Reviewer’s report

Title: HPV infection, anal intra-epithelial neoplasia (AIN) and anal cancer: current issues.

Version: 1 Date: 22 April 2012

Reviewer: Joel Palefsky

Reviewer’s report:

Major compulsory revisions

This well-written article nicely summarizes recent studies documenting the rising incidence of anal cancer in the general population among both men and women and summarizes our limited knowledge of progression from high-grade anal intraepithelial neoplasia (HGAIN) to cancer. Focusing on the role of HGAIN as a precursor to anal cancer highlights the clinical importance of this lesion and the need for more information on its pathogenesis and natural history in risk groups that have been poorly studied. These risk groups include men with no history of receptive anal intercourse and women with or without a history of receptive anal intercourse. The paper rightly points out that the risk of anal cancer is behavior-based, and not based on sexual orientation.

Discussion—first paragraph. The authors should include immunosuppression, both HIV-related and non-HIV sources of immunosuppression such as solid organ transplant as a risk factor.

Discussion—second paragraph. The authors present data on the proportion of Scottish women who have practiced anal intercourse. This figure is lower than that reported from some studies in the U.S., and suggests that there are true population differences or, more likely, some degree of under-reporting among the Scottish women. The authors might want to comment on that.

Discussion—general comment. The article highlights the most important research done to date but should also reference a meta-analysis paper that was recently published online (Machalek DA et al. Anal human papillomavirus infection and associated neoplastic lesions in men who have sex with men: a systematic review and meta-analysis. Lancet Oncol. 2012 Mar 22. Epub ahead of print. This recently published article concludes that the progression rate from HGAIN is not high enough to warrant routine screening and treatment of HGAIN, even in the highest risk groups except in a research setting. Data summarized in this article by Stanley et al. emphasize that the information on HGAIN progression to cancer is limited but suggest that it is similar to that of progression of high-grade vulvar and cervical intraepithelial neoplasia to vulvar and cervical cancer, respectively. The authors might also want to comment on the conclusions of the Machalek paper in this light.
Discretionary revisions

Discussion—second paragraph. The authors describe the higher incidence of anal cancer among women compared with men, and tie that to the relative differences in the proportions of women and men who reported a history of anal intercourse and imply that it is this relative difference that accounts for the differences in anal cancer rates between men and women. The authors could carry the argument a bit further. Further linking risk of anal cancer to anal intercourse, the authors might want to explicitly mention here that it is also likely that among men, MSM account for a disproportionate amount of anal intercourse and anal cancer.

The authors might wish to expand on where they think the field should be going next, e.g., do they believe that there is a need for more studies on progression of HGAIN to cancer, or for data on the efficacy and effectiveness of treatment of HGAIN to reduce the incidence of anal cancer.

Minor essential revisions

Abstract- line 26 should read “There is also less evidence….”
Abstract- line 33 should read “There is strong evidence….”

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

Dr. Palefsky's institution has received research funding from Merck and Co. and funding for participation in Merck scientific advisory boards. Dr. Palefsky has been granted stock options for participation in a scientific advisory board for Aura Biosciences.