incidence also occurred for men 20–24 years of age in the VC (adjusted IRR 0.68, 95% CI 0.51–0.93) and persisted in the post-VC (adjusted IRR 0.51, 95% CI 0.33–0.78); the IRR increased for men 25–29 years of age in the post-VC (adjusted IRR 1.6, 95% CI 1.06-2.43). (Figure).

Overall, rates of gonorrhea dropped among men and women after the vaccination campaign; however, rates had already been in decline since the mid-1970s (*4*). A limited age-specific vaccine effect occurred among men and women 20–24 years of age. No vaccine effect was found among women in other age groups or birth cohorts. Among men 20–24 years of age, the persistent decline occurring among the post-VC could be explained by a herd effect, but rates subsequently increased for men 25–29 years of age. Different effects for men and women may be explained in part by changing transmission patterns and sexual behavior occurring among men who have sex with men and by inadequate adjustment of the underlying gonorrhea trend in men; however, differences by sex are difficult to interpret.

Among study limitations, our ecologic study design could not distinguish between long-term trends or behavioral factors and vaccine effects. For example, in the early 1990s, condom use increased in Norway, especially among persons in their early 20s (*5*), possibly in response to the evolving HIV epidemic (*6,7*). In addition, moderate population vaccine coverage in the VC (i.e., 63%) and a time lag between the vaccination program (1988–1992) and the start of surveillance (1993) may have diluted tangible vaccine effects. For further examination of cross-immunity of MenB vaccines with gonococci, vaccine effectiveness studies in regions where OMV vaccine was used (e.g. New Zealand) and evaluation of new protein-based vaccines are warranted.

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# *Neisseria gonorrhoeae* Resistant to Ceftriaxone and Cefixime, Argentina

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**To the Editor:** Antimicrobial resistance in *Neisseria gonorrhoeae* is increasing globally. In recent years, gonococcal strains with resistance to the extended-spectrum cephalosporin (ESC) ceftriaxone have been reported from many countries (*1*). In South America, 7 ceftriaxone-resistant strains (MICs >0.25 μg/mL) were reported from Brazil in 2007; however, these isolates have not been characterized (*2*). Emergence of cephalosporin-resistant gonorrhea would substantially limit treatment options and represent a major public health concern. We report an *N. gonorrhoeae* isolate in Argentina that was resistant to ceftriaxone and cefixime.

In September 2014, a 19-year-old heterosexual man with no underlying disease was admitted to a hospital emergency department in Rio Negro, Argentina. Physical examination showed a purulent urethral discharge. He reported having had unprotected insertive vaginal sex with multiple partners in the past few months. The patient denied recent travel outside Argentina. He had a history of gonococcal urethritis (March 2014), which was treated with a single dose (500 mg) of ceftriaxone; a gonococcal isolate obtained at that time was not sent to a reference laboratory as part of the Argentinian Gonococcal Antimicrobial Susceptibility Surveillance Program for determination of the antimicrobial susceptibility profile.

At the time of admission, we obtained and cultured a urethral swab specimen and identified an isolate as *N. gonorrhoeae* by using conventional methods (*3*). The isolate was sent to a reference laboratory, and its identity was confirmed by using the Phadebact GC Monoclonal Test (MKL

Diagnostic AB, Sollentuna, Sweden) and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Daltonik GmbH, Bremen, Germany). The patient was given a single dose (500 mg) of ceftriaxone. Five days later, the patient returned for clinical evaluation, and symptoms had resolved. Culture for test of cure was not performed.

We determined MICs of the isolate for penicillin, cefixime, ceftriaxone, tetracycline, ciprofloxacin, and azithromycin by using the agar dilution method according to the standard of the Clinical and Laboratory Standards Institute (*4*). Results were interpreted in accordance with breakpoints of this standard, except for azithromycin, for which we applied breakpoints of the European Committee on Antimicrobial Susceptibility Testing (http://www.eucast.org/).

This isolate was resistant to ceftriaxone and cefixime (MIC 0.5 μg/mL), penicillin (8 μg/mL), tetracycline (8 μg/mL), and azithromycin (1 μg/mL). However, the isolate was susceptible to ciprofloxacin (0.03 μg/mL). We obtained a negative result for β-lactamase by using the chromogenic nitrocefin disk assay (Becton Dickinson, Franklin Lakes, NJ, USA).

Resistance determinants involved in ceftriaxone resistance were amplified by PCR and sequenced as reported (*5*,*6*). We than analyzed full-length *penA* and *pilQ* gene sequences and other genetic determinants, including *mtrR*, *penB*, and *ponA* genes. We purified and sequenced PCR products by using an ABI 3500 Genetic Analyzer (Applied Biosystems, Foster City, CA, USA) and performed molecular epidemiologic characterization by using *N. gonorrhoeae* multiantigen sequence typing (http://www.ng-mast.net).

