



POMERIGGI MICROBIOLOGICI LOMBARDI

Neisseria spp e Moraxella spp: fenotipi attesi, meccanismi di resistenza acquisita, antibiogramma e diagnostica di laboratorio

Arianna Gatti
Microbiologia
ASST Ovest Milanese
Ospedale Nuovo Legnano

1

INTRODUCTION (1)

Neisseria spp e *Moraxella* spp are Gram-negative diplococci with the following general characteristics:

- Kidney bean shaped
 - Arranged in pairs mostly
 - Catalase positive
 - Oxidase positive
 - Non- motile
 - Sensitivity to temperature below 30°C
- *N. gonorrhoeae* e *N. meningitidis* and *M. catarrhalis* are the major human pathogens in the group.
 - Other *Neisseria* species are rarely implicated in human infections . They are commensals of the mouth and upper respiratory tract and hence cause opportunistic infections.

2

INTRODUCTION (2)

Organism	Habitat (Reservoir)	Mode of Transmission
Moraxella catarrhalis	Normal human flora of upper respiratory tract; occasionally colonizes female genital tract	Spread of patient's endogenous strain to normally sterile sites. Person-to-person nosocomial spread by contaminated respiratory droplets also can occur
Neisseria gonorrhoeae	Not part of normal human flora. Only found on mucous membranes of genitalia, anorectal area, oropharynx, or conjunctiva at time of infection	Person-to-person spread by sexual contact, including rectal intercourse and orogenital sex. May also be spread from infected mother to newborn during birth. Asymptomatic carriers are a significant reservoir for increased disease transmission.
Neisseria meningitidis	Colonizes oropharyngeal and nasopharyngeal mucous membranes of humans. Humans commonly carry the organism without symptoms	Person-to-person spread by contaminated respiratory droplets, usually in settings of close contact
Other Neisseria spp.	Normal human flora of the upper respiratory tract	Spread of patient's endogenous strain to normally sterile sites. Person-to-person spread may also be possible, but these species are not common causes of human infections
Neisseria animaloris	Not part of normal human flora. Animal oral and respiratory commensal organism	Animal contact, particularly bites or scratches from dogs and cats

3

Neisseria spp and Moraxella spp: Laboratory Diagnosis

1) Specimen Collection Sites

M. catarrhalis:

- **Nasopharyngeal Swabs:** Recommended for detecting carriers and in pediatric cases.
- **Sputum:** Collected for lower respiratory tract infections.
- **Sinus Aspirates:** Used for confirming sinusitis.
- **Bronchoalveolar Lavage Fluid (BALF):** Used for lower respiratory tract infection evaluation.
- **Blood and Other Fluids:** Can be collected in cases of systematic infection

N. meningitidis

- **Cerebrospinal Fluid (CSF):** A minimum of 200 μ L to 1mL is usually required
- **Blood:** Crucial for septicemia.
- **Nasopharyngeal Swab/Aspirate:** Recommended for screening carriers.
- **Skin Scrapings/Biopsy:** Taken from petechial rash lesions.
- **Other Fluids:** Synovial, pleural, or pericardial fluid

4

N. gonorrhoeae

TABLE 1
Methods of collection of clinical specimens for the laboratory diagnosis of gonorrhoea

Specimen type	Method of collection
Urethral	Express urethral exudates when patients have discharge. If there is no discharge, compress the meatus vertically to open the distal urethra and insert a thin, water-moistened swab (calcium alginate or Dacron) with flexible wire slowly (3 cm to 4 cm in males or 1 cm to 2 cm in females), rotate slowly and withdraw gently.
Urine	Ask patients to collect only the first 10 mL to 15 mL of urine. Patients should not have voided for at least 2 h before specimen collection to increase the chance of detecting the organism.
Cervical	Insert a speculum into the vagina to view the cervix. Insert a swab 1 cm to 3 cm into the endocervical canal and rotate for 10 s to 30 s to allow absorption of exudates.
Vaginal	Collect pooled vaginal secretions, if present. Vaginal wash specimens are most preferred and acceptable to prepubertal girls. If not possible, rub a sterile cotton swab against the posterior vaginal wall and allow the swab to absorb the specimen.
Rectal	Specimens may be obtained blindly or, preferably, through an anoscope. Insert a swab 2 cm to 3 cm into the anal canal. Avoiding fecal material, rotate to sample crypts just inside the anal ring; allow the swab to absorb specimen for 10 s.
Oropharyngeal	Rub sterile swabs over the posterior pharynx and tonsillar crypts, or obtain nasopharyngeal aspirate from infants.
Conjunctiva	Any exudate or pus present in the eye should be carefully removed with a sterile swab. A second swab moistened with saline should be used to rub the affected conjunctiva. This swab should be broken off into a vial of transport medium.
Sterile body fluids	Clean skin puncture site with iodine (1% to 2%, or 10% solution of povidone-iodine [1% free iodine]). If tincture of iodine is used, remove with 70% ethanol to avoid burn. Perform percutaneous aspiration for pleural, pericardial, peritoneal or synovial fluids. Use nonheparinized collection if possible.

Ng and MartinCan J Infect Dis Med Microbiol 2005

5

Neisseria spp and Moraxella spp: Laboratory Diagnosis**2) collection and transport**

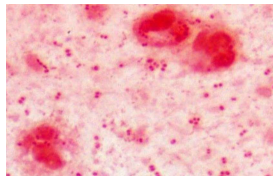
- The appropriate collection and transportation of clinical specimens is essential for isolation, identification, and characterization.
- Clinical specimens suspected of harbouring them should never be refrigerated and culture media should be brought to room temperature before inoculation
- Swabs are acceptable for *N. gonorrhoeae* testing if the specimen will be plated within 6 hours; however, reduced recovery may result within 30 minutes of collection.

