Prof. Jacques Schrenzel
Laboratoire de bactériologie
Laboratoire de recherche génomique
Service des maladies infectieuses
Département de médecine
Service de médecine de laboratoire
Département diagnostique
Hôpitaux Universitaires de Genève
Rue Gabrielle-Perret-Gentil 4
CH-1211 Genève 14
web www.genomic.ch
Tél. (4122) 372 73 08
Fax (4122) 372 73 12
Courriel Jacques.Schrenzel@hcuge.ch

Annual Report of the Swiss National Reference Center for Meningococci, 2023

Address

National Reference Center for Meningococci

Hôpitaux Universitaires de Genève

Laboratoire de Bactériologie

Rue Gabrielle-Perret-Gentil 4

1211 Genève 14

Phone: (022) 372 73 01; Fax: (022) 372 73 12; Jacques.Schrenzel@hcuge.ch

Website: French: http://www.meningo.ch/

Website: German: http://www.meningo.ch/index_DE.html

Website: Italian: http://www.meningo.ch/index_IT.html

Website: English: http://www.meningo.ch/index_EN.html

Table of Content

Hôpitaux Universitaires de Genève Rue Gabrielle-Perret-Gentil 4 CH-1211 Genève 14
Tél. 022 372 73 01 Fax 022 372 73 12 E mail: jacques.schrenzel@hcuge.ch Internet : www.hug-ge.ch

1. Introduction

Neisseria meningitidis is a typical benign colonizer of the healty human nasopharynx, but it can also cause invasive meningococcal disease (IMD). Colonized people spread the bacteria to others by respiratory secretions (e.g., saliva droplets) [1]. When the conditions are met in at risk-people, the transmitted bacteria invade the body and cause different types of illnesses. The most commun clinical picture is meningitis and sepsis [2]. Invasive meningococcal infection is an overwhelming disease that is leading to substantial mortality and morbidity [3]. The case fatality rate of *N. meningitidis* is about 7% in high income countries. However, in low income countries, the fatality rate can reach up to 50% [1]. Developmental disorders, and hearing loss remain among the major neurological sequelae observed in the survivors of the disease [2]. Owing to rapid onset of IMD and the related risk of serious morbidity and mortality, accurate and early diagnosis of the disease coupled to the administration of appropriate treatment are major elements of an adequate patient's management [4]. Additionally, prompt identification of close contacts and post-exposure prophylaxis contribute to prevent secondary cases. The increasing antimicrobial resistance of important human pathogenic bacteria remains a key public health concern. Steady increase of multidrug-resistant *Neisseria gonorrhoeae* isolates represent one of the important threats worldwide [5]. In contrast, *N. meningitidis* seems spared of antibiotic resistance. Nevertheless, since the 1980s *N. meningitidis* isolates exhibiting decrease susceptibility to penicillin were reported in different countries [6]. Nowadays, penicillin-resistant *N. meningitidis* strains are widely reported across the world [7]. The important mechanisms related to penicillin resistance are changes in five critical residues of PBP2 (F504L, A510V, I515V, H541N, and I566V) conferred by mutations in the *penA* gene [8]. Penicillin-resistant strains with high minimal inhibitory concentration (MIC >2 mg/mL) were rarely described. This high penicillin MIC is achieved by chromosomal or plasmid-mediated β-lactamase which is derived from the *Haemophilus influenzae* ROB-1 β-lactamase [9].

N. meningitidis is categorized into 12 defined serogroups, and the major part of invasive meningococcal disease (IMD) cases worldwide are caused by six serogroups: A, B, C, W, X, and Y [10].

Invasive strains of *N. meningitidis* can cause outbreaks and therefore require a continuous surveillance, especially nowadays with the spread of a hypervirulent serogroup W clone in Europe [11]. Also, sporadic cases may occur in any age group and

every effort must be undertaken to optimize the prevention, diagnosis and treatment of such infections.

The last decade has witnessed considerable changes in the epidemiology of invasive meningococcal infections in Europe and Switzerland with the increase in the prevalence of Y and W serogroups. Arthritis, pharyngitis, and pneumonia represent some of the atypical clinical manifestations related to these serogroups.

In Switzerland, invasive meningococcal diseases have to be reported to the Swiss Federal Office of Public Health (SFOPH), and corresponding isolates should be referred to the Swiss National Reference Center for Meningococci (CNM, Centre National des Méningocoques; http://www.meningo.ch) at the University Hospital in Geneva.

The CNM provides reference testing of invasive *N. meningitidis* isolates in collaboration with the SFOPH, and currently performs serotyping and molecular typing following protocols recommended by the European Meningococcal Disease Society (EMGM) (http://emgm.eu). Based on a combination of serogroup and molecular typing data, each strain is classified and data are integrated into national (SFOPH) and international epidemiological databases (European Meningococcal Epidemiology in Real Time [EMERT] database; http://emgm.eu/emert) in order to monitor and share information about trends in meningococcal populations. This methodology is evolving towards Next Generation Sequencing (NGS) [12], a method that we used for a selection of cases collected between 2010 and 2016, to determine the clonality of the meningococcal strains of serogroup W finetype (PorA 5,2:FetA 1-1:ST-11). This was executed as a separate subproject supported by the SFOPH (Decision 16.928412). This annual report describes the methods used and results obtained at the CNM during the calendar year 2023.

2. Materials and Methods

The CNM is investigating invasive isolates of *N. meningitidis* as well as native clinical specimens derived from normally sterile body sites.

Isolates are sub-cultured overnight on chocolate agar plates. The identification is confirmed by PCR using the *N. meningitidis*-specific targets *ctrA*, *sodC*, *tauE, metA*, and *shlA*. Serogroups are assessed by PCR as well as by commercial agglutination kits: A, B and C (Pastorex Meningitis, Bio-Rad) and W135, X, Y, Z and Z' (Difco Neisseria Meningitidis Antisera, Becton Dickinson).

Sequence analysis is performed on each isolate in two variable regions of the gene encoding the antigenic outer membrane protein porin A (*porA*-VR1 and *porA*-VR2) and in one variable region of the *fetA* gene (*fetA*-VR) encoding another outer membrane protein exhibiting sequence data which can be useful for tracing clones emerging or circulating in local populations (World Health Organization Manual – Laboratory Methods for the Diagnosis of Meningitis caused by *Neisseria meningitidis*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*).

