

PRESENT ASPECTS OF HPV INFECTION

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Abstract: People are living surrounded by an environment of omnipresent HPV viruses. A part of these viruses brings about certain lesions, some benign, some of malign potential. Some of these viruses infect the mucous membrane (especially the anogenital one) with a large frequency among the young patients causing cervix cancer (in women), anal and penis cancer, in men. In most of the cases, cervical HPV infection is temporary and asymptomatic. The most spread HPV viruses of oncogenic risks are the types 16 and 18. The screenings for cervix lesions consist in Pap test or liquid-base cytology for detecting HPV virus. Depending on the type of lesion, certain management strategies have been suggested. Today, in order to prevent the HPV cervix infection, the HPV vaccine is being used, being available as a bivalent vaccine (for 16 and 18 HPV types) and as a quadrivalent vaccine (for 6, 11, 16 and 18 HPV types). These vaccines have proved to be very efficient in 5-year studies, so that certain countries have adopted strategies of mass vaccination.

Keywords: HPV, cervix dysplasia, cervix cancer, vaccine

Rezumat: Omul trăieşte înconjurat de un mediu în care virusurile HPV sunt omniprezente. O parte din aceste virusuri provoacă diferite leziuni, unele benigne, altele cu potenţial malign. Unele dintre aceste virusuri infectează mucoasele (mai ales cele anogenitale) cu frecvenţă foarte mare la pacienţii tineri, la femei fiind cauza cancerului de col, iar la bărbaţi, aceste virusuri pot cauza cancer anal şi de penis. Infecţia cervicală cu HPV este în majoritatea cazurilor pasageră şi asimptomatică. Tipurile HPV cele mai răspândite, cu risc mare oncogen sunt 16 şi 18. Screeningul leziunilor de col uterin se face prin citologie pe lamă (examen Papanicolau), sau prin citologie în mediu lichid cu detectarea virusului HPV. În funcţie de leziune, s-au propus o serie de strategii de management. Pentru prevenţia infecţiei cervicale cu HPV, la ora actuală se utilizează vaccinul contra HPV, acest vaccin existând în două forme, vaccin bivalent (contra HPV 16 şi 18) sau un vaccin quadrivalent (contra HPV 6,11,16,18). Aceste vaccinuri s-au dovedit foarte eficiente pe studii de până la 5 ani, astfel încât unele ţări au adoptat strategii de vaccinare în masă.

Cuvinte cheie: HPV, displazie cervicală, cancer de col uterin, vaccin

INTRODUCTION

Human papillomavirus infection is largely spread, existing almost 100 types of HPV that affect humans and out of these types, almost 40 affect the mucosae. Among them, there are types with increased oncogenic risk and others with reduced risks. The most frequent types of HPV involved in the cervix cancer are illustrated in the table 1 bellow; the distribution of these types is relatively the same in the world, with a few exceptions between continents, but the types 16 and 18 remain on the first place, what makes that vaccination be made with the same viral types in all countries. (1,3,4)

HPV types with increased oncogenic risk (16, 18, 45, 33, 31, 58, 52, 35) are involved in the occurrence of the cervix, vulva, penis, oro-pharynx and anal cancer, while the types with reduced oncogenic risk (the most frequent types being the 6 and 11 types) are involved especially in the occurrence of condylomas and of the low-grade squamous intraepithelial lesion (LSIL) and of the vulvar intraepithelial neoplasia (VIN). (2,3)

Prevalence of HPV genital infection is very large at a young age, regarding the population age group between 20 and 24 years old, reaching 45% of the total population. Regarding the age of 50, it is estimated that almost 80% of the women have registered at least one HPV infection (see table 2), HPV infection being the most frequent sexually transmitted infection. (2,3) (http://www.cdc.gov/std/healthcomm/fact_sheets.htm).

HPV infection is of large socioeconomic importance, because the costs directly related to the infection are at the same level with those of HIV infection in the United States of America. HPV infection has also proved to be more expensive than the genital herpes + B hepatitis in the age group between 15 and 25 years old. Falsely negative Babeş smears are among the most frequent causes of malpraxis in USA. (2,3)

HPV infection is a necessary cause (being detected in all cases of cervical neoplasia) but not sufficient for the occurrence of the cervix cancer. There are other co-factors that contribute to the progression from the viral infection to the cancerous lesions. The co-factors which are proved to be involved in the cervix cancer are: long use of oral contraceptives, multiparity, smoking and HIV co-infection; the probable co-factors

are the following: Chlamydia trachomatis infection or herpes simplex, immunosuppression and diet deficiency; the predisposed co-factors that were not clearly proved to be involved in the cervix cancer are the genetic and immunologic factors of the host, the viral factors (the type and the type variants) and the viral load and integration. (5)

