

based on the major capsid protein, L1, which self assembles into virus-like particles. Although HPV L1 is a relatively conserved gene with different HPV types having L1 sequence homology of up to 90%, the vaccine induced protection is HPV type-specific. Both vaccines induce excellent protection against the specific types targeted; however, there is also limited protection from infection with closely related HPV types. The vaccines do not cause regression of established genital lesions: regression is due to cell-mediated immunity. The serological correlates of protection of the vaccines are not defined but it is likely that protection is largely due to neutralising antibodies: animal studies have shown that protection can be transferred by passive immunisation with immune sera. In natural infections, titres of HPV antibodies are much lower than for vaccine induced antibodies, and in fact not all infected people develop detectable antibodies. It is likely that serological correlates of protection will become better defined only if vaccine induced protection starts to wane as the antibody titres potentially drop over time; it may then be possible to define levels of antibody needed for protection. Such information could inform the need for further booster vaccinations.

S12.2 TALES OF WOE: HSV VACCINE AND NULL STUDY RESULTS

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Herpes simplex virus type 2 (HSV-2) infects 530 million people, is the predominant cause of genital ulcer disease, and a key driver of HIV epidemic in sub-Saharan Africa. In human populations with susceptibility to HSV appears universal. In animal models, several candidate preventative and therapeutic vaccines have been successful only to fail in clinical trials, including recent null results from the prophylactic glycoprotein D2 subunit vaccine trial. However, detailed analyses of the immune suggest assays that antibody response may correlate with protective immune response, providing the first evidence of immune correlate of protection from infection. In addition, recent characterization of CD8 tissue memory cells in genital mucosa suggests that we may also identify immune correlate of HSV-2 control in the infected host. In this Symposium, I will discuss HSV-2 vaccine efforts in the context of our understanding of pathogenesis and epidemiology, as well as the current pipeline of candidate vaccines.

S12.3 UNDERSTANDING HOW BROADLY CROSS-NEUTRALISING ANTIBODIES DEVELOP IN HIV INFECTION - CLUES FOR HIV VACCINE DEVELOPMENT?

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Neutralizing antibodies are likely to play a crucial role in a preventative HIV-1 vaccine. Although efforts to elicit broadly cross-neutralising (BCN) antibodies by vaccination have been unsuccessful, a minority of individuals naturally develops these antibodies after many years. Thus understanding how these antibodies evolve could provide a template for HIV vaccine design. To date we have studied ~80 HIV-infected individuals in the long-term CAPRISA cohort and found that approximately a quarter develop cross-neutralising antibodies by 3 years of infection. Analysis of longitudinal samples showed that breadth developed gradually starting from year 2, with the number of viruses neutralised as well as the antibody titer increasing over time, peaking at 4 years post-infection with little activity thereafter. The extent of cross-neutralising activity correlated with CD4 T cell decline and viral load at 6 months post infection, suggesting that early events set the stage for the development of breadth. Mapping of the epitopes targeted by cross-neutralising antibodies revealed that in most cases they recognised one of the 4 well-defined sites of vulnerability on the HIV envelope. This

included the two glycan-dependent epitopes in the V2 and C3 regions of gp120, the CD4 binding site as well as the membrane-proximal external region (MPER). Isolation of monoclonal antibodies from some of these individuals has confirmed the plasma specificities and revealed interesting insights into antibody ontogeny. Furthermore, we have shown how viral escape from earlier strain-specific antibodies contributes to the formation of neutralising antibody epitopes highlighting the dynamic interplay between viral and antibody evolution. Our ongoing work aims to more precisely define the changes in the antibody and viral repertoires that accompany the development of broadly cross-neutralising antibodies with the aim of mimicking these events in a vaccine scenario.

S12.4 CHLAMYDIA TRACHOMATIS

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In vaccine enterprises there are two goals that must be achieved to be successful. Priority is usually given to the vaccine components, which antigen(s) and adjuvants. However an equally important goal is to understand the parameters of protective immunity, or the immunologic goal of vaccination. *Chlamydia trachomatis* infections pose a unique challenge for host immunity. In the majority of infected individuals the invading bacteria replicate only in the epithelial monolayer lining the reproductive tract. The business end (mechanism) of an effective vaccine is likely to be T cells functioning at the epithelial interface. During natural infections individuals' immune responses range from asymptomatic clearance, to asymptomatic infertility, to hospitalisation for PID. Early *Chlamydia* vaccine attempts were associated with enhanced immunopathology. It is possible that *Chlamydia* vaccine candidates will cause enhanced immunopathology, with or without enhanced protection from bacterial replication in the reproductive tract. Evaluation of *Chlamydia* vaccines will need to include their ability to limit bacterial replication and immunopathology. There are some after-the-fact correlates for bad outcomes in women infected with *C. trachomatis* including circulating peripheral mononuclear cells that make too little IFN- γ , too much IL-10 or TNF α when activated by *C. trachomatis* antigens. The *Chlamydia muridarum* mouse model provides an opportunity to define the parameters of protective immunity in the genital tract, and then evaluate/validate them in humans. The mouse model has shown the CD4 T cells are critical to protection and CD8 T cells likely responsible for immunopathology. More recently it was demonstrated that there are redundant mechanisms for clearing *C. muridarum* from the genital tract. This presentation will cover the newest mouse model data, correlating it with what is known in humans. The practicable human correlates of protective immunity and immunopathology are likely to be novel CD4 and CD8 T cell subsets, with antibody possibly falling into disfavour.

