Molecular dynamics of commensal Neisseria species in the human oropharynx in response to antibiotic treatment.

Vellema, SEH[1], Lucchesi, M[1]; Hoebe, CJPA[1][2][3]; Savelkoul, PHM[1]; Wolffs, PFG[1]

1. Department of Medical Microbiology, Infectious Diseases and Infection Prevention, Care and Public Health Research Institute (CAPHRI), Maastricht University Medical Centre (MUMC+), Maastricht, the Netherlands.
2. Department of Sexual Health, Infectious Diseases and Environmental Health, Living Lab Public Health, South Limburg Public Health Service, Heerlen, the Netherlands.
3. Department of Social Medicine, Care and Public Health Research Institute (CAPHRI), Maastricht University, the Netherlands

KEY MESSAGE

- ***Neisseria gonorrhoeae*** **forms antimicrobial resistance through DNA exchange with commensal Neisseria species**
- **Our study finds *Neisseria subflava* to be highly abundant in the oropharynx compared to other commensal Neisseria species and may thus form a more readily accessible reservoir for antimicrobial resistance formation in *Neisseria gonorrhoeae***

Objective

Evaluating the composition of commensal Neisseria communities in the human oropharynx and changes after antibiotic treatment.

Introduction

- Ceftriaxone-resistant *Neisseria gonorrhoeae* poses a threat to successful first-line empirical treatment of gonorrhoeae [1]
- Ceftriaxone resistance is partially conferred through mosaic penA alleles, formed through transformation of DNA from commensal Neisseria species colonizing the oropharynx, visualized in figure 1 [2]
- These commensals themselves may exhibit high-level ceftriaxone resistance and may engage in co-operative or antagonistic interactions with *N. gonorrhoeae*.[3]

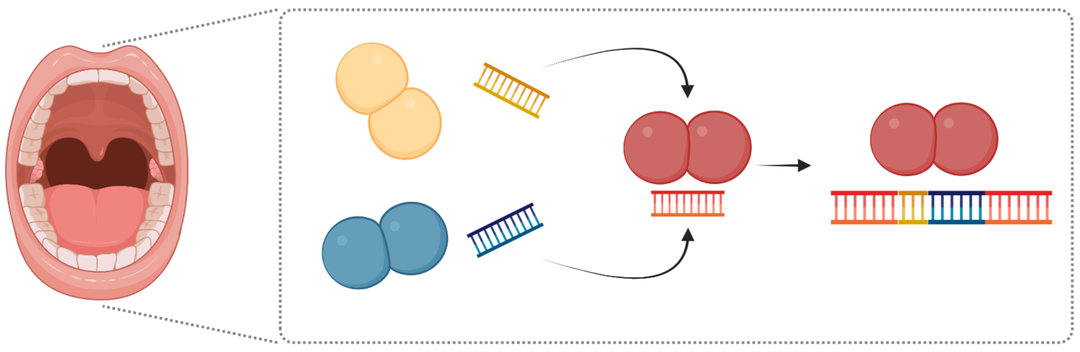

Figure 1. Formation of mosaic penA alleles through DNA transformation by N. gonorrhoeae

Methods

- 96 oropharyngeal swabs were selected from follow-up consultations of 10 patients who visited our STI clinic between 2019 and 2021
- Selection was based on high testing frequency and intermittent positivity for N. gonorrhoeae
- Commensal Neisseria species identification was performed through targeted metagenomic sequencing of penA alleles and species-specific flanking regions using Nanopore sequencing
- Patients were treated with ceftriaxone 500mg IM according to national guidelines when testing positive for N. gonorrhoeae

Results

- The mean relative abundance across all samples was highest for *Neisseria subflava* at 97,8% (see figures 2 and 3)
- Other commensal Neisseria species varied in mean relative abundance from 0,02 to 1,13%
- The relative abundance of *Neisseria subflava* differed significantly between consultations before and after treatment with antibiotics (P-value <0.05), with a mean relative abundance of 98,0% before treatment compared with 85,4% after treatment. See figure 4.
- Relative abundances for other commensal Neisseria species did not significantly differ after treatment.

