Human Papillomavirus (HPV)

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34.1 Epidemiology

Human papillomavirus (HPV) causes warts in humans. It can occur on any part of the skin or mucous membranes but is commonly found on the hands, face, feet, and genital tract of both males and females. There are four main subgroups of warts: common warts, flat warts, plantar warts, and condyloma acuminata (genital warts). It is estimated that common warts are found in 3.5 % of adults and up to 33 % of primary schoolchildren [1]. The incidence of warts increases in immunosuppressed patients.

Transmission of HPV requires viral inoculation in basal epithelial cells. This is usually caused by microinjuries through skin-skin contact, microabrasions, or sexual intercourse [1]. While genital HPV infection most often occurs by intimate contact with an infected person, most cases of HPV transmission are not sexually transmitted. There is usually direct or indirect skin contact, and autoinoculation has been reported [2]. Cutaneous warts are very frequent in children, and among patients in larger households, many of the cohabitants may present with warts as well.

Human papillomavirus is also sexually transmitted and is considered the most common sexually transmitted infection in the United States [3]. HPV is associated with five key risk factors: sexual activity, number of current and lifetime sexual partners, sexual history of the partner(s), immune health, and age of coitarche. It is estimated that 20 million people are currently infected in the United States, and 6.2 million more acquire the virus each year [4]. HPV is widespread among the general population, especially among sexually active young adults; the Centers for Disease Control and Prevention estimates that at least 80 % of women will acquire HPV by age 50. While most strains of the virus involve a transient infection that may or may not involve a wart that will spontaneously regress (termed low-risk strains), certain strains are more oncogenic and persist with clinically significant symptoms (termed high-risk strains). It is well established that the virus is a necessary but insufficient cause of lower genital tract neoplasia. Infected women are at risk of developing

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cervical cancer, the second most common cause of cancer and cancer-related mortality for women worldwide. Men are much less likely to be diagnosed with genital malignancies after having genital warts for unclear reasons [5, 6].

34.2 Etiology

HPV is a non-enveloped virus with an icosahedral protein capsid containing DNA. The virus does not have an envelope, which makes it resistant to many forms of sterilization, such as heat [2]. HPV exclusively infects epithelial cells, though the specific anatomical locations or type of epithelial cell infected may vary by virus strain [4, 7]. Common warts are usually caused by HPV types 1, 2, and 4 [1]. Flat warts, also known as plane warts, are most commonly caused by HPV 3 and 10. Plantar warts are more often associated with HPV 1 and HPV 4. Condylomata are usually sexually transmitted and are most commonly caused by HPV 6, 11, 16, and 18. Types 6 and 11 are considered less oncogenic, while types 16 and 18 are considered high-risk HPV types with greater risk for malignant transformation.

34.3 Clinical Features

34.3.1 Distribution and Arrangement

Common warts (verrucae vulgaris) frequently involve the hands, especially the fingers, but can occur anywhere. Flat warts are generally located on the face, neck, hands, wrists, elbows, or knees and are more common in children. They are usually found in groups of multiple warts. Plantar warts are usually on the heel of the foot or other pressure points on the plantar surface. Condylomata, or genital warts, are usually multiple and may be found anywhere along the anogenital tract, including the vulva, vagina, cervix, scrotum, penis (glans, meatus, shaft), and anal area [1]. Condylomata may also be found in the oropharyngeal tract in rare cases.

34.3.2 Morphology of Lesions

Common warts are usually small, dome-shaped flesh-colored or pink papules with a hyperkeratotic or verrucous surface (Figs. 34.1 and 34.2) They may also appear filiform (Fig. 34.3), especially in certain locations, like periorificial skin [1]. Flat warts are flat-topped, smooth-surfaced papules that often match the patient's skin color (Figs. 34.4 and 34.5). Plantar warts frequently present as a painful, endophytic papules and plaques with a central depression and are surrounded by gentle slopes, resembling an anthill (Fig. 34.6). A clue in identifying warts is that they interrupt normal dermatoglyphic lines on the palmar and plantar surfaces. Condylomata (condyloma acuminatum), or genital warts, present as exophytic papillomas (Figs. 34.7, 34.8,

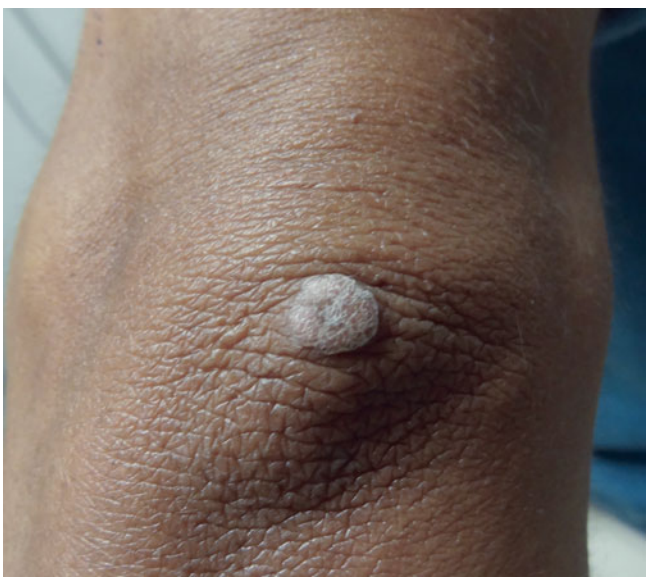

Fig. 34.1 Common wart on the elbow of a Hispanic male

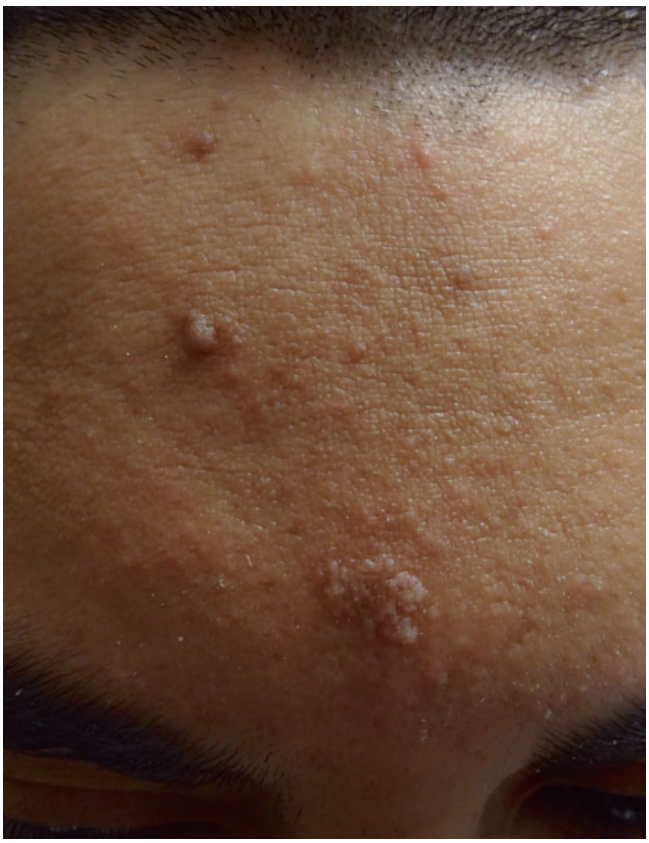

Fig. 34.2 Common warts on the forehead of a Hispanic male

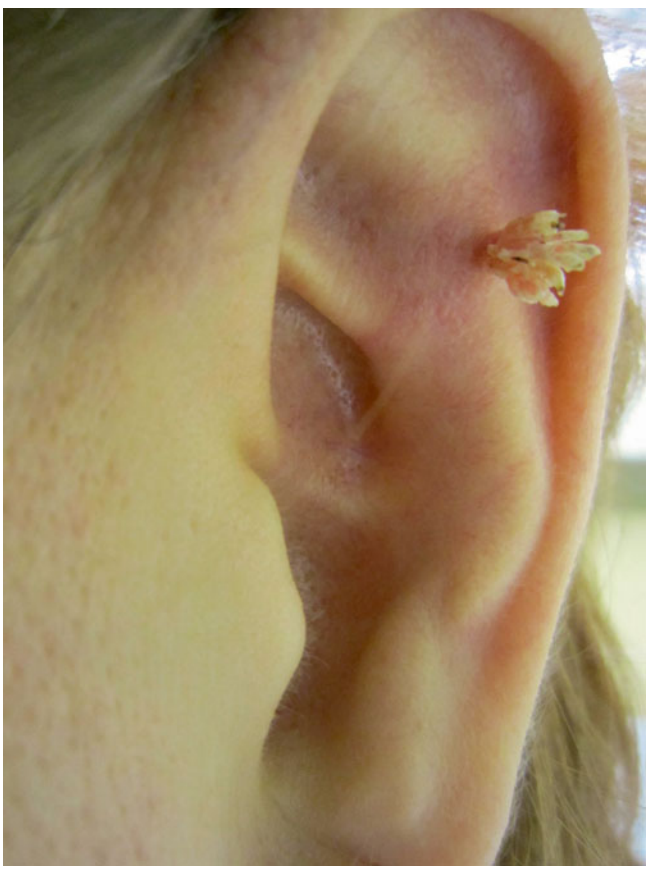

Fig. 34.3 Filiform wart on the ear with fingerlike projections showing thrombosed capillaries

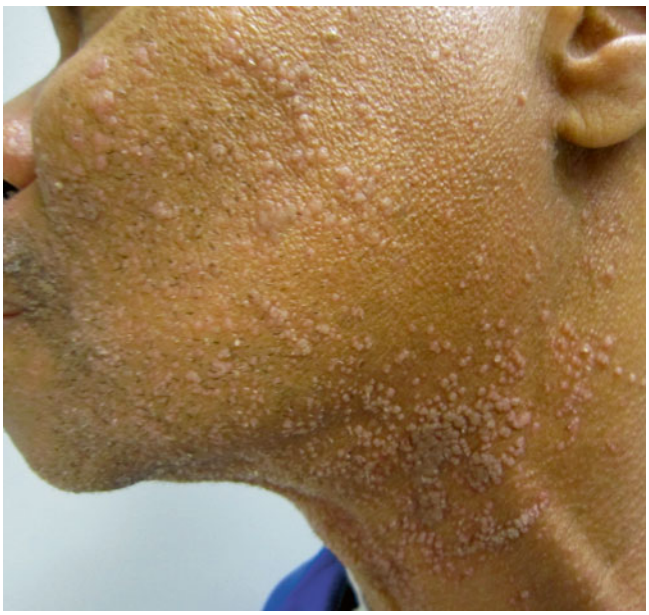

Fig. 34.4 Flat warts on the face and neck of an AA male with HIV infection

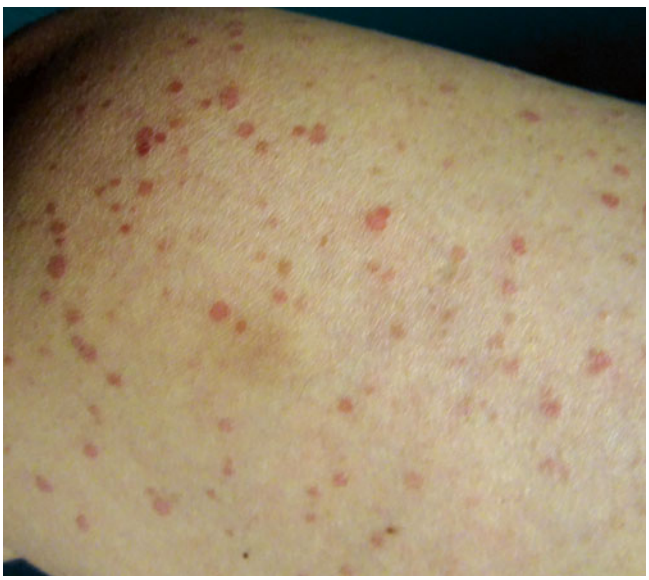

Fig. 34.5 Flat warts on the thigh of a Hispanic male with HIV infection

34.9, and 34.10) [1]. Mosaic warts are plaques composed of several individual small warts coalescing together and are especially recalcitrant to therapy (Fig. 34.11). Cutaneous warts often contain thrombosed capillaries which appear as small black points scattered over the surface of the lesion.