In addition, multilocus sequence typing (MLST) is carried out on each isolate according to protocols recommended by the EMGM (http://emgm.eu). This approach is targeting variable regions of seven house-keeping genes (*abcZ*, encoding a putative ABC transporter; *adk*, adenylate kinase; *aroE*, shikimate dehydrogenase; *fumC*, fumurate dehydrogenase; *gdh*, glucose-6-phosphate dehydrogenase; *pdhC*, pyruvate dehydrogenase subunit, and *pgm*, phophoglucomutase). Each isolate is classified according to its multilocus genotype designated as a sequence type (ST), which is the combination of its alleles over the seven genetic loci tested. STs can be further grouped into clonal complexes (CC), which are defined in the *Neisseria* MLST profile database as groups of STs that share at least four of the seven loci in common with a central ST (http://pubmlst.org/neisseria/).

Isolates are then classified based on a combination of serotyping and molecular typing data according to the following scheme:

Serogroup : *porA*-VR1, *porA*-VR2 : *fetA*-VR : MLST (ST or CC).

The antimicrobial susceptibility testing is performed for each isolate using Mueller-Hinton agar + 5% defibrinated horse blood and 20 mg/L β-NAD (MH-F, bioMérieux). Minimum inhibitory concentrations (MICs) are measured for penicillin, ceftriaxone, meropenem, ciprofloxacin, minocycline and rifampicin by E-test strips (AB Biodisk, bioMérieux). The MICs are interpreted according to the current breakpoints recommended by the European Committee on Antimicrobial Susceptibility Testing (EUCAST, www.eucast.org).

In case of no growth of the strain, clinical specimens are analyzed by qPCR to screen for *N. meningitidis* DNA , and if present, we assess the occurrence of the main serogroups by amplifying their corresponding genetic targets. Nucleic acid extraction from clinical specimens such as cerebrospinal fluid and EDTA blood is performed using the MagPurix 12 Nucleic Acid Extraction System (Zinexts Life science; Taiwan). DNA is amplified by real-time PCR to screen for the presence of the *N. meningitidis*-specific targets described above (panel has been completed based on Diene et al, 2016). PCR assays targeting the polysialyltransferase (*siaD*) gene are performed to assign *N. meningitidis*-positive specimens to serogroups B, C and Y/W135; assignment to serogroup A is achieved by qPCR targeting the *sacC* gene. Finally, differentiation between serogroups Y and W135 is asessed by amplification of the *synF* gene (Y) and *synG* gene (W135) [13].

3. Strain collection

The CNM stores all the received invasive meningococcal isolates at -80°C. The collection currently includes more than 500 isolates (between 2009 and 2023). Previous strains were also stored but their recovery by culture cannot be guaranteed (n=1’914 isolates between 1989 and 2009).

4. National and International quality assurance

There is currently no international quality assurance pertaining to meningococci. We are actively scouting whether this service would become available.

5. Epidemiological research

The precision of NGS permitted us to identify several independent monoclonal outbreaks related to *N. meningitidis* W135 that occurred between 2010 and 2016 in Switzerland. Our meta-analyses included samples from other previously published works and allowed establishing connections between Swiss MenWs and other European outbreaks as published recently in the Journal of Infection [14]. This project was made possible through a specific grant from SFOPH (Decision 16.928412).

We have analyzed the molecular epidemiology of *N. meningitidis* W135 (NmW) between 2017 and 2018 in Switzerland. In this period, we reported the circulation of three main NmW lineages: the Hajj-related, South American and ST-9316. While the first two lineages are part of the same clonal complex 11 and were already present in Switzerland, ST-9316 was new and emerged in 2018 in the canton of Vaud.

We highlighted that the distribution of cc11 lineages is quite heterogenous without a precise geographical localization. We identified several outbreaks that occurred in 2017-2018 due to cc11 lineages. In particular, we observed that some of these outbreaks were sub-variants of already circulating strains. Monitoring the current situation by WGS is strongly recommended as the heterogeneity of circulating lineages detected so far can favor the evolution and emergence of new strains.

Acoording to our analyses, the WGS represents the only technique that can allow to capture a detailed epidemiological picture, nation-wide, of a complex species like *Neisseria meningitidis*.

6. Additional meningococcal research

We published recently two papers to inform clinicians on false negative results when facing very high leucocyte counts in the CSF (De Lorenzi-Tognon et *al*) and about a mixed serogroup W/Y invasive strain (Mauffray et *al*)

M. DE LORENZI-TOGNON, V. LAZAREVIC, N. GAIA, C. CHAABANE, A. CHERKAOUI, M. SCHIBLER, G. RENZI and J. SCHRENZEL: Acute bacterial meningitis due to *Neisseria meningitidis* serotype B missed by a multiplexed PCR panel. Clin Microbiol Infect 2023. 29(12):1613-1615. IF 5.292

F. MAUFFRAY, N. GAIA, C. CHAABANE, G. RENZI, A. FISCHER, A. CHERKAOUI, J. SCHRENZEL, and V. LAZAREVIC: Draft genome sequence of a mixed serogroup W/Y invasive *Neisseria meningitidis* strain. Microbiol Res. Announcements 2023. **12(3):**e0105622.

7. Advisory service and Networking

7.1 Advisory service

Molecular testing:

We systematically conduct molecular assays to define the serogroups using isolates or directly from clinical specimens when the bacterial growth is not possible (or suspicion thereof). As mentioned above, it is likely that the true incidence of invasive *N. meningitidis* infection is missed by rapid empiric therapy (precluding successful cultivation), nor to mention the new clinical presentations related to W135 such as pneumoniae (typically undetected and not referred to the CNM unless presenting with a bacteraemia and thus fulfilling the current definition of invasive infection). Our current molecular approach covers the most frequent serotypes and a result can usually be communicated to the clinicians.

7.2 Networking

We have established contact with the Italian reference center for meningococci to further analyze our peculiar W135 epidemics, in conjunction with their national epidemiology.

7.3 Website

The dedicated website (www.meningo.ch) was fully rebuilt in 2018, and is available in French, German, Italian and English. We are currently updating it to better display the information.

8. Results

8.1. Phenotypic and molecular characterization

During the calendar year 2023, the CNM has received a total of 31 invasive isolates of *N. meningitidis*. These strains were isolated from blood cultures (n=26), cerebrospinal fluid (n=3) joint fluid (n=1), and deep tissue (n=1) (Figure-1).

The Figure-2 depicts the number of *N. meningitidis* strains isolated in 2023 according to gender and serougroups.

