INFECTION WITH HUMAN IMMUNODEFICIENCY VIRUS, HERPES SIMPLEX VIRUS TYPE 2, AND HUMAN HERPES VIRUS 8 IN REMOTE VILLAGES OF SOUTHWESTERN PAPUA NEW GUINEA

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Abstract. To investigate the spread of human immunodeficiency virus (HIV) and other sexually transmitted viruses, two serosurveys (the first in 1999 among 56 adults and the second in 2001 among 351 adults) were conducted in remote villages of the southwestern part of Papua New Guinea. Only one individual was positive for antibodies to HIV. In 2001, the seroprevalence of human herpes virus 8 (HHV-8) was 32.2%, and the seroprevalence of herpes simplex virus type 2 (HSV-2) was 27.4%. Both prevalence rates increased with age, and were lower in the villages near the Bensbach River. The seropositivity of HSV-2 was independently correlated with HHV-8 infection. Our data show that the inhabitants of the southwestern region of Papua New Guinea currently experience an extremely low circulation of HIV. However, the high prevalence of infectious agents that can be sexually transmitted, such as HSV-2 and to a lesser extent HHV-8, indicates the presence of behavioral patterns that may facilitate the spread of HIV in this area of currently low endemicity.

INTRODUCTION

The World Health Organization estimates that there are 42 million people with human immunodeficiency virus (HIV) infection worldwide, most of whom live in developing countries, where the HIV pandemic represents a major threat for individuals and the society. However, the spread of the virus shows wide geographic variation; for example, the Pacific Island region appears to have relatively low rates of HIV infection, with the exception of Papua New Guinea, where HIV infection has been constantly increasing since the first case was reported in 1987.1,2

Early surveillance data were consistent with a late entry and/or spread of the virus in Papua New Guinea, which were attributed primarily to a relatively small aggregation of people in urban centers, a limited highway system, and limited size of the commercial sex sector.1 The small number of HIV-positive cases reported until 1992, all of them diagnosed in the Port Moresby Sexually Transmitted Disease (STD) Clinic,3,4 was followed by an increase in HIV spread; in the same period, high levels of other STDs were reported both in rural and urban areas, suggesting a predominantly heterosexual transmission of HIV infection in Papua New Guinea.1,5,6

As mentioned, limited connections may represent an important obstacle to the spread of HIV and emerging infections in a country such as Papua New Guinea. To explore this issue, we conducted two serosurveys (the first in 1999 and the second in 2001) in remote villages located in the southwestern part of this country where no data on the prevalence of HIV and other sexually transmitted infections had been reported. Approval for the study was given by the Medical Research Advisory Committee of Papua New Guinea.

METHODS

Study population. Serosurvey in 1999. Study participants were Melanesians residing in six remote villages (Korombo, Torwaia, Wando, Balamuk, Bandber, and Bula) in the Morehead District in the Western Province of Papua New Guinea (Figure 1). These villages (total population = 532 inhabitants in the 2000 census) are located in a flat, rural zone, called the Bensbach area, with a low population density. Serum samples obtained from these individuals were tested in 1999 for human herpesvirus 8 (HHV-8) and herpes simples virus type 2 (HSV-2), and the results have been published in a previous report.7 In the present study, the same serum samples (that had been stored frozen) were tested for antibodies to HIV in 2002.

Serosurvey in 2001. Individuals included in this study resided in 18 remote villages (total population = 2,124 inhabitants) in the same geographic area as in the 1999 serosurvey. The six villages that were sampled in the previous survey were included also in this survey, although individuals tested were different. The villages included were classified according to their location as follows (Figure 1): near the Bensbach River (eight villages: Wereave, Weam, Korombo, Bensbach, Torwaia, Wando, Balamuk, and Bandber), near the coast (two villages: Bula and Tais), in the north region (eight villages: Indorodoro, Kandarisa, Tokwa, Mengete, Yokou, Rouku, Wemenevre, and Mibini).

Essential demographic information (i.e., age, sex, village of residence) and approximately 5 mL of venous blood were collected after oral consent from each individual between April and November 2001; sera were separated and handled as described elsewhere.8

Laboratory methods. Serum samples were stored at −20°C and processed at the laboratories of Tor Vergata University (Rome, Italy). Antibodies to the lytic antigen of HHV-8 were detected using an immunofluorescence assay based on BCBL-1 cell line. Samples reactive at a dilution > 1:20 were considered positive. Antibodies to HSV-2 were detected using an IgG-based type-specific HSV-2 enzyme-linked immunosorbent assay (ELISA) (Gull Laboratories, Inc., Salt Lake City, UT). Antibodies to HIV were detected with an ELISA (Vironostika HIV-1 Uni-form II plus O; Organon Teknika, Boxtel, The Netherlands).

