

The thoughts of HPV of the related regional and gender-based features and the differences between different subtypes

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Abstract. HPV is Human Papilloma Virus. It is a sphere DNA virus, which is very common in nature. The only host of HPV is human beings. Currently, 150 subtypes of HPV have been identified. With the severity, it can be divided into high-risk HPV and low-risk HPV. One of the most terrifying features of HPV is that many people with HPV don't have any symptoms but can still infect others through sexual contact. The common symptoms include warts on the surrounding skin. The warts usually appear as rough, occur on hands and fingers. To avoid more people suffering from HPV and make sure public health, we should enhance sex education and strengthen public health publicity. This essay will introduce the differences and features of high-risk HPV and low-risk HPV and different subtypes of HPV. At the same time, the main reason leads to the differences between high-risk HPV and low-risk HPV, which is the virus interacting with host cells, specifically the expression of certain viral proteins, which can significantly disrupt cell growth regulation and leading to the potential for cancer development. Also, the essay contains the production principles, working principles and side effects of HPV vaccine, and why some people still not accept this vaccine.

Keywords: HPV, high-risk, low-risk, vaccine.

1. Introduction

Human Papilloma Virus is referred to as HPV. The HPV virus is sphere with the spike protein locating in the out membrane, forming a flower or mushroom shaped structures, encapsulating the DNA genome. After human infection with HPV, human skin mucosal epithelial cells will proliferate, thereby inducing the formation of tumors. The main mode of transmission of HPV is sexual life and mother-to-child transmission. And the high-risk factors for human papilloma virus infection include early age of first sexual intercourse, having multiple sexual partners and being prolific. The classification of HPV is based on homology and differences in viral nucleotide sequences. HPV is divided into high risk, medium risk and low risk. High risk HPV includes HPV16, HPV18, HPV31, HPV33, HPV35, HPV39, HPV45, HPV51, HPV52, HPV56, HPV58, HPV59 and HPV68. High-risk HPV can lead to various cancers. The order from high to low is as follow anal cancer is 95%, oropharyngeal cancer is 70%, vaginal cancer is 60%, vulvar cancer is 50%, penile cancer is 35% [1]. Medium risk HPV includes HPV26, HPV53, HPV66, HPV73 and HPV82. Low risk HPV includes HPV6, HPV11, HPV15, HPV19, HPV42, HPV43, HPV44, HPV48, HPV81 and HPV84 [2]. In the normal population of cytology, the top ten most common HPV infection types worldwide are HPV16 (2.8%) and HPV52 (1.5%), which are common type of HPV worldwide, HPV31 (1.2%), which is common in Europe and Latin America, HPV53 (1.2%), HPV18 (1.1%), HPV51 (1.1%), HPV58 (1.0%), HPV39 (0.9%), HPV66 (0.9%), and HPV70 (0.8%). High risk HPV usually has a bearing on cervical intraepithelial neoplasia and cervical cancer and low risk HPV usually makes condyloma acuminatum. HPV has significant differences in different regions. In northern China, the familiar HPV types are HPV16, HPV6, HPV56, HPV66, HPV33 and HPV11. In central China, the common HPV types are HPV52, HPV58, HPV16, HPV66, HPV33 and HPV 68. In warm and humid areas, like the hot and rainy summer in southern China, genital warts are widely prevalent. In wealthy regions, like America, and severe cold regions, the probability of virus transmission is relatively small. In immunocompromised areas, like epidemic zones, like Finland, the harm of viruses is relatively significant. The diseases related to HPV virus include condyloma acuminatum. It is often found in the reproductive organs, can cause the excrescence resembles a cauliflower. After infecting the host,

HPV can proliferate extensively, causing abnormal proliferation of epithelial cell nuclei and mitosis, resulting in cervical intraepithelial neoplasia. When HPV infects cervical tissue, The body produces innate and specific responses through immune cells such as specific antibodies and T cells to clear HPV virus. But if HPV infection persists for a long time, it will reduce the immune cells' response to HPV virus invasion, causing tumor cells to undergo immune escape. If HPV continues to infect, it can cause immune inflammatory stimulation and tissue proliferation, allowing tumor cells to escape normal immune surveillance, leading to uncontrolled cell cycle and mediating the occurrence of cervical cancer. It is predicted that there were nearly 291 million HPV positive women worldwide in 2007.

