

HPV – AN INTEGRATED PERSPECTIVE: EMOTIONAL, ECONOMIC, AND THERAPEUTIC DIMENSIONS

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Summary

Human papillomavirus (HPV) infection is one of the most widespread sexually transmitted infections, affecting the majority of sexually active adults at some point. Transmission occurs mainly through sexual contact, but non-sexual or perinatal transmission can also occur. HPV infection can be localized based on the tissue tropism and oncogenic potential of the strain, affecting either the skin or the oropharyngeal or anogenital mucous membranes.

The diagnosis of cutaneous HPV infection is largely clinical, and treatment varies depending on the type and severity of the lesions. There is no treatment that guarantees complete eradication of the virus, and recurrences are common. Prevention is the key to success, both economically and medically. HPV vaccination is the most effective prevention method, being free in Romania for individuals between the ages of 11 and 26, and costing approximately 1800 RON (for three doses) for those over 26. Therapeutic methods include cryotherapy, chemical treatments (trichloroacetic acid, podophyllin), topical treatments (imiquimod, sinecatechins), surgical excision, and CO₂ laser therapy, with estimated costs exceeding 1000 RON in most cases, and the risk of requiring multiple treatment sessions and experiencing recurrences. In the case of anogenital or oropharyngeal infections, the economic burden is significantly higher – tens of thousands of RON – due to the need for specialist consultations, costly diagnostic tests, treatments, and invasive procedures, with long-term recovery both physically and financially.

In addition to physical and financial implications, HPV infection has a significant psycho-emotional impact. Women diagnosed with HPV often report anxiety, depression, and impaired sexual life. The stigma of the disease, fear of rejection, and feelings of guilt can lead to reduced quality of life and strained personal relationships. Studies show that proper education, psychological support, and access to treatment can reduce emotional distress and improve patients' overall well-being.

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General informations

HPV (Human Papillomavirus), part of the *Papillomavirus* genus and the *Papovaviridae* family, is a virus with a diameter of 50–55 nm, containing double-stranded DNA and exhibiting tropism for human squamous or metaplastic cells [1,2].

HPV infection is transmitted in most cases through direct sexual contact, via disruptions in the continuity of the skin or genital mucosa. Non-

sexual transmission, as well as perinatal transmission from mother to fetus, is also possible. HPV gains access to the basal membrane and basal cell layer through microabrasions in the genital epithelium that occur during sexual intercourse. Once infected, these cells become a viral reservoir [3].

HPV strains can be classified based on their oncogenic potential into low-risk (LR) types (e.g., 6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81, etc.) and

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high-risk (HR) types, particularly 16 and 18. Exophytic lesions are caused in 90% of cases by types 6 and 11. Genital warts represent the most common sexually transmitted viral infection, and it is believed that the majority of sexually active adults will acquire it at some point. However, in 90% of cases, the infection is asymptomatic and resolves spontaneously [5].

The most frequent high-risk oncogenic HPV types (16, 18, 31, 33, and 35) are associated with intraepithelial neoplasia (e.g., squamous cell carcinoma in situ, Bowenoid papulosis, erythroplasia of Queyrat, Bowen's disease of the genitals) and with cancers of the cervix, vulva, vagina, penis, anus, and oropharynx [6,7].

Flat genital warts are predominantly located on the cervix and foreskin. They can be considered precursors of intraepithelial neoplasia and are frequently associated with HPV types 16 and 18. Exophytic genital warts are polypoid formations, skin-colored, pink, or gray, grouped together, with a cauliflower-like surface. They can be painful, friable, itchy, and may significantly impact the patient's quality of life. These lesions do not carry a risk of malignant transformation and disappear spontaneously in about 20% of cases within four months [9].

In the case of genital warts, clinical observation is often sufficient for diagnosis. A biopsy is required when: the clinical appearance is not typical; the lesions do not respond to treatment or worsen; the patient is immunocompromised or the genital warts are pigmented, hard, or ulcerated [8,10].

Prophylaxis is primarily achieved by avoiding contact with infectious lesions. Condoms provide protection, but not 100%, as they do not cover all infected areas. Condom use reduces the risk of HPV infection in men by about half. Pap smear screening is essential in the prevention of cervical cancer and is recommended starting at the age of 21, regardless of sexual history. The recommended interval between screenings is every 2 years for women aged 21 to 29, and every 3 years for women over 29 if they have had three consecutive negative Pap tests [3].

