

Partner services are a longstanding component of public health efforts to control sexually transmitted infections (STI). However, they have not been a consistent part of HIV prevention efforts either in high- or lower-income nations. In many areas, partner services for HIV and other STIs have been administratively separated, and the goals of partner services have usually been narrowly conceived to concentrate exclusively on the diagnosis and treatment of sex partners. This is now beginning to change. New evidence suggests that HIV PS in high income nations may be less effective at finding new cases of HIV than previously believed, but could play an important role in linkage to care. In sub-Saharan Africa, HIV PS appears to be highly acceptable and effective.

This session will focus on new opportunities in the area of HIV PS. The speaker will review the following issues: (1) data supporting the efficacy of HIV partner services as an HIV case-finding tool in both in high and low-income nations; (2) cost and cost-effectiveness data on HIV PS; (3) evidence that PS for bacterial STIs can be used to promote HIV case-finding and engagement in care among persons with previously diagnosed HIV infection; and (4) outstanding research questions related to HIV PS.

S.07 - Bacterial virulence and host response

S07.1 INSIGHTS INTO MATERNAL GONORRHOEA: HUMAN PRIMARY CERVICAL AND AMNIOCHORIONIC EPITHELIAL CELL RESPONSES TO NEISSERIA GONORRHOEA INFECTION

doi:10.1136/sextrans-2013-051184.0038

¹J L Edwards, ¹J A Gawthorne, ¹T J Edwards. ¹The Center for Microbial Pathogenesis, The Research Institute at Nationwide Children's Hospital, Columbus, OH, United States; ²The Department of Pediatrics, The Ohio State University College of Medicine, Columbus, OH, United States

Bacterial infection is widely recognised as a factor contributing to adverse pregnancy outcomes (APOs). *Neisseria gonorrhoeae* infections continue to be a universal and intractable problem. In this regard, maternal gonorrhoea increases a woman's risk for APO by 6.5-fold. Bacterial infection is thought to trigger a pro-inflammatory response that initiates those processes involved in (preterm) human parturition. The ability of gonococci to invade and transcytose amniotic sac tissues, *in vivo*, is inferred from the ability to isolate gonococci from these tissues and from amniotic fluid. However, there are currently no data to indicate how gonococcal infection can result in APO, and a physiologically relevant human model of pregnancy that is amenable to scientific analyses has hindered elucidation of factors contributing to APO. Thereby, an understanding of gonococcal infection as it relates to human pregnancy, using human cell models of disease, could provide new insights into the pathophysiology of gonococcal disease and of APO as they likely occur *in vivo*. To this end, we investigated gonococcal infection under conditions reflecting normal pregnancy by using primary epithelial cells derived from the human cervix (i. e. pex cells) and amniochorionic membranes (i. e. pace cells) and by altering the combined concentrations of pertinent steroid hormones. Comparative, quantitative, infection assays indicated that gonococci adhere to and invade amniochorionic cells and tissue, which was further observed to occur by a complement receptor-mediated mechanism. We demonstrate that *N. gonorrhoeae* infection of pex and pace cells elicits the differential production of nitric oxide and complement proteins, as well as the specific matrix metalloproteases, prostaglandins, and cytokines thought to participate in triggering the onset of human parturition. Hence, we provide the first direct evidence to indicate a potential link between gonococcal infection and the induction of APOs.

S07.2 THE EXTRUSION PARADIGM OF CHLAMYDIA PATHOGENESIS

doi:10.1136/sextrans-2013-051184.0039

K Hybiske. University of California, Berkeley, Berkeley, CA, United States

Chlamydia is the most commonly reported bacterial disease in the United States, and remains the leading bacterial cause of sexually transmitted infection, responsible for approximately 90 million new STI cases annually worldwide. Of particular concern is that infections with *C. trachomatis* can lead to severe medical complications in women, such as pelvic inflammatory disease and ectopic pregnancy. Alarming, there remain fundamental gaps in our understanding of *Chlamydia* pathogenesis *in vivo*, for example their natural course of infection in humans and why protective immunity is not established. To help address these questions, our laboratory has been interested in determining how *Chlamydia* disseminate within the host. Our original discoveries elucidated the mechanisms by which chlamydiae exit host cells *in vitro*. Surprisingly, *Chlamydia* possess two mechanisms for cellular escape that are mutually exclusive: (i) Extrusion, a packaged release of *Chlamydia* in which the vacuole pinches off and exits the cell within a membrane-encased compartment; this leaves the original host cell intact, often with a residual chlamydial inclusion. (ii) Lysis, a destructive process that is mediated by proteases and the sequential rupture of vacuole, nuclear and plasma membranes, culminating in the release of free bacteria. The maintenance of two discrete exit mechanisms underscores the fundamental importance of this process for intracellular pathogens such as *Chlamydia*. Extrusions are novel pathogenic structures that we hypothesise confer unique means of interacting with the host's innate immune system, enabling immune evasion and promoting tissue dissemination. To this end, we have recently illuminated key characteristics of chlamydial extrusions that allow direct infection of new cells and their engulfment by professional phagocytes. Bacteria within phagocytosed extrusions are protected from macrophage killing mechanisms for at least 8 h. These results have important implications for *Chlamydia* pathogenesis *in vivo*, including dissemination, transmission and the elicitation of immune responses.