6

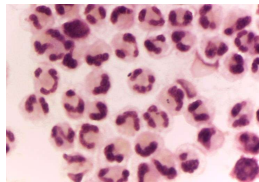
Neisseria spp and Moraxella spp: Laboratory Diagnosis

3) Microscopic examination/gram staining

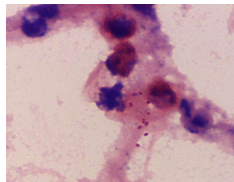
- All Neisseria species and M catarrhalis have very similar microscopic morphology
- Infections of *N. gonorrhoeae*, *N meningitidis* and *M. catarrhalis* are usually highly purulent because the infection causes profuse PMN activity. Phenomena of phagocytosis is often observed.



M. catarrhalis in sputum



N. Meningitidis in CSF



N. Gonorrhoeae in urethral specimen

7

Neisseria spp e Moraxella spp: Microscopic examination/gram staining

- The direct Gram stain of body fluids for either *N. gonorrhoeae* or *N. meningitidis* is best accomplished using a cyto centrifuge, which can concentrate small numbers of organisms 100-fold.
 - Gram stain diagnosis in *N. Gonorrhoeae* infection has a sensitivity and specificity of >95 percent in men with symptomatic urethritis. The specificity of Gram stain diagnosis in women is also high if the cervix is wiped clean to remove cervical secretions before collecting the specimen; however, the sensitivity is only about 50 percent. The sensitivity and specificity of the Gram stain for rectal specimens are lower than with cervical specimens.
 - Clinical practice in bacterial meningitis, should encourage Gram staining due to its affordability, accessibility, ease of application, and speed.
 - Although the specificity of *N. Meningitidis* Gram staining in CSF specimens is high, at 95%, it has a largely variable sensitivity of 75%; it varies between 30% and 89%, mainly related to low bacterial load or early antibiotic Treatment.
 - The sensitivity of *N. Meningitidis* Gram stains on skin lesion samples is 30%-70%.
 - *M. catarrhalis* has a notable tendency to resist decolorization, which can make them appear gram-variable or falsely Gram-positive if the decolorization step is too short or weak.
- Ng and MartinCan J Infect Dis Med Microbiol 2005
- Ciftci et al. Frontiers in Pediatrics 2025

8

Neisseria spp and Moraxella spp: Laboratory Diagnosis

4) Media and cultural conditions for isolation (gold standard for *N. meningitidis* and *M. catarrhalis*)

Neisseria species (spp.) and *Moraxella* spp require enriched and warm environments to grow. They are highly sensitive to temperature changes and dehydration.

They generally grow best at 35-37°C in an atmosphere containing 5% CO₂ ambient air

Primary Culture Media (Non-Selective)

• Chocolate Agar (CHOC)

Selective Culture Media (*Neisseria* spp)

• Modified Thayer-Martin (MTM) Agar: Contains vancomycin (inhibits Gram-positives), colistin (inhibits Gram-negatives), nystatin (inhibits fungi), and trimethoprim (inhibits swarming *Proteus*).

• Martin-Lewis Agar: Similar to MTM but uses anisomycin instead of nystatin, providing better inhibition of fungi.

• New York City (NYC) Medium: medium, a transparent medium containing lysed horse blood, horse plasma, yeast dialysate, and the same antibiotics as MTM, also has been used.

9

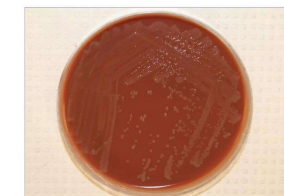
Neisseria spp and Moraxella spp: Laboratory Diagnosis

5) colony morphology on chocolate agar

- ***Moraxella catarrhalis*** on chocolate agar appears as grey-white, opaque, smooth, and convex colonies, typically 1-2 mm in diameter after 24 hours of incubation at 37°C. The colonies are notably non-hemolytic, brittle, and exhibit a distinct, waxy consistency that allows them to be moved across the agar surface intact, known as the "hockey puck sign"



- ***Neisseria* spp** on chocolate agar appears as medium-to-large (1-5 mm), convex, smooth, glistening, and moist colonies after 18-24 hours, often having a bluish-grey or grey color. Colonies are typically non-hemolytic and may appear mucoid, with a distinct, clearly defined edge



10

Neisseria spp and Moraxella spp: Laboratory Diagnosis

6) Identification

Sugar metabolism (useful for identification):

- *N. gonorrhoeae*: oxidizes glucose
- *N. meningitidis*: oxidizes glucose + maltose
- *Moraxella* spp: asaccharolytic

• **MALDI-TOF MS** has been widely adopted for identification of bacteria from clinical samples. it does not yet reliably distinguish between *N. meningitidis* and several non pathogenic *Neisseria* species, such as *Neisseria cinerea* and *Neisseria polysaccharea*. This is most likely due to the high degree of genetic relatedness between *N. meningitidis* and the commensal *Neisseria* species. Therefore, the use of complementary laboratory techniques, including PCR, 16S rRNA sequencing, is typically recommended for identification of *N. meningitidis* and *N. Gonorrhoeae*.

• **Polymerase Chain Reaction (PCR)**: Molecular testing for bacterial DNA is increasingly used for its high sensitivity and ability to detect the bacteria even after antibiotic therapy, providing faster results than culture.

