Abstract O4-S2.04 Table 1 CxBar

No Protection → Protection	Working definition of confirmed infection: Positive NAAT AND Positive culture and Positive IgG/IgM>1:16	Working definition of probable infection: positive NAAT and positive culture & IgG/IgM<1:32 OR negative culture & negative culture IgG/IgM>1:32	Working definition of no infection: negative or self-limited NAAT AND negative culture AND IgG/IgM<1:32
Barrier with buffergel	2	2	4
Barrier only	4	2	2
No Product	5	3	0

Methods Miniature diaphragm-like cervical barriers were manufactured and provided by ReProtect, Inc. BufferGel, previously found ineffective in this model when used alone, was also provided by ReProtect, Inc. Twenty-four pigtailed macaques were randomly assigned to one of three study arms: cervical barrier device alone; cervical barrier with BufferGel; or no barrier device and no gel (control arm). Eight animals were enrolled in each arm. Each macaque underwent baseline exam, product administration if applicable, cervical challenge with C. trachomatis (E: 5×105 IFU), and weekly follow-up exams for 5 weeks. Chlamydia challenge occurred within 30 min of baseline exams. Cervical barrier devices were removed from all test macaques 18 h after insertion. Each exam included cervicovaginal colposcopy, vaginal pH and cervical swabs for chlamydia detection (culture and NAAT: GenProbe Aptima Combo2). Blood for serum antibody testing was collected at baseline and weeks 2 though five post-inoculation.

Results Detection of chlamydial infection is detailed in the Abstract O4-S2.04 table 1 below. Colposcopic exams were comparable across each of the three test arms of the study, and thus did not detect toxic effects of the gel or the cervical barrier. Baseline vaginal pH was somewhat higher in the No Product arm than in either of the test arms. After chlamydial challenge and throughout the duration of the study, mean vaginal pH remained lowest in the barrier with BufferGel arm, but were similar (within 1 pH unit) in all three study arms.

Conclusions In this pilot study, a cervical barrier used alone provided little or no protection, but the barrier used with BufferGel reduced transmission by 50% (p=0.08). These results should encourage further study of the ability of a cervical barrier combined with a microbicide to provide greater protection against sexually transmitted infections than either used alone.

O4-S2.05 MYD-88 DEFICIENT MICE SHOW EVIDENCE OF PRODUCTIVE *T PALLIDUM* INFECTION"

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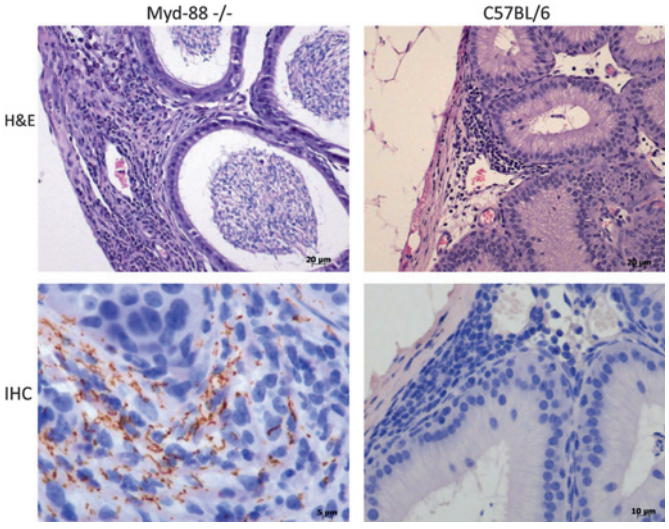
Background Syphilis rates are again increasing in the US and globally and are associated with HIV transmission and rising rates of congenital syphilis. Humans serve as the only natural reservoir of the causative agent, *Treponema pallidum*, and no in vitro cultivation systems are available. Progress towards a vaccine and a better understanding of immune response to syphilis has been hampered over the last half century by lack of a murine model. We hypothesised that previous attempts to establish *T pallidum* infection in mice were unsuccessful because of rapid clearance of the organism by an intact innate immune response. Myd-88 serves as a common signalling molecule stimulated by most toll-like receptors TLRs; pattern recognition receptors of the innate immune system found on most innate immune cells, for example, monocytes, macrophages, and dentritic cells) and is responsible for downstream cytokine responses. We utilised mice bred to be Myd-88 deficient to test this hypothesis and to ascertain whether this mouse strain could be used to study persistent syphilis infection, immune response mechanisms, and eventually vaccine candidates.

