



GGD
Amsterdam

Recent rise in reduced susceptibility to ceftriaxone in *Neisseria gonorrhoeae* is **not** caused by strains with a mosaic *penA* gene




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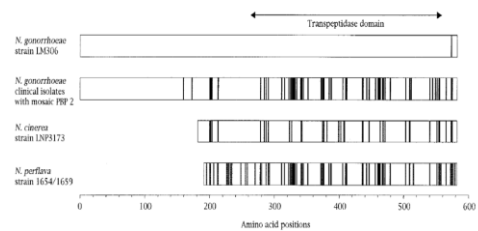
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Disclosures:

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Public Health,
The Netherlands
(Reference laboratory for gonorrhoea)



 Reduced sensitivity against third generations
 cephalosporins: in earlier study related to the
 presence of mosaic *penA* gene



Preceding results 2006-2008

- 2006-2008: routinely MIC cefotaxime determined
 - Increasing number of strains with MIC cefotaxime ≥ 0.125 mg/l
 - Most of these strains also increased MIC against cefixime and ceftriaxone (≥ 0.032 mg/l)
 - Including one large cluster: *penA* mosaic strains, MLVA related, Ng-MAST ST1407

Heymans et al. Antimicrob Agents Chemother. 2012 Mar; 56(3): 1516–1522.



Settings present study, 2010-2013

- STD outpatient clinic: 800-1100 *N.gonorrhoeae* strains/year
- Routine MIC determination for all strains since 2010: ceftriaxone, cefixime, cefotaxime

MICs against cefixime, 2010-2013

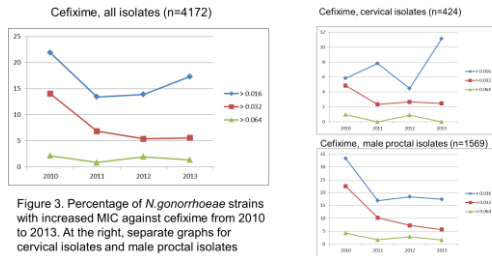


Figure 3. Percentage of *N.gonorrhoeae* strains with increased MIC against cefixime from 2010 to 2013. At the right, separate graphs for cervical isolates and male proctal isolates

MICs against ceftriaxone, 2010-2013

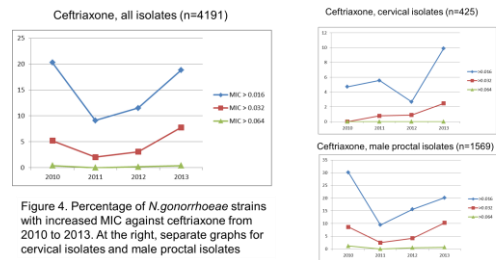


Figure 4. Percentage of *N.gonorrhoeae* strains with increased MIC against ceftriaxone from 2010 to 2013. At the right, separate graphs for cervical isolates and male proctal isolates

- ✘ Strains included in the study:
- ✘ - all strains with ceftriaxone MIC ≥ 0.064 mg/l
- ✘ - all strains with cefixime MIC ≥ 0.064 mg/l
- MIC determined by E-test, whole dilutions

Year	MIC ceftriaxone ≥ 0.064 mg/l	MIC ceftriaxone ≥ 0.064 mg/l OR MIC cefixime ≥ 0.064 mg/l
2010	51	111
2011	21	56
2012	32	59
2013	78	78*
Total	182	305

*2013: only strains with ceftriaxone MIC ≥ 0.064 included

- ✘ Presence of mosaic *penA* gene
- ✘ - as detected by PCR

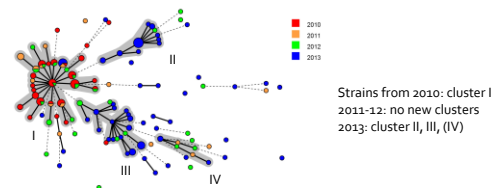
Year	MIC ceftriaxone ≥ 0.064 mg/l	MIC ceftriaxone ≥ 0.064 mg/l OR MIC cefixime ≥ 0.064 mg/l
2010	49/51 (96%)	109/111 (98%)
2011	18/21 (86%)	53/56 (95%)
2012	22/32 (69%)	49/59 (83%)
2013	17/78 (22%)	

*2013: only strains with ceftriaxone MIC ≥ 0.064 included

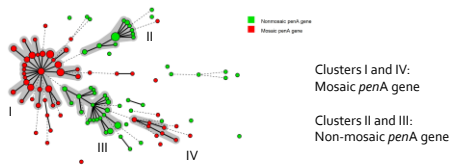
- ✘ MLVA analysis

- Number of tandem repeats
- Five loci
- Rapid test

- ✘ MLVA typing in relation to time



MLVA typing and presence of mosaic *penA* gene



Sequencing of *penA* gene

Note: strain F8g
(highly resistant to
ceftriaxone): A501P
AND mosaic gene

- 16 strains, 2013, non-mosaic *penA*
 - 6 cluster II
 - 1 unrelated
 - 9 cluster III
- All had *penA* XVIII¹ but lacking 543 G-S mutation
- *penA* XVIII also associated with less susceptibility to ceftriaxone (A 501 T mutation)

¹ Whiley et al, Antimicrobial Agents Chemother. 2007 Sep;51(9):3111-6.

Conclusions

- Less strains with mosaic *penA* gene
- More diversity among strains with *penA* mosaic gene
- New clones with reduced susceptibility to ceftriaxone, other mechanism

Further investigations

- Additional Ng-MAST to confirm MLVA results
- Additional *penA* sequencing
- Epidemiological data
- Analysis of strains from 2014 and 2015
 - 2014 resistance data similar to 2013

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