2. The distribution of HPV subtypes influenced by gender and region

The total infection rate of HPV in China is about 13.1-18.8%, among which the infection rate of high-risk HPV is 12.95-17.1%, and the infection rate of low-risk HPV is about 3.28%. The HPV infection rate varies by the changes of region and population, ranging from approximately 14.9% to 16.0% in urban areas and 13.7% to 16.3% in rural areas. Throughout the country, the overall infection rate, high-risk and low-risk HPV infection rates have shown a trend of being higher in the south than in the north. Globally, data from all continents show the highest infection rate of HPV16, with HPV18 being the second most common type [3]. The distribution of HPV types also varies in different regions. HPV33 is more common in Asia, while the infection rates of HPV52 and HPV58 are low. HPV39 is the most common subtype of HPV infection in northern Iran, next are HPV56, HPV51, and HPV68. For HPV16 infected individuals, the most common one is single infection, and the second common one is the infection of HPV16 mixing other HPV virus. But for HPV18 infected individuals, the proportion is totally reversed [4].

The differences of subtypes of HPV between women and men is also very significant. As shown in figure 1, looking globally, the most popular subtypes through women is HPV52, but in men it is HPV58. For the same subtype of HPV virus, for example, HPV 16, in women the prevalence rate is 3.4%, but in men it is only 0.7%. Another subtype of HPV virus, HPV39, in women the prevalence rate is 2.9%, but in men it is only 0.9. Although some subtypes of HPV virus, for example, HPV45, the prevalence rate in men which is 0.5% is higher than the prevalence in women which is 0.4%, in total the prevalence rate of HPV in women is much higher than the prevalence rate of HPV in men.

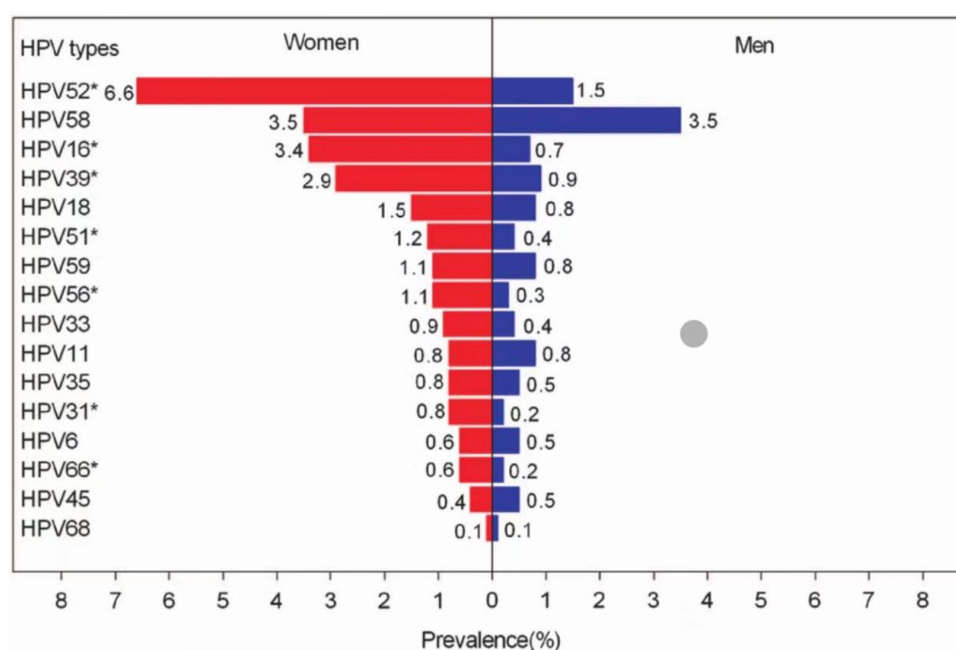


Figure 1. Distribution of HPV subtypes among women and men [5].

3. What leads to the differences between low-risk HPV and high-risk HPV

The main reason of the differences between high-risk HPV and low-risk HPV is the way the virus interacts with host cells. Low-risk HPV types do not significantly change cell cycle regulation, but high-risk HPV types do. So abnormal cell proliferation occurs and the probability of cancer development increases with the persistent infection. E6 and E7 proteins are important proteins for viral replication and can immortalize human cells. E6 binds to the tumor suppressor protein p53, preventing the apoptosis of the cell. E7 binds to the cellular tumor suppressor pRb, preventing it from inactivating transcription factors and favors cell proliferation. But E6 and E7 are overexpressed during cervical transformation and it leads to the invasive cancer phenotype. They change the function of cellular proteins that determine oncosuppressor.