Statistical analysis. The prevalence of HIV seropositivity in 1999 and 2001 was evaluated. The analysis of correlates of specific infections (i.e., HSV-2 and HHV-8) was restricted to participants in the 2001 survey, since the 1999 survey was small and covered only part of the territory.
Seroprevalence rates for each of the three viruses were calculated, and differences by sex, age group, and geographic area were assessed by stratification. Differences were evaluated using the chi-square test and the chi-square test for linear trend. The viral correlates of each infection were evaluated by estimating crude and adjusted odds ratios (ORs) and their associated P values using univariate and multivariate log-binomial linear regression analysis.

RESULTS

1999 serosurvey. A total of 56 individuals were studied; 19 were women. The median age was 35 years (range = 15–85 years). The results of HHV-8 and HSV-2 serology have been previously published. Briefly, 30.4% were positive for antibodies to HHV-8 and 29.6% were positive for antibodies to HSV-2. One individual, a 27-year-old man, was positive for antibodies to HIV (prevalence = 1.8%, 95% confidence interval = 0.04–9.6). He was negative for both antibodies to HHV-8 and antibodies to HSV-2.

2001 serosurvey. A total of 351 individuals were studied. Of the participants, 169 (48.1%) were males and 182 (51.9%) were females. The median age was 32 years (range = 16–79 years, 25th and 75th percentiles = 23 and 44 years, respectively), with no differences between males and females.

No individual had antibodies to HIV. Antibodies to HHV-8 were present in 113 (32.2%, 95% CI = 27.3–37.1) individuals, whereas 94 (27.4%, 95% CI = 22.7–32.1) had antibodies to HSV-2. Forty-five (13.1%) individuals were seropositive for both HHV-8 and HSV-2, 68 (19.2%) were seropositive only for HHV-8, and 49 (14.3%) were seropositive only for HSV-2. The distribution of HHV-8 and HSV-2 seroprevalences by sex, age group, and geographic area is shown in Table 1.

FIGURE 1. Map of the Morehead District (Western Province of Papua New Guinea) with the 18 villages included in the study.
The seroprevalence of HHV-8 was similar between males and females, whereas the seroprevalence of HSV-2 was higher among males ($P = 0.02$, by chi-square test). The seroprevalences of both HHV-8 and HSV-2 tended to increase with age ($P < 0.001$ and $P = 0.006$, respectively, by chi-square test for linear trend), and were similar in the younger age groups.

Villages near the Bensbach River showed a lower seroprevalence for HHV-8 ($P = 0.003$, by chi-square test) and HSV-2 ($P < 0.0001$, by chi-square test) than villages located in the north or on the coast. The highest seroprevalence for HHV-8 was reported in Yokwa (54.2%), whereas the highest seroprevalence for HSV-2 was observed in Rouku (50.0%).

Univariate analysis (Table 1) showed that older age and living in the north were significantly associated with HHV-8 seropositivity, whereas male sex and older age were significantly associated with HSV-2 seropositivity. Moreover, those who were seropositive for HHV-8 had a significantly higher probability of also being positive for antibodies to HSV-2 (39.8%) than those who were seronegative for HHV-8 (20.6%) ($OR = 2.55$, 95% CI = 1.51–4.30).

Multivariate analysis (Table 1) showed that older age and living near the coast or in the north were independently associated with HHV-8 seropositivity; male sex and older age were independently associated with HSV-2 seropositivity. We also conducted a multivariate analysis for HHV-8 seropositivity including HSV-2 seropositivity, in addition to the previous covariates (i.e., sex, age, and geographic area). Older age was significantly associated with the outcome, as was positivity for antibodies to HSV-2, which showed an adjusted $OR$ of 2.14 (95% CI = 1.28–3.60).

**DISCUSSION**

This study provides data on the HIV spread in remote rural villages of southwestern Papua New Guinea, an area close to the border with West Papua (Indonesia). The HIV prevalence rate observed in the 1999 serosurvey, with wide confidence intervals due to the small size of the studied population, led us to investigate a larger population of the same area. The absence of HIV infection in the 2001 serosurvey does not seem to confirm the HIV prevalence observed in the first survey and is most likely due to the limited economic and social exchanges that this region has with Port Moresby, the capital city, and other urban centers.