Methods *T pallidum*, Nicohols strain, was cultivated by intratesticular infection of New Zealand male rabbits housed at 62°C as per protocol. After 12 day incubation, *T pallidum* was extracted and the concentration adjusted to 7×108 organisms/ml. Myd-88 −/− mice and equally-aged C57BL/6 mice were inoculated intradermally, intraperitoneally, intravaginally or in testicles, and intrarectally each mouse receiving total dose of 1×108 organisms divided into the four body site aliquots). Mice were observed daily for signs or cutaneous disease and/or systemic illness and were sacrificed at day 10 and 21. DNA and RNA were extracted from skin, spleen, genitals, rectum, lymph nodes, spinal cord and blood for use in real-time quantitative PCR and RT-PCR, respectively. Corresponding tissue types were also evaluated by histopathology and immunohistochemical staining *T pallidum* Ab, BioCare, Concord, California, USA). The experiment was repeated three times with variable number of mice per experiment.

Results A total of 18 Myd-88 mice and 19 C57BL/6 mice were infected. MyD-88 −/− mice were more likely than B6 control mice to have detectable RNA at day 10 and 21 (day 10, 12/35 sites (35%) +RNA in Myd-88 −/− ; 3/35 sites (8.5%) +RNA in WT. Day 21, 11/40 sites (27.5%) +RNA in Myd-88−/−; 3/40 (7.5%) +RNA in B6). One experiment ongoing past 42 day post-infection reveals at day 42 sacrifice Myd-88 −/− mice with 6/15 sites (40%) +RNA; B6 0/15 sites (0%) +RNA. Histopathology revealed mild to moderate inflammation in MyD88−/− mice and demonstrable organisms by IHC Abstract O4-S2.05 figure 1).

Conclusion These preliminary experiments suggest that the immune recognition impairment caused by deleting Myd88 signalling protein results in productive and longer-lasting *T pallidum* infection in this



Abstract O4-S2.05 Figure 1 Day 21 Post *T.pallidum* infection Epididymis.

murine strain compared to wild-type mice. Further experiments are necessary to further elucidate the kinetics of *T pallidum*-infected Myd-88 −/− mice (relative DNA burden in tissue compartments, carrying out infection to 3 and 6 months and beyond to assess chronicity). MyD-88 deficient mice may hold the promise of serving as one of the first useful murine models to study immunopathogenesis of *T pallidum* infection. Abstract O4-S2.05 figure 1: representative epididymus sections from Day 21 sacrifice. Formalin-fixed tissues were stained with H&E as well as *T pallidum*-specific immunohistochemical stain (IHC).

O4-S2.06 A PRIMATE MODEL OF *MYCOPLASMA GENITALIUM* CERVICAL INFECTION

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Background *Mycoplasma genitalium* (MG) is a newly recognised pathogen associated with acute and persistent reproductive tract infection in men and women. Understanding of the disease mechanisms, persistence and immune avoidance of this organism is hampered by the lack of a suitable animal model.

Methods Female pigtail macaques (Macaca nemestrina) were inoculated cervically with ~109 genome equivalents (~108 ccu's) of MG strain G37, then assessed at intervals over 8 weeks for the persistence of MG in lower tract specimens. Fallopian tube biopsies were collected via laparotomy at Weeks 4 and 8. Specimens were assessed for the presence of MG DNA by qPCR and for viable MG by growth in H broth and Vero cell co-cultures. Serum collected at intervals was evaluated by immunoblot and ELISA for reactivity to MG antigens. Finally the variable regions of the immunodominant surface antigens, MgpB and MgpC, were analysed by PCR cloning and sequencing to evaluate sequence variation during infection.