Since 2014, the number of invasive meningococci isolated was increasing (Figure 3). However, in 2021 and 2022, the number of invasive *N. menigitidis* isolates was very low compared to previous years. Similar to 2020, this downward trend already observed in 2019 was deeply magnified by the sanitary situation linked to Sars-CoV-2. Invasive meningococcal disease cases in the Switzerland have increased moderately since 2021. We have not yet reached the pre-pandemic levels. In 2023, 34 confirmed IMD cases were reported in Switzerland.

The last decade has however witnessed considerable changes in the epidemiology of invasive meningococcal infections in Switzerland. In 2023 serogroup Y was the most frequently invasive serogroup (13/31; 42%), followed by serogroups B (11/31; 35%) and W (7/31; 23%) (Figure 4 and Figure-5).

Figure-6 depicts the number of *N. meningitidis* strains in 2023 as classified by serogroups and age groups.

Figure-7 shows the distribution of serogroups by geographical regions in 2023. Only two strains were referred from the Italian speaking region.

Molecular characterization using MLST (Tables 1a, 1b, and 1c and Figure 8) revealed that ST23 was the most prevalent sequence type among the 13 serogroup Y strains analyzed in 2023 (8/13, 62%) followed by ST1655 (2/13, 15%). The ST11 was the most prevalent sequence type among the 7 serogroup W strains (4/7, 57%).

8.2. Antimicrobial Susceptibility Testing

Table-2 depicts the antimicrobial susceptibility profiles and the MICs ranges by drugs, with the MIC_{50} and MIC_{90} of the 31 invasive *N. meningitidis* strains referred to the Swiss National Reference Center for meningococci in 2023. Applying EUCAST breakpoints (v12; 2023), all invasive *N. meningitidis* strains tested were susceptible to ceftriaxone, meropenem, and rifampicin.

However, 8 strains (26%, 8/31) exhibited low resistance levels to penicillin (MIC ranged between 0.38 and 0.75 mg/l). The molecular analysis of these strains showed the presence of mutations in the five critical residues of PBP2 (F504L, A510V, I515V, H541N, and I566V). In addition, we identified for the first time one penicillin-resistant strain with a high MIC (16mg/l). This strain was a ROB-1 β-lactamase producer, in the addition to the presence of the five key mutations in the PBP2.

In 2023, we identified for the first time in Switzerland one ciprofloxacin-resistant strain (MIC = 0.25 mg/l). WGS analysis confirmed that the resistance mechanism was based on a *gyrA* T91I mutation. This strain was also resistant to penicillin. Table-3 shows the genetic features of the ciprofloxacin-and penicillin-resistant *Neisseria meningitidis* isolates in 2023. These data will be compiled and published, due to their epidemiological relevance.

Summary of key observations

- Invasive meningococcal disease cases in the Switzerland have increased moderately since 2021. We have not yet reached the pre-pandemic levels. In 2023, 34 confirmed IMD cases were reported in Switzerland. In 2023 serogroup Y was the most frequently isolated (13/31; 42%), followed by serogroups B (11/31; 35%) and W (7/31; 23%)
- ST23 was the most prevalent sequence type among the 13 serogroup Y strains analyzed in 2023 (8/13, 62%) followed by ST1655 (2/13, 15%).
- The ST11 was the most prevalent sequence type among the 7 serogroup W strains (4/7, 57%).
- We noticed the rmergence in 2023 of ciprofloxacin- and high levels penicillin-resistance in invasive *Neisseria meningitidis* isolates
- The first *N. meningitidis* strain producing ROB-1 β-lactamase was identified in Basel. This strain was of serogroup Y, like a strain reported by Hong *et al*. [9] in France in 2018.

9. Discussion

The incidence of IMD in 2023 was 0.38 for 100'000, which corresponds to 34 cases reported to the SFOPH. We have reached the pre-pandemic levels. The incidence in 2023 has exceeded the level recorded in 2020 (0.38 *versus* 0.23 in 2020), and has even doubled when compared to 2022 (0.38 *versus* 0.19 in 2022). While antibiotic resistance is still not a concern in the management of *N. meningitidis* infections, the emergence of ciprofloxacin-and penicillin-resistant *N. meningitidis* strains in Switzerland could represent a potential threat to the management of IMD. In Switzerland two new elements about antibiotic resistance took place in 2023: a) the identification of the first penicillin-resistant strain with a high MIC (16mg/l). This strain was indeed a ROB-1 β-lactamase producer (derived from *Haemophilus influenzae* ROB-1 β-lactamase, in the addition of the presence of the five key mutations in the PBP2 gene; and b) the identification of the first ciprofloxacin-and penicillin-resistant *N. meningitidis* strain.

The first acquisition of ROB-1 β-lactamase by *N. meningitidis* through possible horizontal gene transfer was reported in 2018 by Hong *et al*. [9]. This *N. meningitidis* strain was of serogroup Y. The bla_{ROB-1} gene was on the chromosome and was perfectly identical to the bla_{ROB-1} harbored by the pB1000 in *Haemophilus influenzae* [9].

Recent studies reported a resistance to ciprofloxacin in cc4821 meningococci, which was mediated by a *gyrA* T91I mutation. These strains were mostly identified in China [15]. *N. meningitidis* healthy humain carrier rate in Switzerland is not defined, neither in terms of serogroups, nor in terms of antimicrobial susceptibility. It is probably important to study it better, in relationship with the emergence of those two strains. Chemoprophylaxis for the close contacts of IMD patients still represent an important protective measure. Therefore, according to the low incidence of IMD in Switzerland the identification of such strains

could compromise in the future the use of ciprofloxacin as chemoprophylaxis for close contacts if resistance levels do increase.

The proportion of serogroup Y among the invasive strains in 2023 has increased considerably compared to 2022; 42% (13/31) versus 17% (2/12). The *N. meningitidis* ROB-1 β-lactamase producer was of serogroup Y. This strain was isolated in Basel from the bloodstream of a 78-year-old woman. The ciprofloxacin-and penicillin-resistant *N. meningitidis* strain was of serogroup B in Bern from the bloodstream of a 25-year-old man.

The proportion of serogroup B among invasive strains in 2023 was 35%.

The monitoring and the follow-up of the ciprofloxacin-and penicillin-resistant *N. meningitidis* strains among the invasive and the colonizer strains should be enforced.