Features of the methods used for laboratory diagnosis of invasive meningococcal disease

Method	Advantages	Disadvantages	Sensitivity, %	Specificity, %
Gram Staining	<ul style="list-style-type: none"> • Rapid (in minutes) • Inexpensive, accessible, easy • Not affected by antibiotic usage 	<ul style="list-style-type: none"> • Low sensitivity with low bacterial load • Low sensitivity in case of low amount of CSF not allowing centrifugation 	66.0-97.2	97.4-100
Culture	<ul style="list-style-type: none"> • Gold standard, definite identification • Allows for antibiotic susceptibility test • Isolates can be archived, allows for further characterization • Guiding the determination of vaccine content 	<ul style="list-style-type: none"> • Time-consuming (in days) • Difficulty in storage and transport of the samples • Results are affected by antibiotic usage 	55-63	100
rt-PCR	<ul style="list-style-type: none"> • Rapid (in hours) • High sensitivity and specificity • Not affected by antibiotic usage 	<ul style="list-style-type: none"> • Expensive, requires special equipment 	89.5-96	94.5-100
MALDI-TOF	<ul style="list-style-type: none"> • Rapid (in minutes) • Rapid identification from positive blood culture bottle or CSF samples 	<ul style="list-style-type: none"> • Requires approximately 10⁵-10⁶ CFU/ml bacteria • Needs to be updated in the identification of <i>N. meningitidis</i> 	100%	52-92
Antigen tests	<ul style="list-style-type: none"> • Rapid (in minutes) • Requires very little CSF sample • Easy to apply • Easy storage of test kits 	<ul style="list-style-type: none"> • Absence of serogroup B in the panel • The sensitivity range being wide (or variable) 	32.0-95.0	90.0-93.8
qPCR-HRM	<ul style="list-style-type: none"> • Less expensive than the RT-PCR • Probe-free method 		-	-
LAMP	<ul style="list-style-type: none"> • Easy, fast, and inexpensive • CSF, blood, nasopharyngeal swab can be used 		84-100	94-100
			ctRA 89/100	ctRA 100/98.9
			NMO_1242 100	NMO_1242 100
WGS	<ul style="list-style-type: none"> • Extensive characterization of the isolate 	<ul style="list-style-type: none"> • Requires expensive laboratory infrastructure and technical knowledge • Still useful in epidemiology rather than diagnosis 		

CSF, cerebrospinal fluid; rt-PCR, real time polymerase chain reaction; MALDI-TOF, matrix assisted laser desorption ionization time of flight mass spectrometry; qPCR-HRM, qualitative PCR with high-resolution melting; LAMP, loop-mediated isothermal amplification; WGS, whole genome sequencing.

• Ciftci et al. *Frontiers in Pediatrics* 2025

Limitation of ctrA as a Target for Neisseria meningitidis Identification and Potential Alternative Targets

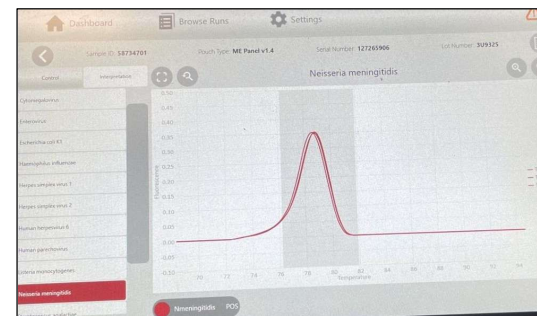
• The ctrA gene (capsule) is highly conserved among the isolates. The sensitivity of ctrA for detecting N. meningitidis was 71.6%, and specificity data were not available.

• These results highlight the importance of using multiple complementary gene targets, including noncapsular genes, for the molecular identification of Neisseria meningitidis from clinical samples

TABLE 1 Cycle threshold values of *Neisseria meningitidis* PCR panel tested for different *N. meningitidis* gene targets

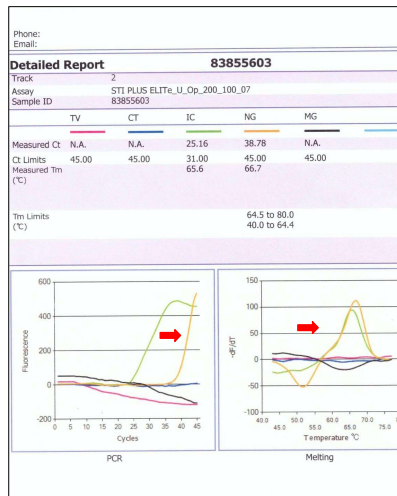
Sample	Specimen type ^a	Serogroup ^b	Serotype ^b	C _t values ^c			
				ctrA	tonf	Mena	sdhC
1	Throat	NE	15	Negative	28.34	29.39	32.7
2	Blood	NE	15	Negative	29.06	29.75	30.99
3	Sputum	NE	NT	Negative	28.22	28.92	29.88
4	Sputum	NE	4	Negative	28.47	29.48	30.13
5	Sputum	NE	NT	Negative	28.7	29.09	30.15
6	Eye	NE	19	Negative	29.6	30.16	31.12
7	BAL	NE	4	Negative	28.88	29.66	30.36
8	Eye	Z	NT	28.42	29.4	29.99	31.03
9	Eye	Z	4	29.41	29.07	29.73	30.5
10	Sputum	AA	NT	27.93	28.15	28.9	Negative
11	Eye	AA	1,19	29.55	29.02	30.07	30.58
12	Sputum	AA	19	28.86	28.1	28.77	29.69
13	Eye	AA	15	Negative	28.98	29.6	30.49
14	Eye	AA	2a	29.22	28.95	29.73	30.61
15	Eye	E	NT	28.78	28.38	29.13	29.91
16	Sputum	E	NT	29.13	Negative	29.56	30.54
17	Eye	E	19	29.84	29.49	30.38	31.46
18	Sputum	E	NT	29.17	28.78	29.67	29.96
19	Eye	E	1,19	28.67	28.07	28.94	29.92
20	Wound	NG	NT	28.65	28.18	28.81	28.87
21	Eye	NG	NT	29.61	28.88	28.87	29.92
22	Sputum	NG	14,19	29.38	28.74	29.6	30.25
23	Urethra	NG	NT	29.12	28.72	29.44	30.08
24	Eye	NE	19	28.18	28.69	29.52	30.23
25	BAL	NE	4	Negative	29.82	29.88	31.75
26	Blood (direct)	W	ND	31.67	31.6	29.55	30.57
27	Blood (direct)	NG	NT	38.92	38.17	39.02	39.62
28	CSF (direct)	B	ND	29.27	28.95	32.09	33.17
29	CSF (direct)	NG	NT	38.39	Negative	39.23	Negative
30	CSF (direct)	Y	ND	28.91	28.98	28.98	29.97
31	CSF (direct)	B	ND	27.48	28.67	28.07	29.91
32	CSF (direct)	B	ND	22.83	22.71	23.46	23.89