S.13 - Challenges to a comprehensive approach to the prevention of HIV and STI among men who have sex with men in Europe (organised by ECDC)

S13.1 CURRENT AND FUTURE CHALLENGES IN GAY MEN'S HEALTH

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Epidemics of HIV in men who have sex with men (MSM) were first recognised in the early 1980s. Since the introduction of antiretroviral treatment (ART) in the mid-1990s incidence of HIV has not, despite

expectations, reduced significantly in many countries. Indeed, the numbers of new diagnoses has increased in some European countries, the USA and Australia. In the UK, for example, over 3000 MSM were diagnosed with HIV in 2010, the highest number since the beginning of the epidemic. As a consequence, the prevalence of HIV is increasing and, for gay communities, a growing number of men are now living with HIV.

Although incidence of sexually transmitted infections (STIs) in MSM fell dramatically in the early years of AIDS, post-ART we have seen a return in some jurisdictions to pre-AIDS incident STIs, and the emergence of new sexually transmitted pathogens.

This paper will focus on behavioural and epidemiological research in the era of ART, with particular reference to the continuing transmission of HIV. It will review current risk factors for HIV infection in negative MSM, sexual risk behaviour and risk reduction interventions among HIV positive MSM, and the emergence and re-emergence of new and established STIs. It will conclude with current challenges to the prevention of HIV and STIs in MSM, and prospects for the future.

S13.2 EVIDENCE-BASED TARGETED REVIEW OF HIV AND STI PREVENTION INTERVENTIONS AMONG MSM

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Background In Europe, men who have sex with men (MSM) are disproportionately affected by STI/HIV. Sex between men is the predominant mode of HIV and syphilis transmission and contributes to a third of gonorrhoea cases in 2011. The main goal of this evidence-based review was to gather and critically appraise the scientific evidence for and to inform European guidance on a comprehensive approach for HIV, STI and hepatitis prevention among MSM.

Methods Relevant data bases were searched for publications related to disease prevention and health promotion among MSM. All kinds of reviews were included but gave presence to systematic reviews, when no reviews were found individual studies were included. A critical appraisal of the quality of each study was performed before inclusion in the targeted review. The Highest Attainable Standard of Evidence (HASTE) was used for grading as the basis for recommendations as HASTE was specifically developed to evaluate evidence regarding HIV/STI interventions among key populations. HASTE takes into account three categories with equal weight: efficacy data; implementation science data; biological and public health plausibility.

Results Seven interventions were identified to be strongly recommended for prevention of HIV, STI and/or hepatitis, and 15 interventions for probable or possible recommendation. Consistent condom use, HIV treatment as prevention, peer outreach and support groups for men testing HIV negative as well as for HIV positive men, together with HSV-2 suppression therapy with acyclovir to prevent genital ulcer disease and hepatitis B vaccination, were all strongly recommended according to the HASTE grading.

Conclusions In general, studies of acceptable quality from the European context were few and made the assessment of context-specific effectiveness difficult. Additionally, effectiveness studies looking into real-life effectiveness of biomedical interventions were very few. Future research would be able to contribute with more information from the specific European settings including (cost-) effectiveness studies.

S13.3 THE STATUS OF HIV PREVENTION AMONG MSM: AN OVERVIEW OF THE EUROPEAN RESPONSE

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Introduction MSM in the European Union and European Economic Area (EU/EEA) are disproportionately affected by STI: 39% of all HIV diagnoses, 33% of gonorrhoea and 55% of syphilis cases were reported among MSM in 2011.

Methods Analyses of surveillance data and information from countries responses for Dublin Declaration monitoring were combined with a review of existing national prevention intervention programmes targeted at MSM. Characteristics of 118 prevention interventions studies were included in the repository.

Results Outbreaks of syphilis, hepatitis C and lymphogranuloma venereum and increasing trends of gonorrhoea and HIV among MSM, observed between 1995–2011, were reported to be associated with high levels of risk behaviour, sexual networking and socio-economic and cultural factors. The national responses included: strengthening of surveillance, prevention and care; enhanced partner notification; and development of a range of prevention intervention programmes. The majority of prevention interventions used media campaigns, education and counselling followed by harm reduction strategies like condom distribution and HIV/STI testing alone or combined with other activities. Nearly half of the behavioural interventions studies reported proper outcome evaluation.

In 2012, HIV/STI prevention programmes targeted to MSM were implemented in 22/30 EU/EEA countries, with non-governmental organisations playing a key role in programme implementation through campaigns, outreach work, information provision and condom distribution. Reported coverage of HIV prevention programmes for MSM ranged from 43% to 76% across countries. Rates of HIV testing among MSM during the last 12 month ranged from 12% to 74% and rates of condom use at last anal intercourse from 42% to 64%.

Conclusion Diversity across EU/EEA in the design and implementation of prevention intervention strategies reflects various characteristics of MSM populations and the changing epidemiology of STI/HIV. A common need exists for improving the effectiveness of prevention intervention programmes, for targeting young, migrant and ethnic-minority MSM and for ensuring adequate funding.

S13.4 WHAT DO GAY MEN NEED? - CHALLENGES REGARDING COMPREHENSIVE APPROACHES IN HIV-PREVENTION INTERVENTIONS FROM A NATIONAL PERSPECTIVE

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Regarding empirical evidence gay men are facing several health problems which can arise from the mastering of living in homo-negative environment. We can e.g. find high levels of substance use, mental health problems, and risky behaviour.

The presentation will raise the question on how these different and interacting health matters work together and how they can be tackled in campaigns focused on gay men and other MSM. What is the experience of the national German campaign "I KNOW WHAT I'M DOING"; what can be done in future work from the MSM community perspective; who are the necessary co-operative partners, what has to be requested from different policy sectors?

S.14 - New strategies and implementation of best practises for dual elimination of mother-to-child transmission of syphilis and HIV (organised by WHO)

S14.1 TESTING FOR SYPHILIS IN PREGNANCY AND ASSOCIATED ADVERSE OUTCOMES IN MOZAMBIQUE

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