compromise the effectiveness of current first-line treatments and lead to more frequent treatment failures.

In this context, actions already underway—or planned at this stage—in France include raising awareness among CeGIDD (free STI clinics) and infectious disease specialists, conducting surveys among laboratories, and promoting systematic culture with antimicrobial susceptibility testing. Reinforced STI prevention and test-of-cure strategies for XDR and MDR strains remain critical.

Tree scale: 0.1

A2059G, S91F, Tet(M)		β-lactamase TEM variant	
☐	Absent	☒	TEM-1
☒	Present	☒	TEM-135
		☐	Absent