I. Sirluck-Schroeder. Journal of Clinical Microbiology 2022



Recent advancements in **multiplex PCR point-of-care panels** enable rapid diagnosis within hours. Commercial kits use the Multiplex assay method to investigate multiple pathogens simultaneously directly in CSF or blood sample with high diagnostic accuracy for *Neisseria meningitidis* detection (The combined sensitivity exceeded 89%, while the specificity surpassed 97%)

The *pivNG* gene (also referred to as *irg* or *pilin inversion gene*) is a specific genetic marker used in molecular diagnostics to identify the bacterium *N. gonorrhoeae*.



15

Nucleic Acid Amplification Testing (NAATs) for *Neisseria Gonorrhoeae*: An Ongoing Challenge

TABLE 1. Overview of Commercial *N. gonorrhoeae* NAATs

	Roche Amplicor	ProbeTec SDA	Abbott LCx	Gen-probe APTIMA
Gene target	Cytosine DNA methyltransferase gene	Multicopy pilin gene-inverting protein homologue	Opacity protein genes	16S ribosomal RNA gene
Amplification technology	PCR	SDA	LCR	TMA
Sensitivity	64.8 to 100%	84.9 to 100%	88.2 to 97.3%	91.3 to 98.5%
Specificity	93.9 to 100%	98.4 to 100%	98.5 to 100%	98.7 to 99.3%
Positive predictive value	31.3 to 100%	54.8 to 100%	59.3 to 100%	88.1 to 97.4%
Negative predictive value	99.5 to 100%	95.2 to 100%	98.5 to 100%	99.2 to 99.9%
Cross-reactivity with other <i>Neisseria</i> species	<i>N. cinerea</i> , <i>N. flavescens</i> , <i>N. lactamica</i> , <i>N. sicca</i> , <i>N. subflava</i>	<i>N. flavescens</i> , <i>N. lactamica</i> , <i>N. subflava</i> , <i>N. cinerea</i>	None identified	None identified

- A disadvantage of NAAT methods is that they are susceptible to inhibition by substances that may be present in samples (urine). These include crystals, hemoglobin and nitrites. These inhibitory substances may lead to the false-negative results in the assay.
- Other disadvantages include cost, risk of carryover contamination, inhibition, and inability to provide antibiotic resistance data

D.M Whiley et al Journal of Molecular Diagnostics 2006

16

Molecular tool for tracking the spread of multidrug-resistant (MDR) *N. gonorrhoeae* strains

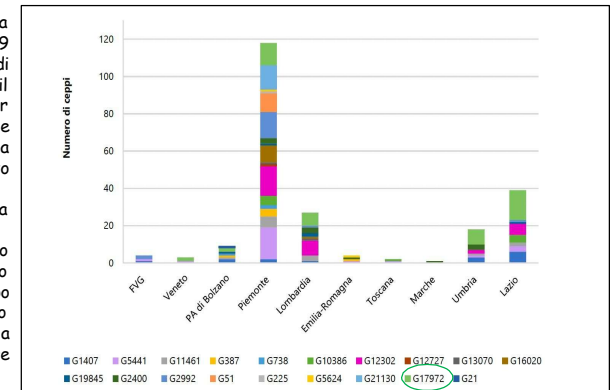
- *N. gonorrhoeae* multiantigen sequence typing (NG-MAST): has become valuable in identifying clusters of resistant strains, such as the internationally spreading G1407 genogroup, which is associated with resistance to cephalosporins, penicillins, and tetracyclines. NG-MAST sequences two variable genes, porB and tpbB.
- *Neisseria gonorrhoeae* Sequence Typing for Antimicrobial Resistance (NG-STAR): is a molecular surveillance tool used to track antimicrobial resistance (AMR) in *N. gonorrhoeae* by analyzing seven specific genes: *penA*, *mtrR*, *porB*, *ponA*, *gyrA*, *parC*, and *23S rRNA*. It assigns sequence types (STs) to identify resistant strains and predict resistance to antibiotics like ceftriaxone, cefixime, and azithromycin, aiding global surveillance.

J.C. Kwong Microb Genom 2016

17

Sorveglianza di laboratorio dell'antibiotico-resistenza in *Neisseria gonorrhoeae* Italia 2018-2022

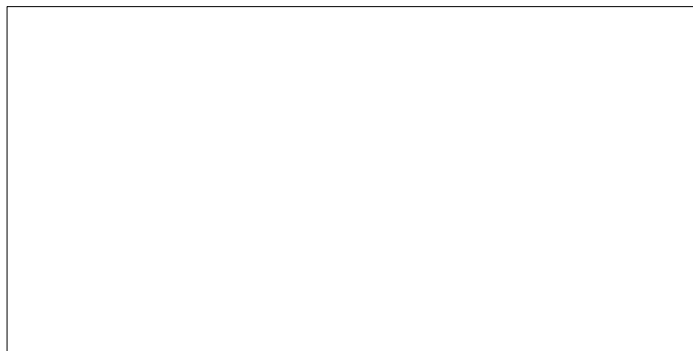
La caratterizzazione molecolare ha permesso di individuare 19 genogruppi nel periodo di osservazione: tra i più frequenti il G17972, identificato nella maggior parte dei centri collaboranti e associato a ceppi resistenti alla ciprofloxacina. Il G12302 è stato identificato in centri collaboranti presenti in 4 Regioni e associato a ceppi resistenti all'azitromicina e ciprofloxacina. In linea con quanto riportato in Europa, si è osservato una diminuzione del genogruppo G1407. Il G21130, identificato solo in alcuni centri collaboranti nella Regione Piemonte, risulta essere associato a ceppi PPNG.