10. Acknowledgements

The authors thank the Laboratory of Bacteriology for excellent assistance, and the SFOPH for financial and scientific support

Hôpitaux Universitaires de Genève Rue Gabrielle-Perret-Gentil 4 CH-1211 Genève 14
Tél. 022 372 73 01 Fax 022 372 73 12 E mail: jacques.schrenzel@hcuge.ch Internet : www.hug-ge.ch

References

[1] Asturias EJ, Bai X, Bettinger JA, Borrow R, Castillo DN, Caugant DA, Chacon GC, Dinleyici EC, Echaniz-Aviles G, Garcia L, Glennie L, Harrison LH, Howie RL, Itsko M, Lucidarme J, Marin JEO, Marjuki H, McNamara LA, Mustapha MM, Robinson JL, Romeu B, Sadarangani M, Saez-Llorens X, Safadi MAP, Stephens DS, Stuart JM, Taha MK, Tsang RSW, Vazquez J, De Wals P (2022) Meningococcal disease in North America: Updates from the Global Meningococcal Initiative. J Infect 85 (6):611-622

[2] Olbrich KJ, Muller D, Schumacher S, Beck E, Meszaros K, Koerber F (2018) Systematic Review of Invasive Meningococcal Disease: Sequelae and Quality of Life Impact on Patients and Their Caregivers. Infect Dis Ther 7 (4):421-438

[3] Shen J, Begum N, Ruiz-Garcia Y, Martinon-Torres F, Bekkat-Berkani R, Meszaros K (2022) Range of invasive meningococcal disease sequelae and health economic application - a systematic and clinical review. BMC Public Health 22 (1):1078

[4] Aye AMM, Bai X, Borrow R, Bory S, Carlos J, Caugant DA, Chiou CS, Dai VTT, Dinleyici EC, Ghimire P, Handryastuti S, Heo JY, Jennison A, Kamiya H, Tonnii Sia L, Lucidarme J, Marshall H, Putri ND, Saha S, Shao Z, Sim JHC, Smith V, Taha MK, Van Thanh P, Thisyakorn U, Tshering K, Vazquez J, Veeraraghavan B, Yezli S, Zhu B (2020) Meningococcal disease surveillance in the Asia-Pacific region (2020): The global meningococcal initiative. J Infect 81 (5):698-711

[5] Lin EY, Adamson PC, Klausner JD (2021) Epidemiology, Treatments, and Vaccine Development for Antimicrobial-Resistant Neisseria gonorrhoeae: Current Strategies and Future Directions. Drugs 81 (10):1153-1169

[6] Botha P (1988) Penicillin-resistant Neisseria meningitidis in southern Africa. Lancet 1 (8575-6):54

[7] Rostamian M, Chegene Lorestani R, Jafari S, Mansouri R, Rezaeian S, Ghadiri K, Akya A (2022) A systematic review and meta-analysis on the antibiotic resistance of Neisseria meningitidis in the last 20 years in the world. Indian J Med Microbiol 40 (3):323-329

[8] Zapun A, Morlot C, Taha MK (2016) Resistance to beta-Lactams in Neisseria ssp Due to Chromosomally Encoded Penicillin-Binding Proteins. Antibiotics (Basel) 5 (4)

[9] Hong E, Deghmane AE, Taha MK (2018) Acquisition of Beta-Lactamase by Neisseria meningitidis through Possible Horizontal Gene Transfer. Antimicrob Agents Chemother 62 (9)

[10] Caugant DA, Brynildsrud OB (2020) Neisseria meningitidis: using genomics to understand diversity, evolution and pathogenesis. Nat Rev Microbiol 18 (2):84-96

[11] Knol MJ, Hahne SJM, Lucidarme J, Campbell H, de Melker HE, Gray SJ, Borrow R, Ladhani SN, Ramsay ME, van der Ende A (2017) Temporal associations between national outbreaks of meningococcal serogroup W and C disease in the Netherlands and England: an observational cohort study. Lancet Public Health 2 (10):e473-e482

[12] Mustapha MM, Marsh JW, Harrison LH (2016) Global epidemiology of capsular group W meningococcal disease (1970-2015): Multifocal emergence and persistence of hypervirulent sequence type (ST)-11 clonal complex. Vaccine 34 (13):1515-1523

[13] Fraisier C, Stor R, Tenebray B, Sanson Y, Nicolas P (2009) Use of a new single multiplex PCR-based assay for direct simultaneous characterization of six Neisseria meningitidis serogroups. J Clin Microbiol 47 (8):2662-2666

[14] Leo S, Lazarevic V, Girard M, Velasco GCG, Anson L, Gaia N, Renzi G, Cherkaoui A, Born R, Basler S, Schrenzel J (2019) Genomic epidemiology of Neisseria meningitidis serogroup W in Switzerland between 2010 and 2016. J Infect 79 (3):277-287

[15] Takahashi H, Morita M, Kamiya H, Fukusumi M, Yasuda M, Sunagawa M, Nakamura-Miwa H, Ohama Y, Shimuta K, Ohnishi M, Saito R, Akeda Y (2023) Emergence of ciprofloxacin- and penicillin-resistant Neisseria meningitidis isolates in Japan between 2003 and 2020 and its genetic features. Antimicrob Agents Chemother 67 (11):e0074423

Figures

Figure 1. Number of *N. meningitidis* strains isolated in 2023 according to the age of the patients and the specimen types.

