Reviewer’s report

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

Version: 1 Date: 13 May 2012

Reviewer: J. Michael M Berry

Reviewer’s report:

Thank you for the opportunity to review “HPV infection, anal intra-epithelial neoplasia (AIN) and anal cancer: current concepts”. It is a concise, excellently written update regarding anal HPV infection, anal cancer precursors and evidence for progression to cancer in the general population as opposed to specific high-risk groups. They summarize recently published data regarding the prevalence of anal HPV infection in groups not generally thought to be at increased risk for anal cancer, indicating that HPV infection is probably more common than most of us realize. This has implications for strategies designed to facilitate more widespread implementation of HPV vaccination. The group also discusses some of the possible differences and similarities to cervical and vulvar neoplasia and puts forth an explanation as to how these may explain the specific prevalence of anal cancer. The authors also elegantly argue the point that HGAIN are potentially pre-cancerous and emphasize the need for clinicians to follow patients carefully when diagnosed with HGAIN because of the potential risk for progression to cancer. This work adds to our body of knowledge and increases awareness among clinicians about this problem that continues to increase annually on a worldwide basis and also highlights important existing gaps in our knowledge.

Minor essential revisions

1. Abstract, pg 2, line 34: Suggest changing some data on the progression of AIN into invasion TO some data on the progression of AIN to invasive cancer
2. Discussion, pg 4, line 71: consider changing 0.37 per 100,000 in men, 0.55 in women to 0.37 per 100,000 in men and 0.55 in women
3. Discussion, pg 5, line 84: consider changing includes to including

Discretionary revisions

1. Background, pg 3, line 48: consider changing other HPV-cancers to other HPV-related cancers
2. Discussion, pg 4, line 74: I think this is a good logical argument but would also consider adding a sentence regarding the anatomic proximity of the vaginal introitus to the anus, which may facilitate a greater amount of auto-inoculation that may also help to explain the gender difference.
3. Discussion, pg 4, line 82: paucity of data from the heterosexual male and non-HIV positive or non-high risk female population (largest sections of the
general population) has been a problem. Consider modifying for clarity to: (largest sections of the general population who make up a substantial number of anal cancer patients) has been a problem in the clinical management of these patients, particularly in determining the rationale and feasibility of instituting a screening program.


5. Discussion, pg 6, line 122: On section describing high-grade intra-epithelial neoplasia … consider adding specific statement: HGAIN can be identified using high-resolution anoscopy (HRA) or colposcopy of the anus and perianus after application of 3-5% acetic acid. In comparison to the number of cervical colposcopists, however, currently there are far fewer trained experts in HRA and this partly explains why there is even less data published on the prevalence of HGAIN in the general population. Since there are no recommendations for screening, many patients are either diagnosed serendipitously during surgery for benign anal conditions or occasionally during colonoscopy or if they present with anal symptoms.


6. Summary, pg 7, Consider adding for clarity: There are supportive data for the contention that HGAIN is a precursor, however, there is limited data on the prevalence of HGAIN in the general population.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

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