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HUMAN PAPILLOMAVIRUS AS A PUBLIC HEALTH CHALLENGE: THE ROLE OF VACCINATION AND SYSTEMIC CARE IN THE ELIMINATION OF HPV-RELATED DISEASES – A REVIEW OF CURRENT RECOMMENDATIONS AND IMPLEMENTATION CHALLENGES

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ABSTRACT

The Human Papillomavirus (HPV) represents a global public health concern that can significantly impact both mental well-being and lead to the development of various diseases, including life-threatening malignancies. A proactive and informed approach is crucial in limiting the spread of the virus, which is why comprehensive education - beginning in early school years and continuing through medical training and ongoing professional development for physicians, nurses and other healthcare workers – is essential. Currently, there is no approved targeted therapy for HPV infection. Available treatment options focus primarily on managing HPV-associated lesions rather than eradicating the underlying viral infection. This review provides a comparative analysis of current HPV prevention strategies and vaccination guidelines, as well as diagnostic and therapeutic recommendations for HPV-related diseases, including cutaneous warts, genital warts, laryngeal papillomatosis, cervical cancer, and HPV-related oropharyngeal cancers.

Review methods: To obtain the most up-to-date information and clinical guidelines, online scientific databases such as Mendeley and PubMed were utilized. Additionally, resources from the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC), as well as websites of various professional medical societies, were consulted.

KEYWORDS

Human Papillomavirus, Vaccine, Prevention, Cervical Cancer, Condyloma Acuminata, Laryngeal Papillomatosis, Cutaneous Warts

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1. Introduction

Over 200 types of human papillomavirus (HPV) habe been identified, among which both low-risk and high-risk types are known to induce either benign or malignant lessions in the human body.

Table1. Genotypes of Human Papillomavirus [1]

Low-risk types of HPV	6, 11, 40, 42, 43, 44, 54, 61, 72, 82
High-risk types of HPV	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68

Low-risk HPV types are responsible for genital warts in both men an women, as well as for cutaneous warts. In contrast, high risk types are assosciated with the development of cancers in the oral cavity, pharynx and genital area, including cervical, vulvar, vaginal, penile and anal cancer. [1]

HPV infection is among the most common sexually transmitted infections. According to a 2010 meta-analysis comprising 194 studies and data from over one milion women, the highest prevalence of HPV was observed in sub-Saharan Africa (20.0%), Eastern Europe (21.4%) and Latin America (16.0%). Among the most frequently detected HPV types 16, 18, 31, 52 and 58 are routinely identified. [2]

According to 2022 WHO data, cervical cancer ranks fourth in incidence and third in mortality among women, with 99% of cases attributable to prior HPV infection. The highest incidence is reported in West and sub-Saharan Africa, as well as in countries such as Bolivia, Guyana and Papua New Guinea, where rates range between 24.6 and 95.5 per 100,000 people in the population. [3]

Cervical cancer mortality follows a similar geographic ditribution, ranging from 16.8 to 64.3 per 100,000 people in the population. [4]

HPV-related cancers and global incidence (2022 data):
- Cervical cancer: approximately 628,000 cases
- Oropharyngeal cancer: 39,794 cases
- Anal cancer: 54,306 cases
- Vulvar cancer: 14,674 cases
- Vaginal cancer: 14,679 cases
- Penile cancer: 19,227 cases. [5]

2. Pathogenesis of HPV Infection

HPV is a non-enveloped DNA virus, 50-60 nm in diameter, classified within the *Papillomaviridae* family. Its genome comprises early (E) and late (L) genes, each responsible for distinct functions during infection.

