NEISSERIA MENINGITIDIS: EVOLUTION OF ANTIMICROBIAL RESISTANCE PATTERNS THROUGHOUT THE YEARS

José Eduardo Oliva Marín[1]
0000_0002_6005_0558

1. Head Clinical Trials Unit
Superintendency of Health Regulation
revista@srs.gob.sv

Literary Review

Received:
March 2, 2026

Accepted:
March 10, 2026

Published:
August 07, 2026

Abstract

Introduction. In the last decades, antimicrobial resistance in *Neisseria meningitidis* has shown significant evolution translating into changes for physicians, and the pressure over the use of antibiotics.

Methods. Research has been made through specialized databases, including PubMed and Google Scholar, using words such as *Neisseria meningitidis*, meningococcal, and antibiotic resistance.

Discussion. Strains with reduced sensitivity to penicillin have been documented gradually. These have been characterized by genetic mutations that encode binding proteins to it, thus, reducing effectivity in standard treatment. Later on, isolated strains have shown resistance to ciprofloxacin, rifampicin, and tetracycline, although these cases are relatively uncommon. The spread of resistance genes through mobile genes and horizontal recombination contribute to the diversity of antimicrobial resistant strains in different geographical regions. This evolution implies challenges in medicine and public health, since it narrows the therapeutic and prophylactic options, requiring constant supervision.

Conclusion. Global surveillance and adopting policies for the rational use of antimicrobials are key to refrain the expansion of resistant strains, and guarantee the future effectivity of treatments against *Neisseria meningitidis.*

Keywords: *Neisseria meningitidis*, meningitis, meningococcal, bacterial resistance, whole genome sequencing

Introduction

Invasive meningococcal disease is a significant threat to public health due to its rapid clinical progression, and high mortality rate. An effective and timely treatment has been a historical cornerstone to reduce mortality rates and sequels, making penicillin the preferred antibiotic for decades.

However, the genetic adaptive capacity of *Neisseria meningitidis* has fostered global emergence and spread of reduced sensitivity strains, and its resistance to antimicrobials, which represents a growing challenge for treatment, and epidemiological surveillance.

Since the end of the 20th century, many regions in the world have reported isolates with intermediate or complete resistance to beta-lactams and fluoroquinolones, and exceptional cases associated to the production of beta-lactamases.

This phenomenon does not only prove meningococcal genetic plasticity but also selective pressure by extended use of antibiotics. In recent years, the identification of strains with multiresistant profiles in Latin America, especially those from a specific clonal lineage (with well characterized molecular mechanisms), highlights the need to strengthen microbiological surveillance systems, and genomic analysis, to comprehend their evolution and spread.

Methodology

A scientific literature review was performed. The bibliographical research was carried out through specialized databases, including PubMed and Google Scholar, using keywords in english and spanish such as "*Neisseria meningitidis*", "meningococcal", "antibiotic resistance" and "resistencia a los antibióticos".

The selections include original articles and reviews, covering signs and symptoms, complications, current

treatments, antimicrobial resistance patterns, and bacterial resistance mechanisms by *N. meningitidis*. The studies were evaluated according to their relevance in the field, methodological clarity, and recentness, to integrate a descriptive and critical analysis.

Discussion

Penicillin has been the main antibiotic to treat meningococcal disease for many years. However, during the 1970s and 1980s, reports emerged about median resistance to penicillin, and eventually, resistant strains were reported around the world (Oppenheim, 1997).

Neisseria meningitidis strains with median resistance to penicillin were isolated in Spain from 1978 to 1986 (Saez-Nieto, 1987), Cataluña in 1986 (Uriz, 1991), in the UK from 1985 - 1989 (Jones, 1990), in Rumania in 1989 (Dorobat, 1990), in Francia from 1999 - 2002 (Antignac, 2003), in Italy from 2002 – 2003 (Stefanelli, 2004), in South Africa from 2001 - 2005 (du Plessis, 2008), and in Belgium from 2000 - 2010 (Bertrand, 2012). In America this sensitivity pattern was described in the US in 1992 (Woods, 1994), in Canada from 1993 - 1994 (Blondeau, 1995) and in Brazil from 2006 - 2008 (Gorla, 2011).