Rapporti ISS Sorveglianza RIS-1/2023

18

Percentuale di ceppi di *N. gonorrhoeae* resistenti alla ciprofloxacina, all'azitromicina, al cefixime e produttori di β -lattamasi (PPNG), 2018-2022



Rapporti ISS Sorveglianza RIS-1/2023

19

Gene	Identification			Screening		
	Identification from databases	Screened	Excluded	Assessed for eligibility	Excluded	Studies included in qualitative and quantitative analysis
<i>penA</i>	226	62	164	19	43	19
<i>gyrA</i> and <i>parC</i>	185	53	132	23	30	23
<i>mtrR</i>	180	66	114	18	48	18
<i>tetM</i>	102	26	76	12	14	12

The gene *penA* (*PenA* family class A beta-lactamase) is related to resistance to penicillins and cephalosporins. The genes *gyrA* (*DNA gyrase subunit A*) and *parC* (*DNA topoisomerase IV subunit A*) are related to resistance to quinolones, the *mtrR* (*multidrug efflux system transcriptional repressor*) gene is related to penicillin, tetracycline, cephalosporins and macrolides, and the gene *tetM* (*tetracycline resistance ribosomal protection protein*) is related to resistance to tetracyclines.

- **Resistance to azithromycin:** *Mtr* (multiple transferable resistance) efflux pumps are triple efflux pumps (*MtrCDE*) that export a variety of antimicrobial agents such as antimicrobial peptides, antibiotics, bile salts and fatty acids.
- **Resistance to ciprofloxacin:** Gene Mutations *gyrA* (*DNA gyrase*) and *parC* (*topoisomerase IV*).
- **Resistance to tetracycline:** *tetM* Abolishes the inhibitory effect of tetracyclin on protein synthesis by a non-covalent modification of the ribosomes.

A. C. Mendes et al. Frontiers in Microbiology 2025

20

Mutations in the *penA* gene of *Neisseria gonorrhoeae*

- Beta-lactam antibiotics, such as penicillin and cephalosporins, inhibit peptidoglycan synthesis in the bacterial cell wall by binding the beta-lactam ring to transpeptidase enzymes called penicillin-binding proteins (PBPs) located in the periplasm.
- Mutations in the *penA* gene alter the PBP protein, preventing antibiotic binding.
- *penA* allelic mosaics are associated with reduced susceptibility to cephalosporins. These alleles in *penA* are called "mosaics" because their DNA sequence appears to have been formed by homologous recombination with DNA from other species of *Neisseria* ssp (*N. cinerea* or *N. flavescens*) that are naturally resistant to third-generation cephalosporin, resulting in a "mosaic" gene structure

A. C. Mendes. *Frontiers in Microbiology* 2025

21

Mutations in the *penA* gene of *Neisseria meningitidis*

- *neisseria meningitidis* generally remains highly susceptible to third-generation cephalosporins (ceftriaxone, cefotaxime), rifampin, and ciprofloxacin, which are standard for treatment and chemoprophylaxis. However, reduced susceptibility to penicillin is increasing due to *penA* gene mutations, though it rarely causes clinical treatment failure.
- Resistance to penicillin is an emerging concern, with resistance rates in Europe ranging from 0.7% to 15.9%
- **Specific Mutations:** Key amino acid substitutions in the C-terminal region of PBP2 are associated with this phenotype, notably **F504L**, **A510V**, **I515V**, **G541N**, and **I566V**.
- Recently, *N. meningitidis* carrying the ROB-1 β -lactamase conferring penicillin resistance has been reported

J.Roca-Grande et al. *Emerging Microbes & Infections* 2025

22

Moraxella catarrhalis: scelta dei test di sensibilità (fenotipo atteso)

MORAXELLA CATARRHALIS: INTERPRETAZIONE DEI TEST

- Praticamente tutti i ceppi vanno considerati potenzialmente produttori di β lattamasi (BRO-1 e BRO-2) e pertanto refrattari ai β lattamici β lattamasi sensibili.
- Si può usare in generale il test del nitrocefina come screening. Se β lattamasi negativi refertare ampicillina S
- L'enzima BRO-1 esprime una resistenza più tenace di BRO-2 e sembra il responsabile della R dei β lattamasi + con ampi R, mentre BRO-2 determina la R dei β lattamasi + con ampi S.
- I ceppi β lattamasi + si considerano penicillina, ampicillina e amoxicillina R anche se S in vitro, mentre amoxicillina/clavulanato supera la resistenza
- Nei ceppi β lattamasi + viene relativamente condizionata anche la sensibilità alle cefalosporine di seconda generazione, SXT e macrolidi (che non sono di prima scelta)
- Non ci sono particolari problemi per i fluorochinoloni

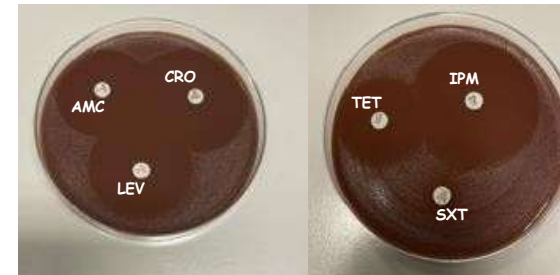
Moraxella catarrhalis:

- 1 - Test indispensabili:
nitrocefina
- 2 - Test di seconda istanza:
ampicillina, amoxicillina, amoxi/clavulanato, cefaclor, cefuroxime, cotrimossazolo
- 3 - Eventuali test di terza istanza:
levofloxacina, eritromicina, cloramfenicolo, tetraciclina