Little HIV prevalence data are available for Papua New Guinea as a whole and, more specifically, for this southwestern area. Early surveys conducted in 1992 showed either the absence of HIV infection in the general population of Papua New Guinea or a very low prevalence among STD patients, whereas more recent studies found high seroprevalence rates among female sex workers. Official reports state that the number of HIV cases in Papua New Guinea has increased rapidly in the last 10 years, but the prevalence data are not supported by recent seroprevalence surveys conducted in the general population.

Our results show that other infections, such as HHV-8 and HSV-2, are widespread in the area of the study, especially in the northern villages. Seroprevalence rates for both infections were similar in 1999 and 2001. Comparison with studies conducted in other countries in Southeast Asia shows that the HHV-8 seroprevalence found in our serosurveys was lower than that observed in rural areas in Cambodia (53.7%), but much higher than the 0.6% observed in the general population of Thailand. The prevalence of HSV-2 was higher than the 14.5% reported in Sydney, Australia among antenatal clinic patients. These results confirm our previous observations suggesting that sexual practices that sustain highly endemic levels of sexually transmitted infections occur in this remote area.

The finding that the seroprevalence of both HHV-8 and HSV-2 increased with age is suggestive of continued exposure to viral agents in the adult population, as occurs with other STDs, and confirms findings of other studies conducted in different geographic areas.

The higher prevalence observed for both HHV-8 and HSV-2 in the northern villages may be attributed to the close proximity of these villages to an important connection route, which may favor social and commercial exchanges. This might also explain the higher HSV-2 prevalence among males, who are more likely to have trading and other work activities outside the Morehead District.

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**Table 1**

<table>
<thead>
<tr>
<th>Geographic area</th>
<th>No. positive/total</th>
<th>% Positive</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>113/351</td>
<td>32.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>58/169</td>
<td>34.3</td>
<td>0.83 (0.52–1.33)</td>
<td>0.90 (0.56–1.43)</td>
</tr>
<tr>
<td>Female</td>
<td>55/182</td>
<td>30.2</td>
<td>1.00</td>
<td>1.04‡ (1.02–1.06)</td>
</tr>
<tr>
<td>Age group (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 30</td>
<td>31/158</td>
<td>19.6</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>30–39</td>
<td>29/73</td>
<td>39.7</td>
<td>2.70 (1.40–5.21)</td>
<td>2.28 (1.16–4.49)</td>
</tr>
<tr>
<td>≥ 40</td>
<td>53/120</td>
<td>44.2</td>
<td>3.24 (1.84–5.72)</td>
<td>2.13 (1.16–2.64)</td>
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<tr>
<td>Geographic area</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>River</td>
<td>29/130</td>
<td>22.3</td>
<td>1.00</td>
<td>1.80§ (1.08–3.01)</td>
</tr>
<tr>
<td>Coast</td>
<td>10/33</td>
<td>30.3</td>
<td>1.51 (0.65–3.54)</td>
<td>1.64 (0.70–3.88)</td>
</tr>
<tr>
<td>North</td>
<td>74/188</td>
<td>39.4</td>
<td>2.26 (1.36–3.75)</td>
<td>1.48 (0.88–2.49)</td>
</tr>
</tbody>
</table>

* HHV-8 = human herpes virus 8; HSV-2 = herpes simplex virus 2; OR = odds ratio; CI = confidence interval.
† Eight sera not available for testing.
‡ Age was considered as a continuous variable; OR per one-year increment.
§ River versus coast and north.
The seropositivity of HSV-2 appears to be a correlate of HHV-8 infection, even after adjusting for age, sex, or geographic area. This association has been also reported in other studies, and suggests that either the two viral agents share, at least in part, similar transmission modalities, or that HSV-2 infection may facilitate the acquisition of HHV-8 through sexual contacts. More specifically, it can be hypothesized that immunologic mechanisms, similar to those that enhance at the mucosal level the sexual transmission of HIV in the presence of HSV-2 genital herpes, may increase the transmission of HHV-8 in HSV-2-infected persons.

In conclusion, despite the fact that Papua New Guinea has the greatest number of HIV infections and acquired immunodeficiency syndrome cases in the South Pacific region, our data show that the inhabitants of the southwestern region currently experience an extremely low circulation of HIV. However, the high prevalence of infectious agents that can be sexually transmitted, such as HSV-2 and to a lesser extent HHV-8, indicates the presence of behavioral patterns that may facilitate the transmission of HIV and contribute to the spread of the epidemic in this area of currently low endemicity. For these reasons, there is an urgent need for prevention campaigns aimed at the containment of the spread of HIV and other sexually transmitted infections, even in these remote and isolated villages.

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