Sequence analysis of the *penA* gene, which encodes penicillin-binding protein 2 (PBP2), identified a nonmosaic PBP2 IX allele. Analysis of the *mtrR* gene and its promoter identified a single nucleotide (A) deletion in the inverted repeat of the promoter region, and a single amino acid substitution at position H105 (H→Y). Amino acid substitutions in the *porB1b* gene were found at positions G120 (G→K) and A121 (A→D). The *ponA* gene, which encodes PBP1, had an amino acid substitution at position L421 (L→P), and full-length PilQ amino acid sequence had sequence type VI. The isolate was assigned to serogroup PorB1b (WII/III), and *N. gonorrhoeae* multiantigen sequence typing showed that it had novel sequence type ST13064 (*porB*-7592 and *tbpB*-33).

Mosaic PBP2 alleles have been strongly associated with decreased susceptibility or resistance to ESCs (*7*). However, the isolate we obtained had a nonmosaic PBP IX allele, which contains the P551L substitution that has been associated with increased MICs for ESCs (*8*). Association of the nonmosaic PBP IX allele, most likely with *mtrR*, *penB*, and *ponA* gene mutations, might be involved in resistance to ESC (*9*). Although Whiley et al. (*6*) did not report an association between sequence type VI and resistance to ESCs, the contribution of this sequence type to ESC resistance requires additional studies.

Isolates with decreased susceptibility and resistance to ESC have now emerged in Argentina (*10*), increasing from 1.1% in 2011 to 5.6% in 2014 (Argentinian Gonococcal Antimicrobial Susceptibility Surveillance Program, unpub. data). Treatment failures and isolates with reduced susceptibilities and resistance to ESC have been reported (*9*). However, in Argentina, syndromic management of gonorrhea has resulted in suboptimal diagnosis and lack of specimens to culture to distinguish between treatment failure and reinfection. Syndromic management represents a major problem that not only compromises surveillance program but also increases selective pressure and facilitates development of drug resistance. Accordingly, surveillance should be strengthened to support detection and verification of asymptomatic infections and treatment failures, identify communities at high risk, and trace sexual contacts. These efforts should be used in public health responses to mitigate emergence and spread of ESC-resistant gonococci.

This study was conducted as part of the reference work of the Argentinian National Reference Laboratory and the Gonococcal Antimicrobial Surveillance Susceptibility Program.

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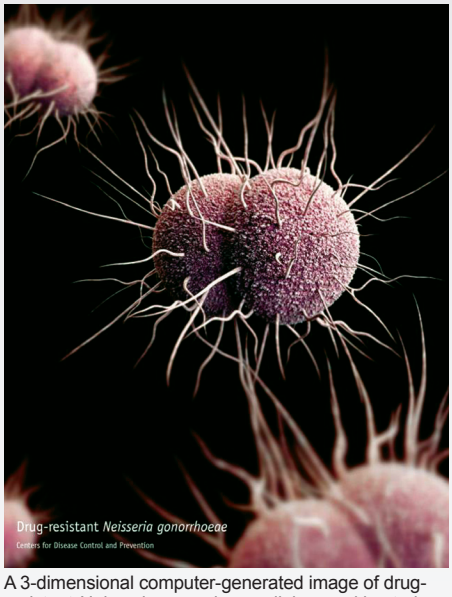
# etymologia

## *Neisseria*

A gram-negative, non-motile diplococcal bacterium, *Neisseria* is named after Albert Ludwig Sigesmund Neisser, a German physician who discovered *Neisseria gonorrhoeae* in 1879.

Gonorrhea comes from the Greek *gonos*, meaning "seed," and rhoe, "flow. The disease caused by this bacterium was known as "gonorrhea" because early physicians incorrectly thought the purulent discharge was semen. As early as 1719, gonorrhea was referred to as "the clap," although theories for why it was called this vary. It may refer to the old French term *clapier*, "brothel," a place where the disease spread easily. Another theory refers to preantibiotic days when the infection was treated by slapping the penis against a board, or clapping it between two boards to force out infected discharge.

*N. gonorrhoeae* is 1 of only 2 *Neisseria* species that is pathogenic to humans. The second, *N. meningitidis*, causes outbreaks of meningitis and septicemia. It was isolated by Anton Weichselbaum in 1887 and designated as *Diplococcus intracellularis meningitidis*.




A 3-dimensional computer-generated image of drug-resistant *Neisseria gonorrhoeae* diplococcal bacteria. Source: Public Health Image Library.

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