Table 2. Functions of the proteins

L1, L2	Capsid protein synthesis
E1	Functions as a helicase regulate viral genome replication
E2	Facilitates binding of E1 protein
E4	Interacts with keratins; involved in virion release, transmission and post-translation modifications
E5	A key oncoprotein implicated in HPV-induced carcinogenesis; supports angiogenesis
E6	Promotes p53 degradation via the ubiquitin-proteasome pathway, ihibiting apoptosis; enhances angiogenesis
E7	Disrupts the cell cycle, promoting cervical dysplasia, facilitating cellular invasion and inducing inflammation

The human papillomavirus exhibits the highesr tropism for keratinocytes, infecting exclusively the undifferentiated basal cells of the skin or mucosal epithelium – known as basal epithelial cells. Following endocytosis, the virus enters the host cel and is transported via vesicles to the endoplasmic reticulum and Golgi apparatus. It then undergoes a series of structual modifications and releases its viral genome near the perinuclear regione. In its episomal form, the viral DNA penetrates the nucleus through nuclear pores, initiating either active or latent replication. [6,7]

The exact mechanism determining why some individuals progress from asymptomatic HPV carriage to clinically apparent infection remain unclear. It is hypothesized that in immuncompromised individuals impaired cellular immune response result in HPV tolerance, preventing effective clearance of the virus. [8]

3. Vaccines

Currently bivalent, quadrivalent and nonavalent vaccines based on virus-like particles (VLPs) are approved for use on the market. The trade names of the bivalent vaccines include Cecolin, Cervarix and Walrinvax; the quadrivalent vaccine is marketed as Gardasil; the nonavalent vaccine as Gardasil-9. Each formulation targets specific HPV types. The latest-generation nonavalent vaccine contains nine genotypes: 6, 11, 16, 18, 31, 33, 45, 52 and 58. [9]

3.1. Safety

There have been isolated reports from individual studies suggesting a potential association between HPV vacciness and various conditions including Complex Regional Pain Syndrome (CRPS), Postural Orthostatic Tachycardia Syndrome (POTS), Primary Ovarian Insufficiency (POI), Venous Thrombosis, Guillain-Barré Syndrome and autoimmune diseases (e.g. celiac disease). In response to concerns about the safety of HPV vaccines, the World Health Organization (WHO) commissioned a review of serious adverse events which found no evidence that the vaccine increases the risk of any of the conditions. Additionally, the Global

Advisory Committee on Vaccine Safety (GACVS) has deemed the vaccine to be exceptionally safe, a conclusion supported by data collected after the administration of over 270 million doses. The benefits of vaccination substantially outweigh any potential risks.

No adverse effects on pregnancy, the fetus or the newborn have been observed, as confirmed by studies conducted in Denmark and the United States. [10]

3.2. Dosage

Table 3. Vaccines dosage

Age/Type of vaccine	Gardasil	Cervarix	Gardasil 9
9-14 years old	2-dose schedule in months: 0, 6 3-dose shcedule in months: 0, 2,	2-dose schedule in months: 0, 6-12 (In case when second dose is given earlier than after 5 months, then a third dose must be given)	2-dose schedule in months: 0, 6-12 3-dose schedule in months: 0, 2, 6
15 years and older	3-dose schedule in months: 0, 2, 6 (Each of the doses should be given within 1 year)	3-dose schedule in months: 0, 1, 6 (Second dose can be given between 1 and 2,5 months after the first dose and third dose between 5 and 12 months after the first dose)	3-dose schedule in months: 0, 2, 6 (Each of the doses should be given within 1 year)

The route of administration of the HPV-vaccines is intramuscular. [1]

3.3. Adverse effects

In clinical trials following vaccination, all HPV vaccines met safety criteria and demonstrated a comparable incidence of adverse post-vaccination reactions. Local reactions primarily included pain at the injection site (35-88%), pain severe enough to impair normal activity (6%), erythema (5-40%) and swelling (4-35%).

Systemic reactions were generally mild and self-limiting, including headache, dizziness, gastrointestinal symptoms (such as nausea, vomiting, abdominal pain), arthritis and myalgia.

Anaphylactic reactions occurred very rarely - approximately 1.7 cases per million does administrated – likely due to hypersensitivity to one of the vaccine components.

