important differences in experimental design, including the route of inoculation, the use of abrasion before inoculation, which could increase the contact between antibody and virus, and most importantly the difference in the time of antibody administration. Others have also reported protection from ganglionic infection by passive antibody administered before inoculation [4, 5], and we have shown that prior HSV immunization of adult guinea pigs can decrease recurrences [6–8] and latency measured by quantitative polymerase chain reaction [8].

To investigate the role of antibody in preventing or reducing latency more thoroughly, we used the well-characterized guinea pig vaginal model of HSV infection and an engineered HSV virus that expresses β-galactosidase in latently infected neurons. Thus, the number of latently infected neurons could be counted after staining. We found that administration of high-titered HSV antibody 24 h after intravaginal challenge significantly reduced the number of latently infected neurons and the number of recurrences; however, when antibody was given 72 h after intravaginal challenge, recurrences were not decreased (latently infected neurons were not quantitated) [9] (unpublished data). We agree with Tenser [1] that although replication does not appear to be a prerequisite for the establishment of latency, when antibody is present before or shortly after virus inoculation, it can prevent or reduce latency, possibly by reducing virus entry into neural tissue.

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Is Human Herpesvirus Type 8 Fairly Prevalent among Healthy Subjects in Italy?

To the Editor—We read with interest the article by Bigoni et al. [1], in which the prevalence of human herpesvirus (HHV) type 8 infection was explored by nested polymerase chain reaction (PCR) in a large series of human immunodeficiency virus (HIV)–positive and –negative samples (peripheral blood lymphocytes [PBL] and lymph nodes [LN]) from Italian subjects with or without lymphoproliferative disorders (Hodgkin’s disease, non-Hodgkin’s lymphoma, or reactive lymphadenitis). The authors, having detected the virus in ~10% of all studied groups, irrespective of underlying pathology and the presence of HIV infection, concluded that HHV-8 infection is quite common in the general population.

The prevalence of this newly discovered virus is, however, a hotly debated issue. Some authors claim that HHV-8 is a ubiquitous virus; others believe that HHV-8 infection is mainly restricted to persons having an increased risk of developing Kaposi’s sarcoma (KS) [2]. The most widely used technique for HHV-8 detection is presently PCR, serologic tests being still under development. Unfortunately, PCR amplification on PBL collected at a single time point does not seem to accurately diagnose HHV-8 infection, since independent reports demonstrate that blood samples of at least 40% of AIDS-associated KS patients are PCR-negative [3, 4]. In addition, by nested PCR we found similar rates of viral detection in a series of PBL samples drawn from 40 subjects with Mediterranean KS [4a], confirming the intermittent character of HHV-8 viremia in these two forms of KS.

On the other hand, PCR studies on LN samples appear more interesting since, as Bigoni et al. [1] suggest, secondary lymphoid organs may be privileged sites of HHV-8 latency or persistence in the infected host [1]. Accordingly, we demonstrated the virus in 100% of LN specimens from AIDS-KS patients and HIV-negative subjects with plasmacellular Castleman’s disease; these specimens were devoid of occult KS foci, as determined by histologic examination and CD34 immunohistochemistry [5, 6]. Moreover, by screening 40 HIV-related and -unrelated lymphomas, we found HHV-8 detection rates (~10%) similar to those reported by Bigoni et al. [1].

However, upon closer examination, of the 4 HHV-8–positive lymphoma patients in our series, 3 (2 HIV-positive, 1 HIV-negative) had a history of or presently had KS, while 1 patient with AIDS-associated non-Hodgkin’s lymphoma had elevated levels of HHV-8, comparable to those seen in a primary effusion lymphoma (PEL) [7]. In addition, HHV-8 DNA sequences were not detected by PCR in LN from HIV-negative subjects (0/5) or HIV-positive drug users (0/22) without KS [5–7].

Our data on Italian subjects thus indicate a strong association between the presence of HHV-8 and the occurrence of well-defined pathologic events (i.e., KS, PEL, and Castleman’s disease). Unfor-

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Unfortunately, this association failed to emerge from the article by Bigoni et al., as they did not provide any clinical information relative to their HHV-8-positive subjects.

Moreover, even if restricted areas of Italy show relatively high incidences of endemic Mediterranean KS [8], during the last decade the incidence of KS has increased nationwide by several hundred-fold, mainly due to the emergence of the epidemic AIDS-associated form of the disease. It is therefore puzzling that Bigoni et al. could not document any difference in HHV-8 prevalence between HIV-seropositive and -seronegative patient groups.

Perhaps this apparent paradox could be clarified by providing detailed demographic data and risk factors for or history of KS, PEL, or Castleman's disease of the patients in their series. Until then, it would be premature to consider HHV-8 infection as fairly frequent in the general Italian population.

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Reply

To the Editor—Until now, the presence of human herpesvirus (HHV) type 8 DNA has been detected mainly, but not exclusively [1, 2], in patients with specific disorders, such as Kaposis's sarcoma (KS) [3], multicentric Castleman's Disease (MCD) [2], and body cavity-based lymphoma (BCBL) [4], as well as in human immunodeficiency virus (HIV)—seropositive patients [5].

Recently, we described the presence of HHV-8 DNA by nested polymerase chain reaction (PCR) in ~10% of biopsies from lymphoproliferative disorders, in peripheral blood mononuclear cells (PBMC) from healthy blood donors, as well as in corresponding samples from HIV-positive patients [6]. Not unexpectedly, the virus load was increased in HIV-immunodepressed patients: Samples from HIV-negative persons harbored 1 viral genome in ~37,000 diploid cells, but samples from HIV-infected patients showed a 10- to 1000-fold increase of viral DNA content. These results suggested that HHV-8 DNA is fairly common in the population and that it can be reactivated during immunosuppression.

With regards to the presence of HHV-8 in the general population, Corbellino et al. [7] report their results and, suggesting a strong association between the presence of HHV-8 and specific pathologic conditions, raise an interesting point. The presence of HHV-8 in HIV-negative patients could be indicative of history or risk factors for the development of KS, MCD, or BCBL. If that is the case, is it correct to suggest that HHV-8 infection is fairly frequent in the general population?

Here we address this concern, providing clinical data, analysis of risk factors, and history of the patients described in our study [6].

The large majority of our HHV-8—positive patients was from the northeast part of Italy, and none had a history of putatively HHV-8—associated diseases (KS, MCD, or BCBL). Of the 10 HIV-seronegative patients carrying HHV-8 DNA sequences, only the patient with reactive follicular hyperplasia had Hodgkin's disease (HD) as a concomitant disease. Likewise, none of the 4 HIV-infected patients with PBMC positive for HHV-8 has thus far developed KS or other relevant diseases (mean follow-up, 1.5 years). Moreover, no evidence of previous or concomitant KS was present in 2 HIV-seropositive patients with HHV-8 DNA sequences in their pathologic lymph nodes, 1 with HD and the other showing features of HIV-associated lymphadenopathy syndrome (LAS). Of note, both of these patients were intravenous drug users. Only 1 HIV-seropositive homosexual man with LAS later developed KS.

Therefore, the analysis of clinical data of our series of patients confirms that the presence of HHV-8 DNA is not necessarily associated with particular risk factors or the development of specific diseases. In addition, the positivity of PBMC from healthy blood

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