The first cases of penicillin resistant *Neisseria meningitidis* were reported during the 1980s. In South Africa in 1987 (Botha, 1988), in Spain in 1985 and 1989 (Saez-Nieto, 1992), in Malawi in 1988 (Round, 1988), in Taiwan in 2000 (Ben, 2001), in USA in 2005 (Glikman, 2006), and in Australia in 2010 (Abeysuriya, 2010). Mexico, Central America, and the Caribbean (Cuba and Dominican Republic) reported cases from 2008 to 2015: 19 penicillin resistant *Neisseria meningitidis* isolates (14 cases in México in 2010 (WHO, 2011), one in Cuba in 2011 (WHO, 2012) and 4 cases in Mexico 2012 (WHO, 2013).

The first cases of penicillin resistant *Neisseria meningitidis* by beta-lactamase production were reported during the 1980s: one case in Canada in 1983 (Dillon, 1983), two in South Africa in 1987 (Botha, 1988), one case in Spain in 1988 (Fontanals, 1989) and again one in Spain in 1996 (Vasquez, 1996). Although, up to now, the presence of beta-lactamase in meningococcus in exceptional, there are reports from different parts of the world: two cases in Sweden in 2000 (Backman, 2000), one case in France in 2018 (Hong, 2018), and one in Canada in 2018 (Tsang, 2019).

In regard to *Neisseria meningitidis* with median resistance to ciprofloxacin, the first strains were reported as follows: one meningococcal serogroup B isolate from an asymptomatic patient in France in 1999 (Casin, 1999), one meningococcal serogroup C isolate from a nursing student with invasive disease in Australia in 2000 (Shultz, 2000), and a meningococcal serogroup B isolate from cerebrospinal fluid in Spain in 2003 (Alcalá, 2004).

In the American continent, two *N. meningitidis* strains with median resistance to fluoroquinolones were reported for the first time, in Argentina between 2002 and 2003 (Corso, 2005). Afterwards, *N. meningitidis* strains with median resistance to ciprofloxacin were reported around the world: one in Israel in 2003 (Strahilevitz, 2008), 12 strains in India in 2005 (Singhal, 2007), another one in Israel in 2006 (Strahilevitz, 2008), and one in Hong Kong in 2006 (Chu, 2007); three strains in the USA between 2007 and 2008 (Wu, 2009), and one in Italy in 2009 (Lapadula, 2009).

Over time, *Neisseria meningitidis* became resistant to ciprofloxacin. These strains have been reported since the 1990s: ten in Spain from 1999 to 2006 (Enriquez, 2008), 31 isolations in patients with invasive illness in China from 2005 to 2013 (Chen, 2015), and two cases in Brazil between 2012 and 2013 (Gorla, 2018).

Also, for over three decades, rifampicin resistant *Neisseria meningitidis* strains have been reported. The first case caused an invasive disease in a 5-month-old infant in Minnesota, USA, in 1996. The isolate was a serogroup B meningococcus and showed resistance for rifampicin with a MIC > 32 µg/ml (Rainbow, 2005).

From 2017 to 2019, six invasive meningococcal disease cases were identified in El Salvador. These were caused by *N. meningitidis* serogroup Y, resistant both to penicillin (MIC > 8,0 mg/l) and to ciprofloxacin (MIC 0,125 mg/l). The genomic analysis revealed that penicillin resistance was caused by beta-lactamase ROB-1 (bla_{ROB-1}), but ciprofloxacin resistance was related to a Thr91Ile substitution in the DNA gyrase (*gyr*A). All isolated strains belonged to ST3587, clonal complex 23, and showed a high genetic similarity among them, according to the SNP central genome analysis. This was the first report of invasive strains in Latin America regarding serogroup Y *N. meningitidis* isolates, resistant to both fluoroquinolones and beta-lactamic agents (Marín, 2021).

Between January 2020 and June 2025, ten more cases of serogroup Y *N. meningitidis* were detected, all resistant to beta-lactamic antibiotics and with median sensitivity to fluoroquinolones. These isolates were sent to Instituto Adolfo Lutz (IAL, for its acronym in Portuguese) in São Paulo, Brazil, to develop confirmation tests on antimicrobial sensitivity, and a complete genome sequencing.

