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SPECIAL ARTICLE

Ten years of human papillomavirus vaccination. From dermatology to oncology via infectology☆

Fernando A. Moraga-Llop

Asociación Española de Vacunología, Barcelona, Spain

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Abstract Human papillomavirus (HPV) was first identified in dermatology, and it was subsequently demonstrated that is was required for the development of uterine cervical cancer and other tumours, after a persistent infection by any of its oncogenic genotypes. Ten years ago, the most common infections and cancers associated with HPV could be prevented by immunization with 2 vaccines, one bivalent, and another tetravalent, and having just marketed a nonavalent one. During the period 2007–2008, the HPV vaccine was included in the Autonomous Communities vaccination calendar, and it is the second vaccine, after that of Hepatitis B, that prevents cancer. In these 10 years that these vaccines have been available the knowledge has progressed and there have been significant advances in vaccination strategies, as well as in the indications and recommendations. These include, lowering the age in the vaccination schedule, prescribing of 2 doses at 9 years and at 13–14 years, systematic vaccination of the male in some countries, immunization of the woman after adolescence, implementation of vaccination programmes in developed countries, prevention of other cancers, recommendations for vaccinations for populations at high risk of HPV infection, scientific evidence on the impact and effectiveness of vaccination, and confirmation of the safety of these vaccines, with more than 270 million doses administered, as has already been observed in clinical trials. The role of health professionals is essential to achieve and maintain high vaccine coverage.

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E-mail address: fmoraga@acmcb.es

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Diez años de vacunación frente al virus del papiloma humano. De la dermatología a la oncología a través de la infectología

Resumen El virus del papiloma humano (VPH) se identifica en primer lugar en dermatología y posteriormente se demuestra que es una causa necesaria para el desarrollo de cáncer de cuello uterino y de otros tumores, tras una infección persistente por alguno de sus genotipos oncogénicos. Desde hace 10 años, las infecciones y neoplasias más frecuentes relacionadas con el VPH pueden prevenirse mediante la inmunización con 2 vacunas, una bivalente y otra tetravalente, y acaba de comercializarse una nonavalente. Durante el periodo 2007-2008 se incluyó la vacuna frente al VPH en el calendario de las comunidades autónomas y es la segunda vacuna, después de la de la hepatitis B, que previene el cáncer. En estos 10 años de disponibilidad de estas vacunas se ha progresado en su conocimiento y se han producido avances importantes en las estrategias de vacunación y en las indicaciones y las recomendaciones: adelanto de la edad de vacunación en el calendario, pautas de 2 dosis desde los 9 hasta los 13-14 años, vacunación sistemática del varón en algunos países, inmunización de la mujer más allá de la adolescencia, implementación de programas de vacunación en países en desarrollo, prevención de otras neoplasias, recomendaciones de vacunación para poblaciones de riesgo elevado de infección por el VPH, evidencia científica del impacto y la efectividad de la vacunación, y confirmación de la seguridad de estas vacunas, con más de 270 millones de dosis administradas, como ya se había observado en los ensayos clínicos. El papel de los profesionales de la salud es fundamental para alcanzar y mantener coberturas vacunales elevadas.

''If men are not vaccinated, the prevalence of HPV will not decrease, as they are transmitters of infection.''

Zur Hausen, *La Vanguardia*, September 18, 2009.

Introduction: a century of human papillomavirus

More than one century ago, in 1907, Ciuffo proved the infectious aetiology of warts and suggested that the cause was a virus, since he was able to transmit the infection through injection of lesion filtrates in human volunteers[1]; later, evidence emerged that genital warts were a manifestation of a sexually transmitted infection. In the 1940s, the advent of electronic microscopy allowed the identification of viral particles in these warts (human papillomavirus [HPV]). In 1953, Bunting was the first to visualize a virus, HPV, within the cells of a wart (papilloma).[2] Thus, dermatology and venereology are found in the origins of the history of the pathology of HPV.

In the 1970s, Orth[3] demonstrated the oncogenic potential of the virus in epidermodysplasia verruciformis, and in the 1980s, Zur Hausen[4] found that HPV DNA is present in most cervical cancers. This author was awarded for his discovery of the role of infection in the pathogenesis of cervical cancer with the Nobel Prize in Physiology or Medicine ten years ago, in 2008, sharing the honour with Barré-Sinoussi and Montaigner, who received the award for their discovery of human immunodeficiency virus. In the 1990s, Bosch et al.[5] and Walboomers et al.[6] confirmed that HPV was present in nearly every case (99.7%) in a series of cervical cancer biopsies from patients in 22 countries; presence of the virus is necessary, although not sufficient, for the development of this cancer along with other cofactors that determine the malignant progression of infection by HPV. Persistent infection by any of the 12–15 oncogenic or high-risk genotypes out of the 150 HPV types that cause cutaneous or genital disease is necessary for the development of cervical cancer preceded by preneoplastic lesions (cervical intraepithelial neoplasia [CIN]: CIN1, CIN2 or CIN3).[7,8]

Thus, infection by HPV plays a role in the pathogenesis of these cervical tumours as well as anogenital and oropharyngeal tumours, and its role in other types of tumours is currently under investigation. The risk of progression from low- to high-grade lesions (from dysplasia to neoplasia) is greater in individuals with persistent infection by any of the oncogenic genotypes, although most HPV infections are silent and temporary and resolve spontaneously within 2 years from transmission. Five percent of all human cancers worldwide are associated with HPV.[9]

Last of all, the most significant breakthrough in regards to HPV has been the development of vaccines in the past 10 years that can prevent the most frequent HPV-related infectious diseases and cancers (primary prevention), conditions that we may be able to treat in the future with therapeutic vaccines that are currently being investigated. The virus-like particles used in preventive vaccines are not infectious or oncogenic, as they contain no viral DNA, but they can induce production of antibodies against the virus. Vaccinology enters the history of HPV one century after it starts and plays a key role in the complex and fascinating chapter that is currently unfolding, in which various medical and surgical specialties are converging, collaborating and participating.