**Changing Trends in Decreased Susceptibility of Neisseria Gonorrhoeae to Cephalosporins in England and Wales: 2012 Data from the National Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP)**

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**INTRODUCTION**

- Gonorrhoea is the second most commonly diagnosed STI in the United Kingdom.
  - In 2012, 25,525 new cases were diagnosed in England, a 21.4% increase relative to 2011 (1).
  - Effective control and treatment of gonorrhoea has repeatedly been threatened by resistance development in Neisseria gonorrhoeae (2-4).
  - Between 2007 to 2010, there was an increase in the proportion of isolates exhibiting DS and reports of treatment failure to cefixime in England and Wales (2, 5).
  - Hence changes to first-line treatment were recommended in 2011 from orally administered cefixime to injectable ceftriaxone (500mg) administered in combination with 1g of oral azithromycin.
  - We investigated recent patterns and risk factors associated with gonococcal isolates exhibiting DS to currently recommended first and second line therapies.
  - We also explored associated risk factors at a reduced cut-off for cefixime.

- 1670 gonococcal isolates were received during the sampling period of which 1535 (91.9%) had MIC data, representing ~5.9% of gonorrhoea diagnoses in England and Wales in 2012.
- Three isolates (0.2%) exhibited DS to ceftriaxone at MIC>0.125mg/L and 263 (17.1%) isolates were less susceptible at MIC>0.15mg/L.
- MIC distributions varied by sexual orientation with a bi-modal distribution of ceftriaxone MICs among isolates from men who have sex with men (MSM) (Figure 1).
- 5.6% of isolates exhibited DS to cefixime at MIC>0.20mg/L in 2012, a significant decline (p<0.001) from 10.8% reported in 2011 (Figure 2).

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**METHODS**

- GRASP (Gonococcal Resistance to Antimicrobials Surveillance Programme) is a national sentinel surveillance system set up to monitor antimicrobial resistant Neissera gonorrhoeae in England & Wales.
- Between July-September, 2012 gonococcal isolates from consecutive patients diagnosed with gonorrhoea attending 25 STD clinics were submitted for antimicrobial susceptibility testing to determine the Minimum Inhibitory Concentrations (MICs).
- Cefixime cut-off at ≥0.125mg/L and lower cut-off at ≥0.015mg/L for cefixime (first line therapy).
- MIC cut-off at ≥0.125mg/L for cefixime (second line therapy).
- Antimicrobial results were linked to patient’s clinical data extracted from the national STD surveillance database (Genitourinary Medicine Activity Dataset version 2).
- Pearson’s chi-square test and univariate logistic regression was used to determine risk factors associated with isolates exhibiting DS to cefixime and ceftriaxone.
- Only isolates with MIC and linked patients’ clinical data were included in the analysis.

- 1. Standard GRASP MIC cut-off
- 2. Lower MIC cut-off to explore emerging less susceptible isolates

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**RESULTS**

- Isolates less susceptible to cefixime at MIC>0.015mg/L were associated with increasing age (p<0.05), being an MSM (OR 2.06; 95% CI 1.44-2.95); 6 or more sexual partners (OR 1.86; 95% CI 1.20-2.87); sex abroad (OR 1.19; 95% CI 1.30-2.75); a history of gonorrhoeae (OR 1.58; 95% CI 1.15-2.19); and being HIV positive (OR 1.94; 95% CI 1.30-2.88) (Table).
- Isolates exhibiting DS to cefixime at MIC>0.20mg/L were more likely to be from older patients (p<0.005), and those reporting sex abroad (OR 2.05, 95% CI 1.15-3.66) but less like to be from females (OR 0.28, 95% CI 0.09-0.84) (Table).

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**LIMITATIONS**

- There is a degree of sampling bias as GRASP over-represents MSM, symptomatic patients and those living in London.

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**DISCUSSION/CONCLUSIONS**

- This analysis shows a continuing downward trend in the prevalence of DS to cefixime in England and Wales, which may in part reflect changes to treatment guidelines.
- Isolates exhibiting DS to cefixime (MIC ≥0.125mg/L) were more likely to be from older patients, men and those reporting sexual contact abroad.
- There is evidence of isolates exhibiting DS to cefixime (MIC ≥0.125mg/L) for the first time since it was last reported in 2009.
- Isolates less susceptible to cefixime (MIC ≥0.015mg/L) were more likely to be from older HIV positive MSM, with high rates of sexual partner change.
- Monitoring MIC drifts is crucial for detecting drift towards emerging resistance.
- To maintain the usefulness of the currently recommended cefixime regimen, adherence to treatment guidelines remains paramount to ensure gonorrhoea remains a treatable bacterial infection.

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**REFERENCES**