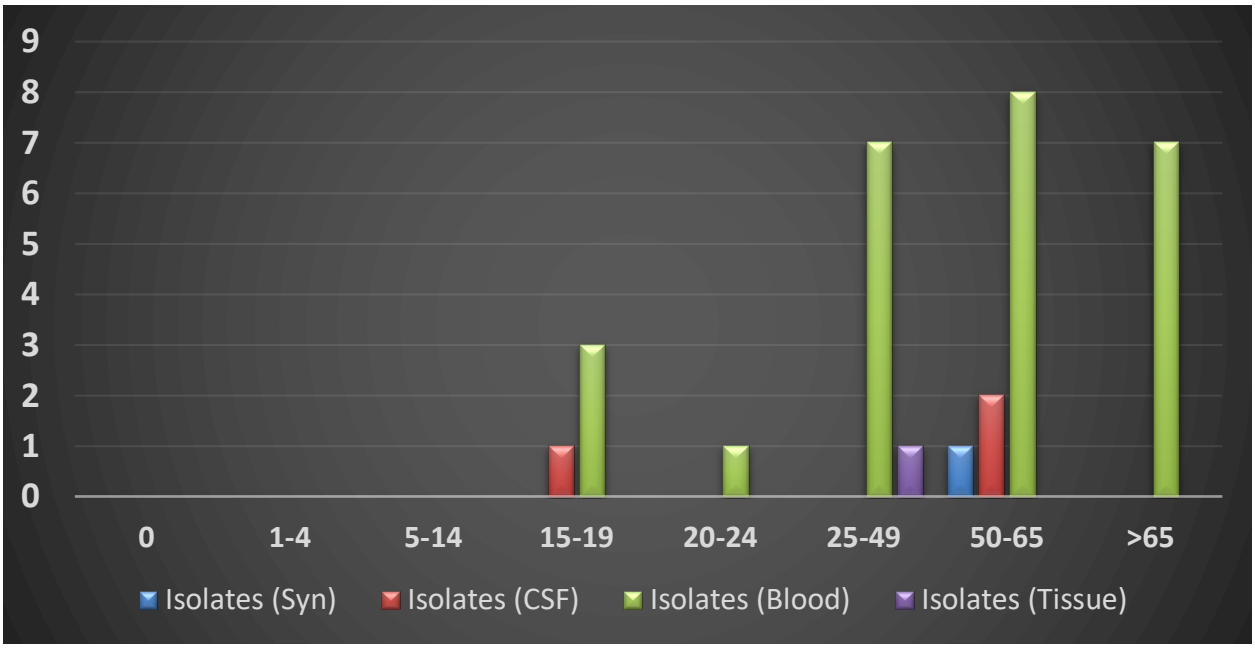


Figure 2. Number of *N. meningitidis* strains isolated in 2023 according to gender and serogroups.

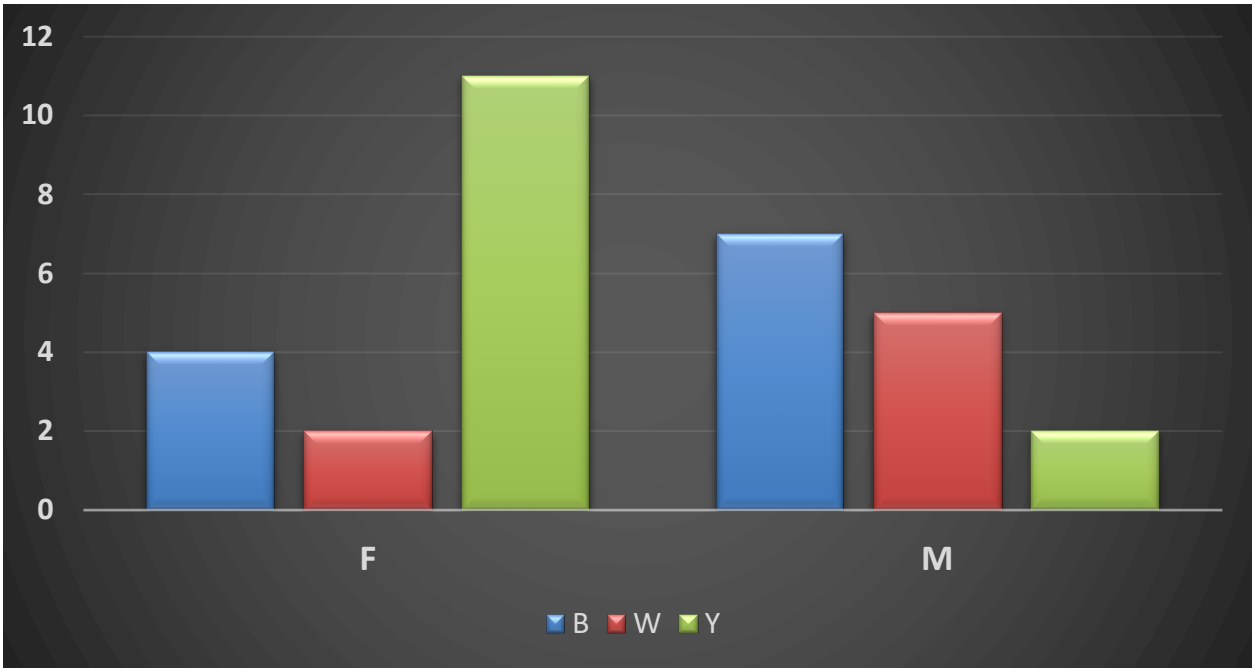


Figure 3. Annual number of cases of invasive meningococcal diseases reported to the Swiss Federal Office of Public Health (SFOPH) and number of *N. meningitidis* strains referred to the Swiss National Reference Center for Meningococci (SNRCM) from 2009 to 2023

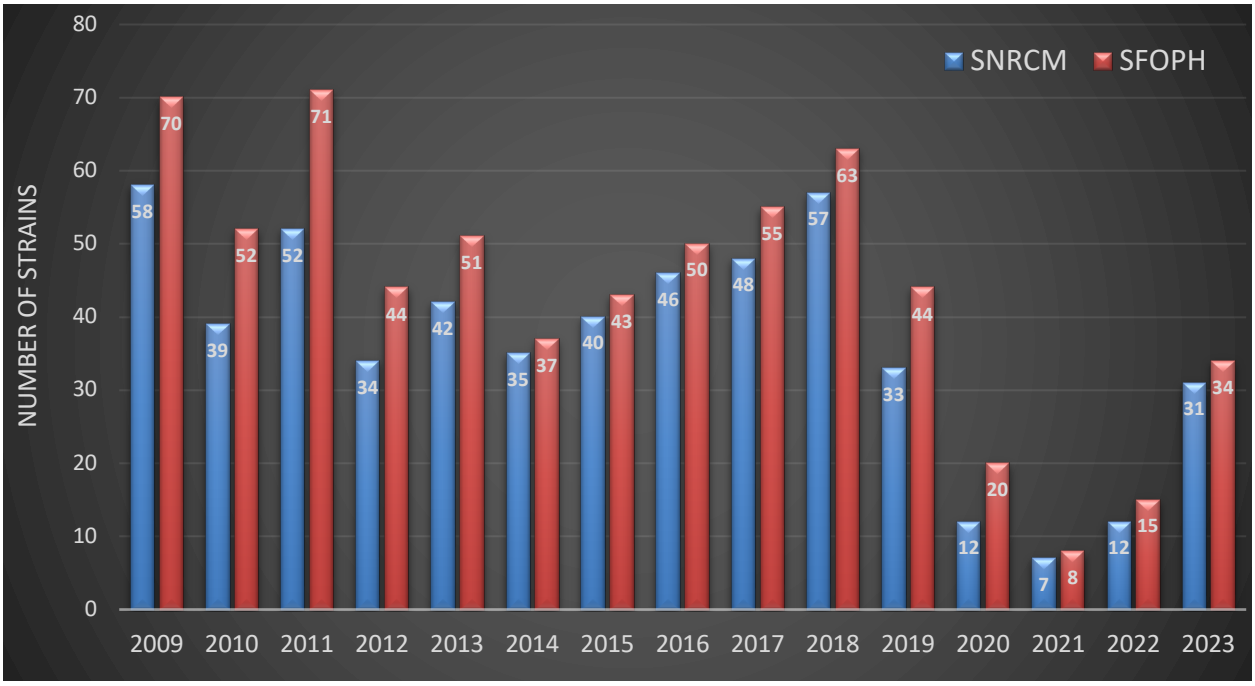


Figure 4. Serogroups distribution in 2023 (n=31)