Results Of the five primates inoculated cervically with MG, three were infected throughout the 8 weeks of the study, one maintained infection for 4 weeks and one resisted infection. Recovery of viable MG from lower reproductive tract sites was improved by co-culture in Vero cells followed by qPCR to measure an increase in MG genomes during culture. Growth in H broth, as determined by colour change proved an unreliable indicator of the presence of viable MG in the specimen possibly due to the presence of primate microorganisms that inhibit the growth of MG. No viable MG or MG DNA was detected in upper tract tissues in any of the primates perhaps suggesting that longer infection times or repeated inoculations are needed to achieve ascension in this model. Analysis of mgpB variable regions B and G indicated that after 8 weeks of infection the predominant expressed sequence changed from that of the G37C inoculum to 1 to 5 novel sequences consistent with recombination between the expression site and the MgPars. In contrast, no sequence variation was observed in the inoculum grown in vitro for a similar duration. Antibodies reactive with MG antigens, including the variable regions of MgpB and MgpC, were detected by immunoblot and ELISA in serum and cervical exudates.

Conclusions The cervical inoculation model of pigtail macaques results in long-term infection and can be used to study the persistence of MG, development of antibodies and antigenic variation.

Health services and policy oral session 1—Innovation technology

O5-S1.01 EMPLOYING SCHOOL NURSES AS A HEALTHCARE POINT OF CONTACT FOR MALE HIGH SCHOOL STUDENTS: A SCHOOL-BASED INTERVENTION TO PREVENT STD, HIV, AND TEEN PREGNANCY

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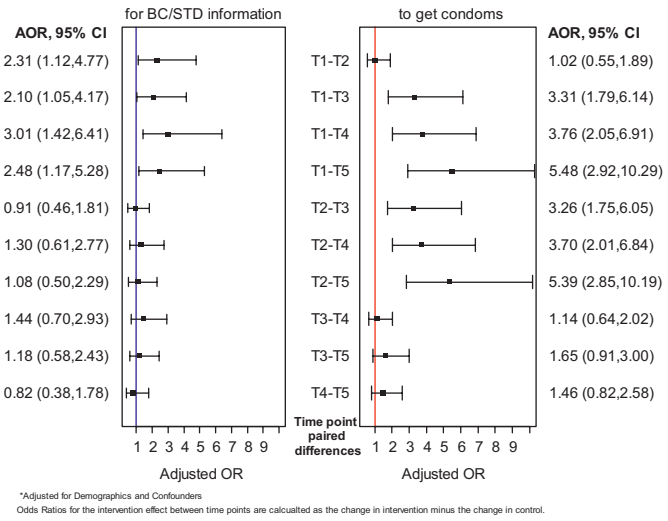
Background Adolescent males tend to have lower levels of knowledge about sexual and reproductive health (SRH), and access health care less frequently than adolescent females. Innovative strategies are needed to reach males with accurate information and resources regarding their SRH needs. Such strategies may improve adolescent males' access to SRH services, including STD screening, treatment, and contraception.

Methods A multi-level intervention was delivered and evaluated across 5 years in a large public school district in Los Angeles, California. One intervention component sought to improve students' awareness and utilisation of condom availability programs (CAPs) in schools by working with key school personnel, particularly nurses, to more effectively implement district CAP policies. Six intervention and six control high schools participated in the study . Analyses included survey data from 13 733 high school males across 5 years (T1–T5). A mixed model logistic regression analysis was used to test for an intervention effect on males' reports of services sought from the school nurse. Random effects on the student level were included to control for repeated measures on the same student.

Results The sample was 80% Latino and 9% African American; the mean age was 16.3. In the intervention as compared to the control condition, statistically significant increases were observed across 5 years of intervention in respondents' reports of going to the school nurse for information about birth control, STDs, pregnancy, or sex (see Abstract O5-S1.01 figure 1), as well as reports of going to the school nurse for condoms. For example, 5.4% of intervention school males reported going to the nurse for condoms at T1; reports increased to 9.6% at T5 for this group, whereas an opposite trend was observed for control school males.



Abstract O5-S1.01 Figure 1 Adjusted ORs* for the change between time points in males going to the school nurse.