

Annual Report for the National Reference Laboratory for *Neisseria meningitidis*, 2024

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Background

All invasive cases of meningococcal infection in Sweden are reported to the communicable disease surveillance system Sminet, and the isolates or culture-negative sample are sent to the National Reference Laboratory (NRL) in Örebro in most of the cases. At the laboratory, national and global epidemiology is monitored, along with developments in knowledge and methodology within the field.

Analyses performed at the NRL include identification, serological and/or genetic grouping of all invasive *Neisseria meningitidis* isolates, as well as isolates from other sites when needed. Typing is conducted using whole genome sequencing on all culture-positive invasive isolates. Antibiotic susceptibility is verified through MIC determination of all invasive *N. meningitidis* isolates and, when necessary, isolates from other sites. For culture-negative samples from sterile sites, PCR diagnostics, genogrouping, and genosubtyping (including Sanger sequencing) are performed.

Epidemiology of *Neisseria meningitidis* 2024

The incidence of invasive meningococcal disease continued to rise in 2024 following several years of very low occurrence. During 2024, 46 cases of invasive meningococcal disease were reported in Sweden, corresponding to an incidence of 0.4 cases per 100,000 inhabitants (see Figure 1). The median age among the cases was 50 years (range 0–85 years), with the highest number of cases reported in the 15–19 age group (n=9), see Figure 2. The gender distribution was balanced (46% female). Of the reported cases, two individuals (4%) died (source: Epidemiological Annual Report, Public Health Agency of Sweden, FoHM).

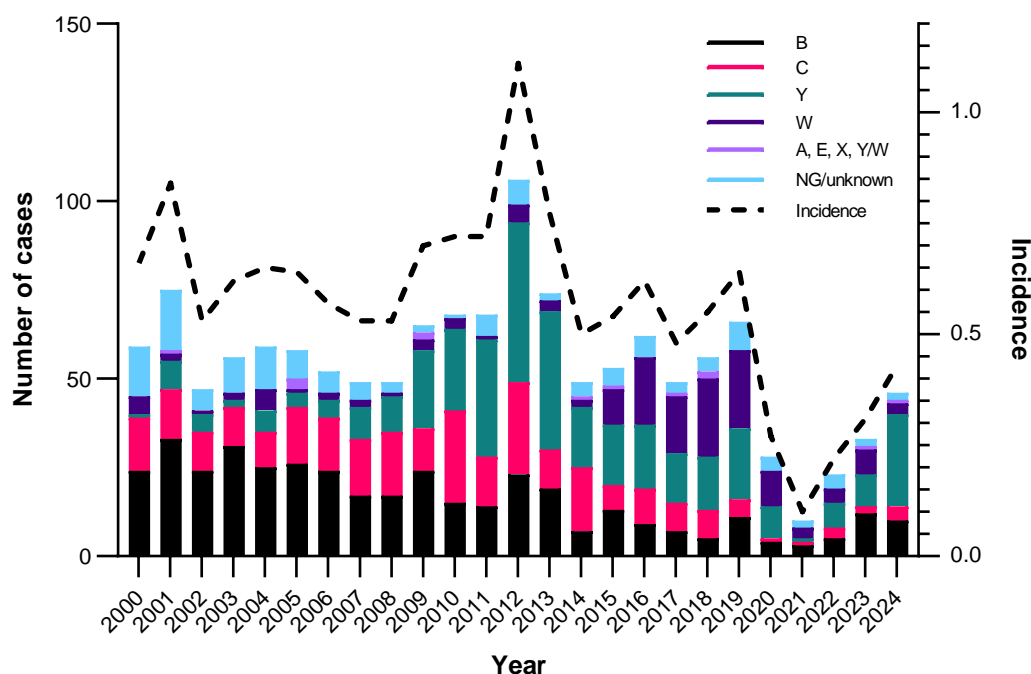


Figure 1. Number of cases, serogroups, and incidence (number of cases per 100,000 inhabitants) of invasive meningococcal disease from 2000 to 2024.

