

Last-line antibiotics increasingly ineffective against gonorrhoea

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The last remaining antibiotics used to treat gonorrhoea (cefixime and ceftriaxone) in England and Wales are becoming less effective. But recent changes in prescribing practice, based on new recommendations that challenge previous public health thinking, seem to have delayed or reversed this trend, and may help to delay the growing threat of multi-drug resistant gonorrhoea, suggests new research published Online First in *The Lancet Infectious Diseases*.

"Fears continue that the current cephalosporins will become ineffective. Decreased susceptibility and increasing evidence of treatment failures to cefixime, with no new licensed agents, and no alternative drugs to which resistance has not been reported raise the very real possibility that gonorrhoea could become untreatable", explains Professor Catherine Ison from [Public Health](#) England who led the research.

Gonorrhoea is a global public health concern, with an estimated 106 million cases reported every year. It is the second most common bacterial sexually transmitted infection in the UK; cases rose by 21% in 2012, with more than 25 000 new diagnoses and by 37% in men who have sex with men (MSM).

To help clarify the current usefulness of cephalosporins in England and Wales, the [investigators](#) looked at data from the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) coordinated by Public Health England.

[Bacteria](#) were isolated from patients diagnosed with gonorrhoea attending 26 genitourinary medicine clinics and 24 laboratories every year between 2007 and 2011, and tested for their sensitivity to cephalosporins.

The findings show that the effectiveness of cephalosporins declined rapidly between 2007 and 2010, particularly cefixime.

Isolates with cefixime minimum inhibitory concentrations (MICs; a measure of [drug susceptibility](#)) of 0.125mg/L or more (indicating decreased susceptibility) among people infected with gonorrhoea rose from 1.5% in 2007 to 17.1% in 2010, followed by a substantial fall to 10.8% in 2011. Decreased susceptibility to cefixime was most prominent in MSM with most isolates belonging to genogroup G1407, indicating they were a largely clonal population.

According to the authors, one explanation for this decline in the prevalence of isolates with decreased susceptibility to cefixime in 2011 was the change in national treatment guidelines in 2010 to prolong the use of cephalosporins, replacing [cefixime](#) with high-dose ceftriaxone plus azithromycin before resistance reached the 5% threshold.

"Although we cannot attribute causality to this observation, the progressive accumulation of isolates with decreased cephalosporin susceptibility from 2007 to 2010 seems to have been delayed or reversed", they write.

They add, "The proactive approach used here challenges previous dogma that public health control of gonorrhoea is best achieved with one preference for antimicrobial agent that should only be replaced once resistance and treatment failures cross a 5% threshold, the recommended cutoff for treatment change. We postulate that public health is best served if changes are made pre-emptively, before an emerging resistance

phenotype reaches 5% prevalence, and becomes well established in sexual networks, particularly those with high rates of unprotected intercourse and partner change. We further propose that a combination of high-dose (500 mg) ceftriaxone with a second drug, specifically azithromycin, will better militate against the rapid emergence of resistance than use of any one agent alone."*

Commenting on the paper, David J M Wright and Berge Azadian from Chelsea and Westminster Hospital in London, UK, say that combined use of antimicrobials is the most promising approach to delaying the emergence of resistant N gonorrhoeae, adding that "Use of a molecular probe in men who have sex with men could help to control the [gonorrhoea](#) epidemic, with rapid detection of resistant strains of N gonorrhoeae and the mosaic penA gene and improved contact-tracing".

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