A. Camporese. Riv Med Lab - JLM, Vol. 3, N. 4, 2002

23

Moraxella catarrhalis: scelta dei test di sensibilità (fenotipo atteso)



Reports of resistance to tetracycline varied from 0.8% to 12.9% and to cotrimoxazole from 0.8% to 19% (Kim M. Hare Journal of Medical Microbiology 2019)

24

Moraxella catarrhalis: macrolide susceptibility

- Recently, the prevalence of macrolide-resistant *Moraxella catarrhalis* has been reported, especially among Chinese children, often with high-level resistance (MIC > 256 mg/L and with rates of 40-80%.
- The most common mechanisms of macrolide resistance include ribosomal modification by methylation or mutation which prevents binding of the antibiotic to its target, or efflux of the antibiotic by efflux pumps.
- High-level resistance is often associated with a mutation in the 23S rRNA gene (A2330T).

Ya-li Liu Emerging Microbes & Infections 2022

25

Neisseria spp and *Moraxella* spp: Antibiogramma

<i>Neisseria gonorrhoeae</i>			EUCAST Clinical Breakpoint Tables v. 16.0, valid from 2026-01-01	
Expert Rules and Expected Phenotypes			Guidance documents	
For comments on dosages related to breakpoints, see the table of dosages.			For abbreviations and explanations of breakpoints, see the Notes sheet	
			Disk diffusion criteria for antimicrobial susceptibility testing of <i>Neisseria gonorrhoeae</i> have not yet been defined and an MIC method should be used. If a commercial MIC method is used, follow the manufacturer's instructions. Laboratories with few isolates are encouraged to refer these to a reference laboratory for testing.	
Penicillins ¹	MIC breakpoints (mg/L)			Notes
	S ≤	R >	ATU	
Benzylpenicillin (surrogate agent) ¹	0.06 ¹	1		1. Always test for beta-lactamase (tests based on a chromogenic cephalosporin can be used). If beta-lactamase positive, report resistant to ampicillin and amoxicillin. If beta-lactamase negative, determine the MIC of benzylpenicillin. Infer the susceptibility to ampicillin and amoxicillin from the benzylpenicillin MIC (do not report benzylpenicillin susceptibility).
Ampicillin ¹	Note ¹	Note ¹		
Ampicillin-sulbactam	IE	IE		
Amoxicillin ¹	Note ¹	Note ¹		
Amoxicillin-clavulanic acid	IE	IE		
Piperacillin	-	-		
Piperacillin-tazobactam	-	-		
Ticarcillin-clavulanic acid	-	-		
Temocillin	IE	IE		
Phenoxyethylpenicillin	-	-		
Oxacillin	-	-		
Cloxacillin	-	-		
Dictyoxacillin	-	-		
Flucloxacillin	-	-		
Mecillinam oral (pivmecillinam) (uncomplicated UTI only)	-	-		

26

Neisseria gonorrhoeae
Expert Rules and Expected Phenotypes [Guidance documents](#)

Cephalosporins	MIC breakpoints (mg/L)			Fluoroquinolones	MIC breakpoints (mg/L)			
	S ≤	R >	ATU		S ≤	R >	ATU	
Cefaclor	-	-	-	Ciprofloxacin	0.03	0.06		
Cefadroxil	-	-	-	Delamanid	IE	IE		
Cefalexin	-	-	-	Levofloxacin	IE	IE		
Cefazolin	-	-	-	Moxifloxacin	IE	IE		
Cefepime	-	-	-	Nalidixic acid (screen only)	NA	NA		
Cefepime-avibactam	-	-	-	Norfloxacin (uncomplicated UTI only)	-	-		
Cefiderocol	IE	IE	-	Oxazolidinones	0.125	0.25		
Cefixime	0.125	0.125	-	Tetracyclines	MIC breakpoints (mg/L)			
Cefotaxime	0.125	0.125	-		S ≤	R >	ATU	
Cefoxitin	IE	IE	-		Doxycycline	IE	IE	
Cefpodoxime	-	-	-		Erythromycin	IE	IE	
Ceftaroline	-	-	-		Minocycline	IE	IE	
Ceftazidime	-	-	-	Tetracycline	0.5	0.5		
Ceftazidime-avibactam	-	-	-	Tigecycline	IE	IE		
Ceftibuten	-	-	-	Miscellaneous agents	MIC breakpoints (mg/L)			
Ceftolozane-tazobactam	-	-	-		S ≤	R >	ATU	
Ceftrozone	0.125	0.125	-		Spectinomycin	64	64	
Cefuroxime iv	-	-	-					
Cefuroxime oral	-	-	-					

No MIC breakpoints for Aminoglycosides Carbapenems Macrolides Monobactams



Neisseria meningitidis				EUCAST Clinical Breakpoint Tables v. 16.0, valid from 2026-01-01	
Expert Rules and Expected Phenotypes		Guidance documents		For abbreviations and explanations of breakpoints, see the Notes sheet	
Disk diffusion criteria for antimicrobial susceptibility testing of <i>Neisseria meningitidis</i> have not yet been defined and an MIC method should be used. If a commercial MIC method is used, follow the manufacturer's instructions.					
Penicillins ¹	MIC breakpoints (mg/L)			Notes	
	S ≤	R >	ATU	Numbered notes relate to general comments and/or MIC breakpoints.	
Benzyloxybenzylpenicillin (all indications)	0.25	0.25		1. All breakpoints pertain to iv administration.	
Ampicillin (indications other than meningitis)	0.125	1			
Ampicillin (meningitis)	IE	IE			
Ampicillin-sulbactam	IE	IE			
Amoxicillin (indications other than meningitis)	0.125	1			
Amoxicillin (meningitis)	IE	IE			
Amoxicillin-clavulanic acid	-	-			
Piperacillin	-	-			
Piperacillin-tazobactam	-	-			
Ticarcillin-clavulanic acid	-	-			
Temocillin	-	-			
Phenoxyethylpenicillin	-	-			
Oxacillin	-	-			
Cloxacillin	-	-			
Dicloxacillin	-	-			
Flucloxacillin	-	-			
Mecillinam oral (pivmecillinam) (uncomplicated UTI only)	-	-			

