# RAMATIC RISE OF RESISTANCE TO FLUOROQUINOLONES P.O. Box 5, Smolensk, 214019, Russia C2-1887 IN NEISSERIA GONORRHOEAE IN CENTRAL RUSSIA

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# Abstract

- Background: Several reports showed the increase of fluoroquinolones (FQ) resistance in gonococci in the past few years. In 1998 only 1.3% of N. gonorrhoeae strains were intermediately resistant to FQ in Central Russia. Present study was performed to evaluate the resistance of clinical strains of N. gonorrhoeae to FQ and its molecular mechanisms.
- Methods: A total of 213 N. gonorrhoeae clinical strains from Smolensk and Moscow isolated in 2002-2003 were analyzed. Susceptibility testing to ciprofloxacin was performed by agar dilution (NCCLS, 2003). For 21 randomly selected strains with MICs of ciprofloxacin >=4 µg/ml mechanisms of FQ resistance were determined by PCRamplification and direct sequencing of the gyrA and parC QRDRs.
- Results: The 34.7% of strains were non-susceptible to this FQ including just 3.3% of intermediately resistant ones (MIC90 = 4  $\mu$ g/ml, MIC's range 0,001 - 8  $\mu$ g/ml). In 8 of the 21 isolates with high level FQ resistance, only dual mutations (S91F, D95G) in the gyrA were detected, while in 12 isolates the same mutations were combined with the additional S87R substitution in the parC. Another combination of mutations in the gyrA (S91F, D95N) and parC (D86N) was found in a single isolate.
- Conclusions: The incidence of resistance to FQ in Central Russia has increased almost 30 times over the period of time from 1998 to 2003. This fact together with identification of the known mechanisms of resistance suggests that FQ can no longer be used for empiric treatment of gonorrhea in this part of Russia.

# Background

Gonorrhea remains one of the most common STI which accounted for 114 thousands of new cases in 2003 in Russia [1]. Several reports showed the increase of fluoroquinolones (FQ)

resistance in gonococci in the past few years. In 1998 only 1.3% of *N. gonorrhoeae* strains were intermediately resistant to FQ in Central Russia [2]. Present study was performed to evaluate the resistance of clinical strains of N. gonorrhoeae to FQ and its molecular mechanisms.

#### Methods

A total of 213 N. gonorrhoeae clinical strains from Smolensk and Moscow isolated in 2002-2003 were analyzed. Susceptibility testing to ciprofloxacin was performed by agar dilution (NCCLS, 2003). For 21 randomly selected strains with MICs of ciprofloxacin >=4 µg/ml the quinolone resistancedetermining regions of /gyrA/ and /parC/ genes were amplified by PCR as previously described [3, 4], and the PCR products were directly sequenced on both strands using a BigDye Terminator Cycle Sequencing Kit v 3.1 on an ABI 310 automated sequencer (Applied Biosystems, USA).

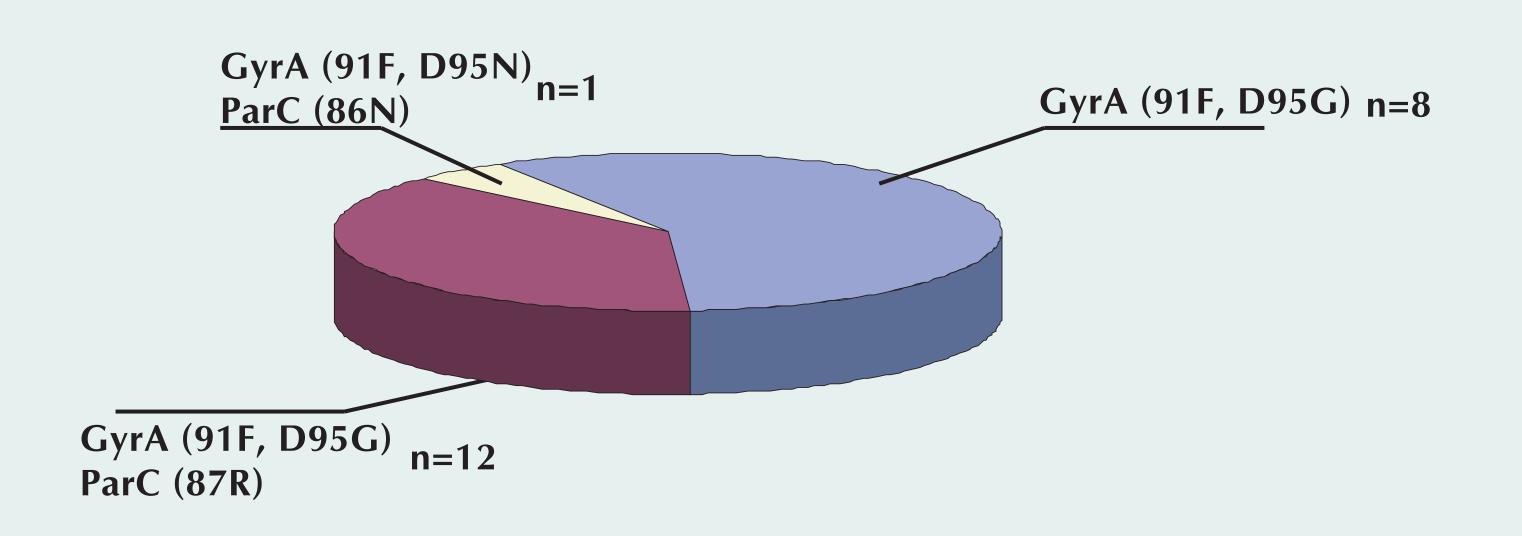
# Results

The 74 (34.7%) of strains were non-susceptible to this FQ including just 7 (3.3%) of intermediately resistant ones  $(MIC_{90} = 4 \text{ g/ml}, MIC's range 0.001 - 8 \text{ g/ml}).$ 



In 8 of the 21 isolates with high level FQ resistance, only dual mutations (S91F, D95G) in the gyrA were detected, while in 12

isolates the same mutations were combined with the additional S87R substitution in the parC. Another combination of mutations in the gyrA (S91F, D95N) and parC (D86N) was found in a single isolate.



# Conclusions

- The incidence of resistance to FQ in Central Russia has increased almost 30 times over the period of time from 1998 to 2003
- FQ can no longer be used for empiric treatment of gonorrhea in this part of Russia
- All tested strains had known mechanisms of FQ resistance that have been previously detected throughout the world

#### References

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