Unexpected increase in *ompA*-genotype L1 variants responsible for anorectal lymphogranuloma venereum in France

Investigations into circulating *Chlamydia trachomatis* genotypes are useful to elucidate the dynamics and evolution of lymphogranuloma venereum. *ompA*-genotype L2b was the causative agent of the first cases of rectal lymphogranuloma venereum in Europe in 2003, which then spread globally.[1] Since 2013, the evolution of the ongoing lymphogranuloma venereum epidemic has been marked by a shift to *ompA*-genotype L2 and emergence of *ompA*-genotype L2 and L2b variants.[2]

In France, the diversity of *ompA*-genotypes responsible for lymphogranuloma venereum is monitored by sequencing the *ompA* gene from all lymphogranuloma venereum-positive rectal samples collected as part of a 3-month prospective nationwide survey with universal lymphogranuloma venereum screening.[3] This surveillance was initiated in 2020 and has been conducted every year by the National Reference Center for Bacterial Sexually Transmitted Infections, Bordeaux, France.

Collection and analysis of 652 anorectal lymphogranuloma venereum-positive specimens between 2020 and 2024 indicated a significant decrease in the *ompA*-genotype L2 ($p<0·0001$) and disappearance of the *ompA*-genotype L2b variant (appendix p 1). In contrast, the proportions of the *ompA*-genotype L1 variants increased markedly: two (1·5%) of 137 in 2020, two (1·6%) of 128 in 2021, 12 (8·9%) of 135 in 2022, 15 (15·3%) of 98 in 2023, and 40 (26%) of 154 in 2024.

We identified three *ompA*-genotype L1 variants that differed from the L1/440 reference strain. The first, GenBank accession number MN563611.1, differed by ten mutations and was the most frequent (58 [81·7%] of 71 samples). The first variant was identified in two samples in 2020 and 2021 each, 12 samples in 2022, 14 samples in 2023, and 28 samples in 2024. The second, PQ151388, differed by 11 mutations and was detected in one sample in 2023 and 11 samples in 2024. The third, PQ1656811, differed by 12 mutations and was identified in one sample in 2024. All the *ompA*-genotype L1 variants identified in our study had the characteristic nine-bp insertion in the *pmpH* gene of variant L2b,[2] suggesting recombination between the genomes of lymphogranuloma venereum strains. The L1 variants were not geographically clustered and were distributed throughout France. No associations were found between the L1 variants and anorectal symptoms, HIV status, or pre-exposure prophylaxis use.

Lymphogranuloma venereum cases with the *ompA*-genotype L1 variant (GenBank GQ413956) were first described in the 1980s among men who have sex with men.[4] This strain did not spread further during the lymphogranuloma venereum outbreak. *OmpA*-genotype L1 variants were sporadically reported in Europe since 2014.[2] Conversely, *ompA*-genotype L1 variants accounted for 27 (31%) of 88 of the lymphogranuloma venereum cases in Argentina from 2017 to 2019.[5]

In conclusion, our results highlight the unique genotype distribution of lymphogranuloma venereum in France in 2024, which is characterised by the presence of *ompA*-genotype L1 variants in about a quarter of the cases. The occurrence of ompA-genotype L1 variants is unprecedented among lymphogranuloma venereum cases in Europe and reflects changes in the operating sexual networks of men who have sex with men and distinct migration or travel patterns.

We declare no competing interests. This work did not receive any funding. CB and OP designed the study. CL-N collected the demographic, clinical, and biological data. AT sequenced the *ompA* and *pmpH* genes. CL-N, AT, and OP analysed the data. AT and OP prepared the first draft of the manuscript. All authors reviewed and approved the final version of the manuscript. We would like to thank all clinicians and biologists who participated in the lymphogranuloma venereum surveillance network. The French national sentinel surveillance for anorectal *Chlamydia trachomatis* infections was approved by the French Data Protection Authority, Commission Nationale de l'Informatique et des Libertés (approval number 10.362), and data were collected after written informed consent was obtained from the affected patients.

*Arabella Touati, Cécile Laurier-Nadalié, Cécile Bébéar, *Olivia Peuchant*
olivia.peuchant@u-bordeaux.fr

Centre Hospitalier Universitaire de Bordeaux, Department of Bacteriology, National Reference Centre for Bacterial Sexually Transmitted Infections, Bordeaux 33000, France (AT, CL-N, CB, OP); University of Bordeaux, UMR 5334 CNRS Microbiologie Fondamentale et Pathogénicité, Antimicrobial Resistance in MYcoplasmal and gram-NEgative bacteria (ARMYNE), Bordeaux, France (CB, OP)

1 Harris SR, Clarke IN, Seth-Smith HM, et al. Whole-genome analysis of diverse *Chlamydia trachomatis* strains identifies phylogenetic relationships masked by current clinical typing. *Nat Genet* 2012; **44:** 413–19.
2 Seth-Smith HMB, Bénard A, Bruisten SM, et al. Ongoing evolution of *Chlamydia trachomatis* lymphogranuloma venereum: exploring the genomic diversity of circulating strains. *Microb Genom* 2021; **7:** 000599.
3 Peuchant O, Laurier-Nadalié C, Albucher L, et al. Anorectal lymphogranuloma venereum among men who have sex with men: a 3-year nationwide survey, France, 2020 to 2022. *Euro Surveill* 2024; **29:** 2300520.
4 Christerson L, de Vries HJ, de Barbeyrac B, et al. Typing of lymphogranuloma venereum *Chlamydia trachomatis* strains. *Emerg Infect Dis* 2010; **16:** 1777–79.
5 Büttner KA, Entrocassi AC, Gallo Vaulet ML, et al. *ompA* sequencing and multilocus sequence typing of lymphogranuloma venereum cases in Buenos Aires reveal new *Chlamydia trachomatis* genotypes. *Microorganisms* 2024; **12:** 587.

Lancet Microbe 2025; 6: 101097
Published Online February 25, 2025
https://doi.org/10.1016/j.lanmic.2025.101097

See online for appendix