Fainting episodes were sporadically reported and are considered stress-related rather than a direct adverse effect of the vaccine. Preventive measures, such as having the patient seated and observing them for 15 minutes post-vaccination, are recommended. [10,12]

3.4. Efficacy

Numerous clinical trials and randomized controlled studies – including a 9-year prospective cohort study in Denmark, a 10-year prospective cohort study in Greece, a population-based cohort study in Sweden, a registry-based cohort study in Denmarks and a randomized clinical trial in Costa Rica – have been conducted across different regions of the world. These studies consistently confirm the preventive efficacy of the HPV vaccine and its long-term protective effects. [12,13,14,15,16]

4. Diseases

Depending on the genotype of the human papillomavirus (HPV) to which an individual is exposed, various clinical manifestations may develop. HPV is responsible for common cutaneous warts, which are classified into four types: verruca vulgaris (common warts), verruca plantaris (plantar warts), mosaic warts (resulting from coalescence of multiple plantar warts) and verruca plana (flat warts). These are benign lesions, although they exhibit a high tendency for recurrence. The likelihood of ocurrence increases with age, due to persistent viral replication. Cutaneous warts are typically more frequent in males and are most commonly observed in individuals with compromised immune function.

Warts that develop ont mucosal surfaces of the anogenital regios are referred to as condyloma acuminata (anogenital warts). These lesions typically arise at sites of microtrauma in HPV carriers and represent the most prevalent clinical manifestation of HPV infection worldwide. They are most commonly associated with low-risk genotypes 6 and 11. [7] The same genotypes of HPV are are also responsible for another condition – recurrent respiratory papillomatosis (RRP) – characterized by benign papillomatous growths within the respiratory tract. Although histologically benign, these lesions carry the potential for malignant transformation, particularly when the disseminate to the pulmonary system. RRP is classified into juvenile-onset and adult-onset forms. Juvenile-onset RRP, more commonly associated with HPV type 11, is typically diagnosed before the age of 12 and tends to follow a more aggressive clinical course, often necessitating tracheotomy. Transmission in such cases is primarily vertical, occuring during natural birth. In contrast, adult-onset RRP is more frequently caused by HPV type 6, usually diagnosed after puberty and is generally less aggressive. In adults, transmission most commonly occurs through orogenital contact.

In contrast, warts ocurring in the throat are diagnosed as laryngeal papillomatosis, which may undergo malignant transformation, particularly if the lesions spread into the lungs. [8]

The most serious HPV-related diseases include cancers of the oral cavity and pharynx, as well as malignancies of the genital tract. Cervical cuncer is currently the fourth most common malignancy among women worldwide. It is most frequently caused by HPV genotypes 16 and 18. An untreated HPV infection can progress to cancer, typically over a period of 15 to 20 years. In immunocompromised women (e.g. those infected with HIV), this progression may occur more rapidly – within approximately 5 to 10 years. Risk factors for the development of cervical cancer include: early age at first pregnancy, high number of childbirths (more than five deliveries), early onset of sexual activity, a high number of sexual partners, presence of other sexually transmitted diseases, immune competence, long-term use of hormonal contraception, cigarette smoking and the oncogennic potential of the HPV genotype involved. [17] Head and neck squamous cell carcinomas (HNSCC), originating from the mucosal epithelium of the oral cavity, pharynx and larynx are most commonly associated with tobacco smoking and/or excessive alcohol consumption. However, there is a subset of HPV-positive HNSCCs, whose development is primarily attributed to infection with HPV genotype 16. [18] The increasing incidence of HNSCC is associated with changes in sexual practices. Risk factors include high number of sexual partners, early initiation of sexual activity, oral sex, direct contact between genital infection and oral infection (of HPV), open-mouth kissing and lack of condom use. [19]

5. Strategies

5.1. New Strategies

The Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem was proposed and published by the World Health Organization (WHO) in 2020. The straetgy is centered around a „triple intervention” approach:

1. HPV vaccination
2. Cervical cancer screening
3. Treatment

The WHO aims to implement these measures by 2030 in order to reach a target incidence of 4 cases per 100,000 woman-years by 2120. The key interim targets to be acheived by 2030 are known as the 90-70-90 goals, where:

- 90% of girls are fully vaccinated against HPV by age 15
- 70% of women are screened with a high-performance test at ages 35 and 45
- 90% of women diagnosed with cervical disease receive appropriate treatment and care.