HPV vaccination is a safe and effective method of preventing genital warts, and more importantly, cervical, vaginal, vulvar, and anal intraepithelial neoplasia, as well as cervical

cancer. There are three types of vaccines: Bivalent (Cervarix – protects against types 16 and 18), Quadrivalent (Gardasil – protects against types 6, 11, 16, and 18), Nonavalent (Gardasil 9). The last one protects against the most frequently implicated types (6, 11, 16, 18, 31, 33, 45, 52, and 58). In countries where large-scale HPV vaccination has been implemented, a significant decrease in the incidence of HPV-related diseases has been observed. Vaccination is permitted for breastfeeding women but not recommended during pregnancy. Moreover, vaccination is encouraged even after previous HPV exposure, as it protects against future infections and helps boost immunity [3]. In Romania, HPV vaccination is free of charge for girls and boys aged 11 to 26.

Treatment

The indications for treating genital lesions caused by HPV include: symptomatic condylomas that cause physical or psychological discomfort; high-grade neoplasia and invasive cancer [3]. There is no evidence that current therapeutic options can eradicate the infection or alter its natural progression. Unrealistic attempts to eliminate HPV infection, which is typically self-limiting, may cause unnecessary physical harm to the lower genital tract. No therapeutic method has major advantages or guarantees 100% healing; personalized treatment is necessary based on the lesion's characteristics and the patient's preferences [4].

The social costs of treating HPV infection are complex and extend beyond basic medical expenses. These include direct, indirect, psychosocial, and public healthcare system costs. Direct costs include vaccination and medical expenses related to specialist consultations, screening tests and lesion treatment. Indirect costs cover productivity loss due to medical leave or work incapacity. Psychosocial costs involve the stress of long-term monitoring of HPV infection and its progression risk, stigma and anxiety linked to having a sexually transmitted disease, and the emotional impact on quality of life and intimate relationships. Public healthcare system costs consist of screening programs, public awareness campaigns, HPV vaccination (fully subsidized only for men and women under 26), and therapy [3].

In addition to various treatment methods for HPV infection, there are also adjuvant products that support the immune system in fighting the virus. Among these are Hupavir and Isoprinosine. Hupavir is a dietary supplement used as an adjuvant in HPV infections, particularly genital or cervical infections. However, it is not a true antiviral medication. The adjuvant indications for Hupavir include: persistent HPV infections (that are not spontaneously cleared after 12–24 months), mild cervical lesions, and use as part of a combined protocol with Isoprinosine, HPV vaccination, and/or local treatments. In most cases, the recommended dosage is 1 sachet per day, for 3–6 months. The benefits of Hupavir include good tolerance, immune system support, acceleration of viral clearance, and promotion of spontaneous lesion regression [11,12].

Isoprinosine contains the active substance inosine acedoben dimepranol and is used for the treatment of cell-mediated immune suppression associated with viral infections. The indications for Isoprinosine in HPV infection include: genital warts – external lesions (excluding perianal or meatal locations), either as monotherapy or as an adjuvant to conventional topical or surgical procedures; persistent HPV infections involving cutaneous or mucosal areas, vulvovaginal sub-clinical infections, or endocervical lesions. The aim of treatment is likewise to support the immune system in eliminating the virus. The usual dose for adults and elderly patients is 6–8 tablets per day, divided into 3–4 doses, administered for 14 days per month, over a period of 1–3 months [13].

Therapeutic methods include cryotherapy; trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80–90%; podophyllin 10–25%; electrocautery; surgical excision; CO₂ laser; podophylotoxin 0.5%; imiquimod 5%; and sinecatechins. Alternative options may include interferons, 5-fluorouracil 5%, or photodynamic therapy (Table 1) (Figure 1) [3,4,5].

Psycho-emotional impact

Human Papillomavirus (HPV) infection, particularly with high-risk oncogenic types, is increasingly associated with significant psychological consequences for affected women.

Existing studies consistently show that HPV infection negatively impacts psychological well-being, manifesting in heightened levels of anxiety, depression, and disturbances in sexual life and personal identity [14].

A quantitative study using standardized assessment tools found that HPV-positive women scored significantly lower across all domains of the Female Sexual Function Index (FSFI) and reported higher levels of depression, anxiety, and hopelessness compared to the control group. These results suggest that HPV infection is associated with reduced sexual functioning and negative psychological effects. Strengths of the study included the use of validated instruments and a demographically diverse sample. However, limitations included its cross-sectional design and recruitment from a single medical center, which restricts causal interpretation and generalization of the results. The study did not account for HPV vaccination status or the severity of infection, both of which may influence psychological outcomes [15].