Neisseria meningitidis				Expert Rules and Expected Phenotypes	
Cephalosporins	MIC breakpoints (mg/L)			Notes	
	S ≤	R >	ATU	Numbered notes relate to general comments and/or MIC breakpoints.	
Cefaclor	-	-		1. Resistant isolates are rare or not yet reported. The identification and antimicrobial susceptibility test result on any such isolate must be confirmed and the isolate sent to a reference laboratory.	
Cefadroxil	-	-			
Cefalexin	-	-			
Cefazolin	-	-			
Cefepime	-	-			
Cefepime-enmetazobactam	-	-			
Cefiderocol	IE	IE			
Cefixime	-	-			
Cefotaxime (all indications) ¹	0.125	0.125			
Cefoxitin	-	-			
Cefpodoxime	-	-			
Cefuroxime	-	-			
Ceftazidime	-	-			
Ceftazidime-avibactam	-	-			
Ceftibuten	-	-			
Ceftiofole	-	-			
Ceftolozane-tazobactam	-	-			
Ceftriaxone (all indications including prophylaxis) ¹	0.125	0.125			
Cefturoxime iv	-	-			
Cefuroxime oral	-	-			
Carbapenems ^{1,2}	MIC breakpoints (mg/L)			Notes	
	S ≤	R >	ATU	Numbered notes relate to general comments and/or MIC breakpoints.	
Doripenem	Note ³	Note ³		1. Resistant isolates are rare or not yet reported. The identification and antimicrobial susceptibility test result on any such isolate must be confirmed and the isolate sent to a reference laboratory.	
Ertapenem	IE	IE		2. Breakpoints for serious <i>N. meningitidis</i> systemic infections (meningitis with or without septicemia) have been determined for meropenem only.	
Imipenem	Note ³	Note ³		3. The addition of a beta-lactamase inhibitor does not add clinical benefit.	
Imipenem-celebactam ³	Note ³	Note ³			
Meropenem (all indications) ^{1,2}	0.25	0.25			
Meropenem-azborbactam ³	Note ³	Note ³			

Neisseria meningitidis
Expert Rules and Expected Phenotypes

Fluoroquinolones	MIC breakpoints (mg/L)		
	S ≤	R >	ATU
Ciprofloxacin (all indications, including meningitis and prophylaxis)	0.016	0.016	
Delafloxacin	IE	IE	
Levofloxacin	IE	IE	
Moxifloxacin	IE	IE	
Nalidixic acid (screen only)	NA	NA	
Norfloxacin (uncomplicated UTI only)	-	-	
Ofloxacin	IE	IE	

Miscellaneous agents	MIC breakpoints (mg/L)		
	S ≤	R >	ATU
Chloramphenicol (meningitis) ¹	2	2	
Colistin	-	-	
Daptomycin	-	-	
Fosfomycin iv	-	-	
Fosfomycin oral	-	-	
Fusidic acid	-	-	
Lefamulin	-	-	
Metronidazole	-	-	
Nitrofurantoin (uncomplicated UTI only)	-	-	
Nitroxoline (uncomplicated UTI only)	-	-	
Rifampicin (prophylaxis only)	0.25	0.25	
Spectinomycin	-	-	
Trimethoprim (uncomplicated UTI only)	-	-	
Trimethoprim-sulfamethoxazole	-	-	

Tetracyclines	MIC breakpoints (mg/L)			Notes
	S ≤	R >	ATU	
Doxycycline	-	-		1. Tetracycline can be used to predict susceptibility to minocycline for prophylaxis against <i>N. meningitidis</i> infections.
Eravacycline	IE	IE		
Minocycline (prophylaxis only)	1 ¹	1 ¹		
Tetracycline (screen only)	2 ¹	2 ¹		
Tigecycline	IE	IE		

Moraxella catarrhalis
Expert Rules and Expected Phenotypes

EUCAST Clinical Breakpoint Tables v. 16.0, valid from 2026-01-01
For abbreviations and explanations of breakpoints, see the Notes sheet

Guidance documents

Penicillins	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes
	S ≤	R >	ATU		S ≥	R <	ATU	
Benzylpenicillin	-	-			-	-		Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method. 1. Most <i>M. catarrhalis</i> produce beta-lactamase, although beta-lactamase production is slow and may give weak results with <i>in vitro</i> tests. Beta-lactamase producers should be reported resistant to penicillins and aminopenicillins without inhibitors. 2. For susceptibility testing purposes, the concentration of sulbactam is fixed at 4 mg/L. 3/A. Susceptibility can be inferred from amoxicillin-clavulanic acid. 4. For susceptibility testing purposes, the concentration of clavulanic acid is fixed at 2 mg/L.
Ampicillin	1 ^{1,2}	1 ^{1,2}			-	-		
Ampicillin-sulbactam	1 ^{1,2}	1 ^{1,2}			Note ^a	Note ^a		
Amoxicillin	1 ¹	1 ¹			-	-		
Amoxicillin-clavulanic acid	1 ¹	1 ¹		2-1	19	19		
Piperacillin	1 ¹	1 ¹			-	-		
Piperacillin-tazobactam	Note ^b	Note ^b			Note ^a	Note ^a		
Ticarcillin-clavulanic acid	IE	IE			IE	IE		
Temocillin	IE	IE			IE	IE		
Phenoxyethylpenicillin	-	-			-	-		
Oxacillin	-	-			-	-		
Cloxacillin	-	-			-	-		
Dicloxacillin	-	-			-	-		
Flucloxacillin	-	-			-	-		
Mecillinam oral (pivmecillinam) (uncomplicated UTI only)	-	-			-	-		