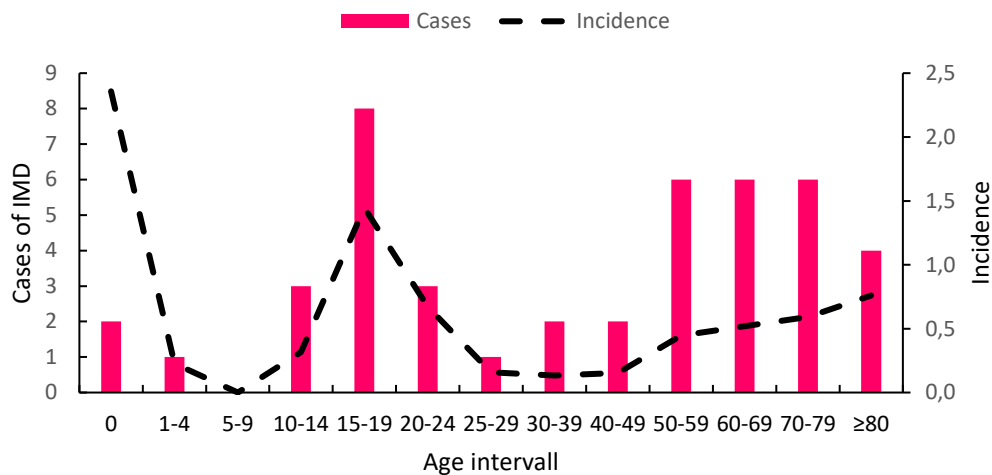


Figure 2. Distribution of invasive meningococcal disease by age group in 2024.

At the NRL in 2024, 37 culture-positive *N. meningitidis* isolates and seven culture-negative cerebrospinal fluid samples or DNA preparations were received for *Neisseria* classification. These originated from 44 cases of invasive disease. In addition, two more cases were reported based on both clinical and laboratory notification but not sent to the NRL for further typing.

The invasive isolates were primarily derived from blood cultures, with exceptions including six isolates from cerebrospinal fluid, one from joint fluid, and two from secretions. The serogroup distribution of these invasive isolates (one per patient) was as follows: Y (n=25), B (n=6), W (n=3), C (n=2), X (n=1).

Seven culture-negative samples were verified and genogrouped using a PCR-based method with the following results: B (n=4), C (n=2), Y (n=1).

All culture-positive isolates were whole-genome sequenced and uploaded to the *Neisseria* PubMLST database (<http://PubMLST.org/neisseria>), an international public database for molecular typing and microbial diversity. Results from fine typing using genosubtype (*porA*), multilocus sequence typing (MLST), and whole-genome similarity comparisons are presented in Table 1 and Figure 3.

Methodological changes

Development of a rapid sequencing method using Oxford Nanopore Technology is underway to enable faster whole genome sequencing for determining similarities between isolates, which can be of great importance in outbreak investigations.

Due to the discontinuation of a reagent used for serogrouping (specifically for serogroup 29E), the serogrouping algorithm will be updated during 2025.

Table 1. Fine Typing of *porA* for all 37 culture-positive invasive *Neisseria meningitidis* isolates submitted to the NRL.

Genosubtype	B	C	W	X	Y	Totalt
P1.5-2,10-1,36-2					11	11
P1.5-1,2-2,36-2					6	6
P1.5-1,10-4,36-2					5	5
P1.5,2,36-2		1	2	1		4
P1.5-2,10-23,36-2					2	2
P1.7,16,35	1					1
P1.7,16-29,35		1				1
P1.19,15,36	1					1
P1.21,16-36,37-1	1					1
P1.22,14,36	1					1
P1.18-1,30-1,38	1					1
P1.22-1,14,38	1					1
P1.5-1,10-1,36-2					1	1
P1.5-2,2-2,36-2			1			1
Totalt	6	2	3	1	25	37

Educational initiatives

Internally, a biomedical analyst at the NRL was trained in *Neisseria* diagnostics during 2024.

Externally, an annual epidemiological report is published in collaboration with the Public Health Agency of Sweden, and resistance data are reported to Swedres.

Additionally, telephone contact has been maintained with various stakeholders, including treating physicians and infectious disease control doctors.