As of June 2025, 147 countries have integrated HPV vaccination into their national immunization programs. Among them, 86 countries Focus on vaccinating only girls/women, while the reamining 81 countries include both sexes in their vaccination strategies. [20]

5.2. Vaccines against HPV

In April 2022, the World Health Organization (WHO) issued updated immunization recommendations, including guidance on HPV vaccination. The Strategic Advisory Groups of Experts (SAGE) recommends administering the HPV vaccine to young girls and boys aged 9 to 14 years, with the aim of providing immunization as early as possible and prior to the onset sxual activity. Depending on the vaccine type, the appropriate dosing schedule- based on the manufacurer.s guidelines – should be followed. Typically, a 2-dose

schedule is recommended for girls aged 9-14, while 3-dose schedule is advised for those 15 years and older and for immuncompromised individuals (including those living with HIV), to be completed within one year.

However, numerous randomized climical trials have demomnstarted that. A single-dose regimen offers comparable efficacy, effectivenes and duration of protection in immunocompetent females under the age of 18, relative to the standard two-dose schedule. Although the one-dose regimen is not currently incluuded in vaccine manufacturer's guidelines, it is endorsed by SAGE (Strategic Advisory Group of Experts) due to its simplified immplementation, lower cost and high effectivenes.

HPV vacciantion is a form of primary preventin, but it does not eliminate the risk of infection or cancer entirely, as current vaccines do not cover all HPV genotypes. [10, 21]

5.2.1. Recommendations for Poland

Recommendations for poland (March 2022) regarding prophylaptic HPV vaccination were developed in cooperation with the Polish Society of Gynecologists and Obstetricians, the Polish Pediatric Society, the Polish Society of Family Medicine, the Polish Society of Gynecologic Oncology, the Polish Vaccinology Society and the Polish Society of Colposcopy and Cervical Pathophysiology.

The guidelines identify firls aged 11-13 years at the priority group of vaccination. The next steps should Focus on vaccinating girls over the age of 13 as well as boys aged 11-13 years. In older groups vaccination may also be beneficial – for indtance, in women previously diagnosed and treated for cervical precancerous lesions, the HPV vaccine may reduce the risk of recurrence.

Under the National Immunization Program, the selection of the vaccine should be based on efficacy, the genotype composition most revelant to the epidemiology of HPV in Poland and cost-effectiveness.

The qualification proces for HPV vaccination is the same as for other vaccines and the contraindications are no different. Pregnancy testing prior to vaccination is not required. Co-administration of HPV vaccines with vacinnes against pertussis, tetanus, diphteheria, inactivated polio, hepatitis A and B, meningococcal disease or COVID-19 is considered safe. In such cases, an injection site distance of at least 2.5 cm should be maintained or the vaccines should be administered in opposite arms.

It is important to consider the risk of syncope, which can occur due to stress related to vaccination. Proper patient preparation is essential to reduce the risk – it is advised that the patient sits or lied down during injection and offerring a drink or snack may also help. Post-vacination observation for at least 30 minutes is recommended to monitor for anaphylaxis or other acute adverse events.

The final point of the recommendations emphasizes the importance of education about vaccination among both patients and healthcare professionals. Suggested measures include public campaigns, conferences and educational initiatives within clinic and hospitals. [1]

Poland introduced HPV vaccination into its National Immunization Program in 2023 and the success of implementation largely depends on the active involvement of medical institutions. [22]

5.3. Recommendations for the Western Pacific Region

In response to the growing burden of cervical cancer, Member States, in collaboration with the World Health Organization (WHO) and partners in the Western Pacific Region, have developed strategic approaches aimed at eliminating cervical cancer from the region. The three core pillars of this strategy are:

1. Strengthening health services and health system
2. Sustainble financing mechanisms
3. Health education, health promotion, improved communication and community engagement

Significant disparities across the region pose a major challenge to implementing a unified prevention and treatment action plan. In many countries, health system remain underdeveloped and in resource-limited settings, there is often a lack of funding to implement even the basic components of cervical cancer prevention and care.

The recommendations for the Western Pacific Region highlight the updated 2022 WHO guidance on the use of a one- or two-dose HPV vaccination schedule for girls 9-14 years, as well as for older adolescent girls and women aged 15-20 who have not been previously vaccinated. Currently, countries in the region are at different stages of introducing or integrating HPV vaccination into their national immunization programmes.

