How does *T. pallidum* cause the many manifestations of syphilis and still evade immune clearance? How does macrolide resistance develop and spread? Is there a biological basis for determining which patients can be reinjected or when the incidence of syphilis will decline in a given population? Molecular studies involving the laboratory and the clinic have shed insights into pathogenic mechanisms involved in invasion and dissemination, induction of host responses, and immune evasion by *T. pallidum*. Molecular epidemiology studies have begun to unravel the movement of *T. pallidum* strains throughout communities, and to shed light on the appearance of macrolide resistance. Our evolving knowledge about these issues will be discussed in the context of the natural history of syphilis.

In the highest HIV prevalence regions, women wishing not to conceive have limited contraceptive choices - typically injectable progestins, oral oestrogen/progestin combinations or male condoms. None of these are in the top tier of contraceptive effectiveness.

For nearly a quarter century, the hypothesis that women using hormonal contraceptives may be at increased risk of HIV acquisition has persevered. However, the results across multiple human studies have been mixed - some demonstrate increased HIV risk, but others do not. The strongest evidence that use of hormonal contraception may increase HIV susceptibility is for injectable progestin-only contraceptives. Observational studies have estimated that this method may increase HIV acquisition risk 1.4–2.0-fold. Their limitations include few endpoints, measurement error in contraceptive use, and likely confounding by behavioural factors. Evidence on HIV acquisition risk is weaker for oral contraceptives, and few data are available for other hormonal formulations including progestin implants or IUDs.

In addition, trade-offs between the alleged risks of hormonal contraception and those of an unintended pregnancy must be considered.

Four mathematical models have addressed this question. Using different assumptions, analytic algorithms and levels of rigour, they all reached similar conclusions. Withdrawal of injectable progestins has adverse pregnancy consequences, switching to implants/IUDs has better outcomes than injectables, while switching to orals/condoms was worse. While the current situation creates a public health conundrum, it also presents an opportunity to expand contraceptive choice, and concomitant reproductive rights, for women exposed to HIV.

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**PL04 - Plenary session 4**

**PL04.1 SEXUAL BEHAVIOUR AND STIS IN MEN WHO HAVE SEX WITH MEN: A GLOBAL PERSPECTIVE**


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Sexual and gender minorities have been present throughout human history, but recently there has been increased public awareness of their prevalence, because of human rights activism and the recognition of the increased STI and HIV burden among some subpopulations, particularly men who have sex with men (MSM) and transgender women. Behavioral and biological factors explain some of the disparities noted in their higher rates of STI and HIV. The colorectal mucosa has the highest concentration of cells that can bind HIV in the body, and single layer columnar epithelial cells may be readily traumatised and inflamed during anal intercourse. MSM who are versatile in their sex roles may efficiently acquire HIV/STI by being the receptive partner, and then can readily transmit infections to new partners if they are insertive. STI and HIV potentiate the transmission of each other, and certain venues that enable MSM to meet partners readily, such as saunas and specific internet sites, have been associated with rapid expansion of micro-epidemics. MSM in many parts of the world have been found to have higher rates of many bacterial and viral STIs than demographically matched peers, and may have unique STIs based on specific behaviours (e.g. association of faecal contact and enteric pathogens) and the concentration of new infections within subpopulations (e.g. recent outbreaks of MRSA and LGV). The stigmatisation of homosexuality and gender nonconformity creates barriers to effective STI and HIV control, since many MSM may defer seeking health care because of the expectation of receiving insensitive care, and concerns about confidentiality, as well as liability, in many jurisdictions. In order to mitigate the disproportionate rates of STI and HIV among MSM, public health officials and clinicians need to become culturally competent, to develop services that conduct appropriate screening (e.g. rectal NAAT) in a sensitive manner.