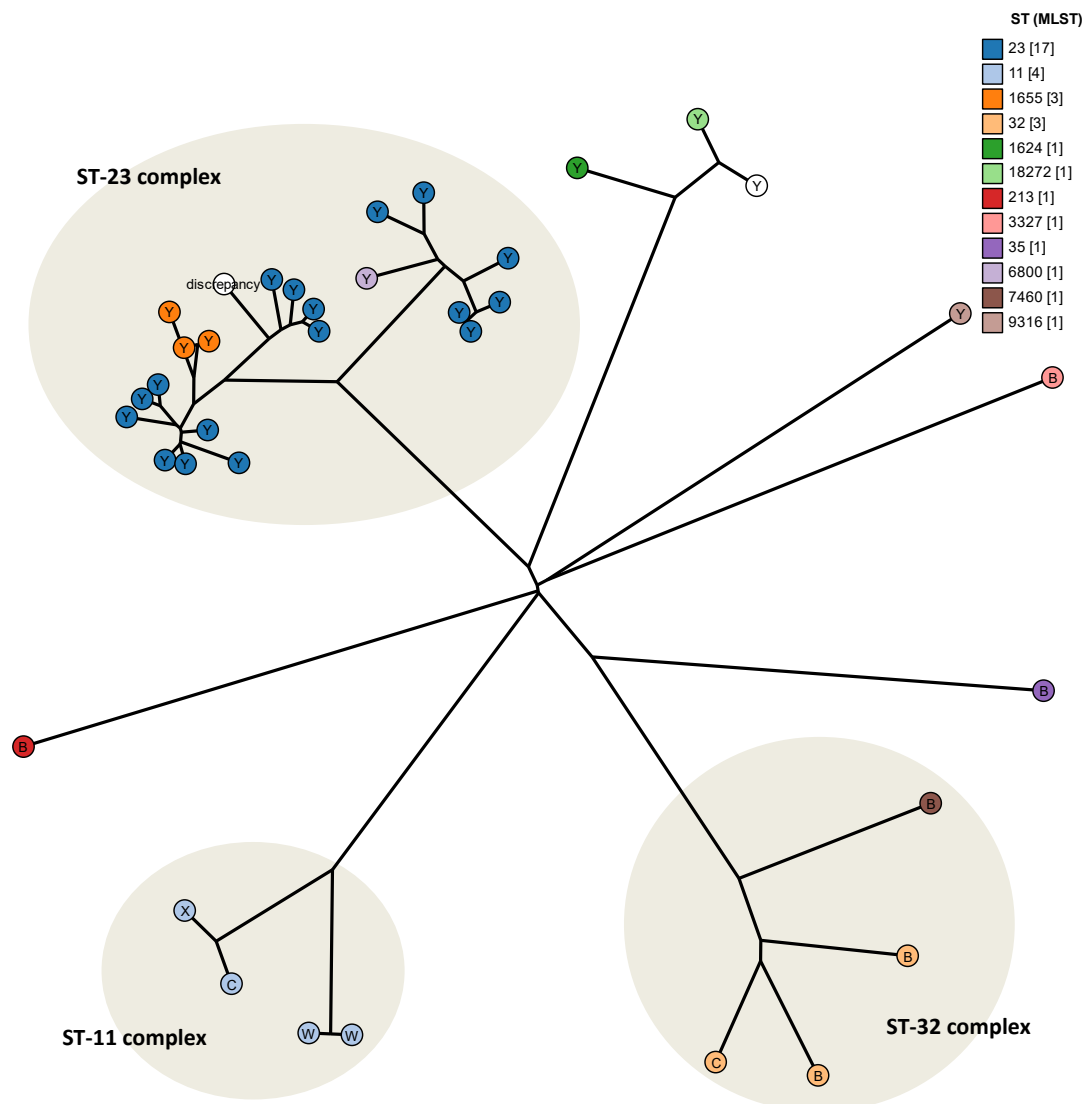


Figure 3. GrapeTree Analysis of all whole-genome sequenced culture-positive isolates (n=37) in 2024, <https://pubmlst.org/software/bigsdb>. Genetic similarity is illustrated through clustering and branch distances, where each circle represents an isolate and its corresponding serogroup. The colours of the circle are based on sequence type (ST), with the three most common clonal complexes (ST-23, ST-11, ST-32 complex) highlighted. No epidemiological links between disease cases were observed in 2024.

Global Surveillance and Epidemiological Developments

The number of invasive meningococcal disease cases dropped significantly during the COVID-19 pandemic but has since rebounded internationally, a trend also observed in Sweden. While many European countries reported an increase in *N. meningitidis* serogroup B during 2024, this was not reflected in Sweden, where most invasive cases were caused by serogroup Y.

Throughout 2024, the NRL represented by Paula Mölling and Susanne Jacobsson, continued its participation in the global laboratory network, the Invasive Respiratory Infections Surveillance (IRIS) Initiative. This network includes reference laboratories from 30 countries across six continents. Initially established to monitor changes in invasive diseases caused by *N. meningitidis*, *Streptococcus pneumoniae*, and *Haemophilus influenzae* during the COVID-19 pandemic, the project has now extended its scope to track post-pandemic epidemiology of these pathogens.

