

Increasing trends of gonorrhoea and syphilis and the threat of drug-resistant gonorrhoea in Europe

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Sexually transmitted infections (STI) notifications have been on the rise in several European countries since the early 2000s, most likely due to multiple factors like increased screening, use of more sensitive diagnostics, improved reporting and also due to high levels of unsafe sexual behaviour among certain subpopulations. Across Europe, 32,000 cases of gonorrhoea, 18,000 cases of syphilis and over 345,000 cases of chlamydia were reported in 2010 [1]. Certain subpopulations appear to be more affected than others: Men who have sex with men (MSM) are disproportionately affected by gonorrhoea and syphilis, and young people between 15 and 24 years of age are affected mainly by chlamydia and gonorrhoea. The increases in gonorrhoea and syphilis reported in this edition of *Eurosurveillance* are worrying as they are identified in MSM and young adults and seem to be associated with high levels of unsafe sexual behaviour and co-infection with human immunodeficiency virus (HIV). The increases in gonorrhoea are of particular concern as they coincide with decreasing susceptibility of *Neisseria gonorrhoeae* to currently used antimicrobial drugs in England [2] and across Europe [3].

The increases reported in this edition can be partly explained by increased testing of risk groups. Bremer et al. [4] report that the increase in syphilis diagnoses in Germany could be linked to increased uptake of screening by HIV-negative MSM and incorporation of syphilis testing in the clinical monitoring of HIV-positive MSM. In Sweden, the increase in gonorrhoea seen over the last five years, particularly among young women (who are more often asymptomatic than men) is similarly linked to the increasing use by youth clinics of nucleic acid amplification tests which are more sensitive and test for both chlamydia and gonorrhoea in the same sample [5]. Similarly, increased testing of MSM in the United Kingdom (UK) due to the recent increases in lymphogranuloma venereum (LGV), and new testing guidance is thought to have contributed to the increase in gonorrhoea notification there [6].

Intensified testing does not, however, completely explain the reported rises in STI notifications. Increased

risk behaviour among both MSM and young adults may have contributed to these changes. The rise in gonorrhoea among heterosexuals in Sweden and the UK in particular cannot be linked solely to increased testing, and unsafe sexual behaviour is an important contributor. In addition, Velicko and Unemo [5] report that half of the diagnoses among heterosexual men in Sweden appear to be acquired outside Sweden; this adds to the risk of importation of resistant strains. These observations indicate the need to implement behavioural surveillance in addition to biological surveillance as a useful tool to gain more insight into current trends of unsafe sexual behaviour.

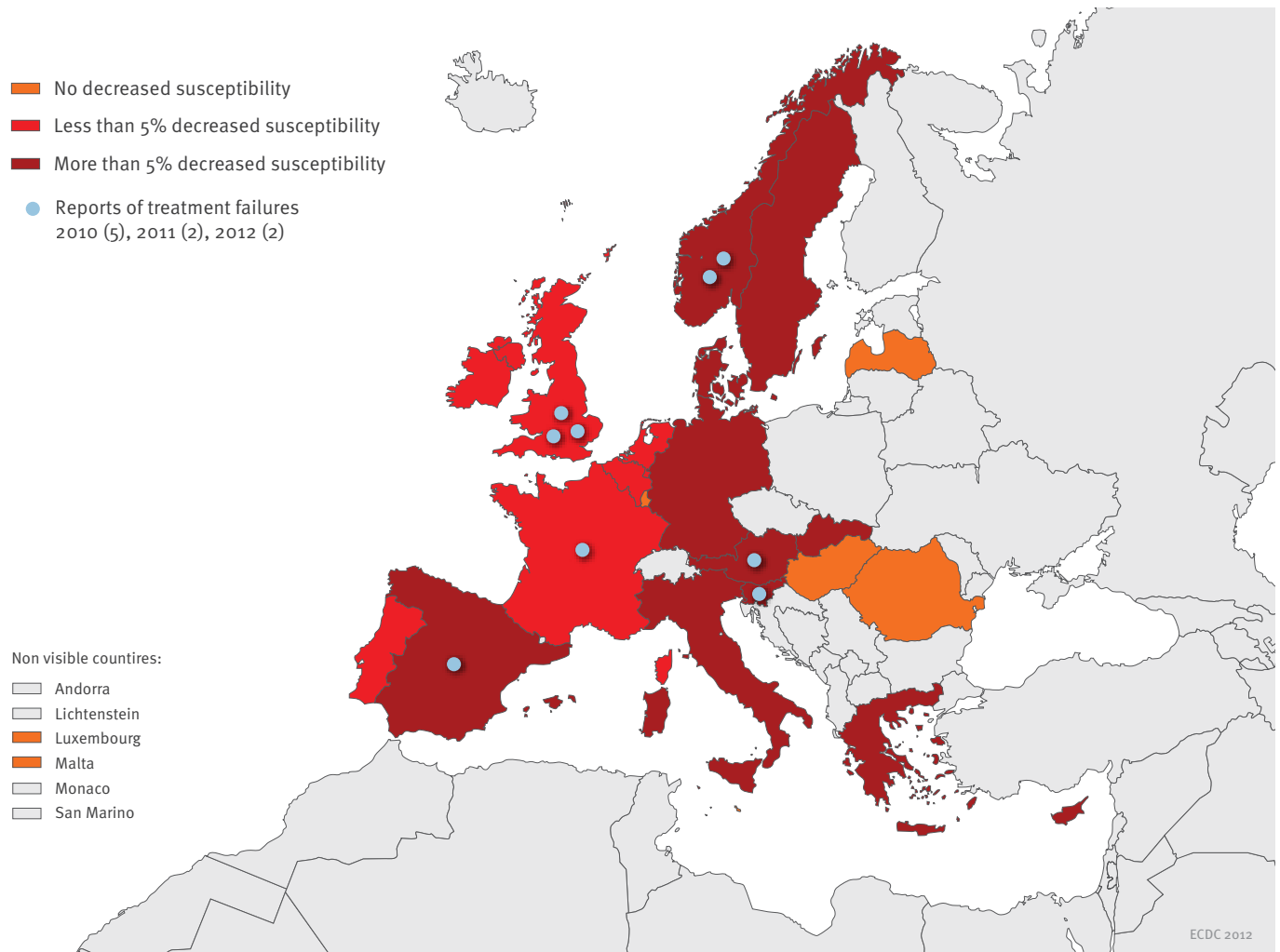
Effective control of gonorrhoea relies entirely on successful antimicrobial treatment. Untreated infections can lead to severe secondary sequelae, including pelvic inflammatory disease, first trimester abortions, ectopic pregnancy and infertility, and may contribute to facilitating HIV transmission. Current treatment guidelines in Europe recommend the use of single-dose injectable (ceftriaxone) or oral third-generation cephalosporins (cefixime) [7].

