



Resistance Alert: High-level azithromycin resistance in *Neisseria gonorrhoeae*

- There is an ongoing outbreak in northern England of high-level azithromycin resistant (HL-AziR) *Neisseria gonorrhoeae* (GC). This is a threat to the current front-line dual therapy for gonorrhoea.

In response it is recommended that:

- All laboratories should screen all GC isolates for azithromycin resistance. This can be done by
 - using a 15 µg azithromycin disc, or
 - determining the MIC (eg by gradient strip).
- Any isolates classified as resistant by disc (≤ 27 mm) or MIC (MIC > 0.5 mg/L) should be referred to the Sexually Transmitted Bacteria Reference Unit for confirmation and to distinguish strains with HL-AziR from those with lower levels of resistance.
- Isolates referred to STBRU for this purpose will be processed free-of-charge.

Background

Few antimicrobials remain effective for the empiric treatment of *Neisseria gonorrhoeae* infection and gonorrhoea could become untreatable in the future. In 2011 the British Association of Sexual Health and HIV (BASHH) gonorrhoea treatment guidelines (<http://www.bashh.org/documents/3920.pdf>) were changed to ceftriaxone 500mg i.m. in combination with azithromycin 1g p.o., as first-line dual therapy, in order to delay the accumulation of treatment failure and extend the useful life of ceftriaxone.

Basis for alert

The Sexually Transmitted Bacteria Reference Unit (STBRU) at Public Health England (PHE) has recently detected an outbreak of high-level azithromycin resistant gonorrhoea (HL-AziR; MIC > 256 mg/L) in northern England. The outbreak was first detected in Leeds in March 2015 and now appears to have spread to neighbouring areas in the north of England. Fifteen

cases have been reported in Leeds, and a further four cases have been detected in patients from Macclesfield, Bury and Grimsby. Some of the cases have reported partners from other parts of England. All cases to date have been heterosexual patients. HL-AziR is otherwise a rare phenotype previously observed only sporadically in the UK and elsewhere; the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) identified six cases in 2007, no cases between 2008 and 2011, two in 2012 and three in 2013.

Ten isolates from the 2015 northern England outbreak have been characterised by whole genome sequencing; this showed that the genomes were identical, with the same mutation in all four alleles of the chromosomal 23S rRNA gene; this type of resistance is NOT transferable between strains. The isolates identified to date remain susceptible to ceftriaxone, ciprofloxacin and spectinomycin. Treatment should be guided by the resistance profile, and to date this has been ceftriaxone as all cases have been sensitive. If any in future are also ceftriaxone-resistant this would require specialist advice from a PHE microbiologist.

Urgent intervention is required to prevent further dissemination of strains with this resistance phenotype, which presents a significant threat to the current front-line dual therapy for gonorrhoea.

Action advised:

- all laboratories should test gonococci for azithromycin resistance
- all isolates categorised as resistant to azithromycin (disc zones ≤ 27 mm or MICs > 0.5 mg/L) should be referred to the STBRU for investigation of possible HL-AziR.
- STBRU hopes in future to recommend sensitive and specific interpretive criteria for distinguishing strains with HL-AziR
- an alert to clinicians has been issued through BASHH. This highlights that if a strain of HL-AziR gonorrhoea is detected in one of their patients that they should make particularly rigorous efforts to ensure patients are followed up and receive a test of cure, and that their partners are contacted. In order for this to occur in a timely manner, it is important that clinicians are promptly notified of potential HL-AziR

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