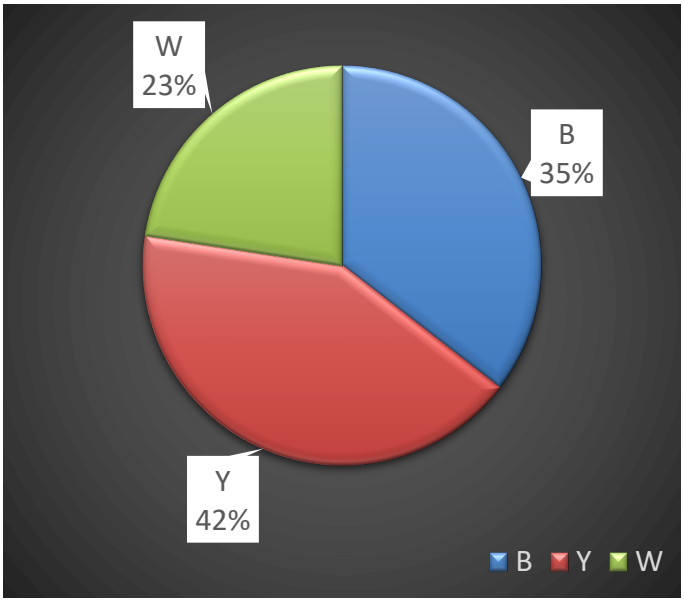


Figure 5. Annual number of strains representing the main serogroups B, C, X, Y and W135 of invasive *N. meningitidis* as determined at the Swiss National Reference Center for meningococci from 2009 to 2023