The recommandations note that the primary barier to implementation is the cost of introducing HPV vaccines, In many countries, there are insufficient public funds to provide vaccination free of charge and individuals must bear the cost themselves, For low-income countries, suport from the global Alliance for Vaccines and Immunization (Gavi) may offer a solution, as the organization co-finances the procurement of vaccines in selceted eligible countries. [23]

5.4. Recommendations for the African Region

The strategic plan for African countries includes the integration of a one-dose HPV vaccination schedule, as well as the incorporation of cervical cancer screening and treatment into essential health system service packages. Similar to other regions, particular emphasis is places on the importance of education regarding HPV vaccination, in order to eliminate misconceptions among patients and increase awareness of HPV-related diseases.

The plan also outlines the need to expand access to high-quality, affordable screening tests. The African Region aims to utilize existing multipurpose molecular testing platforms to improve the availability of HPV ttesting. In addition, it seeks to enhance access to surgical treatment, chemotherapy and radiotherapy sevices.

The strategy includes the establishment of robust monitoring and evaluation mechanisms to assess the effectiveness of cervical cancer elimination programmes, as well as the strengthening of national research infrastructure to advance scientific knowledge in the fields of cervical cancer prevention and treatment.

One of the most significant challenges facing the African Region is securing sustainable funding for these initiatives. However, several African countries benefit form support provided by the global Alliance for Vaccines and Immunization (Gavi), which has facilitated the implementation of these objectives. [24]

5.5. Recommendations for the European Region

As o 2025, 47 out of 53 countries in the WHO European Region have incorporated the HPV vaccine into their national immnization progrsmmes, with 39 of tchem offering the vaccine to both girls and boys. Currently, only 15 countries have achieved a vaccination coverage rate of 70% or higher. The WHO has outlined several steps that should be taken to improve exisiting outcomes.

It has emphasized the importance of evidence-based decision-making, particularly in countries that have not yet implemented HPV vaccination in their national schedules. In countries where the vaccination coverage remains suboptimal, catch-up vaccination startegies should be developed to ensure access for individuals outside the primary target group, including those from hard-to-reach areas.

Moreover, it is essential to strengthen the competencies of healthcare professionals in communicating with adolescents and their parents regarding the safety and importance of HPV vaccination. [25]

5.6. Recommendations for the Region of the Americas

The Pan American Health Organization (PAHO) recommends that one or two doses of the HPV vaccine be administered to girls betweeen the ages of 9 and 14. In immunocompromised individuals (e.g. patients living with HIV), two doses should be given at an interval of six months, or -if feasible- a three-dose schedule should be used.

Member States are encouraged to strengthen school-based immunization programmes, as this significantly increases vaccine coverage rates. To ensure the most effective population-level protection and to accelerate elimination of cervical cancer, HPV vaccination should also be introduced for girls and women over 15 years of age, as well as for boys and men.

A regional health protection fund should guarantee access to HPV vaccines at affordable prices throughout the Americas. [26]

5.7. Recommendations for Eastern Mediterranean Region

The Eastern Mediterranean Region has developed five strategic directions aimed at eliminating cervical cancer.

The first area focuses on primary prevention-countries in the region must be prioritze accelerating the implementation of Human Paillomavirus vaccination programs in order to improve vaccination coverage rates. The second pillar emphasizes early detection through the expansion of cervical cancer screening programs and the treatment of precancerous lesions.

The third component involves comprehensive treatment and care, with an emphasis on ensuring continuity of services, including improved access to early diagnosis, therapeutic interventions, rehabilitation and palliative care.

The fourth and fifth strategic directions are supportive in nature-addressing the strengthening of health systems and the enhancement of communication, advocacy and community engagement. These complementary efforts aim to promote service integration and improve overall health outcomes across the region. [27]

6. Screening

6.1. Molecular Diagnostics

Molecular diagnostics for the detection of HPV have been recommended as the primary screening test for cervical cancer in the guidelines of the American Society of Clinical Oncology (ASCO) published in 2021, as well as in the WHO recommendations issued in 2021. The recommended method is primary high-risk HPV (HR-HPV) testing, which involves genotyping for HPV types 16 and 18 in the initial phase of screening, followed by cytology for those who test positive for HR-HPV. These recommendations apply to women aged over 25 years, with the suggestion to continue testing until at least the age of 74 (up to the age of 70, according to the ASCOs recommendations). [28, 29]

