

Textbox

Antimicrobial resistance in *Neisseria gonorrhoeae* in Switzerland

Nicola Low¹

¹ Professor of Epidemiology and Public Health, Institute of Social and Preventive Medicine, University of Bern, 3012 Bern.

Antimicrobial resistance to *Neisseria gonorrhoeae* continues to be a problem for both clinical management and control of gonorrhoea. Gonorrhoea is the second most common sexually transmitted bacterial infection in Switzerland, with 3,463 laboratory confirmed cases reported in 2020, a more than five-fold increase since 2004 [1]. Of these cases, 83% were in men and 17% in women. Men who have sex with men (MSM) accounted for 65% of male gonorrhoea cases in 2020 [1].

N. gonorrhoeae evolves rapidly and, through a wide range of mechanisms, has developed resistance to all classes of antimicrobials widely used to treat it [2]. The World Health Organization recommends changing the first-line antimicrobial used when the level of resistance exceeds 5%; above this level, blind treatment is not recommended because of the risk of treatment failure [3]. Ceftriaxone is the only antimicrobial that has fulfilled this requirement during the whole study period, and there are no other licensed drugs to replace it.

Antimicrobial susceptibility testing (AST) of cultured isolates is essential for monitoring and early warning. Molecular diagnostic tests have, however, largely replaced bacterial culture-based methods to detect *N. gonorrhoeae* in Switzerland and many other countries. Molecular diagnostic tests are highly sensitive and specific for detection of the organism, but these tests do not detect the markers of antimicrobial resistance, so resistant strains will not be identified unless they cause clinical treatment failure [3]. AST is conducted in a minority of gonorrhoea cases. The Swiss Centre for Antibiotic Resistance (anresis.ch) network collects data about *N. gonorrhoeae* from laboratories across Switzerland. A report on *N. gonorrhoeae* AMR was published in the anresis.ch report in 2015. The number of laboratories contributing to anresis.ch is increasing to include those that serve outpatient clinics that treat large numbers of people with gonorrhoea.

From 2004 to 2020, a total of 26,208 laboratory-confirmed gonorrhoea cases were reported to the national surveillance system. During this period, results of AST for 2,611 patients were reported to anresis.ch. The proportion of reported cases for which any sample had AST increased from 7.9% in the period 2004–2007 to 10.9% from 2016 to 2020. This report covers reports about the antibiotics ciprofloxacin, azithromycin, cefixime and ceftriaxone. Results of AST are reported as delivered by laboratories (susceptible, intermediate or resistant). Most laboratories changed from CLSI to EUCAST breakpoints

between 2011 and 2013. Minimal inhibitory concentration (MIC) values were available for about a third of all reported samples.

The proportion of samples resistant to ciprofloxacin is stable (50% above the clinical breakpoint 0.064 mg/L in 2020). Owing to persistently high levels of resistance, ciprofloxacin has not been recommended as a treatment for gonorrhoea for many years. Overall, the proportion of isolates with resistance to cefixime, an oral extended-spectrum cephalosporin, is low (0.8%). Cefixime has been discontinued as a recommended treatment for gonorrhoea, because levels of resistance started to exceed 5% from 2011 on. But small numbers of isolates continue to be reported as resistant (>0.125 mg/L) each year (Figure 1). Cefixime is no longer available in Switzerland. The current recommendation for treatment of gonorrhoea is intramuscular ceftriaxone 1 g. The number of isolates with resistance to ceftriaxone remains extremely low (0.2% in 2020, Figure 1). Where MIC values are available, there has been a slight drift within the range of susceptible values since 2015. For azithromycin, the proportion with resistance has increased (15% in 2020). This level is based on a EUCAST epidemiological cut-off value of 1 g/L with uncertain clinical significance. Where MIC values are available, a drift towards higher values over time is seen.

The pattern of gonococcal antimicrobial resistance in Switzerland follows that seen in other European countries. Resistance to ceftriaxone remains rare in Switzerland. But, anresis.ch covers only one in ten diagnosed gonorrhoea infections and of these, only one third has the MIC values reported. To monitor the drift towards samples with higher levels of resistance, MIC values should be reported for all samples. Surveillance for AMR in *N. gonorrhoeae* in Switzerland could be improved if more samples were sent for culture. Physicians should be encouraged to take swabs as well as urine samples before giving empirical treatment for suspected gonorrhoea. Whole genome sequencing would also help by allowing genetic markers of AMR and strains involved in outbreaks to be monitored. These measures would contribute to improved control of AMR gonorrhoea in Switzerland.

References

- [1] Bundesamt für Gesundheit. Sexuell übertragene Infektionen und Hepatitis B/C in der Schweiz im Jahr 2020: eine epidemiologische Übersicht. *BAG Bulletin*. 2021; 48/21: 12–60.
- [2] Unemo M, Shafer WM. Antimicrobial Resistance in *Neisseria gonorrhoeae* in the 21st Century: Past, Evolution, and Future. *Clin Microbiol Rev*. 2014; 27(3): 587–613.
- [3] Low N, Unemo M, Skov Jensen J, Breuer J, Stephenson JM. Molecular diagnostics for gonorrhoea: implications for antimicrobial resistance and the threat of untreatable gonorrhoea. *PLoS Med*. 2014; 11(2): e1001598.

Figure 1: *Neisseria gonorrhoeae* isolates in Switzerland, 2004–2020, with results of antimicrobial susceptibility testing. Panel A, ciprofloxacin; B, azithromycin; C, cefixime; D, ceftriaxone.

