Methods A comprehensive review of randomised trials of behavioural and biomedical interventions aimed at decreasing HIV transmission and acquisition was performed and will be presented.

Results In addition to male circumcision, the most successful biomedical intervention has been the use of antiretroviral drugs (ARVs) for prevention of HIV perinatal transmission and sexual transmission among HIV discordant couples, and for the prevention of HIV acquisition via microbicides and oral pre-exposure prophylaxis (PrEP). All of the transmission studies have demonstrated that reductions in viral load with ARVs to undetectable viral blood levels during birth, breast-feeding, or sexual intercourse reduces transmission by > 96%. This has been the greatest success in the HIV prevention field over the past two decades and continual scale-up of access to ARVs can be associated with marked reductions in HIV transmission and incidence. Decreasing acquisition with use of ARVs is totally dependent on high adherence (> 90%) to the medications in an uninfected population. Studies have had mixed results with some populations with high adherence demonstrating high efficacy using PrEP (> 70% efficacy) or microbicide (> 50% efficacy), while others with low adherence as measured by non-detectable blood levels of ARVs demonstrated no efficacy.

Conclusion Multiple studies have confirmed that effective use of ARVs substantially reduces transmission and emphasise the critical importance of integrated behavioural and biomedical strategies. When treatment with ARVs is combined with other interventions involving voluntary counselling and testing, condoms, adherence to medications, and circumcision, the possibility of controlling HIV becomes a feasible and achievable goal.

PL.03 - Plenary session 3: Anton Luger Memorial

PL03.1 STIS - 2013: RESURGENCE OF EARLY SYPHILIS, PERSISTENCE OF HIGH STI MORBIDITY AND MORTALITY, AND EMERGENCE OF ANTIMICROBIAL RESISTANT STIS: IMPLICATIONS AND POTENTIAL RESPONSES

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Recent directions in clinical-epidemiologic research on STIs include (1) population-level estimates of STI prevalence (e.g., WHO's 2011 publication of global estimates), and formal population-level surveys of STI prevalence and risk determinants; (2) analysis of global mortality and disability attributable to major diseases, including STIs (the Global Burden of Disease Study, published in the December 2012 triple issue of The Lancet); (3) conceptualization and implications of the "Treatment and Care Cascade" and the "Prevention Cascade" currently focused on HIV infection; and (4) emerging interest in Program Science, linking programme implementers and scientists in needs assessments, conceptualization, design, advocacy for funding, implementation, evaluation, cost-effectiveness, and continuous strengthening of STI/HIV programmes. The global emergence and rapid spread of anti-microbial resistant pathogens, suggests the clinical mantra of "first do no harm" to the individual patient must be mirrored in a similar public health mantra - "first do no harm" to the population. This means selective use and more systematic evaluation of the impact of antimicrobial use on human and animal pathogens and microbiomes. The reemergence of syphilis and persistence of other STIs in vulnerable populations, and the limited implementation of cost-effective interventions for STI control reflects global neglect of STI programmes, and perhaps increasing failure to effectively integrate STI, HIV/AIDS, and reproductive health programmes globally (for example, the very limited integration of HIV PMTCT with elimination of congenital syphilis programmes). Nonetheless, progress in sexual health promotion and STI control can be made possible with cost-effective use by clinicians and public health leaders of effective, available tools, such as scale up of HPV and HBV vaccines, and linked delivery of other sociobehavioral and biomedical STI interventions in vulnerable populations. Rigorous evaluation of the impact of such programmes, with assessment of what is not working as well as what is working, is essential.

PL03.2 CONTROL OF SYPHILIS IN THE WORLD'S MOST POPULOUS COUNTRY: OPPORTUNITIES AND CHALLENGES

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As one of the major sexually transmitted infections (STIs), syphilis has made a strong resurgence in China at a rate faster than any other country since 1980s. Epidemic of the infection has focused on the groups most at risk, such as men who have sex with men (MSM), female sex workers (FSWs), particularly those women working in the service venues or on the streets, and migrants. In recent years, the Chinese government has increased its efforts to respond the epidemic. Specifically, the Ministry of Health's recently launched 10-year national syphilis control and prevention plan includes the national milestone of achieving an explicit decline in the reported syphilis incidence and the elimination of congenital syphilis by 2020, indicating specific targets for percentages of target populations educated about syphilis, tested and treated for syphilis. Increasing political commitment, innovative screening technologies, and functional health systems have provide opportunities for China to develop the comprehensive intervention package consisting of "One integration of behavioural prevention, Two systems to be strengthened, and Three active screening accesses to high-risk groups to link One standardised treatment at clinic" to highlight the combination of behavioural and biomedical interventions for achieving the goals of the national plan. However, many significant challenges at programing and implementation levels, such as capacity of health system, affordability to STI care, trust between public health providers and clients, access to hidden populations, social stigma, confidentiality, and micro-environment to support delivery of intervention and care, still remain.

PL03.3 SYPHILIS: FROM PATHOGENESIS TO CONTROL

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Syphilis is one of the most fascinating of all infections. Although its origin is still debated, the history of syphilis includes many famous (and infamous) persons, and the disease is featured in art and literature. Syphilis is caused by a corkscrew-shaped bacterium, *Treponema pallidum*, that was first identified over 100 years ago. It has a miniscule genome, and it lacks many of the common metabolic pathways. It is so fragile that it dies within hours outside of the host, yet it is capable of evading host defences to persist for decades within the host.

Syphilis is known as "the great imitator" because its clinical manifestations, which can range from an ulcer or rash to blindness and insanity, can be mistaken for many other clinical conditions. In contrast, the infection can lie smouldering for many years, without any clinical evidence. After 70 years of use, penicillin continues to be an effective treatment, yet resistance to macrolide antibiotics like azithromycin has erupted in *T. pallidum* in many regions of the world. Physicians recognise that some persons who are treated for syphilis can be reinfected, sometimes multiple times. At the population level, the incidence of syphilis can wax and wane, often shifting from one population group to another.

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 reinfected 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.

PL.04 - 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 greatest 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 create 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.

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-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.

PL04.3 PROTECTIVE AND NON-PROTECTIVE IMMUNITY IN STIS

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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. scabie*) 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 sensitization 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 by 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.

PL.05 - Plenary session 5

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

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