HIV-2 in West Africa. Epidemiological studies
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Summary

This thesis is an investigation of the epidemiology of human immunodeficiency virus type 2 (HIV-2) infection in two West African countries, Guinea-Bissau and The Gambia.

Chapter 1 discusses the setting of the studies and puts them into the perspective of previous research conducted at the Medical Research Council (MRC) Laboratories in The Gambia.

Chapter 2 is a review of the epidemiology of HIV-2, and describes the key differences of HIV-2 infection compared to HIV-1, including a lower transmission rate, a more limited geographical spread, stable or decreasing prevalences and a better prognosis.

Chapter 3 describes the results of the first round of the Gambian HIV sentinel surveillance programme in 2000-1. The HIV-1 prevalence, 15 years after detection of the first case in the country, was still relatively low at 1.0%, and HIV-2 prevalence was 0.8%. In comparison to an earlier cross-sectional study among pregnant women carried out in 1993-5, this shows a reversal, as then HIV-2 was the more prevalent virus (1.1%) and HIV-1 was less common (0.6%).

Chapter 4 describes the incidence of HIV-2 in a rural area in north-west Guinea-Bissau. The incidence was 4.6 per 1000 persons per year, which is lower than expected in view of the high prevalence (8%). Among the risk factors independently associated with incident infection in women were active syphilis, history of vaginal discharge, having been divorced, living in the central part of the village, and having lived elsewhere in Guinea-Bissau. Among men age below 30 years and active syphilis were significantly associated with new infections.
Chapter 5 examines the hypothesis, put forward by researchers from Dakar and Boston, that HIV-2 infection might offer protection against subsequent infection with HIV-1. In the same rural population in Guinea-Bissau as described in Chapter 3, we found that the incidence of HIV-1 infections was higher among those already infected with HIV-2, so HIV-2 could possibly be a risk factor for HIV-1 acquisition, rather than a protective factor.

Chapter 6 examines the mortality in a cohort of patients attending a sexually transmitted disease clinic at the MRC facilities in Fajara. This study confirmed that the survival of HIV-2 infected patients was better than that of HIV-1 infected patients. In the group of patients with normal CD4 count (> 500 cells / µl) the mortality of HIV-2 infected subjects was half of that in HIV-1 infected subjects, but among those with a low CD4 count (< 200 cells / µl), there was no difference in mortality between those infected with HIV-1 or HIV-2. This study also described the survival of patients who are infected with both viruses. These patients had a poor prognosis; their mortality rate was similar to those of patients with HIV-1. This indicates that HIV-2 is not able to mitigate the course of HIV-1 disease.

Chapter 7 compares the survival of HIV-2 infected women with that of HIV-1 infected and HIV-uninfected women. Unlike the study population in Chapter 6, these women were not recruited because they were ill, but were screened for HIV at their first visit to an antenatal clinic as part of a study examining mother-to-child transmission rates of HIV-1 and HIV-2 in 1993-5. This study population is more representative of the general population than the highly selected patients of Chapter 6. In 2001 we re-visited these women and established their vital status. The results confirmed some earlier findings: prognosis with HIV-2 infection was better than with HIV-1 infection, and the mortality rate is predicted by the plasma viral load in both infections. The surprising result was that in this seroprevalent cohort more than 50% of women with HIV-1 were still alive eight years after recruitment. This indicates that the survival with HIV-1 in West African women is similar to that of women in Europe or North America prior to the use of highly active antiretroviral treatment (HAART). Another important finding was that it is
not the virus type *per se* that is predictive of mortality, but the plasma viral load. In other words, if a person has HIV-2 infection with a high plasma viral load, then the prognosis is as bad as that of a person with HIV-1 and high plasma viral load. This suggests that the start of treatment in HIV-2 disease should be guided by the same indicators as in HIV-1 disease.

Chapter 8 describes survival of eight children who were infected with HIV-2 by their mothers around the time of delivery. Perhaps surprisingly, this is the world's largest cohort of perinatally HIV-2 infected children. An earlier study following up these children had found that all eight had survived to 18 months of age. After 5-7 more years three of the eight children had died. This was a significantly higher mortality rate than in an HIV uninfected control group of children, but was lower than in an HIV-1 infected group of children. The numbers were very small though and few firm conclusions can be drawn. It does suggest however, that children with perinatally acquired HIV-2 infection need the same care and prophylaxis as HIV-1 infected children.

Finally, Chapter 9 draws conclusions from these studies, and identifies outstanding research questions. It remains unclear what initiated the HIV-2 epidemic, and why it is in decline now. The plasma viral load in HIV-2 infected people is generally lower than in HIV-1 infected people, but the reasons for this are unknown. Another unresolved question is why only a limited proportion of HIV-2 infected people have a high plasma viral load and develop AIDS, and how large this proportion is. If a preventive vaccine were to be developed, very large field trials would be needed to test the protective efficacy of such a vaccine, as the incidence of HIV-2 is low. HIV-2 prevalence is stable or declining in most countries, and HIV-2 is not a global threat. Nevertheless many people in West Africa infected with this virus will develop immunodeficiency and die from AIDS. Trials and cohort studies are needed to identify appropriate treatment regimens.
HIV-2 in West Africa