6.2. Cytology

Cytology is a screening test capable of detecting early neoplastic changes within cervix. The procedurę involves collecting a sample from the ectocervix and endocervical canal using a cytobrush, which is then either smeared onto a glass slide and fixed with 96% ethanol (in the case of conventional cytology) or placed in a vial containing a liquid fixative (for liquid-based cytology – LBC). [30]

Recent studies have demonstrated that HPV DNA-based tests offer higher sensitivity, particularly in detecting CIN3 lesions and more advanced cervical intraepithelial neoplasia. In 2021, the World Health Organizations (WHO) recommended the broader implementation of HPV DNA testing to enhance the detection of HPV-associated precancerous or cancerous lesions in women. [31]

However, it should be noted that, compared to cytology, HPV DNA testing more frequently leads to the detection of CIN2 lesions in younger women, which are known to have higher likelihood of spontaneous regression. [32]

6.3. WHO Recommendations on Diagnostic Testing

According to the World Health Organization (WHO), women should undergo cervical cancer screening every 5 to 10 years, starting at the age of 30. In contrast, women who test positive for HIV should begin screeening at the age of 25 and repeat it every 3 years. Precancerous lesions, as well as early-stage cervical cancer, are frequently asymptomatic and painless; therefore, regular screening is crucial for early detection.

Currently, liquid-based cytology is commonly used, allowing for the identification of infections with specific HPV genotypes. In cases where HPV infection is confirmed, colposcopy should be performer accompanied by targeted biopsies and endocervical curettage. [21]

6.4. Recommendations of the Polish Society of Gynecologists and Obstetricians

In June 2022, the Polish Society of Gynecologists and Obstetricians published guideline for primary cervical cancer screening, introducing five diagnostic algorithms aimed at facilitating the interpretation and practical application of screening models. The proposed system enables gynecologists to initiate preliminary screening and refer more advanced cases to colposcopy specialists.

The position statement recommends initiating screening at the age of 25, with no upper age limit, though it advises continuing testing at least until the age of 74. The preferred screening method is high-risk HPV (HR-HPV) testing with genotyping for typed 16 an 18. As alternative methods, co-testing (HR-HPV testing and cytology) or cytology alone (conventional or liquid-based) may be used. In cases of equivocal cytological findings (when it is unclear whether the lesion corresponds to LSIL or HSIL), the use of p16/Ki-67 dual-satin testing is recommended. Increased expression of p16 suggests a high-grade squamos intraepithelial lesion (HSIL), in which case colposcopy and biopsy are indicated.

Recommended screening intervals for patients with HR-HPV-negative results and NILM (Negative for Intraepithelial Lesion or Malignancy) cytology are every 3 to 5 years. For HR-HPV-negative cases with abnormal cytology results, such as ASC-US (Atypical Squamos Cells of Undetermined Significance) or LSIL (Low-grade Squamos Intraepithelial Lesion), annual follow-up testing is advised.

When cytology is used as the primary screening test, follow-up intervals should range from 1 to 3 years depending on the results. [33]

As of Huly 1, 2025, the National ealth Fund has introduced free HPV-HR testing with genotyping triage using liquid-based cytology (LBC). Cervical samples will be collected from patients for primary HPV-HR molecular screening. In the event of a positive result, cytological examination (liquid-based) will be performed on the previously collected sample. [34]

7. Treatment

7.1. Management of Anogenital Warts

Anogenital warts (condyloma acuminata) are most often diagnosed during physical examination; however, in some cases, a biopsy and histopathological assessment may be required. These lesions may regress spontaneously or proliferate extensively in number and size. Management largely depends on patients, as well as the locaion and size of the lesions.

For at-home treatment, the following topical agents may be used: imiquimod cream (3.75% or 5%), podophyllotoxin gel (0.5%) or sinecatechin ointment (15%). Physician-administered therapies include surgical excision (using scissors, electrosurgery, curettage or CO_2 laser ablation), cryotherapy or chemical ablation using 80-90% trichloroacetic acid or dichloroacetic acid.

