

## Selected Summary

### Human papilloma virus and squamous cell carcinomas of the head and neck

Mork J, Lie K, Glatte E, Hallmans G, Jellun G, Koskela P, Mfiller B, Pukkala E, Schiller JT, Youngman L, Lehtinen M, Dillner J. (Cancer Registry of Norway, Oslo; Department of Otolaryngology, National Hospital, Oslo; Department of Pathology, Norwegian Radium Hospital, Oslo; the Northern Sweden Health and Disease Study, Umea, Sweden; the Janus Committee, Norwegian Cancer Society, Oslo, Norway; the National Public Health Institute, Oulu, Finland; the Finnish Cancer Registry, Helsinki, Finland; the Laboratory of Cellular Oncology, National Cancer Institute, Bethesda, Maryland, USA; the Clinical Trial Service Unit and Epidemiological Studies Unit, University of Oxford, Oxford, UK; the National Public Health Institute, Helsinki, Finland; the Microbiology and Tumor Biology Center, Karolinska Institute, Stockholm, Sweden). Human papilloma virus infections: A risk factor for squamous cell carcinoma of the head and neck. *N Engl J Med* 2001;**344**:1125–31.

#### SUMMARY

Mork *et al.* have reported the probability of human papilloma virus (HPV) as a risk factor for squamous cell carcinomas of the head and neck (SCCHN). In a unique study, the authors have collected prediagnosis serum samples of 292 patients with SCCHN from a serum sample bank of 900 000 subjects. Serum samples of SCCHN patients and controls collected on an average of 9.4 years after enrollment in the serum bank were analysed for antibodies against HPV-16, 18, 33 and 73. Although the authors discuss the drawbacks of the serological assay, they believe that the risk associated with seropositivity was largely attributable to infection at the site of the tumour. The odds ratio (OR) was significantly higher for tumours that were positive for HPV-16 (37.5) than those that were negative (2.1). There was significant heterogeneity in the ORs across anatomical sites with elevated ORs detected for cancers of the tongue and oropharynx. A hundred and sixty tumour tissues from the 292 patients were subjected to DNA extraction and polymerase chain reaction (PCR) analysis for HPV. Detection of HPV-16 by PCR in tumours correlated significantly with prediagnostic seropositivity for HPV-16 ( $p < 0.001$ ). The risk of having SCCHN that contained HPV-16 DNA in HPV-16 seropositive subjects was significant. However, the authors were limited in their ability to control for risk factors other than smoking in the present study.

#### COMMENT

There is a growing concern about the increasing incidence of SCCHN in young adults.<sup>1</sup> Though tobacco is a strong causative factor, with its increased consumption among the younger popu-

lation, there are a large number of patients with no attributable addictive or environmental causative factors. What is the cause of cancer in these patients? Is HPV really a risk factor for SCCHN? This question, has been addressed in various studies but without a definite answer. In India HPV is important since the infection is said to be more prevalent in developing countries and in individuals from a lower socio-economic status. There are two reports from India on the status of HPV in oral cancer patients; one reports 15% of oral tumours positive for HPV-16 and 39.5% of the corresponding normal mucosa positive<sup>2</sup> and another reports 47% of oral cancers positive for HPV-16.<sup>3</sup>

HPV as an aetiological factor has been studied in detail. The ability of HPV-16 to immortalize keratinocytes and its oncoproteins E6 and E7 to deactivate the tumour suppressor gene p53 and pRb has been noted *in vitro*. The synergistic action of HPV-16 and tobacco nitrosamines to convert HPV-immortalized oral keratinocytes to a transformed phenotype has been demonstrated *in vitro*.

At present, it is difficult to pinpoint HPV as a causative factor, but its role in oral carcinogenesis needs to be defined. Several cumulative events apart from virus affliction seem to lead to cancer. Elimination of viruses from host cells could reduce the incidence of human cancers.

This study does not conclusively demonstrate a cause and effect relationship between HPV-16 infection and cancers arising from the mucosal squamous cell epithelium, but does give more credence to their association; thus meriting further study.

#### REFERENCES

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- 3 Balaram P, Nalinakumari KR, Abraham E, Balan A, Hareendran NK, Bernard HU, *et al.* Human papillomaviruses in 91 oral cancers from Indian betel quid chewers—high prevalence and multiplicity of infections. *Int J Cancer* 1995;**61**:450–4.

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