Other evidence suggests that the psychological impact of HPV infection evolves with disease progression. In asymptomatic cases, individuals may remain unaware of the infection, experiencing minimal psychological distress. However, an HPV diagnosis during cervical screening – even without cytological abnormalities – can cause confusion and anxiety. The psychological response depends on the patient's understanding of the virus and the extent to which an STI diagnosis aligns with her sexual history and identity. In more advanced stages, when precancerous lesions or cancer are present, psychological stress intensifies, particularly fears related to cancer. The stigma associated with sexually transmitted infections can exacerbate this burden [16].

Further studies show that HPV-positive women experience greater psychosocial impact, sexual dysfunction, and higher levels of negative affect. Factors such as younger age and emotional vulnerability (high negative affect and low positive affect) are significant predictors of psychological distress. Social stigma surrounding HPV transmission contributes to feelings of shame, fear of disclosure, and concerns about intimate relationships [17].

Table I. Treatment methods for genital warts

<i>Therapeutic methods</i>	<i>Application</i>
Hupavir	1 sachet /day, in 200ml water
Isoprinosine	6-8 tablets divided into 3-4 doses per day, 14 days/month, 1-3 months
Podophyllotoxin solution 0,5% - Condylox	Apply with a cotton swab directly to the wart twice daily for 3 consecutive days, followed by a 4-day break. The cycle may be repeated up to 4 times. The total treated area should not exceed 10 cm ² , and the amount of product should be under 0.5 ml per day.
Imiquimod cremă 5% - Aldara	It induces the secretion of multiple cytokines by macrophages, with interferon- γ being the most important, stimulating a cell-mediated immune response against HPV, leading to the elimination of genital warts. It is applied by the patient once a day (at bedtime) and removed after a maximum of 10 hours, 3 times per week, for up to 16 weeks. It should not be applied on an area larger than 60 cm ² . Adverse reactions include itching, edema, erythema, and burning sensation, and it is contraindicated during pregnancy.
Sinecatechins oitment 15% - Veregen	Apply three times per day, using up to 0.5 ml per lesion, for a maximum of 16 weeks. It does not need to be washed off. Sexual contact should be avoided during treatment.
Cryotherapy with liquiud nitrogen	Destroys genital warts through thermally induced cytolysis. Applications are repeated every 1-2 weeks. Can be used during pregnancy. Therapeutic efficacy: 50-100%.
Podophyllin 10-25%	Apply a small amount directly on the wart and allow it to dry. The area must be washed a few hours later to reduce the risk of local reactions such as erythema, edema, itching, blistering. Systemic toxicity may occur due to absorption. Therefore, no more than 0.5 ml should be applied in one session, and only on areas smaller than 10 cm ² . It is contraindicated during pregnancy and in cases of anorectal warts. If no regression is observed after a maximum of 4 applications (once per week), a different treatment is recommended. Therapeutic success rate: 10-20%.
Trichloroacetic acid or Bichloroacetic acid 80-90%	Caustic agents that destroy genital warts through chemical protein coagulation. A small amount is applied directly to the lesion and left to dry until a frost-like appearance is achieved. Applications can be repeated weekly. Can be used during pregnancy. Not effective for vaginal or cervical warts and may damage surrounding healthy tissue if applied incorrectly.
CO2 Laser	Used for large lesions, intraurethral growths, or therapy-resistant cases.
Invasive excision methods	Recommended for large, multiple, or nonresponsive lesions. Surgical excision, curettage or electrocautery (Figure 1). Surgical excision may involve additional costs for anesthesia, consultation, lab tests, or postoperative care. More complex treatments may require multiple sessions.



*Figure 1: Treatment of genital HPV infection by electrocautery:
A. First presentation of the patient in the clinic and B. Post-procedural appearance.*

A diagnosis of genital warts often brings feelings of shame and embarrassment, with many patients blaming themselves for acquiring the condition. This stigma can be overwhelming and significantly damage self-image. It is important to remember that HPV infection is extremely common and the presence of genital warts does not reflect a person's character or worth [17].

Genital warts can lead to anxiety and depression. Concerns about how others perceive the patient, fear of rejection, and worry about transmitting the virus to partners can result in significant psycho-emotional distress. This anxi-

ety affects interpersonal relationships, work, and daily activities, leading to a reduced quality of life. While wart treatments do not cure HPV, they can help manage symptoms and improve the quality of life for affected individuals [18].

These findings highlight the complex psychological burden of HPV infection and emphasize the need for integrated interventions that include psychological support and proper education to reduce distress, fight stigma, and enhance the overall well-being of women diagnosed with HPV.

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Conflict of interest
NONE DECLARED

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