E3 ubiquitin ligases are a family of proteins that regulate protein homeostasis by transferring ubiquitin to target proteins. This process regulates cellular protein homeostasis and is involved in many cellular responses. E6-associated protein, also called E6AP, is a protein that targets proteins for degradation with cells. It has two main functions. One is directing proteins to the ubiquitin proteasome system, one is acting as cofactor for transcription. The 26S proteasome is a large protein complex that breaks down proteins in eukaryotic cells. It uses ATP hydrolysis to disrupt the higher-order structures of its substrates, then moves the unfolded polypeptides into a chamber for proteolytic cleavage. High risk HPV E6 proteins target the cellular E3 ubiquitin ligase E6AP to p53, resulting in the ubiquitin peptides transfer from E6AP to p53, marking p53 for degradation by the 26S proteasome [6].

4. HPV vaccine

Vaccination is the most useful way of preventing HPV virus. To make HPV vaccine, people use recombinant DNA technology to produce virus-like particles which mimic the HPV virus. Firstly, they let a protein from the surface of the HPV virus grown in yeast cells, so the protein self-assembles into virus-like particles which look like the HPV virus. Next, people add other ingredients, which include aluminum, sodium chloride, water, and so on, to the virus-like particles to make the vaccine stable, and stimulate the immune system. The principle of vaccine is by removing HPV nucleic acid, retaining its nucleocapsid protein L1, and forming virus like particles, owing to the presentation of viral antigens after intramuscular injection, it can stimulate humoral immunity, produce neutralizing antibodies, which can bind to viral antigens when HPV infection next time, thereby preventing specific types of HPV entry and development of cervical intraepithelial neoplasia. HPV vaccines are divided into bivalent vaccines, quadrivalent vaccines and nonavalent vaccines. The bivalent vaccine mainly targets HPV16/18 and can prevent about 70% of cervical cancer associated with these two HPV types. The quadrivalent vaccine targets approximately 70% of cervical cancers associated with HPV16/18 and 90% of genital warts caused by low-risk HPV6 or HPV11. The nonavalent vaccine can prevent cancers such as cervical cancer, vulvar cancer, anal cancer, and vaginal cancer, as well as diseases such as genital warts. The increased types increase the protective efficacy of cervical cancer to 90%. According to WHO and UNICEF estimates, the proportion of women in the target age range who have completed their first dose and all immunizations worldwide by 2022 is as the data shown: 21% of women have completed their first dose and 15% have completed all immunizations, 6% of men have completed their first dose and 5% have completed all immunizations. The overall vaccination rate in Asia is the lowest, with a vaccination rate of less than 6% for the first dose and less than 4% for completing all vaccinations [7]. There are many factors that affect people's willingness to get vaccinated. Many people choose not to receive the HPV vaccine due to a lack of relevant knowledge. On a personal level, many people are unaware of the dangers of the HPV virus and its associated diseases, as well as the susceptibility of the HPV virus to infection, thus neglecting the importance of getting vaccinated against HPV. From a societal perspective, due to some religions being incompatible with vaccination, some people with religious beliefs may choose not to receive the HPV vaccine. Furthermore, insufficient dissemination of knowledge related to sexuality in society can also lead to people making incorrect choices. In terms of healthcare, the lack of human resources

can also hinder the popularization of HPV vaccines. After promoting the vaccine for 5-8 years, the infection rates of high-risk HPV16 and HPV18 significantly decreased by 83% in women aged 13-19, 66% in women aged 20-24, and 54% in women aged 13-19 [8].

5. Conclusion

There are many different subtypes of high-risk and low-risk HPV. Different subtypes have dissimilar regional distribution characteristics and probability of infection. Different subtypes of HPV distribute in different countries, different climatic region. Also, the region with other epidemics or not also influence the distribution of subtypes of HPV. The differences of principles of working lead to the difference of the severity of the resulting disease, and other aspects, between high-risk HPV and low-risk HPV. Vaccination can prevent HPV virus to a big extent. But unfortunately, because of a range of reasons, like the unawareness of HPV virus and the related diseases, the lack of the promotion of sex education, and so on, there are still a number of people are unwilling to vaccination. To treat HPV in the future, people should base on the subtypes of HPV and connect their feature with patients' actual condition. Nowadays, HPV vaccine still has some limitations, for example, it doesn't prevent all HPV-related cancers, or it is not recommended for certain people, like people who are pregnant. To make more people accept HPV vaccination, by ensuring that the HPV vaccine can effectively activate the immune system and establish immune response, it can reduce the rejection of vaccines against other diseases. Also, attach more importance on publicity work on sex education, introduction of HPV to raise people's awareness of getting the HPV vaccine.

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