Moraxella catarrhalis									
Expert Rules and Expected Phenotypes									
Cephalosporins	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes	
	S ≤	R >	ATU		S ≥	R <	ATU		
Cefaclor	-	-	-	-	-	-	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Cefadroxil	-	-	-	-	-	-	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Cefazolin	-	-	-	-	-	-	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Cefepime	4	4	-	30	20	20	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Cefepime-avibactam ^a	Note ^a	Note ^a	-	Note ^a	Note ^a	Note ^a	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Cefiderocol	IE	IE	-	IE	IE	IE	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Cefixime	0.5	0.25	-	5	21	21	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Cefotaxime	1	2	-	5	20	17	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Cefoxitin	IE	IE	-	IE	IE	IE	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Cefprozime	IP	IP	-	10	IP	IP	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Cefuroxime	IE	IE	-	IE	IE	IE	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Ceftazidime	-	-	-	-	-	-	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Ceftazidime-avibactam	-	-	-	-	-	-	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Ceftibuten	IE	IE	-	IE	IE	IE	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Cefibiprolol	IE	IE	-	IE	IE	IE	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Ceftiozanone-avibactam	IE	IE	-	IE	IE	IE	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Ceftriaxone	1	2	-	30	24	21	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Cefuroxime iv	4	8	-	30	21	18	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Cefuroxime oral	0.001	4	-	30	20	21	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Carbapenems	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes	
	S ≤	R >	ATU		S ≥	R <	ATU		
Meropenem	1	2	-	10	22	22	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Imipenem	1	2	-	10	22	22	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Ertapenem	1	2	-	10	22	22	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Meropenem-avibactam	1	2	-	10	22	22	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Imipenem-cilastatin	1	2	-	10	22	22	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Ertapenem-avibactam	1	2	-	10	22	22	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	

Moraxella catarrhalis									
Expert Rules and Expected Phenotypes									
Fluoroquinolones	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes	
	S ≤	R >	ATU		S ≥	R <	ATU		
Ciprofloxacin	0.125	0.125	-	5	11 ^a	11 ^a	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Delamanid	IE	IE	-	IE	IE	IE	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Levofloxacin	0.125	0.125	-	5	29 ^a	29 ^a	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Moxifloxacin	0.25	0.25	-	5	28 ^a	28 ^a	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Nalidixic acid (screen only)	NA	NA	-	30	23 ^a	23 ^a	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Norfloxacin (uncomplicated UTI only)	-	-	-	-	-	-	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Ofloxacin	0.25	0.25	-	5	28 ^a	28 ^a	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Macrolides, lincosamides and streptogramins	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes	
	S ≤	R >	ATU		S ≥	R <	ATU		
Azithromycin	0.25 ^a	0.25 ^a	-	Note ^a	Note ^a	Note ^a	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Clarithromycin	0.25 ^a	0.25 ^a	-	Note ^a	Note ^a	Note ^a	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Erythromycin	0.25	0.25	-	15	23 ^a	23 ^a	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Roxithromycin	0.5 ^a	0.5 ^a	-	Note ^a	Note ^a	Note ^a	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Clindamycin	-	-	-	-	-	-	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Quinupristin-dalfopristin	-	-	-	-	-	-	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Tetracyclines	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes	
	S ≤	R >	ATU		S ≥	R <	ATU		
Doxycycline	1 ^a	1 ^a	-	Note ^a	Note ^a	Note ^a	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Eravacycline	IE	IE	-	IE	IE	IE	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Minocycline	1 ^a	1 ^a	-	30	25 ^a	25 ^a	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Tetracycline	2 ^a	2 ^a	-	30	26 ^a	26 ^a	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	
Tigecycline	IE	IE	-	IE	IE	IE	-	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.	

Moraxella catarrhalis
Expert Rules and Expected Phenotypes

Miscellaneous agents	MIC breakpoints (mg/L)			Disk content (µg)	Zone diameter breakpoints (mm)			Notes
	S ≤	R >	ATU		S ≥	R <	ATU	
Chloramphenicol	Note ¹	Note ¹			Note ¹	Note ¹		Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.
Colistin	-	-			-	-		1.A. For topical use of chloramphenicol, see table of topical agents. 2. Trimethoprim-sulfamethoxazole in the ratio 1:19. Breakpoints are expressed as the trimethoprim concentration.
Daptomycin	-	-			-	-		
Fosfomycin iv	IE	IE			IE	IE		
Fosfomycin oral	-	-			-	-		
Fusidic acid	-	-			-	-		
Levofloxacin	IE	IE			IE	IE		
Methicillin	-	-			-	-		
Nitrofurantoin (uncomplicated UTI only)	-	-			-	-		
Nitroxoline (uncomplicated UTI only)	-	-			-	-		
Rifampicin	-	-			-	-		
Spectinomycin	-	-			-	-		
Trimethoprim (uncomplicated UTI only)	-	-			-	-		
Trimethoprim-sulfamethoxazole ²	1	1		1.25-23.75	15	15		

TAKE HOME MESSAGES

- *Neisseria* spp. and *Moraxella* spp. are Gram-negative diplococci that, although sharing similar morphological characteristics, exhibit distinct clinical phenotypes, pathogenicity and resistance profiles.
- Although culture is the gold standard, molecular tests for *Neisseria* spp and *Moraxella* spp identification are increasingly used for their high sensitivity and for the ability to detect the bacteria even after antibiotic therapy, faster than culture.
- *Neisseria* spp. and *Moraxella* spp Whole Genome Sequencing is increasingly used to understand strain variation and antimicrobial resistance.
- Resistance to so many treatment options, including penicillins, sulphonamides, tetracyclines, quinolones and macrolides (including azithromycin), makes *N. gonorrhoeae* a multidrug resistant organism.