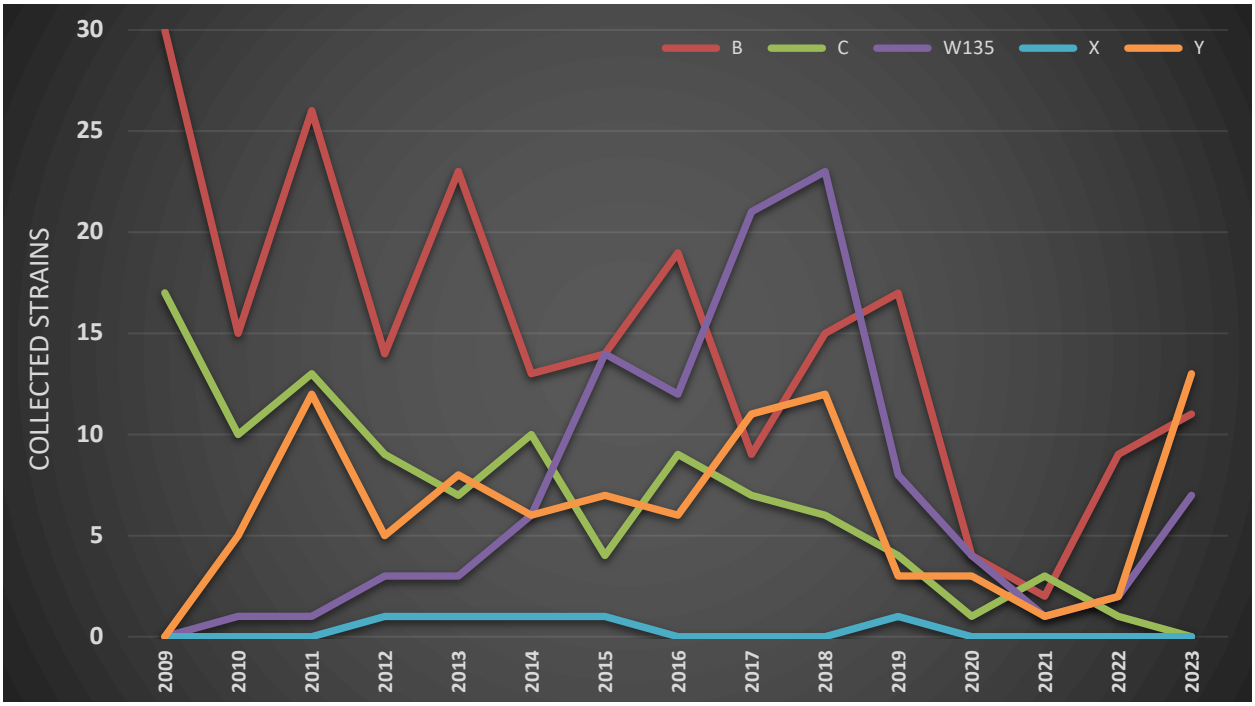


Figure 6. Number of isolates in 2023 by serogroups and age groups

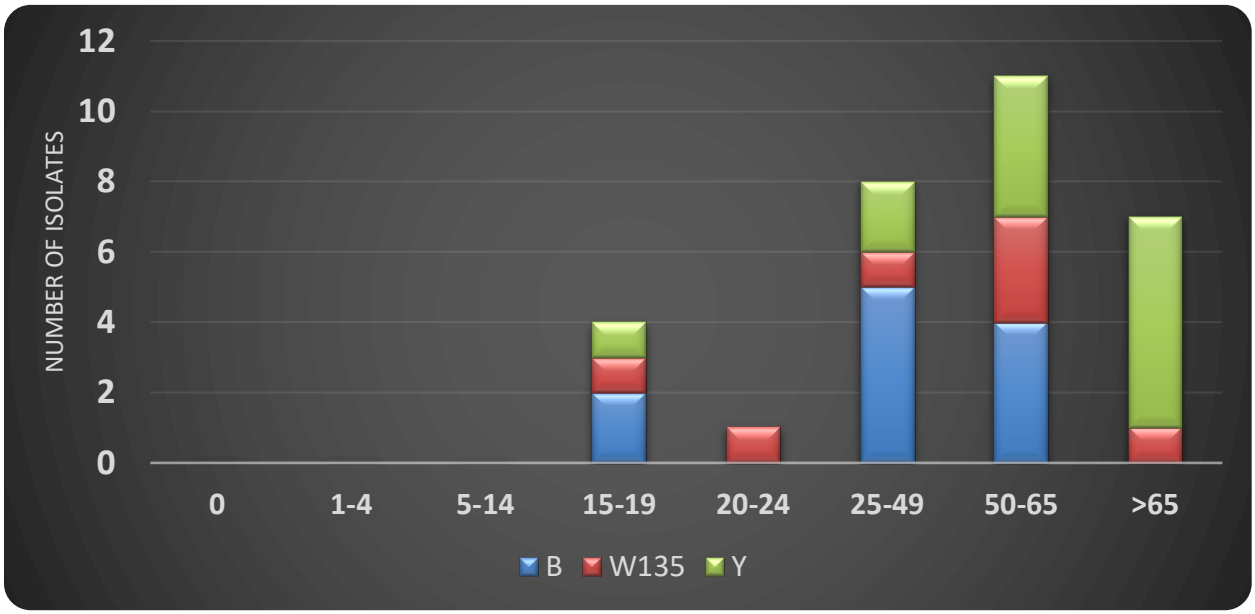


Figure 7. Distribution of serogroups by geographical regions in 2023

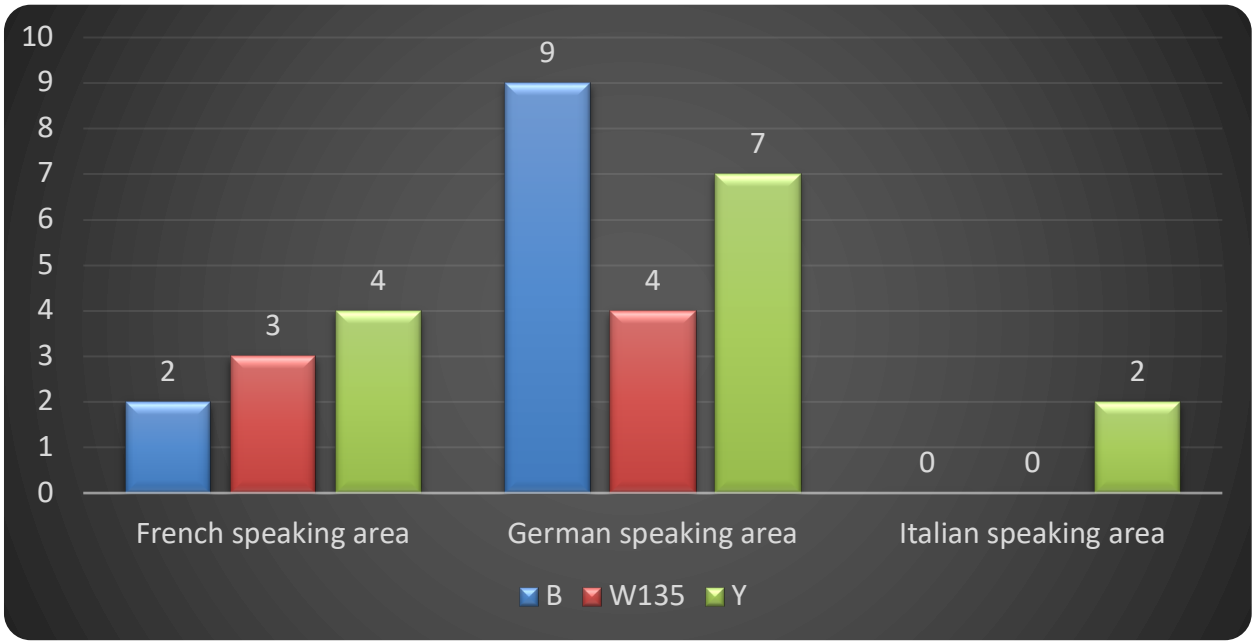
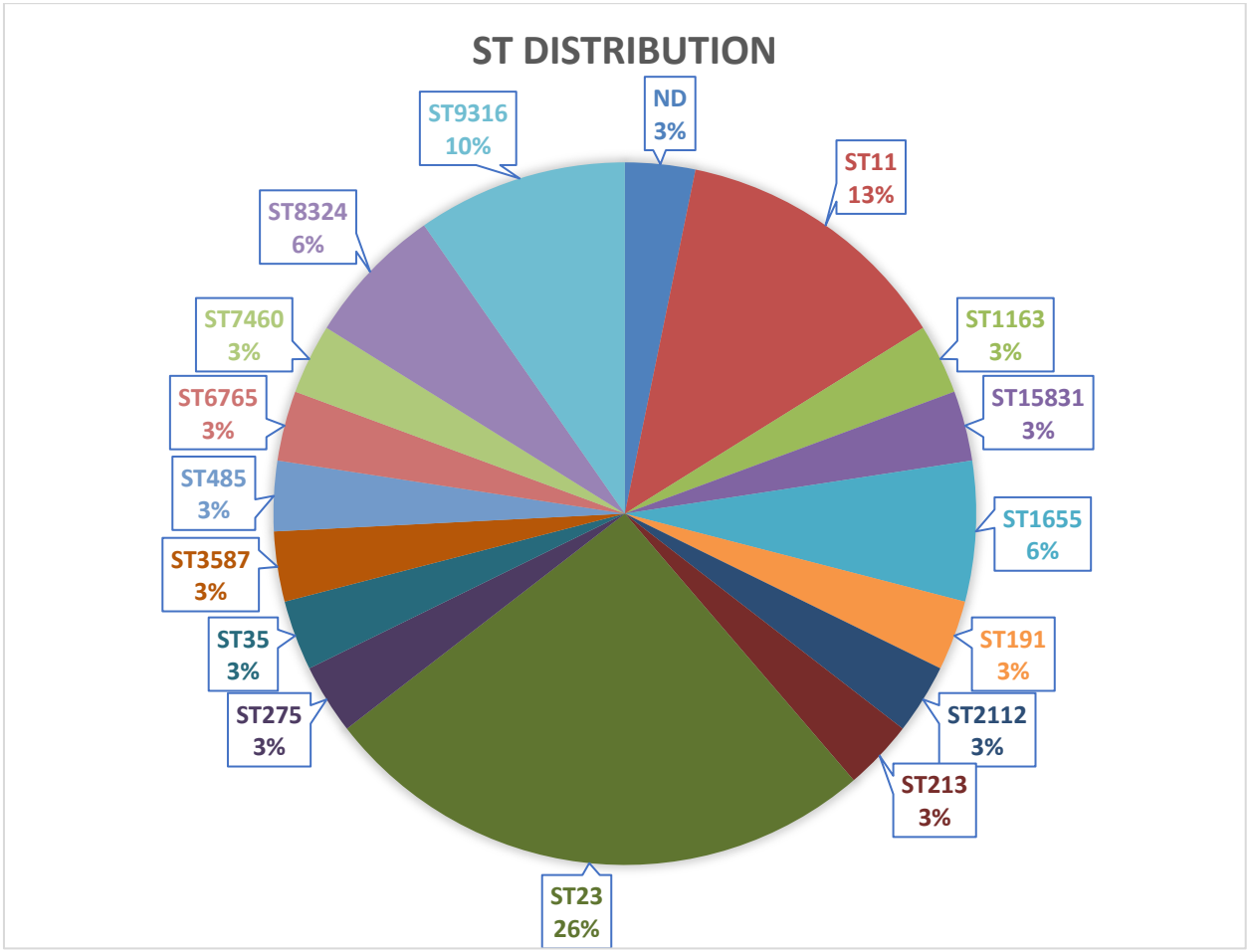