All analyzed cases belonged to the sequence ST3587, clonal complex 23, same as the 2017 – 2020 isolates. Genomic analysis confirmed the presence of beta-lactamase ROB-1 gen (bla_{ROB-1}, allele 2), related to penicillin resistance, the substitution GyrA Thr91Ile (allele 242), related to lower sensitivity to ciprofloxacin. Compared to the isolates from 2017-2019, the isolates from 2020-2025 conserved the resistance to penicillin, but their ciprofloxacin resistance was modified to intermediate sensitivity. The resistance mechanisms against both antibiotics remained the same (Marín, 2026).

It is worth noting that two isolates from 2020-2025, carried the gen tetB, defining a triple resistant phenotype (penicillin, ciprofloxacin-intermediate y tetracycline) with elevated minor inhibitor concentrations of tetracycline (6 µg/mL), approximately 40 times greater than sensitive isolated strains. At the same time, it showed increased values for minocycline and doxycycline. Sensitivity for more recent derivatives such as tigecycline and eravacycline, remained (Marín, 2026).

Conclusion

The heightened genetic adaptability of *Neisseria meningitidis,* caused by horizontal transfer of genes, recombination and phase variation, allows the isolates an efficient evasion of the host's immune response, developing resistance to different antimicrobial agents. This adaptation capacity not only makes the invasive meningococcus more difficult to treat, but also represents a challenge for epidemiological control, since it fosters the emergence and spread of resistant strains in the population.

Hence, it is key to maintain constant surveillance on bacterial sensitivity, optimize treatment regime, and reinforce prevention strategies, including vaccination campaigns towards populations at risk. Applying these measures is essential to limit the spread of resistant strains, reduce the morbidity and mortality rate, and ensure an effective control of this potentially serious disease.

References

Abeysuriya, S. (2010). Penicillin-resistant Neisseria meningitidis bacteraemia, Kimberley Region, 2010. Communicable Diseases Intelligence Quarterly Report, 34(3), 342–344. https://doi.org/10.33321/cdi.2010.34.36

Alcalá, B., et al. (2004). Neisseria meningitidis showing decreased susceptibility to ciprofloxacin: First report in Spain. Journal of Antimicrobial Chemotherapy, 53(2), 409. https://doi.org/10.1093/jac/dkh075

Antignac, A., et al. (2003). Neisseria meningitidis strains isolated from invasive infections in France (1999–2002): Phenotypes and antibiotic susceptibility patterns. Clinical Infectious Diseases, 37(7), 912–920. https://doi.org/10.1086/377739

Backman, A., et al. (2000). Complete sequence of a β-lactamase-encoding plasmid in Neisseria meningitidis. Antimicrobial Agents and Chemotherapy, 44(1), 210–212. https://doi.org/10.1128/AAC.44.1.210-212.2000

Ben, R. J., et al. (2001). Meningitis due to penicillin-resistant Neisseria meningitidis in a 20-year-old man. Journal of the Formosan Medical Association, 100(10), 696–698. PMID: 11760376

Bertrand, S., et al. (2012). Evolutionary changes in antimicrobial resistance of invasive Neisseria meningitidis isolates in Belgium from 2000 to 2010: Increasing prevalence of penicillin nonsusceptibility. Antimicrobial Agents and Chemotherapy, 56(5), 2268–2272. https://doi.org/10.1128/AAC.06310-11

Blondeau, J. M., et al. (1995). Neisseria meningitidis with decreased susceptibility to penicillin in Saskatchewan, Canada. Journal of Clinical Microbiology, 33(7), 1784–1786. https://doi.org/10.1128/jcm.33.7.1784-1786.1995

Botha, P., et al. (1988). Penicillin-resistant Neisseria meningitidis in Southern Africa. The Lancet, 331(8575–8576), 54. https://doi.org/10.1016/S0140-6736(88)91029-X

Casin I, Gandry B, Lassau F, Janier M, Lagrange P, Collatz E. (1999) Decreased susceptibility to penicillin G (Pen), tetracyclines (Tet), and fluoroquinolones (Fq), and characterization of DNA gyrase mutations, in oropharyngeal and anogenital isolates of Neisseria meningitidis (Nme) in patients presenting at an STD clinic. In: Program and Abstracts of the 39th Interscience Conference on Antimicrobial Agents and Chemotherapy; San Francisco, CA.