Table no. 1. Prevalence of the oncogenic HPV infection in the general population

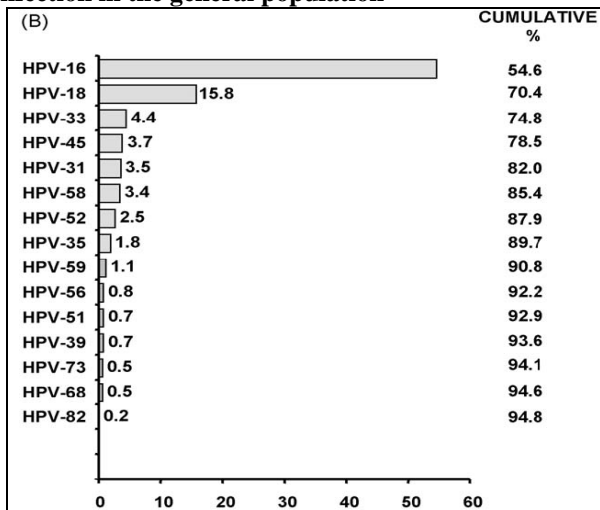


Table no. 2. Prevalence of the HPV infection in the women living in the USA per age groups (2)

Age	Prevalence (%)	95% CI
14-19	24.5	(19.6-30.5)
20-24	44.8	(36.3-55.3)
25-29	27.4	(21.9-34.2)
30-39	27.5	(20.8-36.4)
40-49	25.2	(19.7-32.2)
50-59	19.6	(14.3-26.8)

In order to produce lesions, HPV must reach the basal level of the epithelium, at the level of the undifferentiated cells, the access being possible through the micro-abrasions of the mucosal surface or through the junction area. In the moment in which the virus reaches these cells, it uses the cell division mechanism for replication, inhibiting the differentiation of the host cell and thus creating the condition for an infinite replication. (3)

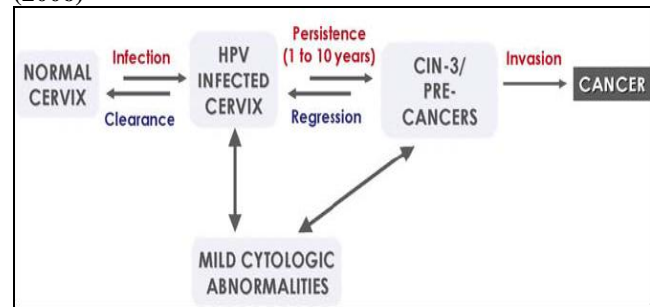
In most of the people, HPV infections are transitory and asymptomatic. 70% of the new infections disappear during one year and 90% in two, with an average of 8 months. An increased risk of infection is registered in the young female patients, with a large number of intimate partners, with frequent sexual relations, who practice anal sex and use alcohol. Virus persistence more than 6 months is possible especially in the patients of an advanced age, in the case of the HPV infection with an increased oncogenic risk and in case of an infection with more types of HPV. Viral persistence is the first step towards carcinogenesis. (2,3)

HPV infection, genital condylomatosis and LSIL lesions are the most frequently encountered in the women

below 25; approximately 70% of these lesions disappear spontaneously in a period of three years. (3)

Cervical carcinogenesis follows well-defined successive stages. The starting point is the viral infection of the epithelium of the transformation area; the infection may suffer a rapid clearance through the intervention of the inborn immune system or through other mechanisms. Otherwise, the persistent infection once installed, it may produce microscopic cellular lesions (this is mostly "solved" by the immune response of the host). The viral persistence (essential condition for carcinogenesis) leads to the clonal expansion of the infected epithelium and to the occurrence of CIN 3 lesions in a period of almost 2-3 years, in the susceptible subjects, and afterwards, it may lead to cervix cancer (picture no. 1). The period of time covered after the occurrence of the cervix cancer is of 12-15 years on average (5-30 years). (2,3,7)

Picture no. 1. HPV type - distribution in women with and without cervical neoplastic diseases. Vaccine 24S3 (2006)



Cervix cancer is the second neoplasia in terms of frequency, in the women of the developed countries and is on the first place in the poor countries. In 2002, there were reported 493000 new cases and 274000 deaths, 83% of the cases belonging to the developing countries. (3,6)

HPV infection has become a more and more important cause of morbidity in men. Infection prevalence was proved to be similar with that of women, although it was observed that the majority of the oncogenic HPV penile infections are asymptomatic and do not lead to penis cancer. Certain studies showed that the HPV infection in the partner of a patient with cervical lesions is more frequent than in the general population and the vice versa – a woman with a male partner with penis cancer may register higher risks to develop cervical cancer. Men who have homosexual relations register an increased risk to develop anal cancer. (3)

Penis cancer is a rare entity, having a proportion of 0,5% of the totality of the cancer types in men. It was observed that this disease, as well as the sexually transmitted diseases, has a smaller incidence in the circumcised men, while the oncogenic HPV (especially the 16 and 18 types) is detected in 40-50% of cases. (3,6)

The anal cancer does not have a well known natural history, but it is suspected that the progression from the pre-cancerous lesions to cancer follows the same steps as in the case of the cervix cancer; in analogy with the cervical region in women, the anus has also a transition region where the rectal mucosa meets the

squamous epithelium. It was proved that, although practicing anal sex may increase the incidence of the HPV infection, it is not compulsory to bring about the infection. (3,6)

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