Reviewer's report

Title: Incidence of Human Herpesvirus 8 (HHV-8) Infection Among HIV-uninfected Individuals at High Risk for Sexually Transmitted Infections

Version: 1 Date: 13 February 2007

Reviewer: Philip Pellett

Reviewer's report:

General:
Many of the specifics of HHV-8 transmission are unknown, which has inhibited development of meaningful prevention messages and strategies. This paper provides useful information on the important issue of HHV-8 incidence in HIV-uninfected individuals at high risk for sexually transmitted infections. In addition, there were interesting observations about HHV-8 seroprevalence in heterosexuals vs. MSM. In all, this is a nicely done study that will be of interest to many in the field. The paper is relatively cleanly prepared. Most of the points raised below can be addressed easily.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached):
1. Confidence intervals are needed on the incidence estimates (HHV-8, HIV, etc.). This is important because in the current text, these values are being compared as hard numbers. For example, in line 6 of p. 12, something is made of the seroincidence being lower in females than males (2.3/100 py vs. 3.1 py). I imagine that the confidence intervals for the female estimate are very wide, given how few were studied. Some sort of statistical test is needed to have confidence that the difference is meaningful. Several parts of the text will need revision in this regard.

2. I want to know whether individuals who were seropositive at the first time point remained seropositive through the study period. This is important because we need to understand whether the “incident” seroconversions are true seroconversions or are some form of seroreversion (antibody levels fluctuating above and below the serologic cutoff, as has been seen for HSV gG serology). If seroreversion is frequent, this will confound attempts to identify risks for infection. 72 of the 456 individuals studied were HHV-8 seropositive at the time of enrollment, and were not tested further. I would like to know the serostatus of at least 20 of them in specimens equivalent to those used for the seroincidence part of the study. The robustness of your conclusions will be much greater with this information.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct):
1. The NEJM paper by Hladik et al. from 2006 should be cited in the context of transfusion-transmission of HHV-8.

2. I assume that “persistently HHV-8 negative” means negative on the two dates sampled (p. 7). As expressed, it sounds stronger than it is.

3. I don’t understand the ranges listed at the end of the penultimate paragraph on p. 9. The overall young end of the range (0.3 years) is smaller than the minimum for either of the two sub-categories.

Discretionary Revisions (which the author can choose to ignore):
1. The Abstract mentions the “large difference” between HHV-8 incidence and incidence of HIV and other STIs, but there is no mention elsewhere in the abstract of such information.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions.
Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests.