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Anorectal Manifestations of Sexually Transmitted Diseases

Human Papillomavirus and Squamous Cell Carcinoma of the Anus.

A Major Nuisance and Growing Menace.

PART II

At any given time in the United States, twenty million men and women have an active Human papillomavirus (HPV) infection. Five million new cases are diagnosed each year. These represent one third of all cases of newly diagnosed sexually transmitted infections. In addition to the morbidity of the disease itself, HPV is strongly associated with the development of squamous cell carcinoma of the anus. Hence, this ubiquitous virus has taken on a more menacing significance than simply that of an inconvenient sexually transmitted disease.

Human papillomavirus is a small double-stranded DNA virus with a diameter of 55 nm. It is encased in a protein capsid with the viral genome existing in a circular or epitomal configuration. An intact capsid is necessary for HPV to be infectious. The viral genome is divided into 3 regions. the Upstream Regulatory Region (URR), the Early Region (E) and the Late Region (L). Each region

is responsible for a part of the transcription, replication or capsid production process.

Many people have a genital HPV infection without exhibiting any signs or symptoms. Even without signs or symptoms however, the disease can be transmitted sexually and complications of the infection may become manifest.

A MAJOR NUISANCE

The most common clinical manifestation of HPV is that of genital warts. Sometimes called condyloma accuminata or venereal warts, these lesions are the most easily recognized sign of a genital HPV infection. Human papillomavirus types 1, 2, and 4 together comprise the major cause of cutaneous papillomas in the general population.

Genital warts are soft, moist, or flesh colored and appear in the genital area within weeks or months after infection. They sometimes appear in clusters that resemble cauliflower-like bumps, and can be either raised or flat, small or large. Genital warts may be found in women on the vulva and cervix, inside

“Prevention of disease transmission is the goal in any illness... Many people have a genital HPV infection without exhibiting any signs or symptoms.”

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and surrounding the vagina, or around the anus. In men, genital warts may appear on the scrotum or penis or in and around the anus. There are cases where genital warts have been found on the thigh and groin.

Oftentimes, patients are unable to relate the appearance of genital warts with any specific activity. However, genital warts are very contagious and may be spread during oral, vaginal, or anal sex with an infected partner. They may be transmitted by skin-to-skin contact during sexual activity.

About two-thirds of people who have sexual contact with a partner with genital warts will develop warts, usually within 3 months of contact.

The diagnosis of warts is easily made by visual inspection. Topically applied disclosing agents such as acetic acid (vinegar) will sometimes show otherwise invisible lesions.

There are many forms of treatment for anal warts. These include chemical methods such as 20 percent podophyllin antimitotic solution, Trichloroacetic acid (TCA), 0.5 percent podofilox solution, and 5 percent imiquimod cream (Aldara®). Common side effects of treatment include burning, redness and itching. These medications should be utilized only by physicians trained in their use. Podophyllin, podofilox and 5-FU should not be used during pregnancy.

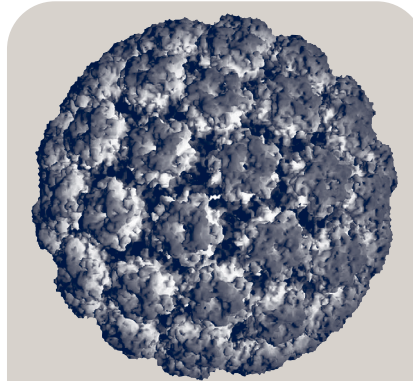
While chemical methods may be curative, treatment may ultimately require some form of physical removal or destruction. This can be accomplished through freezing, electrodesiccation (cautery) or laser ablation. Surgical excision offers the most thorough and complete means of eradication. Subdermal injection of Interferon, more commonly used in the past, may be used to augment the treatment. **Even with the best of treatments, recurrence is common, and focused long term surveillance is necessary in order to spot recurrences as soon as they arise.**

A GROWING MENACE

Genital warts are strongly associated with the development of squamous cell carcinoma of the anal canal. Integration of the Human papillomavirus DNA into the host cell genome is believed to be essential for malignant progression. Human papillomavirus type 16 is present in 30-75% of cases of anal cancer. Additionally, types 6, 11, and 18 are present in an additional 10% of cases. HPV appears to play a central yet unknown role in the development of the disease.

Recently, many physicians have begun to use cytological testing to aid in the early diagnosis of pre-malignant or malignant changes in the anal epithelium. The anal area is brushed with a small brush and the specimen is sent for cytological evaluation. This is similar to Pap smear testing for pre-malignant

changes of the cervical epithelium in women. The results may be normal or may show atypia or any of the three grades of Anal Intraepithelial Neoplasia (AIN). AIN I is the earliest manifestation of dysplasia, while AIN III is associated with severe dysplasia (Bowen's disease). It is not yet clear that progression of AIN necessarily leads to carcinoma of the anus. It is also unclear as to whether or not eradication of these affected areas of the anal canal will lead to the prevention of carcinoma. Extrapolation from the gynecological literature and cervical dysplasia studies has prompted further research into evaluating the natural history of Anal Intraepithelial Neoplasia.



Atomic model of the Papillomavirus capsid.

If anal carcinoma is diagnosed, the standard treatment of 5-FU, mitomycin-C and radiation is used. Five year cure rates approach 84%. Follow up biopsies may be used to examine the treated area. In patients experiencing an incomplete response, or in those patients exhibiting a recurrence of the disease, an abdominoperineal resection may be used as a salvage technique.

Prevention of disease transmission is the goal in any illness. Latex condoms are helpful but not completely protective as lesions may arise in covered areas. Misuse or failure to cover all exposed areas can also lead to the spread of disease. Regular examinations of susceptible individuals may aid in the control of early disease. The larger the load of condyloma, the more difficult is the treatment. Cytological swabbing and testing with early diagnosis may one day enable the practitioner to treat HPV while it is in the microscopic stages. Further research is necessary to clarify this issue.

As of now, HPV vaccines are still in the experimental stages and prevention remains the best cure. ■

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