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Introduction

Antimicrobial resistance in *Neisseria gonorrhoeae* (NG) is a global public health concern [1]. In France, the annual ENGON program has been implemented to monitor gonococcal resistance at the national level. The program involves collecting metadata (e.g., demographic, epidemiological, and clinical data) from individuals, as well as the phenotypic and genotypic characterization of isolates. NG isolates were collected from voluntary public and private laboratories during the period from September to December each year, from 2018 to 2023.

Methods

Each **NG** isolate received by the National Reference Center was confirmed by MALDI-TOF MS. Antimicrobial susceptibility testing was performed using Etest (bioMérieux) for spectinomycin (SPT), gentamicin (GEN), tetracycline (TET), azithromycin (AZI), ciprofloxacin (CIP), cefixime (FIX), and ceftriaxone (CRO), following EUCAST guidelines [2]. Whole-genome sequencing was carried out using Illumina technology and analyzed with an in-house pipeline [3]. Ceftriaxone-resistant isolates (n=6) identified outside of the survey periods were included in the calculation.

Results

Patient characteristics from ENGON

A total of 2,966 NG isolates were sent by 112 laboratories from 2018 to 2023. NG was mostly isolated in males (80%), with a the median age of 28 years. Most isolates were obtained from urogenital samples (86%). All patient characteristics are presented in the Table 1.

Table 1 – Characteristics of gonorrhea Patients in France from 2018 to 2023

	2018 No. (%)	2019 No. (%)	2020 No. (%)	2021 No. (%)	2022 No. (%)	2023 No. (%)
Number of isolates	158	375	423	803	551	656
Sex						
Male	123 (78.3)	308 (82.1)	334 (79.0)	647 (80.7)	415 (75.5)	552 (84.5)
Female	34 (21.7)	66 (17.6)	84 (19.9)	155 (19.3)	134 (24.4)	101 (15.5)
Transexual	0 (0.0)	1 (0.3)	5 (1.2)	0 (0.0)	1 (0.2)	0 (0.0)
Not reported	1	0	0	1	1	3
Age (years)						
<25	58 (36.9)	124 (33.3)	158 (37.4)	306 (38.2)	198 (36.1)	209 (32.0)
≥25	99 (63.1)	248 (66.7)	265 (62.6)	495 (61.8)	351 (63.9)	444 (68.0)
Not reported	1	3	0	2	2	3
Sex and sexual orientation						
Females	34 (51.5)	66 (35.9)	84 (39.6)	155 (57.6)	134 (54.9)	101 (49.8)
Heterosexual males	3 (4.5)	21 (11.4)	21 (9.9)	42 (15.6)	38 (15.6)	32 (15.8)
MSM	28 (42.5)	92 (50.0)	96 (45.3)	67 (24.9)	61 (25.0)	66 (32.5)
Bisexual males	1 (1.5)	4 (2.2)	6 (2.8)	5 (1.9)	10 (4.1)	4 (2.0)
Transexual	0 (0.0)	1 (0.5)	5 (2.4)	0 (0.0)	1 (0.4)	0 (0.0)
Not reported	92	191	211	534	307	453
Site of infection						
Urogenital	110 (71.0)	287 (76.5)	360 (85.7)	729 (91.1)	487 (88.9)	566 (86.8)
Oropharyngeal	1 (0.6)	14 (3.7)	4 (1.0)	5 (0.6)	6 (1.1)	8 (1.2)
Anorectal	42 (27.1)	66 (17.6)	47 (11.2)	60 (7.5)	39 (7.1)	65 (10.0)
Other	2 (1.3)	8 (2.1)	9 (2.1)	6 (0.8)	16 (2.9)	13 (2.0)
Not reported	3	0	3	3	3	4
HIV status						
Negative	75 (87.2)	191 (88.0)	267 (91.1)	432 (93.9)	312 (93.4)	376 (92.2)
Positive	11 (12.8)	26 (12.0)	26 (8.9)	28 (6.1)	22 (6.6)	32 (7.8)
Not reported	72	158	130	343	217	248
Region						
Paris area	64 (40.5)	122 (32.5)	144 (34.0)	255 (31.8)	235 (42.6)	244 (37.2)
North-East	19 (12.0)	30 (8.0)	43 (10.2)	108 (13.4)	59 (10.7)	91 (13.9)
North-West	14 (8.9)	45 (12.0)	41 (9.7)	114 (14.2)	82 (14.9)	113 (17.2)
South-East	26 (16.5)	122 (32.5)	101 (23.9)	163 (20.3)	121 (22.0)	133 (20.3)
South-West	35 (22.2)	55 (14.7)	94 (22.2)	150 (18.7)	54 (9.8)	74 (11.3)
Overseas area	0 (0.0)	1 (0.3)	0 (0.0)	13 (1.6)	0 (0.0)	1 (0.2)

MSM: Men who have sex with men

Antimicrobial resistance of isolates from ENGON

Eight percent of the isolates were susceptible to all of the tested antibiotics, ranging from 7.5% in 2023 to 13.9% in 2018. All isolates were susceptible to SPT and GEN. The most frequent phenotype was TET and CIP resistance combined with AZI, FIX, and CRO susceptibility. Figure 1 presents the resistance rates.