**PL04.2 SEX HORMONES, HIV INFECTION AND UNINTENDED PREGNANCY: EVER SINCE ADAM AND EVE**


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Regardless of the Genesis interpretation, human sexual behaviour is necessary for species survival. Biologically, steroidal sex hormones affect sexual function, reproductive capacity, and possibly infection risk. Women have 2 main sex hormones - oestrogen and progestin. These hormones function in two ways - endogenously to regulate the reproductive cycle and exogenously to control fertility.

**PL05 - Plenary session 5**

**PL05.1 PREP & TREATMENT AS PREVENTION FOR HIV: FINDING THE BALANCE**


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Protective and non-protective immunity in STIs.

It is certainly remarkable that the causative agents of sexually transmitted infections (STIs) induce long-lasting protective immune responses only occasionally and insufficiently (*T. pallidum, human papilloma viruses, herpes simplex virus, S. scabiei*) or not at all (*C. trachomatis, N. gonorrhoeae*, *C. albicans*, *human immunodeficiency virus, T. vaginalis*).

The reasons for this phenomenon are often microbe-related, but may also be due to peculiarities of the mucosal immune system. Evidence exists, for instance, that density and function of epithelial dendritic cells in the mucosa are different from those in the epidermis and, perhaps as a consequence of this, mucosal sensitisation more often results in T cell non-responsiveness or anergy than epicutaneous sensitization.

The relatively poor functionality of the adaptive immune response in the defence against the various STI-causing microorganisms can sometimes be compensated by cells and molecules of the innate immune system. Good examples of this are the overexpression of certain anti-microbial peptides in the vaginal epithelium and the imiquimod-induced cytotoxic response of plasmacytoid dendritic cells against HPV-infected targets.

At a time where we are challenged with increased anti-microbial resistance to anti-microbial chemotherapy, research efforts are needed to better understand the mechanisms of microbe-host cell interactions and to use this knowledge for the development of better therapeutic strategies.
Antiretroviral-based HIV-1 prevention strategies - including antiretroviral treatment (ART) to reduce the infectiousness of HIV-1 infected persons and antiretroviral pre-exposure prophylaxis (PrEP) for uninfected persons to prevent HIV-1 acquisition - are promising new approaches for decreasing HIV-1 spread. The past two years have seen significant new advances in knowledge regarding ART and PrEP for HIV-1 prevention, including definitive demonstration in randomised trials that both ART and PrEP reduce HIV-1 risk and the development of normative guidance for prescribing these HIV-1 prevention strategies. Adherence is key to efficacy of antiretrovirals for HIV-1 prevention, both as ART and PrEP. There are numerous parallels in the challenges and opportunities ahead for ART and PrEP, including how to target to realise maximum population benefits, whether HIV-1 infected persons at earlier stages of infection would accept ART to reduce their risk for transmitting HIV-1 and highest-risk HIV-1 negative persons would use PrEP, whether high adherence could be sustained to achieve high effectiveness, and how to integrate these strategies into HIV-1 prevention programmes. Delivering these strategies in order to achieve population-level benefits is the next step, balancing costs, optimism, and realistic appreciation of the challenges ahead.

**Methods** To discern where we are heading in the field of HIV/STI diagnostics research, new assays and new approaches to enhance care were reviewed.

**Results** There are commercial NAATs for CT/NG by 4–5 companies. Some are available on expensive robotic platforms, limiting their use in resource-constrained settings. Additionally, a new CT/NG NAAT that can return results in 90 minutes is available. Other rapid NAAT and hybridization POC assays are in the pipeline. There are two NAATs and a POC test for trichomonas. POC syphilis serology tests have proliferated, which is important to syphilis elimination. Several platforms offer NAAT tests for HPV and there is a NAAT for HSV ulcers. Rapid HIV POC and 4th generation tests have advanced earlier detection of HIV. A home oral-fluid HIV test can be purchased in the US. Patients perform their own HIV tests in Emergency Departments with excellent accuracy.

**Conclusions** Learning how to wisely and effectively use these tools can improve the detection of STIs and provide cost-effective ways to increase the number of patients being treated.