Chen, M., et al. (2015). Shifts in the antibiotic susceptibility, serogroups, and clonal complexes of Neisseria meningitidis in Shanghai, China: A time trend analysis of the pre-quinolone and quinolone eras. PLoS Medicine, 12(6), e1001838. https://doi.org/10.1371/journal.pmed.1001838

Chu, Y. W., et al. (2007). A blood isolate of Neisseria

meningitidis showing reduced susceptibility to quinolones in Hong Kong. International Journal of Antimicrobial Agents, 30(1), 94–95. https://doi.org/10.1016/j.ijantimicag.2006.11.028

Corso, A., et al. (2005). Emergence of Neisseria meningitidis with decreased susceptibility to ciprofloxacin in Argentina. Journal of Antimicrobial Chemotherapy, 55(4), 596–597. https://doi.org/10.1093/jac/dki048

Dillon, J. R., et al. (1983). Spread of penicillinase-producing and transfer plasmids from the gonococcus to Neisseria meningitidis. The Lancet, 321(8328), 779–781. https://doi.org/10.1016/S0140-6736(83)91846-9

Dorobat, O., et al. (1990). Characteristics of Neisseria meningitidis strains isolated in Romania between 1986 and 1989. Archives Roumaines de Pathologie Expérimentale et de Microbiologie, 49(3), 215–221. PMID: 2134148

du Plessis, M., et al. (2008). Neisseria meningitidis intermediately resistant to penicillin and causing invasive disease in South Africa, 2001–2005. Journal of Clinical Microbiology, 46(10), 3208–3214. https://doi.org/10.1128/JCM.00221-08

Enriquez, R., et al. (2008). Fluoroquinolone resistance in Neisseria meningitidis in Spain. Journal of Antimicrobial Chemotherapy, 61(2), 286–290. https://doi.org/10.1093/jac/dkm452

Fontanals, D., et al. (1989). Penicillin-resistant β-lactamase-producing Neisseria meningitidis in Spain. European Journal of Clinical Microbiology & Infectious Diseases, 8(1), 90–91. https://doi.org/10.1007/BF01964130

Glikman, D., et al. (2006). Pneumonia and empyema caused by penicillin-resistant Neisseria meningitidis: A case report and literature review. Pediatrics, 117(5), e1061–e1066. https://doi.org/10.1542/peds.2005-1994

Gorla, M. C., et al. (2011). Antimicrobial susceptibility of Neisseria meningitidis strains isolated from meningitis cases in Brazil from 2006 to 2008. Enfermedades Infecciosas y Microbiología Clínica, 29(2), 85–89. https://doi.org/10.1016/j.eimc.2010.07.016

Gorla, M. C., et al. (2018). Emergence of resistance to ciprofloxacin in Neisseria meningitidis in Brazil. Journal of Medical Microbiology, 67(3), 286–288. https://doi.org/10.1099/jmm.0.000685

Hong, E., Deghmane, A. E., & Taha, M. K. (2018). Acquisition of beta-lactamase by Neisseria meningitidis through possible horizontal gene transfer. Antimicrobial Agents and Chemotherapy, 62(9), e00831-18. https://doi.org/10.1128/AAC.00831-18

Jones, D. M. (1990). Meningococci with reduced susceptibility to penicillin. The Lancet, 335(8693), 863–864. https://doi.org/10.1016/0140-6736(90)90985-E

Lapadula, G., et al. (2009). Imported ciprofloxacin-resistant Neisseria meningitidis. Emerging Infectious Diseases, 15(11), 1852–1854. https://doi.org/10.3201/eid1511.090833

Marín, J. E. O., Villatoro, E., Luna, M. J., Barrientos, A. M., Mendoza, E., Lemos, A. P. S., et al. (2021). Emergence of MDR invasive Neisseria meningitidis in El Salvador, 2017–2019. Journal of Antimicrobial Chemotherapy, 76(5), 1155–1159. https://doi.org/10.1093/jac/dkab010