Alternative therapies include apllication of podophyllin resin, topical cidofovir, interferon therapy (administered locally) and photodynamic therapy. However, these options should be discussed with the patient, as current evidence supporting their efficacy is limited and potential risks must be considered. [35]

7.2. Management of Cutaneous Warts

The treatment of cutaneous warts depends on their type and localization. For common warts, cryotherapy is considered the first-line treatment when well tolerated by patient. However, for individuals preferring home-based therapy, topical preparations cointaining salicylic acid – often in combination with lactic acid – may be used. Thermotherapy is also an available option for wart removal.

Plantar warts may be treated with intralesional bleomycin injections, laser therapy, cryotherapy or thermotherapy in the case of primary lesions. In recurrent cases, CO_2 laser ablation combined with intralesional injection of recombinant human interleukin-2 is recommended.

Flat warts, especially when present in multiple lesions, can be managed with CO_2 laser therapy or intralesional injections of bleomycin or *Candida albicans* antigen. In cases of intolerance or contraindications to the aforementioned methods, photodynamic therapy may be considered. [36]

7.3. Treatment of Laryngeal Papillomatosis

Currently, due to the lack of targeted therapies, surgical excision remains the gold standard. In cases where the disease exhibits an agressive course, complete eradication often requires multiple surgical intervention. [8]

7.4. Treatment of Cervical Cancer

Cervical cancer treatment is based on the clinical stage of the disease.

In early-stage cervical cancer (i.e. stages IA-IB1), with tumor size ≤ 2 cm, the recommended treatment is surgical. The procedure of choice for stage IA1 is laser or electrosurgical loop excision (conization) with adequate margins; for stage IA2, simple hysterectomy is preferred. Sentinel lymph node biopsy should be performer for staging. For women who have completed childbearing and present with IA1 or IA2 lesions, simple hysterectomy i salso recommended.

For stage IB1 tumors, conization and sentinel lymph node assessment should be performed. If lymph node involvement is confirmed histologically, chemioradiation is the preferred treatment. As an alternative to surgery, radiotherapy may be considered in stage IB1 depending on the risk-benefit assessment especially in cases where reoperation may be required.

In locally advanced stages (i.e. IB2-IIA1) without lymph node involvement and with clear surgical margins and/or no residual tumor, concurrent chemoradiotherapy is recommended. Radical surgery (including removal of the parametrium, upper vagina and pelvic lymph node) may be considered when adjuvant chemoradiotherapy is not expected postoperatively. If imaging shows residual tumor, suspicious lymph nodes or positive surgical margins at these stages, chemoradiotherapy with or without brachytherapy is the treatment of choice. Para-aortic lymph node dissection should be performed for diagnostic purposes even when these nodes appear uninvolved, particularly if pelvic nodes are positive.

In advanced, disseminated, inoperable cases (i.e. IB3-IVA), imaging (PET-CT) and nodal staging should be performed. If lymph node metastases are present, radical concurrent chemoradiotherapy is indicated. If lymph nodes are not involved, treatment should be individualized based on risk factors such as tumor size, histopathological findings and patient age. Surgical treatment with intraoperative lymph node assessment may be considered. If nodes are negative, a radical hysterectomy can be performed; if nodes are positive, definitve chemoradiotherapy with image-guided brachytherapy is recommended. [38]

Table 4. Staging of Cervical Carcinoma [37]