NRL also participated, through Paula Mölling, in the international online conference *Global Meningococcal Initiative (GMI) 12th Regional Meeting – Meningococcal Disease in Western Europe*, held in March 19–20, 2024, where the *Meningococcal Disease in Sweden* was presented.

Additionally, in 2024, the NRL joined a collaborative application to the European Centre for Disease Prevention and Control (ECDC) alongside 13 European reference laboratories within the European Meningococcal Disease Society (EMGM), with the aim of establishing a European reference network: the European Union Invasive Bacterial Diseases Laboratory Network (IBDLabNet).

Research

Ongoing research on *N. meningitidis* is conducted at the NRL, with both national and international collaborations. Current projects include:

- Studying the changing epidemiology over time, with increasing incidence of *N. meningitidis* serogroups Y and W in Sweden as well as globally
- Investigating *N. meningitidis* carriage and its interaction with other bacterial species
- Examining the pathogen's ability to cause disease in mice infected with isolates associated with either invasive disease or carriage
- Identifying genetic variants linked to invasive disease or carriage of *N. meningitidis*

At the NRL, Cecilia Klanger (junior physician) is supervised in her PhD project titled *Genetic variants of Neisseria meningitidis linked to phenotypic outcome of infection vs carriage*.

In May 2024, Lorraine Eriksson (Licensed Biomedical Analyst) defended her doctoral thesis *Exploring genomic and phenotypic differences in Neisseria meningitidis – understanding carriage and invasive disease*, ISSN: 1652-4063.

Active research collaborations are ongoing with Professor Muhamed Taha (Pasteur Institute, Paris, France), Professor Eva Särndahl and Associate Professor Alexander Persson (Örebro University), Associate Professor Edmund Loh (Karolinska Institute), and Associate Professor Olof Herting (Karolinska University Hospital), along with their respective teams.

Publications in 2024

The following scientific articles were published during 2024, reflecting active research and international collaboration in the field of *Neisseria meningitidis* and infectious disease surveillance:

- **Säll O, Eriksson L, Berhane IA, et al.** Prevalence and persistence of *Neisseria meningitidis* carriage in Swedish university students. *Epidemiol Infect.* 2024 Aug 22;152:e99. PMID: 3916865.
- **Belayneh M, Mengesha M, Idosa BA, et al.** *CARD8* polymorphisms among bacterial meningitis patients in North-West Ethiopia. *BMC Infect Dis.* 2024 Oct 1;24:1084. PMID: 39354402.
- **Shaw D, Torreblanca RA, Amin-Chowdhury Z, et al.** The importance of microbiology reference laboratories and adequate funding for infectious disease surveillance. *Lancet Digit Health.* 2024 Dec 20. PMID: 39709282.
- **Borrow R, Campbell H, Caugant DA, et al.** Global Meningococcal Initiative: Insights on antibiotic resistance, control strategies and advocacy efforts in Western Europe. *J Infect.* 2024 Nov. PMID: 106335.
- **Persson A, Koivula T, Jacobsson S, Stenmark B.** Diverse proinflammatory response in pharyngeal epithelial cells upon interaction with *Neisseria meningitidis* carriage and invasive isolates. *BMC Infect Dis.* 2024 Mar 6;24(1):286. PMID: 38443838.

Plans for the next Year

The culture media used for the culture and isolation of *N. meningitidis* (GCAGP and GVCNTP) will no longer be CE-marked under IVDR regulations, according to the manufacturer. A decision has therefore been made to explore in-house production or alternative agar plates. This work will continue throughout 2025.

There is an ongoing initiative to provide electronic diagnostic results to clients outside the region to improve turnaround times. This effort will also continue in 2025.

The EUCAST laboratory contacted the reference laboratory to discuss the development of a disc diffusion method for antimicrobial susceptibility testing of *N. meningitidis*. The project has progressed positively, with the NRL contributing well-characterized strains. Completion is expected in 2025.

Efforts are ongoing to ensure that all European countries upload data from PubMLST to EMERT-II and EpiPulse. The NRL joined this initiative in 2024. The ECDC distributes monthly surveillance reports both nationally and internationally, with the goal of transitioning to real-time reporting to enhance outbreak-related surveillance across borders.

Collaboration within IBDLabNet and with ECDC will continue in 2025, focusing on the distribution of external quality assessments to compare laboratory performance, identify training and capacity-building needs, support member countries, advance whole genome sequencing, and pinpoint areas requiring further and expanded research.

Professional development

The training of existing staff in the NRL will continue, with the goal that the entire team will be fully qualified in *Neisseria* diagnostics.