substantial synergistic and/or additive effects (34%), without any observed antagonistic effects. Nevertheless, the results of *in vitro* antimicrobial synergy testing need to be interpreted with some caution, because these may not absolutely correspond to the *in vivo* situation.

Conclusion This study demonstrates *in vitro* synergy between several of the antimicrobials currently used or potentially considered for dual antimicrobial therapy of gonorrhoea and this is also the first study using Etest as an objective, easily performed and reproducible *in vitro* method for dual antimicrobial synergy testing of *N. gonorrhoeae*. Such method might be crucial if susceptibility testing for combination antimicrobial therapy will be performed prior to treatment of gonorrhoea.

P2.088 N. GONORRHOEAE ANTIMICROBIAL RESISTANCE IN URUGUAY: PERIOD 2010 – 2011

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Background The increasing antimicrobial resistance in *N. gonorrhoeae* threatens the effectiveness of single-dose treatment compromising the control of the infection.

Recent reports of third generation cepahalosporins and azithromycin resistance coupled with the already described frequent ciprofloxacin resistance makes it mandatory to monitor the local susceptibility patterns.

Methods Susceptibility by agar dilution technique to ciprofloxacin, azythromycin, ceftriaxone, penicillin and tetracycline was performed to 59 and 56 isolates received in 2010 and 2011 respectively. GASP - LAC MIC interpretative criteria standards were used. Betalactamase production was detected by chromogenic cephalosporin method.

Results In 2011 CIM 90 shifted for ciprofloxacin (8-fold), azithromycin (4-fold) and ceftriaxone (2-fold). The rates of resistant isolates reached 28% and 10% for ciprofloxacin and azithromycin respectively. All the isolates tested were susceptible to ceftriaxone.

Isolates showing resistance to one drug frequently shared resistance or decreased susceptibility to other antibiotics.

One isolate showed decreased susceptibility to ceftriaxone (CIM 0.125 μg/mL) and ciprofloxacin (CIM 0.5 μg/mL), resistance to azythromycin (CIM 2 μg/mL) and is a TRNG.

Conclusions In 2011 an overall increase in either resistance, decreased susceptibility and multidrug resistance was observed. These observed increasing antimicrobial resistance and multidrug resistance to first line treatment antibiotics is worrisome and reinforces the need of continuous surveillance.

P2.089 ANTIMICROBIAL SUSCEPTIBILITY PROFILE OF *NEISSERIA GONORRHOEAE* ISOLATES IN THE PROVINCE OF QUÉBEC: 2012

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Background Since 1988, the LSPQ (Laboratoire de santé publique du Québec) coordinates the *Neisseria gonorrhoeae* antimicrobial resistance programme, to support treatment guidelines updates. In the context of decreasing susceptibilities to 3rd generation cephalosporins, azithromycin and cefixime were added to our antibiotic susceptibility panel.

Methods All *N. gonorrhoeae* strains isolated in clinical laboratories throughout the province were submitted to the LSPQ. The susceptibility profiles to azithromycin (AZI), cefixime (CEF), ceftriaxone (CFX), ciprofloxacin (CIP), ertapenem (ERT), gentamicin (GEN), penicillin (PEN), spectinomycin (SPE), tetracycline (TET), and tigecycline (TIG) were determined by the agar dilution method according to CLSI guidelines. WHO criteria were used to determine decreased susceptibility (DS) to cephalosporins. In 2010 and 2011, 5 antibiotics were tested (AZI, CEF, CFX, CIP and SPE) and 5 other antibiotics were added in 2012 (ERT, GEN, PEN, TET and TIG).

Results In 2012, a total of 502 strains isolated from 352 males (70%), 145 females (29%) and 5 unknown (1%) were tested. All strains were susceptible to cefixime, ceftriaxone and spectinomycin, 47.4% were resistant to ciprofloxacin, 35.7% to tetracycline, 26.3% to penicillin, and 1.4% to azithromycin (MIC = 16 mg/L). Gentamicin MICs ranged from 2 to 16 mg/L (MIC50 = 8 mg/L and MIC90 = 16 mg/L). Tigecycline MICs ranged from 0.03 to 2 mg/L (MIC50 = 0.5 mg/L and MIC90 = 1 mg/L). Ertapenem MICs ranged from ≤ 0.004 to 0.12 mg/L (MIC50 = 0.03 mg/L and MIC90 = 0.06 mg/L). DS to cefixime, DS to ceftriaxone and resistance to azithromycin data are presented in the attached table. Cefixime MIC of 0.125 mg/L was identified in 61 strains (6.6%) in 2010, 72 (9.0%) in 2011 and 20 (4.0%) in 2012.

Conclusions Although DS to cefixime has emerged in Québec, it remains at low level. Resistance to an alternative treatment option, azithromycin, is also emerging. This highlights the need to continue our resistance monitoring programme to support public health interventions.

Abstract P2.089 Table 1

Antibiotic susceptibility	AB2010 (n = 920)	AB2011 (n = 797)	2012 (n = 502) *
DS to cefixime (≥ 0.25 mg/L)	0.2%	0.8%	0.8%
DS to ceftriaxone (≥ 0.125 mg/L)	0.1%	0.1%	0.6%
Resistance to azithromycin (≥ 2 mg/L)	1.2%	1.0%	1.4%

Legend: * partial data, DS: decreased susceptibility

P2.090 MULTI-DOSE CEFIXIME FOR REDUCED SUSCEPTIBILITY GONORRHEA: A PHARMACOKINETIC MODEL

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Background Gonococcal minimal inhibitory concentrations (MIC) to 3rd generation-cephalosporins have been rising worldwide. New treatments for resistant gonococci are urgently needed. We developed pharmacokinetic models to assess whether multiple doses of 600mg or 800mg of cefixime would achieve serum levels sufficient to treat gonococcal isolates with elevated cefixime MICs (≥ 0.5 μg/mL).

Methods Based on published data, we assumed 800mg of cefixime has a peak total concentration (Cmax) of 4.9 μg/mL, an elimination half-life of 3.5 hours, and a volume of distribution of 32 L. We extrapolated a 600mg dose Cmax as the midpoint (4.25 μg/mL) between the 400mg Cmax (3.7 μg/mL) and 800mg. We created simulation models to identify regimens which could achieve total serum cefixime concentrations that exceed 4 times the MIC for over 20 hours, a previously proposed criterion for defining pharyngeal gonorrhoea treatment regimens. We also assessed the pharmacokinetics of free serum cefixime concentrations assuming a 30% unbound fraction, an alternative criterion for gonorrhoea therapy.

Results Simulations suggest that 600mg or 800mg every 12 hours for two doses would achieve total serum cefixime levels sufficient to