Epidemiology of HIV-1, HHV-8 & HSV among homosexual man
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Citation for published version (APA):
Dukers, N. H. T. M. (2002). Epidemiology of HIV-1, HHV-8 & HSV among homosexual man s.n

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SUMMARY
The present thesis concerns the epidemiology of three viruses: human immunodeficiency virus (HIV-1), human herpesvirus 8 (HHV8) and herpes simplex virus (HSV). Prevalence and incidence of these viruses are investigated as well as time trends herein. Also the role of risk behaviour in acquiring these viruses is investigated. Most research is performed among homosexual men participating in the Amsterdam Cohort Study on HIV-1 and AIDS. Some topics were further explored among participants in the Cohort Study among drug users and among homosexual men attending a sexually transmitted diseases (STD) clinic in Amsterdam.

In Chapter 1, we report recently increasing rates of HIV-1 and other sexually transmitted diseases (STD), and in HIV-1 related sexual risk behaviour among homosexual men in Amsterdam. The mid-nineties were marked by the availability of revolutionary new treatment possibilities in HIV-1 infection, called highly active antiretroviral therapy (HAART). People are no longer dying from AIDS, and the mere availability of such potent anti-HIV-1 treatment holds new promise for anyone. We have demonstrated that the recent availability of HAART, as well as the successful use of this treatment by HIV-1 infected persons was associated with sexual risk taking. Moreover, the occurrence of lipodystrophy, a relatively common side effect of HAART was likely to have unfavourable effects on a persons sexual activity and well being. It is still difficult to fully comprehend to what extent HAART use accounts for the general rise in STD and risk behaviour, though our studies indicate that some aspects of treatment may play a role. To fully grasp the course of the HIV-1 epidemic, it is necessary to monitor the HIV-1 incidence in different subgroups (high and low risk groups), since estimates may differ substantially between populations. Along with cohort studies, a recently developed laboratory method to detect recent HIV-1 infections (the so-called STARHS or detuned assay) made it possible to estimate HIV-1 incidence. Using this method, we demonstrated a rising HIV-1 incidence among homosexual men who comprise a high risk group for infection (being attendees of an STD clinic).

In Chapter 2, we evaluated several aspects of HHV8, the virus causing Kaposi’s Sarcoma; prevalence and incidence, and changes herein over calendar time as well as possible transmission routes and symptoms in primary infection are investigated. Both prevalence and incidence were shown to be high among homosexual men and low among drug users. Contrary to HIV-1, the prevalence and incidence of HHV8 was more or less stable over time. Among homosexual men, seropositivity for HHV8 was associated with several factors including Mediterranean nationality, HIV-1 infection and a higher number of sexual partners. Among drug users, seropositivity was associated with history of sexual contact with homo- or bisexual men, Mediterranean nationality and commercial unprotected sex (for women). Strikingly, HHV8 seropositivity was not associated with presence of parenterally transmissible viruses or with injecting drug use. Among homosexual men, seroconversion was associated with oral-genital sex, whereas in drug users the number of new infections was too small to examine risk factors for seroconversion. The presented studies provide strong evidence for sexual transmission, possibly by the oral-genital route, among homosexual men and lack of transmission by injecting drug use with shared equipment suggesting that blood-borne transmission of HHV8 is highly unlikely. Furthermore, primary infection among HIV-1 negative homosexual men was accompanied by a mild flu-like illness, which is consistent with infection of HHV8 in the oropharynx. Along with the unique character of the presented studies on HHV8, providing longitudinal information for a large number of persons, our experiences with this
virus proved the importance of using an optimal serological assay to detect infection.

In Chapter 3, we investigated another herpesvirus, HSV. This virus was in 1995-1997 considerably less prevalent among young homosexual men than in 1995-1997. This decrease was not markedly influenced by a change in demographic and socioeconomic factors over time. We have shown that the decline in HSV seroprevalence over the studied period was explained by a decrease in sexual activity (as measured by the number of sex partners, HIV-1 infection and past episode(s) of gonorrhea). It is known that HSV2 can be transmitted sexually. We showed that, although childhood non-sexual transmission of HSV1 is still the most common mode, sexual transmission of HSV1 seems to be increasing.

After the start of the HIV-1 epidemic in the early eighties, a drastic reduction of HIV-1 related sexual risk behaviour and several sexually transmissible viruses, including HIV-1 and HSV, was noted among homosexual men. Now we face a new challenge with HIV-1 rising again, and with increasing rates of STD and sexual risk behaviour. It is only sensible to renew prevention efforts and to target programs especially to HIV-1 positive individuals who hold the key in limiting the spread of HIV-1. The continuous monitoring of sexual risk behaviour and incidence of STD and HIV-1 is essential to keep track of the current risk of these infections. Cohort studies are excellent monitoring tools and hold the potential to discover new transmission routes and new STD, such as HHV8 infection. It is recommended though that HIV-1 incidence rates obtained from such cohorts are validated in other populations, since cohort participants may represent a selected group. To monitor HIV-1 accurately in populations other than cohorts, will become possible by application of a newly developed laboratory method, STARHS or 'detuned' assay. Applying this test in a high risk population, we showed an increasing HIV-1 incidence. This trend would not have been noticed when HIV incidence estimates would have been based solely on the cohort participants This assay is still being validated, but shall, considering its usefulness, no doubt eventually be put to wide use.