S07.3 SURVIVAL STRATEGIES OF HAEMOPHILUS DUCREYI: ROLE OF TRANSPORTERS

doi:10.1136/sextrans-2013-051184.0040

S D Rinker, M E Bauer. Indiana University School of Medicine, Indianapolis, IN, United States

During human disease, *Haemophilus ducreyi* leads a primarily extracellular lifestyle, in which the organism is under constant pressure from the immune system. To survive in this environment, *H. ducreyi* expresses multiple mechanisms that counteract various antimicrobial activities of innate immunity. Key among these is secretion of LspA proteins to prevent phagocytosis, allowing *H. ducreyi* to reside extracellularly. When phagocytes cannot engulf bacteria, they secrete granule contents, including antimicrobial peptides (APs) such as cathelicidin and defensins, to kill the pathogens extracellularly. APs bind and destabilise cell membranes to lyse bacteria. Our laboratory is studying two transporter systems that protect *H. ducreyi* from human APs, including cathelicidin LL37 and beta-defensins. To prevent lethal interactions between LL37 and the inner membrane, *H. ducreyi* utilises the Sap (sensitive to antimicrobial peptides) transporter, which takes up periplasmic LL37 for cytoplasmic degradation. By mutagenizing structural components of the Sap transporter, we have found a direct correlation between the effectiveness of Sap-mediated LL37 resistance *in vitro* and the contribution of the transporter to virulence in humans. Further, we found that *H. ducreyi*

OppA (oligopeptide binding protein A), the periplasmic component of another uptake transporter, appears to cooperate with the Sap transporter for LL37 uptake. For beta-defensin resistance, *H. ducreyi* utilises the MTR efflux transporter. MTR is a member of the resistance-nodulation-division family of multidrug resistance transporters that pump hydrophobic agents from the periplasm and cytoplasm out of the cell. Our data demonstrate that the *H. ducreyi* MTR transporter confers resistance to both LL37 and beta-defensins. Interestingly, we also found that the MTR transporter affects activation of CpxRA, which globally regulates virulence factors in *H. ducreyi*. The role of MTR in human virulence is under investigation. Together, these studies highlight the significance of AP resistance mechanisms to pathogen survival in the human host.

S07.4 IDENTIFICATION OF DETERMINANTS TRIGGERING ANTIGENIC VARIATION IN *MYCOPLASMA GENITALIUM*

doi:10.1136/sextrans-2013-051184.0041

R Burgos, P A Totten. *University of Washington, Seattle, WA, United States*

Mycoplasma genitalium (MG) is an emerging sexually transmitted pathogen associated with reproductive tract disease in men and women. Despite the development of a robust antibody response, MG can persist for months to years, potentially increasing the risk for sexual transmission and serious upper reproductive tract infection in women. The molecular basis of MG pathogenesis is poorly understood, in part due to its fastidious nature, extremely small genome lacking known virulence genes, and the limited genetic tools available for molecular investigations. Nevertheless, previous studies have linked MG virulence to its unique terminal organelle, a complex structure that mediates adherence, motility, and cell division. The terminal organelle is composed of a complex array of unique proteins, including MgpB and MgpC which serve as major adhesins and are required for terminal organelle biogenesis. Remarkably, these two surface-exposed proteins also undergo phase and antigenic variation through a unique process of segmental recombination between discrete variable regions within *mgpB* and *mgpC* and multiple homologous archived sequences, termed MgPa repeats (MgPar). Our goal is to identify the molecular factors required to promote this genetic diversity, a mechanism which likely contributes to the ability of MG to adapt to different host conditions and maintain persistent infections. Recently, we have shown that RecA is required for *mgpB/C* gene variation and that this protein is expressed in several isoforms. We have now expanded these studies by showing that these RecA isoforms originate from different translational start sites and that specific *recA* upstream sequences regulate the expression ratio of these isoforms and *mgpB/C*-MgPar recombination. Together, these studies suggest the presence of novel regulatory mechanisms that may allow this genetically challenged organism to cause disease, evade the host immune response, and persist in infected individuals.

