HPV and ENT; should we vaccinate boys?

BY DAVID BLACK AND CHARLIE HALL

David Black and **Charlie Hall** reiterate Vin Paleri's pleas for a common sense evidence-based approach by those who allocate healthcare resources to the now urgent issue of HPV-related disease. They discuss the merits of different vaccines and the need for vaccination of boys if we are to get to grips with a growing epidemic.

Human papillomavirus (HPV) is a DNA virus from the papillomavirus family that is capable of infecting humans. HPVs establish productive infections only in keratinocytes of the skin or mucous membranes. Most of these infections are subclinical and will cause no physical symptoms; however, others will present as benign papillomas on the skin or mucous membranes. More than 30 to 40 types of HPV are transmitted through sexual contact and infect the anogenital region, presenting typically as genital warts. Persistent infection with certain 'high risk' HPV types, notably types 16, 18, 31, 33 and 45, may result in progression to precancerous lesions and invasive cancer. High risk HPV infection is a cause of nearly all cases of cervical cancer (70% HPV type 16 and 18).

The recognition and rise of HPV types 16 and 18 as a major cause of oropharyngeal squamous cell carcinoma (OSCC) represents perhaps the most significant development in the epidemiology of head and neck cancer in the last 20 years. It has significantly changed the age and risk factor profile of patients; oropharyngeal cancer is no longer the preserve of heavy smokers and drinkers of low social class. Furthermore, HPV-related OSCC differs in its pathophysiology, opening the door not only to different treatment regimes, but also the possibility of primary prevention. HPV is estimated to be associated with up to 55% of OSCC [1], it is the most common sexually transmitted infection worldwide, and in the UK it is thought up to 80% of sexually active men will contract HPV during their lifetime [2]. The increasing prevalence of HPV-related OSCC appears to partially reflect changing sexual practices and a normalisation of oral sex [3]. The identification of the HPV virus in the pathogenesis of cervical and head and neck carcinomas has led to what may be reasonably considered the first vaccine against cancer.

There are currently three prophylactic vaccines available, all of which were originally developed for the prevention of cervical cancer; Cervarix (types 16 and 18), Gardasil (types 6, 11, 16, 18) and Gardasil-9, a nine-valent vaccine. The quadrivalent Gardasil vaccine carries the added benefit of acting against types 6 and 11, which are also associated with laryngeal papillomatosis.

At least 64 countries worldwide currently have national HPV vaccination programmes [4]. These have all initially focused on vaccinating adolescent and pre-adolescent girls, as nearly 100% of cervical cancer is HPV-associated [5] and this represents the largest burden of disease. There is increasing recognition that the other carcinomas associated with HPV, oropharyngeal SCC amongst them, have an equal or greater prevalence in men [6]. In the USA 91% of anal cancers, 72% of oropharyngeal cancers and 63% of penile cancers are HPV-related [7]. In the UK these three diseases affect 2000 males every year, while 48,000 are diagnosed with genital warts [6]. In fact, such is the success of female vaccination for cervical cancer, and the rise in incidence of HPV-related OSCC, that it is predicted cases of the latter will overtake the former within four years globally [8]. The absence of an early-detection screening tool akin to cervical smear tests means HPV-related OSCC patients will usually present with late stage disease, increasing cost and long-term morbidity of treatment while reducing disease-free survival. The need for primary prevention through vaccination is, therefore, even more vital.

It has been argued that a comprehensive vaccination programme in girls will provide sufficient herd immunity and that immunisation of boys is therefore unnecessary. Mathematic models have shown this to be at least partially accurate [9]. However, these models fall down when considering men who have sex with men (MSM) and men who have sex with women from other countries: 15% of 24-35-year-old men have had sex with someone from outside the UK in the last five years [2]. Despite the numerous vaccination programmes, worldwide coverage remains poor, with only 3.5% of women reached. Even in the developed world, uptake can be disappointing: in 2014 just 37% of girls and 13% of boys in the USA received the three-dose course [10]. In response to this, many countries, including Australia, Austria, Canada, Israel, Switzerland, the USA and areas of Germany and Italy, have now begun to vaccinate both sexes.

Despite this, there are currently no plans in the UK to extend vaccination to boys. The Joint Committee of Vaccination and Immunisation (JCVI) began considering this issue in 2013 and, although a

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decision was expected in 2015, this has now been delayed to 2017, meaning that implementation of a vaccination programme is unlikely to begin before 2020 at the earliest. As of June 2016, a pilot programme has been put in place to vaccinate MSM. However, vaccination is only offered on an opportunistic basis to patients already attending sexual health clinics. Vaccination is known to be most effective if given before sexual debut; however, the average age of these patients first clinic attendance is 28. HPV Action, a pressure group of 44 patient and professional bodies including ENT UK, recently wrote to the Secretary of State for Health, urging him to reconsider this delay by the JCVI. With the recent announcement that both New Zealand and Brazil will begin vaccination programmes for boys by 2017, the UK looks increasingly in danger of falling behind the curve.

The health economic arguments appear straightforward. It has been estimated that extending the vaccination programme to boys would cost £22million a year whilst the current cost of treating ano-gential warts alone runs to £54million, and the secondary care costs of treating HVP related OSCC exceeds £21million [6]. HPV Action continues to pressure parliament to act earlier to bring in full vaccination, noting that with each year's delay a further 400,000 boys go unvaccinated.

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David Black, BM BCh, MA (Cantab) MRCS, DOHNS,

ENT ST6, Gloucestshire Royal Hospital, ENT Dept, Great Western Road, Gloucester, GL1 3NN, UK.

E: davidblack@doctors.org.uk

Charlie Hall, BMsc (Hons), MB.BS., FRCS (ORL-HNS),

Consultant ENT Head & Neck and Thyroid Surgeon, Gloucestershire Hospitals NHS Foundation Trust, Great Western Road, Gloucester, GL1 3NN, UK.

T: +44 (0)300 422 6433
E: charlie.hall@glos.nhs.uk

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ABOUT THE AUTHORS

David Black is an ENT registrar on the Severn deanery rotation. He has particular interests in head and neck cancer and education. He is the current President of SWEAM.

Charlie Hall qualified in 1995 from St Bartholomew's Hospital, London, and did his registrar training at the Marsden and South West ENT Rotation. He undertook a one-year fellowship in head and neck, skin cancer and thyroid surgery in Melbourne, Australia in 2008 before being appointed consultant in Gloucester and Cheltenham in 2009. He is the Co-chair of the Head and Neck Three Counties Cancer Network and Honorary Secretary of the South Western Laryngological Association. Charlie is also the Training Programme Director for ENT in the Severn Deanery.