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

doi:10.1136/sextrans-2013-051184.0352

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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

doi:10.1136/sextrans-2013-051184.0353

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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

doi:10.1136/sextrans-2013-051184.0354

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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

treat pharyngeal infections caused by gonococci with an MIC ≤ 0.5 μg/mL. A regimen of 800mg orally every 8 hours for three doses would achieve total levels high enough to treat gonococci with an MIC ≤ 1.0 μg/mL. Free cefixime levels attained with 800mg of cefixime every 12 hours for two doses would exceed 0.5 μg/mL for over 24 hours; 800mg every 6 hours for three doses would achieve free levels that exceed 1.0 μg/mL for nearly 24 hours.

Conclusion Two-to-three 800mg doses of cefixime could be an effective therapy for pharyngeal infections with gonococci with cefixime MICs of 0.5–1.0 μg/mL. A pharmacokinetics trial to evaluate the accuracy of these simulations and the safety and tolerability of the proposed regimens is currently underway.

P2.091 A REPEATED LOW DOSE CO-CHALLENGE MODEL OF SHIV-RT AND HSV-2 IN RHESUS MACAQUES

doi:10.1136/sextrans-2013-051184.0355

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Background HIV acquisition is facilitated by HSV-2 infection, making microbicides that block both viruses desirable for limiting HIV transmission. We have tested microbicides in a stringent efficacy model: vaginal co-challenge with a single high dose of SHIV-RT (10^3 $TCID_{50}$) and HSV-2 (2×10^8 pfu) in DepoProvera (DP)-treated macaques. Here we established a model mimicking real world exposure: repeated low dose SHIV/HSV-2 co-challenge in non-DP-treated animals.

Methods Two groups of macaques were co-challenged weekly for 11wks with SHIV (10 or 50 $TCID_{50}$) and HSV-2 (10^7 pfu) after which the SHIV dose was increased to 200 $TCID_{50}$ in all animals for 9 more co-challenges. HSV-2 shedding in vaginal swabs and SHIV plasma viremia were determined. Antibodies (Abs) to SIV and HSV-2, HSV-2-specific T cell responses and the hormones estradiol and progesterone were measured in the blood.

Results After 11 co-challenges, SHIV infections were detected in 1/3 animals from the 10 $TCID_{50}$ SHIV group and 1/3 from the 50 $TCID_{50}$ SHIV group (after 2 and 8 challenges, respectively). Upon increasing the SHIV dose, two more animals became infected (after 1 and 5 more co-challenges), but the last two remained uninfected. SHIV viremia was similar in all infected animals, which all developed SIV-specific Abs. All animals (6/6) became HSV-2 infected. Initial analyses suggest that the frequency of HSV-2 shedding was greater in non-DP-treated animals repeatedly exposed to 10^7 pfu than we previously observed for DP-treated animals that received a single 2×10^8 pfu dose of HSV-2 with SHIV ($p < 0.0001$). HSV-2-specific IgG responses were not detected; T cell responses are being analysed.

Conclusion We have developed a repeated low dose co-challenge model to evaluate microbicides against SHIV and HSV-2. SHIV infection frequency was 67% in this model, similar to the single high dose co-challenge. HSV-2 infection was enhanced compared to the single high dose model.

P2.092 *IN VITRO* AND *IN VIVO* EVALUATION OF CARRAGEENAN-BASED FORMULATIONS TO PREVENT HPV ACQUISITION

doi:10.1136/sextrans-2013-051184.0356

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Background Human papillomavirus (HPV) constitutes one of the major sexually transmitted viral infections. Vaccines against HPV are commercially available but vaccination rates are currently low around the world due to parental autonomy, three dose regimen, cost and the need for cold chain storage. *In vitro* and *in vivo* data have indicated that carrageenan (CG)-based microbicide formulations may prevent HPV infection but additional data is needed to assess the durability of this antiviral activity and the effect of biological fluids.

Methods A proprietary 3% CG gel formulation (Population Council) and the commercial sexual lubricant Divine 9 were tested for their anti-HPV activity against HPV16, 18, and 45 pseudoviruses (PsVs). The anti-HPV PsV activity was estimated using the *in vitro* luciferase assay in HeLa cells and IC_{50} values were calculated using a dose-response-inhibition analysis on GraphPad Prism v5.0 software. The HPV PsV luciferase mouse model was performed to test the *in vivo* activity of the gels. The formulations were applied intravaginally in a BAT24 (–2h/+2h) dosing regimen or in a single –24h application before challenging with HPV16 or 45 PsV in PBS or seminal plasma. *In vivo* luciferase expression was measured 24h later and the Mann Whitney U test ($P < 0.05$) was used for statistical analyses.

Results Both CG and Divine 9 showed broad-spectrum anti-HPV activity *in vitro* (IC_{50}: 1–20ng/ml) and significantly decreased HPV PsV infection in the mouse model; the in-house formulation afforded better protection than Divine 9 in the BAT24 ($p = 0.0101$) or the single –24h application ($p = 0.0008$) dosing regimens. CG formulations retained full activity in the murine model when PsVs were mixed with human seminal plasma.

Conclusions The potential broad-spectrum activity of CG formulations and the durability of protection, even in the presence of seminal plasma, supports further advancement of CG to prevent HPV acquisition.

P2.093 ROLE OF 5% KOH SOLUTION FOR THE TREATMENT OF GENITAL MOLLUSCUM CONTAGIOSUM IN ADULT FEMALE PATIENTS

doi:10.1136/sextrans-2013-051184.0357

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Background To evaluate the role of 5% KOH solution in the treatment of genital Molluscum contagiosum (MC) in adult female patients.

Methods All total 19 female patients with multiple genital MC were included for this study. All the patients were seronegative for the human immunodeficiency virus. Pregnant and lactating woman were not included in the study. It was a clinic based study. 5% KOH solution was applied to the skin lesions with swab stick. After 5 minutes skin lesions were washed with cold water gauge sponge. The procedure was repeated at 4 days interval. Patients were evaluated at the end of every 5 sittings and results were recorded.

Results 5 patients had complete clearance of their skin lesions by the end of 5 sittings. Another 11 patients had complete clearance of their skin lesions by the end of 10 sittings. Remaining patients had complete clearance of their skin lesions by the end of 15 sittings. Side effects of the treatment noted in the study were very few and very mild in nature

Conclusion This study showed that 5% KOH solution is a safe, inexpensive & effective clinic procedure for the treatment of genital MC in adult female patients. It is a simple technique with wide patient acceptance and with excellent cosmetic results. Side effects of the treatment noted in the study was very mild and well tolerated by the patients.