The upward trend in gonorrhoea cases is particularly worrying as it comes at a time when treatment failures with third generation cephalosporins are being reported, also in Europe. In June this year, the World Health Organisation has warned that drug-resistant gonorrhoea is becoming a major public health crisis [8]. The European Centre for Disease Prevention and Control (ECDC) has recently launched the first regional public health response plan to control and manage the threat of resistant gonorrhoea. [9]

N. gonorrhoeae has developed resistance to most of the antimicrobial drugs successively introduced for treatment over the years. The first treatment failures to the less potent cephalosporins were reported in 2000 in Japan [10] and other countries [11] with recent reports from Norway [12], England [13,14] and Austria [15]. The emergence of a highly ceftriaxone-resistant strain Ho41 in Japan in 2011 [16] triggered worldwide concerns as ceftriaxone is the last remaining option for

FIGURE

Decreased susceptibility to cefixime in 2010 and reported cefixime treatment failures in 2010-2012, EU/EEA



EU/EEA: European Union/European Economic Area.

Decreased susceptibility to cefixime is defined as a minimum inhibitory concentration (MIC) ≥ 0.25 mg/L.

This figure has been adapted with permission from a map published in [9].

empirical first-line treatment. Ceftriaxone treatment failures of pharyngeal gonorrhoea have been reported in Sweden [17] and Slovenia [18]; treatment failure for genital infection has been reported from France [19]. A suspected ceftriaxone-resistant strain has also been reported from Spain [20].

The European gonococcal antimicrobial surveillance programme (Euro-GASP) is a sentinel surveillance system implemented through the European STI network; it involved laboratories across 21 Member States of the European Union (EU) and European Economic Area (EEA). Euro-GASP results from 2009 and 2010 show that decreased susceptibility to cefixime is becoming more frequent and is spreading across Europe (Figure 1). Susceptibility to ceftriaxone also appears to be decreasing [3,21,22]. These results are extremely worrying as the loss of both cefixime and ceftriaxone as

treatment options for gonorrhoea would have a significant impact on public health.

The ECDC plan details the response to this development across the EU/EEA and guides the individual Member States in their national interventions [9]. The goal of the plan is to minimise the impact of resistant gonorrhoea in Europe, and specific objectives are directed at national authorities as well as ECDC:

- Surveillance of gonococcal antimicrobial susceptibility in the EU/EEA will be strengthened to inform national treatment guidelines. ECDC plans to include another four to five countries in Euro-GASP in 2012 and 2013 in a capacity building project, to reinforce the collection of epidemiological and demographic information on patients. Through Euro-GASP, ECDC supports countries in performing antimicrobial

testing and ensures the comparability of results through training courses and an external quality assurance programme.

- Minimum capacity for bacterial culture and susceptibility testing will be either available or developed at national level in EU/EEA Member States.
- A strategy will be developed to rapidly detect patients diagnosed with gonorrhoea who experience a clinical treatment failure with recommended cephalosporins, including the clinical management of affected patients and their sexual partners. ECDC will implement treatment failure reporting to inform (inter)national authorities and professional societies to contribute to the revision of the European treatment guidelines.
- A set of recommended public health actions will be outlined for use in the EU/EEA Member States where resistant cases are detected. A communication strategy will be established to disseminate the surveillance results and increase awareness among public health authorities, professional societies, physicians and the public about the threat of resistant gonorrhoea.

The increasing rates of gonorrhoea and syphilis need to be closely monitored, and public health interventions need to be targeted at the affected groups. These intervention programmes need to be evidence-based and monitored rigorously and systematically to ensure their quality. Multidrug-resistant *N. gonorrhoeae* is a serious public health threat which could result in the loss of the last remaining options for effective treatment in the near future. The spread of strains with reduced antimicrobial susceptibility to third generation cephalosporins across Europe needs to be further investigated using tools such as molecular typing. Public health experts and clinicians need to be informed about the current critical situation and should be vigilant for treatment failures.

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