Marín, J. E. O., Boza, M. J. L., Camargo, C. H., Campos, K. R., Santos, M. B. N., Yamada, A. Y., Sacchi, C. T., & Lemos, A. P. S. (2026). Stepwise evolution of triple antimicrobial resistance in Neisseria meningitidis. The Journal of Infectious Diseases. https://doi.org/10.1093/infdis/jiag113

Oppenheim, B. (1997). Antibiotic resistance in Neisseria meningitidis. Clinical Infectious Diseases, 24(Suppl. 1), S98–S101. https://doi.org/10.1093/clinids/24.supplement_1.s98

Rainbow, J. (2005). Rifampin-resistant meningococcal disease. Emerging Infectious Diseases, 11(6). https://wwwnc.cdc.gov/eid/article/11/6/04-1288_article

Round, A. (1988). Penicillin and meningococci. The Lancet, 331(8587), 702. https://doi.org/10.1016/S0140-6736(88)91496-1

Saez-Nieto, J. A., et al. (1987). Isolation of Neisseria meningitidis strains with increased penicillin minimal inhibitory concentrations. Epidemiology and Infection, 99, 463–469. https://doi.org/10.1017/S0950268800067960

Saez-Nieto, J. A., et al. (1992). Epidemiology and molecular basis of penicillin-resistant Neisseria meningitidis in Spain: A 5-year history (1985–1989). Clinical Infectious Diseases, 14(2), 394–402. https://doi.org/10.1093/clinids/14.2.394

Shultz, T. R., Tapsall, J. W., & White, P. A. (2000). An invasive isolate of Neisseria meningitidis showing decreased susceptibility to quinolones. Antimicrobial Agents and Chemotherapy, 44(4), 1116. https://doi.org/10.1128/AAC.44.4.1116-1116.2000

Singhal, S., et al. (2007). Ciprofloxacin-resistant Neisseria meningitidis, Delhi, India. Emerging Infectious Diseases, 13(10), 1614–1616. https://doi.org/10.3201/eid1310.060820

Stefanelli, P., et al. (2004). Emergence in Italy of a Neisseria meningitidis clone with decreased susceptibility to penicillin. Antimicrobial Agents and Chemotherapy, 48(8), 3103–3106. https://doi.org/10.1128/AAC.48.8.3103-3106.2004

Strahilevitz, J., et al. (2008). Serogroup A Neisseria meningitidis with reduced susceptibility to ciprofloxacin. Emerging Infectious Diseases, 14(10),

1667–1669. https://doi.org/10.3201/eid1410.080252
Tsang, R. S. W., et al. (2019). WGS analysis of a penicillin-resistant Neisseria meningitidis strain containing a chromosomal ROB-1 β-lactamase gene. Journal of Antimicrobial Chemotherapy, 74(1), 22–28. https://doi.org/10.1093/jac/dky391
Uriz, S., et al. (1991). Neisseria meningitidis with reduced sensitivity to penicillin: Observation in 10 children. Scandinavian Journal of Infectious Diseases, 23, 171–174. https://doi.org/10.3109/00365549109023396
Vigilancia Sanitaria, Prevención y Control de Enfermedades. (2011). Informe regional de SIREVA II, 2010. Organización Panamericana de la Salud. https://www.paho.org/es/sireva
Vigilancia Sanitaria, Prevención y Control de Enfermedades. (2012). Informe regional de SIREVA II, 2011. Organización Panamericana de la Salud. https://www.paho.org/es/sireva
Vigilancia Sanitaria, Prevención y Control de Enfermedades. (2013). Informe regional de SIREVA II, 2012. Organización Panamericana de la Salud. https://www.paho.org/es/sireva
Woods, C. R., et al. (1994). Invasive disease caused by Neisseria meningitidis relatively resistant to penicillin in North Carolina. Journal of Infectious Diseases, 170(2), 453–456. https://doi.org/10.1093/infdis/170.2.453
Wu, M., et al. (2009). Emergence of ciprofloxacin-resistant Neisseria meningitidis in North America. New England Journal of Medicine, 360(9), 886–892. https://doi.org/10.1056/NEJMoa0806414