Figure 8. Distribution of sequence types in 2023



Tables

Table 1. Synopsis of MLST profiles and serogroups of invasive *N. meningitidis* strains referred to the Swiss National Reference Center for meningococci in 2023

Table-1a

Samples	Canton	Serogroup	Sequence types (STs)
Blood culture	LU	**Y**	**ST23**
Blood culture	BL	**Y**	**ST23**
Joint puncture	GE	**Y**	**ST23**
Blood culture	GE	**Y**	**ST23**
Tissue	TI	**Y**	**ST23**
Blood culture	VD	**Y**	**ST23**
Blood culture	FR	**Y**	**ST23**
Blood culture	SO	**Y**	**ST23**
Blood culture	TI	**Y**	**ST1655**
Blood culture	TG	**Y**	**ST1655**
Blood culture	BL	**Y**	ST3587
Blood culture	BE	**Y**	ST2112
Blood culture	LU	**Y**	ST15831

Table-1b

Samples	Canton	Serogroup	Sequence types (STs)
Blood culture	BL	**W**	**ST11**
Blood culture	VD	**W**	**ST11**
Blood culture	ZH	**W**	**ST11**
Blood culture	ZH	**W**	**ST11**
Blood culture	NE	**W**	**ST9316**
Blood culture	GE	**W**	**ST9316**
Blood culture	SO	**W**	**ST9316**

Table-1c

Samples	Canton	Serogroup	Sequence types (STs)
Blood culture	ZH	**B**	**ST8324**
Blood culture	AG	**B**	**ST8324**
Blood culture	ZH	**B**	ST1163
Blood culture	VD	**B**	ST35
Blood culture	BL	**B**	ST191
Cerebrospinal fluid	LU	**B**	ST485
Blood culture	BE	**B**	ST7460
Blood culture	ZH	**B**	ST6765
Blood culture	BE	**B**	ND
Cerebrospinal fluid	BE	**B**	ST213
Cerebrospinal fluid	VS	**B**	ST275

Table 2. Antimicrobial susceptibility testing (EUCAST breakpoints) of the 31 invasive *N. meningitidis* strains referred to the Swiss National Reference Center for meningococci in 2023

	Minimum inhibitory concentration (MIC)			Breakpoint susceptible (≤ µg/mL)	% of strains considered susceptible
	Range	MIC50	MIC90		
Penicillin	0.094-16	0.094	0.5	0.25	71
Ceftriaxone	0.002-0.032	0.002	0.003	0.12	100
Meropenem	0.006-0.094	0.016	0.047	0.25	100
Ciprofloxacin	0.002-0.25	0.004	0.006	0.016*	96.8
Minocycline	0.064-2	0.25	0.5	1	96.8
Rifampicin	0.002-0.125	0.012	0.094	0.25	100

*: EUCAST changed ciprofloxacin breakpoint from 0.03 µg/mL to 0.016 µg/mL in 2023

Red: increased (resistance) vs 2022
Green: decreased (resistance) vs 2022
Black: identical to 2022

Table 3. Ciprofloxacin-and penicillin-resistant *Neisseria meningitidis* isolates in 2023 and their genetic features

Samples	Patient gender	Patient age	Canton	Serogroup	Sequence types (STs)	Penicillin		*penA* allele	Presence of mutation in the 5 critical residues of PBP2	Ciprofloxacin	
						MIC	Profil			MIC	Profil
Blood culture	F	19	ZH	**B**	ST1163	**0.38**	**PCG^R**	14	**YES**	0.006	CIP^S
Cerebrospinal fluid	F	62	LU	**B**	ST485	**0.38**	**PCG^R**	7	**YES**	0.006	CIP^S
Blood culture	M	25	BE	**B**	ST7460	**0.5**	**PCG^R**	9	**YES**	**0.25**	**CIP^R**
Blood culture	M	27	ZH	**B**	ST6765	**0.38**	**PCG^R**	7	**YES**	0.004	CIP^S
Cerebrospinal fluid	M	51	BE	**B**	ST213	**0.38**	**PCG^R**	295	**YES**	0.004	CIP^S
Blood culture	F	87	BL	**Y**	ST3587	***16**	**PCG^R**	9	**YES**	0.003	CIP^S
Blood culture	M	66	BL	**W**	ST11	**0.75**	**PCG^R**	9	**YES**	0.008	CIP^S
Blood culture	M	55	ZH	**W**	ST11	**0.75**	**PCG^R**	14	**YES**	0.006	CIP^S
Blood culture	M	22	ZH	**W**	ST11	**0.38**	**PCG^R**	14	**YES**	0.006	CIP^S

Resistant to penicillin **PCG^R**
Changes in five critical residues of PBP2 (**F504L, A510V, I515V, H541N, and I566V)**
* **ROB-1** penicillinase-producing
Resistance to ciprofloxacin **(CIP^R)** based on a ***gyrA* T91I mutation**

Hôpitaux Universitaires de Genève Rue Gabrielle-Perret-Gentil 4 CH-1211 Genève 14
Tél. 022 372 73 01 Fax 022 372 73 12 E mail: jacques.schrenzel@hcuge.ch Internet : www.hug-ge.ch

Hôpitaux Universitaires de Genève Rue Gabrielle-Perret-Gentil 4 CH-1211 Genève 14
Tél. 022 372 73 01 Fax 022 372 73 12 E mail: jacques.schrenzel@hcuge.ch Internet : www.hug-ge.ch