S07.5 UNDERSTANDING DISSEMINATION OF *TREPONEMA PALLIDUM* WITHIN THE HOST - IS THERE HOPE FOR A SYPHILIS VACCINE?

doi:10.1136/sextrans-2013-051184.0042

S Houston, R Hof, C Wetherell, A Phillips, Y Denchev, C E Cameron. *Department of Biochemistry and Microbiology, University of Victoria, Victoria, BC, Canada*

Treponema pallidum is a highly invasive spirochete that disseminates to organ sites distal to the site of primary infection and is able to cross both the blood-brain and placental barriers during the course of infection. The corkscrew motility used by *T. pallidum* undoubtedly contributes to its invasive nature. However, this signature motility is shared with other spirochetes and thus the factors responsible for the widespread dissemination capability that is

unique to *T. pallidum* remain unknown. We have identified the treponemal-specific, surface-localised protein pallilysin as a dual functioning adhesin/metalloprotease that exhibits specific attachment to, and degradation of, multiple extracellular matrix components. Pallilysin is produced as an inactive proprotease that can be activated via either autocatalytic cleavage or host-originating thrombin cleavage. Purified recombinant pallilysin, as well as a non-invasive model treponeme heterologously expressing pallilysin on its surface, exhibit specific degradation of fibrin clots. Pallilysin immunisation alters the course of *T. pallidum* dissemination following challenge within the rabbit model of syphilis infection, with immunised rabbits exhibiting a reduced bacterial burden within organs distal to the site of challenge compared to unimmunized control rabbits. Further, rabbit infectivity tests (RIT) showed that rabbits receiving lymph nodes from challenged, unimmunized rabbits seroconverted and developed orchitis by 30 days post-transfer, while 66% of RIT rabbits receiving lymph nodes from challenged, pallilysin-immunised rabbits remained seronegative and had no signs of orchitis at the termination of the experiment (day 185 post-transfer). Collectively these studies identify pallilysin as a *T. pallidum*-specific metalloprotease that (1) exploits the host coagulation cascade to facilitate protease activation, (2) plays a central role in treponemal dissemination and (3) shows promise as a novel syphilis vaccine candidate.

S.08 - STI/HIV treatment guidelines: Important areas of clinical uncertainty

S08.1 TREATMENT OF GONORRHOEA IN AN ERA OF EMERGING CEPHALOSPORIN RESISTANCE AND RESULTS OF A RANDOMISED TRIAL OF NEW POTENTIAL TREATMENT OPTIONS

doi:10.1136/sextrans-2013-051184.0043

R D Kirkcaldy. *CDC, Atlanta, GA, United States*

Background Cephalosporins are the mainstay of recommended gonorrhoea treatment, and there is an urgent need for treatment options for cephalosporin-allergic patients or infections with suspected cephalosporin resistance. We evaluated the efficacy and tolerability of two novel combinations of existing antimicrobials for treatment of uncomplicated urogenital gonorrhoea.

Methods We conducted a non-comparative trial, randomising patients with urogenital gonorrhoea to one of two regimens: gentamicin 240 mg intramuscularly plus azithromycin 2 g orally (GENT/AZI), or gemifloxacin 320 mg orally plus azithromycin 2 g orally (GEMI/AZI). The primary outcome was microbiologic cure of urogenital infections (negative follow-up culture) at 10–17 days post-treatment. All participants who returned for follow-up and had evaluable follow-up cultures were included in this per protocol analysis.

Results For 401 evaluable participants (GENT/AZI-202; GEMI/AZI-199), the mean age of both groups was 30 years. Most participants were heterosexual men (GENT/AZI, 57%; GEMI/AZI, 51%), followed by men who have sex with men (GENT/AZI, 33%; GEMI/AZI, 39%), and women (GENT/AZI, 9%; GEMI/AZI, 11%). Microbiological cure was achieved by 100% (lower one-sided 95% confidence interval, 98.5%) of GENT/AZI participants, and 99.5% (lower one-sided 95% confidence interval, 97.6%) of GEMI/AZI participants. GENT/AZI cured 10/10 pharyngeal and 1/1 rectal infections; GEMI/AZI cured 15/15 pharyngeal and 5/5 rectal infections. In the GENT/AZI arm, the most common adverse events (AEs) were mild-moderate nausea (27% of participants), diarrhoea (19%), abdominal discomfort/pain and vomiting (both 7%). In the GEMI/AZI arm, the most common AEs were nausea (37% [8% moderate-severe]), diarrhoea (23%), and abdominal discomfort/pain (11%).