Human papillomavirus and cervical dysplasia in Nunavut: prelude to a screening strategy

Sylvia M Healey 1, Kristan J Aronson 2, Yang Mao 3, Eduardo L Franco 4

1 Health Protection Unit, Department of Health, Government of Nunavut, Iqaluit, Nunavut, Canada;
2 Department of Community Health and Epidemiology, Queen’s University, Kingston, Ontario, Canada;
3 Environment Risk Assessment and Case Surveillance Division, Cancer Bureau, Center for Chronic Disease Prevention and Control, Population and Public Health Branch, Health Canada, Ottawa, Ontario, Canada;
4 Department of Oncology and Epidemiology, McGill University, Montreal, Quebec, Canada;

Alphabetical list of abbreviations: ASCUS, atypical squamous-epithelial cells of undetermined significance; HC-II, hybrid capture II; HPV, human papillomavirus; NWT, Northwest Territories; OR, odds Ratio; Pap, Papanicolaou; RLU, relative light units; SIL, squamous intraepithelial lesions.

ABSTRACT
Objectives. To determine the prevalence of oncogenic human papillomavirus (HPV) in Nunavut and to assess the association between HPV and squamous intraepithelial lesions (SIL) as a prelude to planning a better screening strategy. Study Design. A cross-sectional study was conducted on the Pap-screened populations in 19 communities in Nunavut, Canada. SIL was determined using Liquid-based cytology, and HPV testing was done using the Hybrid Capture II assay. Results. Prevalence of oncogenic HPV in 1,290 women ages 13-79 was 26% and of Cervical Dysplasia was 7.2%. Over 90% of women with SIL had positive HPV tests. Over 75% of women who were HPV positive but SIL negative were under 30 years of age. Conclusion. Consideration should be given to using liquid-based cytology for Pap testing. Also consider concurrent HPV testing in those over 30 years old and reflex testing of HPV in those under 30 years old with a positive HPV test.

Key Words: papillomavirus, Papanicolaou test, cervix neoplasms, screening, Inuit

INTRODUCTION
The high rate of cervical cancer in the aboriginal population of Nunavut and the Northwest Territories (1), despite having screening rates comparable to British Colombia and Ontario, has led to concerns about current screening methods. Recent reports in the literature have indicated that although the conventional Pap test is the best tool we have at present, it is less than ideal for screening for cancer of the cervix, and has a sensitivity of approximately 51% (2). This has generated interest in evaluating the potential of incorporating new technologies, including liquid based cytology and Human Papillomavirus (HPV) testing into the screening process.

METHODS AND RESULTS
As a prelude to this process, the prevalence of high-risk HPV types in Nunavut was determined and the association between these high-risk HPV types and cervical dysplasia was examined (3). A cross-sectional study was done from May 1st 1999 to December 31st 1999. Figure 1 shows the 19 communities in Nunavut from where women who went to the clinic for a routine Pap test were invited to participate. The Pap test was done using liquid cytology and HPV testing was done on the residual sample using the Hybrid II capture method. Age, ethnicity, health region, highest level of education in the household and smoking were controlled for as potential confounders.
As shown in Figures 2 and 3, the proportion of women in this study who had a Pap test during the study period ranged between 20% and 45% of the general population of Nunavut. Of those women who did receive a Pap test, study participants were equally represented across age groups with 70% participation.

The prevalence of high-risk HPV types in the participating communities in Nunavut was 26%. Comparative studies in Newfoundland and Ontario found prevalence rates of 9.2% and 13%, respectively. The prevalence of cervical dysplasia was 7.2%, also higher than other provinces reporting comparative data (4,5). Women in Nunavut with high-risk HPV were 28.6 times more likely to get cervical dysplasia. This after adjusting for age, ethnicity, region, education and smoking. In the Nunavut study, the risk of SIL also correlated positively with increasing viral load.

As seen in Figure 4, over 90% of those with cervical cancer precursors tested positive for oncogenic HPV types. 21% of women with negative cytology were also positive for oncogenic HPV types. Most of these women (75%) were under 30 years old. In a prospective study in the US (Kaiser Permanente) involving 17,654 women, who were followed for the development of incident squamous intra-epithelial lesions (SIL), it was found that presence of oncogenic HPV preceded and predicted the first cytological detection of SIL (6,7).

CONCLUSIONS
Based on all the information from this study and other recent reports in the literature, consideration should be given to incorporating the new technologies to make screening for cervical cancer more effective. In parti-
cular, consideration should be given to using liquid based cytology for Pap testing. Also, consider concurrent HPV testing in women over 30 years old and reflex testing for HPV in those less than 30 years who have a positive Pap test.

Acknowledgements:
The authors would like to thank all the women who participated in the study, the Baffin and Keewatin Regional Health Boards, Dr. Andre Corriveau, Chief Medical Health Officer for the North West Territories for their support.

REFERENCES

1. Corriveau A. Cancer incidence and mortality in the NWT 1991 to 1996. Epi-North 1997; 9(2):5.
2. McCrory DC, Matchar DB, Bastian L, et al. Evaluation of Cervical Cytology. Evidence Report/ Technology Assessment No. 5. AHCPR Publication No. 99-E010. Agency for Health Care Policy and Research, U.S. Department of Health and Human Services, Rockville, MD, February 1999.
3. Healey SM, Aronson KJ, Mao Y, Franco. Oncogenic Human Papillomavirus Infection and Cervical Lesions in Aboriginal Women in Nunavut, Canada. Sexually Transmitted Diseases 2001;28(12): 694-700
4. Ratnam S, Franco EL, Ferenczy A. Human papillomavirus testing for primary screening of cervical cancer precursors. Cancer Epidemiol Biomark Prev 2000; 9:945-951.
5. Sellors JW, Mahony JB, Kaczorowski J, et al. Prevalence and predictors of human papillomavirus infection in women in Ontario, Canada. Can Med Assoc J 2000;163:503-508.
6. Liaw K, Glass A, Manos MM, et al. Detection of human papillomavirus DNA in cytologically normal women and subsequent cervical squamous intraepithelial lesions. J Natl Can Inst 1999;9:954-60.
7. Rosendaal L, Westerga J, van der Linden JC, et al. PCR-based high-risk HPV testing is superior to neural network based screening for predicting incident CIN III in women with normal cytology and borderline changes. J Clin Pathol 2000; 53:606-611.

Sylvia Healey
Department of Health & Social Services
Bag 1000, Station 1000,
Iqaluit, Nunavut
Canada, X0A 0H0

Email: shealey@cov.nu.ca