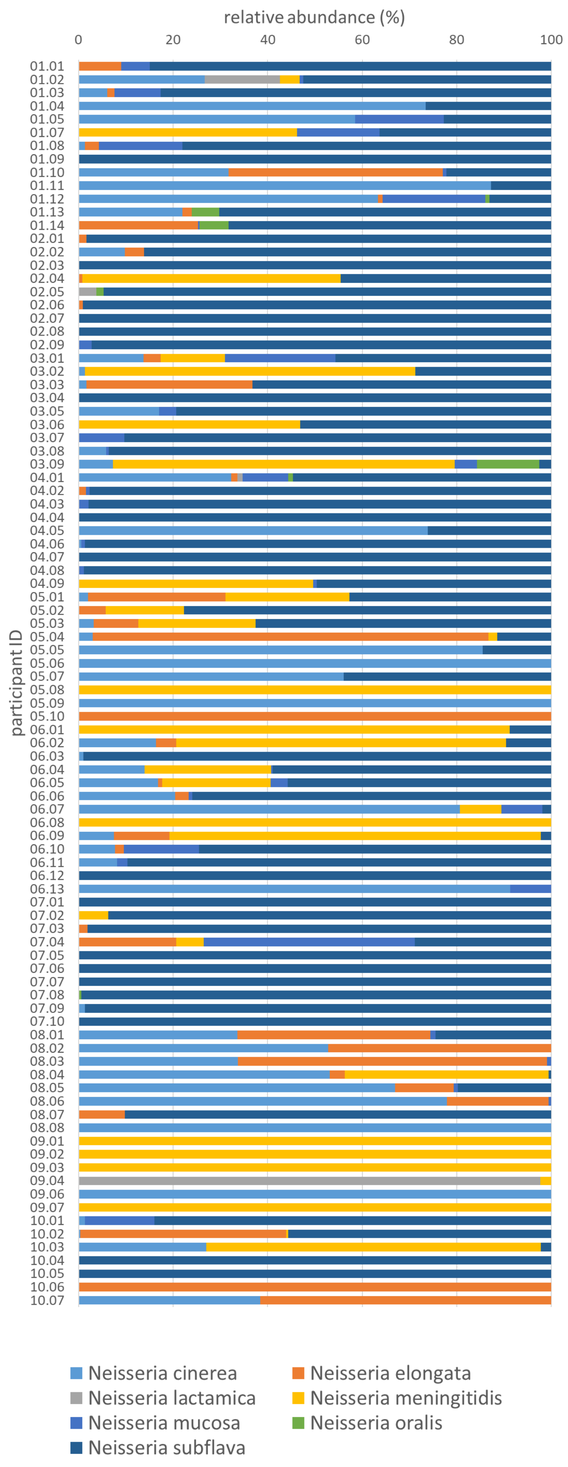

Figure 2. Relative abundances of commensal Neisseria species at participant level

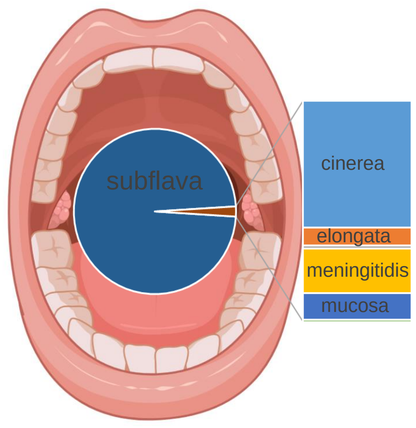

Figure 3. Mean composition of commensal Neisseria species in the oropharynx

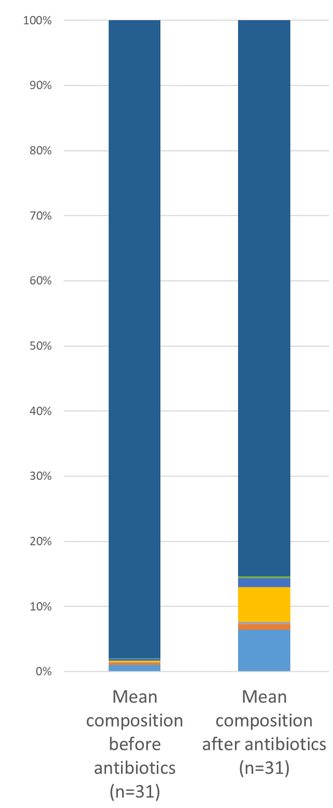

Figure 4. Relative abundances of commensal Neisseria species before and after antibiotic treatment

Conclusion

- *Neisseria subflava* is highly abundant in the oropharynx compared to other commensal Neisseria species and may thus form a more readily accessible reservoir for AMR.
- Furthermore, *Neisseria subflava* decreased in relative abundance after treatment, suggesting that many strains remain susceptible to ceftriaxone despite reported intrinsic resistance.

References

1. Unemo, M., & Shafer, W. M. (2014). Antimicrobial resistance in Neisseria gonorrhoeae in the 21st century: past, evolution, and future. Clin Microbiol Rev, 27(3), 587-613.
2. Ameyama, S., Onodera, S., Takahata, M., Minami, S., Maki, N., Endo, K., Goto, H., Suzuki, H., & Oishi, Y. (2002). Mosaic-like structure of penicillin-binding protein 2 Gene (penA) in clinical isolates of Neisseria gonorrhoeae with reduced susceptibility to cefixime. Antimicrob Agents Chemother, 46(12), 3744-3749.
3. Baerentsen, R., Tang, C. M., & Exley, R. M. (2022). Et tu, Neisseria? Conflicts of Interest Between Neisseria Species. Front Cell Infect Microbiol, 12, 913292.

Correspondence to
Sem Vellema

Department of Medical Microbiology, Infectious Diseases, and Infection prevention, MUMC, Maastricht

Email
sem.vellema@maastrichtuniversity.nl

Telephone
+31 43 387 6644