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Human papillomavirus types 6 and 11 seropositivity: Risk factors and association with ano-genital warts among homosexual men

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Summary *Objectives:* Human papillomavirus (HPV) types 6 and 11 are most commonly associated with ano-genital warts. There are few data on the sero-epidemiology of HPV6 and HPV11 among homosexual men.
Methods: Behavioural data and sera for antibodies to HPV6 and HPV11 capsid protein L1 were collected annually for 1427 HIV negative and 245 HIV positive homosexual men. For HIV negative men, a combined variable, HPV6/11, was created (HPV 6 and/or 11) to analyse predictors of seroprevalence and seroincidence.
Results: High rates of HPV6 and HPV11 seroprevalence were found (39.2—53.2% of men). For HPV6/11 (HIV negative men only), seroprevalence was associated with higher numbers of sexual partners, longer history of sexual activity and seropositivity for several sexually transmissible infections. Each year, 12.6% of men younger than 25 years seroconverted. Seroincidence (5.9/100PY) was associated with younger age, more recent male sexual partners, receptive anal fingering and anal chlamydia. Seropositivity and seroconversion were strongly associated with past and incident anal warts.

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Conclusions: HPV6 and HPV11 seropositivity were common among homosexual men. Among HIV negative men, HPV6/11 seroprevalence and seroincidence correlated closely with markers of sexual activity. The high numbers of young men seroconverting each year suggests a role for prophylactic vaccination of young gay men.

Summary: Ano-genital warts, caused by human papillomavirus, are very common. In a community cohort of Australian homosexual men, HPV6 and 11 seroprevalence and seroincidence were high and were associated with past and incident anal warts and other markers of sexual activity.

Introduction

Ano-genital warts are an extremely common, highly infectious, sexually transmissible disease manifestation of human papillomavirus (HPV) infection.[1] Nearly all ano-genital warts are related to HPV infection with types 6 or 11[2–5] which are primarily transmitted through genital skin-to-skin contact.[6] Ano-genital warts are associated with psychological morbidity and substantial health-care costs.[7–9] Since 2007, when the quadrivalent HPV (qHPV) vaccine for girls and young women was added to Australia's National Immunization Program, there has been a major reduction in the incidence of ano-genital warts in young women. In addition, there has been evidence of herd immunity among young heterosexual men. However, no decline in genital warts has been seen in homosexual men.[10]

Among homosexual men globally, anal HPV6 and HPV11 infection have been reported to be highly prevalent.[11–14] Ano-genital warts disproportionately occur in homosexual men, where they are associated with a higher lifetime number of sexual partners[15–17] and positive HIV status,[16,18] among other factors. HPV serology provides an estimate of lifetime cumulative exposure to or infection with HPV, but there are few data on the seroepidemiology of HPV6 and HPV11 in men and even fewer among homosexual men.[12,19–21]

From 2013, Australia will be the first country in the world to extend its national publicly funded qHPV vaccination program of young girls to boys. By establishing the seroprevalence of qHPV types HPV6 and HPV11 and their correlation with disease, may have on future HPV-associated disease among Australian homosexual men can be measured. To achieve this aim, we explored firstly the prevalence, incidence and risk factors for HPV6 and HPV11 seropositivity, and secondly the association between ano-genital warts and HPV6 and HPV11 seropositivity in two prospective cohorts of HIV negative and positive homosexual Australian men.

Materials and methods

Study populations

Two prospective community based cohort studies of homosexual men were conducted in Sydney, Australia. The Health in Men (HIM) study involved HIV negative homosexually active men. The methodology for the HIM study has been published previously.[22] Men who were 18 years or older, tested HIV negative, had sexual contact with at least one man in the past 5 years, lived in Sydney or had regular contact with gay events and venues in Sydney were eligible to enrol. The study recruited 1427 participants from June 2001 to December 2004 and concluded interviews in June 2007. The Positive Health (pH) study recruited HIV positive men from 1998 to 2006, who reported sex with at least one man during the previous 5 years or who identified as homosexual, using similar community based methods as the HIM study.[23] The HIM and pH studies and the serological research within the two studies received ethics approval from the University of New South Wales Human Research Ethics committee.

Data collection

Participants underwent annual structured face-to-face interviews on a wide range of topics, including sexual relationships and practices. Quantitative sexual behaviour data were collected. At approximately 6 months between annual face-to-face interviews, information on recent sexual relationships and practices and injecting drug use was collected from HIM participants via a short-version telephone interview. In the HIM study, serological testing for HIV and storage of serum samples were undertaken annually. In the pH study, annual serological testing was only performed from 2005 to 2007.

Serum sample collection, shipment and testing

The laboratory methodology has been previously published.[24] Briefly, serological analysis was performed at the German Cancer Research Center (DFKZ), Heidelberg, Germany. The samples were analysed for antibodies to the capsid (L1) proteins of the mucosal alpha HPV types 6, 11, 16, 18, 31, 33, 35, 45, 52 and 58 as previously described.[25,26] All samples were analysed for HPV antibodies by glutathione S-transferase (GST)-L1 serology[27,28] in combination with fluorescent bead technology.[25,29] Cut-points to determine antibody positivity were selected by visual inspection of the distribution of median fluorescence intensity (MFI) values among all study participants[30,31] and seropositivity was defined as having an MFI value of 400 or more for all HPV types, except HPV 6 and HPV 35 where more stringent cut-offs of 800 and 600 MFI were used. Seroconversion was defined by two conditions: 1) at least 2-fold increase of the previous serum MFI-value, and 2) MFI-value above the cut-off. The current manuscript describes only the results of the HPV6 and HPV11 L1 data.

Statistical analysis

Firstly, seroprevalences and seroincidences were calculated separately for HPV6 and for HPV11. Seroincidences