<table>
<tr><th>Stage</th><th colspan="3">Stage Description</th></tr>
<tr><td rowspan="5">I</td><td rowspan="5">Stromal invasion</td><td colspan="2">IA – Stromal invasion < 3 mm</td></tr>
<tr><td rowspan="4">IB - Stromal invasion ≥ 3 mm to < 5 mm</td><td>IB1 – Stromal invasion ≥ 5 mm or positive surgical margins after conization; tumor size < 2 cm</td></tr>
<tr><td>IB2 – Tumor size ≥ 2 to < 4 cm</td></tr>
<tr><td>IB3 – Tumor size ≥ 4 cm</td></tr>
<tr><td rowspan="3">II</td><td rowspan="3">Tumor extends beyond the uterus but does not reach the lower third of the vagina or the pelvic wall</td><td rowspan="2">IIA – No parametrial invasion</td><td>IIA1 – Tumor size < 4 cm</td></tr>
<tr><td>IIA2 – Tumor size ≥ 4 cm</td></tr>
<tr><td colspan="2">IIB – Parametrial invasion not reaching the pelvic wall</td></tr>
<tr><td rowspan="4">III</td><td rowspan="4">Tumor involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney and/or has pelvic or para-aortic lymph node metastases</td><td colspan="2">IIIA – Tumor involves the lower third of the vagina, not the pelvic wall</td></tr>
<tr><td colspan="2">IIIB – Tumor extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney</td></tr>
<tr><td rowspan="2">IIIC – Lymph note metastases</td><td>IIIC1 – Involvement of pelvic lymph nodes (e.g. obturator, iliac)</td></tr>
<tr><td>IIIC2 – Involvement of para-aortic lymph nodes</td></tr>
<tr><td rowspan="2">IV</td><td rowspan="2">Tumor extends beyond the true pelvis and/or invades the mucosa of the bladder or rectum</td><td colspan="2">IVA – Tumor invades the bladder or rectal mucosa</td></tr>
<tr><td colspan="2">IVB – Distant metastases present</td></tr>
</table>

7.5. Treatment of HPV-Related Oropharyngeal Cancers

HPV-related orophraryngeal cancer exhibit increased sensitivity to chemotherapy and radiotherapy, which often makes these modalities the treatment of choice. This translates into a more favorable prognosis and higher overall survival rates. Lesions identified at an early stage (i.e. T1-T2, N0-N1) can be managed surgically, either via transoral approach or through open excision combined with selective neck dissection. Definitive rdiotherapy serves as an alternative treatment modality.[39]

Management of intermediate and advanced stages centers on radiochemotherapy using standardized protocols. A common approach involves dose de-escalation of radiation therapy by 15-20% while maintaining concurrent chemotherapy. Clinical outcomes show no evidence of disease progression in 92% of patients at two years post-treatment, along with lower incidence of adverse effects.[40]

A 2019 study presented a novel treatment strategy that combined the administration of an HPV-16 vaccine in a three-dose schedule (on days 1, 22 and 50) with nivolumab (a PD-1 inhibitor), given biweekly starting on a day 8 and continuing for up to one year. The findings demonstrated good tolerability and safety, with a one-year overall rate of 70%, representing an improvement compared to nivolumab monotherapy. [41]

In randomized controlled trial involving patients with HPV-positive, low-oncogenic-risk oropharyngeal and oral cavity cancers, standard treatment with cisplatin and radiotherapy was compared to a regimen using cetuximab. These results showed no significant difference in tratment-related toxicity; however, cisplatin demonstrated superiority in terms of 2-year overall survival and 2-year disease recurrence risk. [42]

Conclusions

The Human Papillomavirus (HPV) is a globally widespread pathogen, which is why education on modes of transmission, prevention, diagnostics and treatment should begin as early as school age. While there is no targeted therapy against HPV infection, effective preventive measures - namely vaccination – are available.

Despite the lack of evidence linking HPV vaccines to the development of various previously mentioned diseases, the Global Advisory Committee on Vacine Safety (GACVS) reports that unfounded allegations and fears persist, undermining public trust in vaccines and contributing to reduced vaccination coverage in certain countries, The anti-vaccine movement ha salso significantly affected HPV immunization rates both in Poland and wordlwide. This highlights the critical importance of educational initiatives introduced in schools (targeting both children and parents), as well as training medical personel in effective patient communication to address and dispel vaccine-realted concerns.

Lack of awareness about HPV-related risks and fear of potential side effects are only part of the barriers to implementing the WHO strategy. Due to financal constraints, many countries are unable to independently fund HPV prevention programs. In this context, suport from international organizations such as Gavi plays a vital role. However, prevention efforts must be complemented by comprehensive, specialized healthcare systems that ensure access to appropriate diagnostics and treatment for HPV-related diseases.

The successful implementation of the WHO's global strategy for HPV elimination by 2120 depends on the commitment of all member states to adopt and integrate the recommended interventions within their national healthcare systems.

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