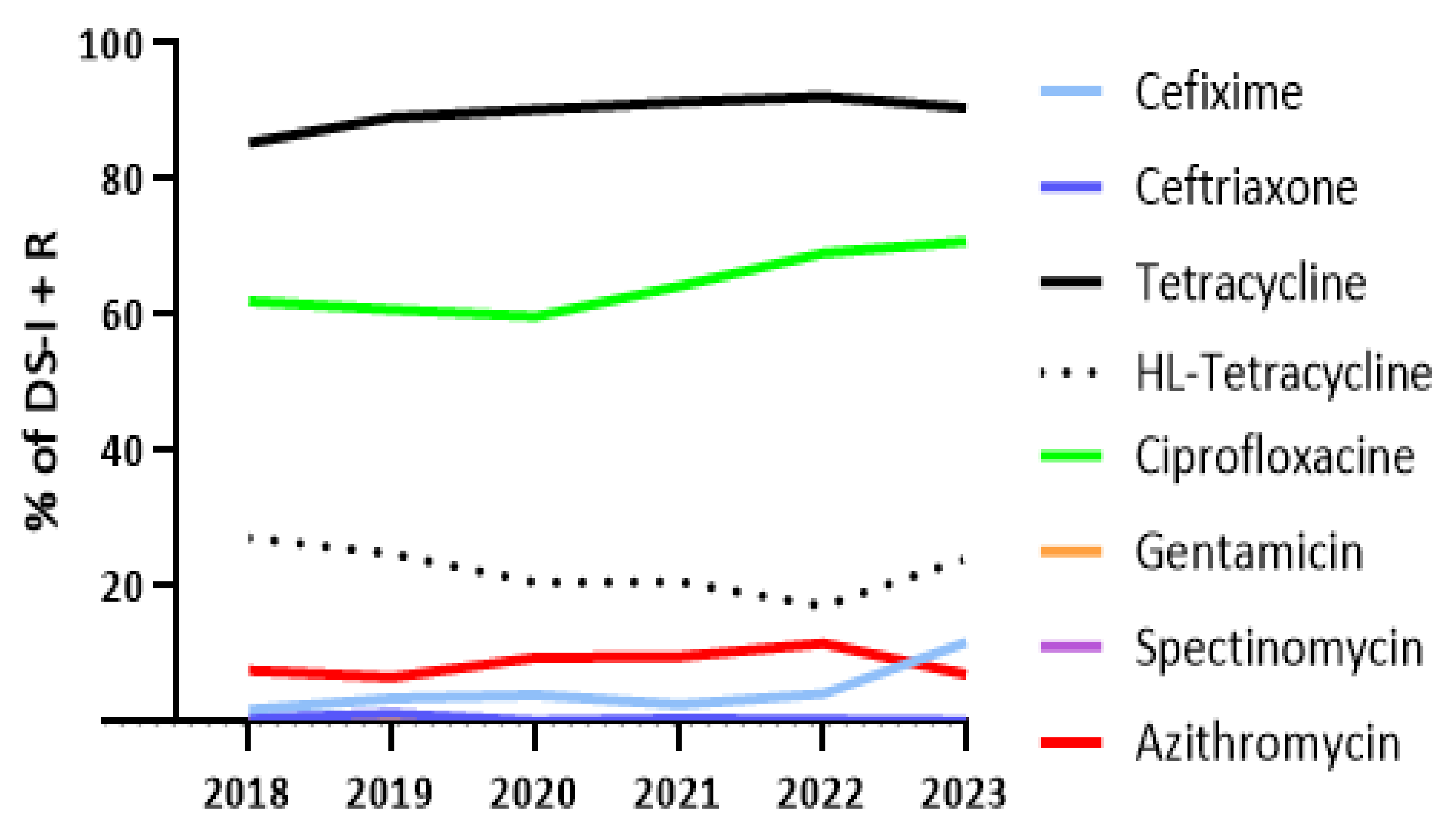


Figure 1 – Proportion (%) of resistant and decreased susceptibility/intermediate isolates by antimicrobial and year from 2018-2023. This graph includes all ENGON and CRO-resistant isolates collected each year. Decreased susceptibility corresponds to a FIX MIC between 0.032 mg/L and 0.125 mg/L. HL: high level of resistance

Genomic characterization of ENGON Isolates

Most resistance to tetracycline was due to the V57M mutation in RpsJ (88%), followed by the acquisition of the **tet(M)** gene (22%). A mutation in **the** 23S rRNA was observed in 2% of NG. The most frequent GyrA and ParC mutations were S91F+D95A (60%) and S87R (37%), respectively (**Escherichia coli numbering** ?). Mosaic *penA* was identified in 9% of the isolates, **increasing** consistently year after year, from 1% in 2018 to 23% in 2023 (p < 0.001). The most common NG-MLST types were ST9362 (10%), followed by ST11706 (8%) and ST7822 (8%). Mosaic *penA* alleles were identified in 20 different STs, including five STs (ST1580, ST7363, ST8123, ST9362, and ST16676), which represented 82% of the isolates. Notably, ST1580 and ST16676 represented 72% (36% each) of all NG isolates with mosaic *penA* in 2023, whereas ST16676 had not been detected prior to this year.

Conclusion

A concerning rise in NG strains with diminished susceptibility to FIX was noted in France in 2023. This increase is associated with the presence of ST16667 and ST1580 clones that carry a mosaic *penA34* allele. Surveillance of decreased susceptibility to cefixime in NG strains in France and other European countries is needed to better understand this rapid shift in the gonococcal population.

[1] Sati et al., The WHO Bacterial Priority Pathogens List 2024: a prioritisation study to guide research, development, and public health strategies against antimicrobial resistance. Lancet Infect Dis, 2025, 11:S1473-3099(25)00118-5. [2] EUCAST. Clinical breakpoints and dosing of antibiotics. 2024. [3] Caméléna et al., Emergence of Extensively Drug-Resistant *Neisseria gonorrhoeae*, France, 2023. Emerg Infect Dis, 2024, 30(9):1903-1906