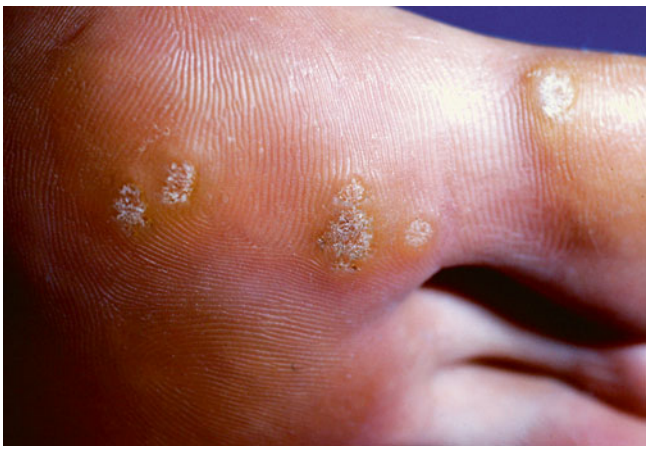

Fig. 34.6 Plantar warts on the great toe and foot of a Hispanic male showing an endophytic papule interrupting dermatoglyphic lines

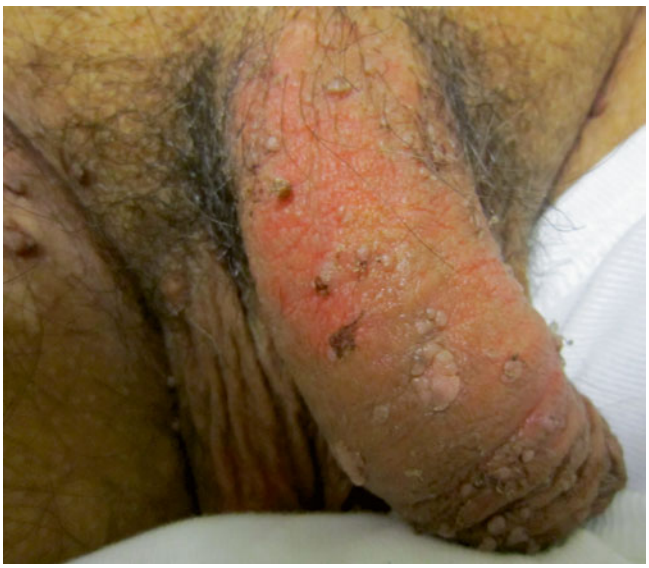

Fig. 34.7 Condyloma acuminata on the penis of a Hispanic male

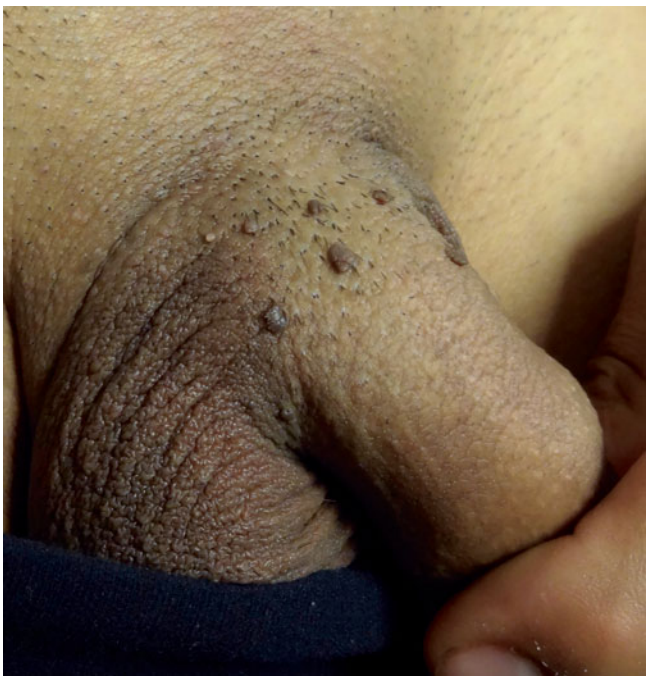

Fig. 34.8 Condyloma acuminata on the penis of a Hispanic male

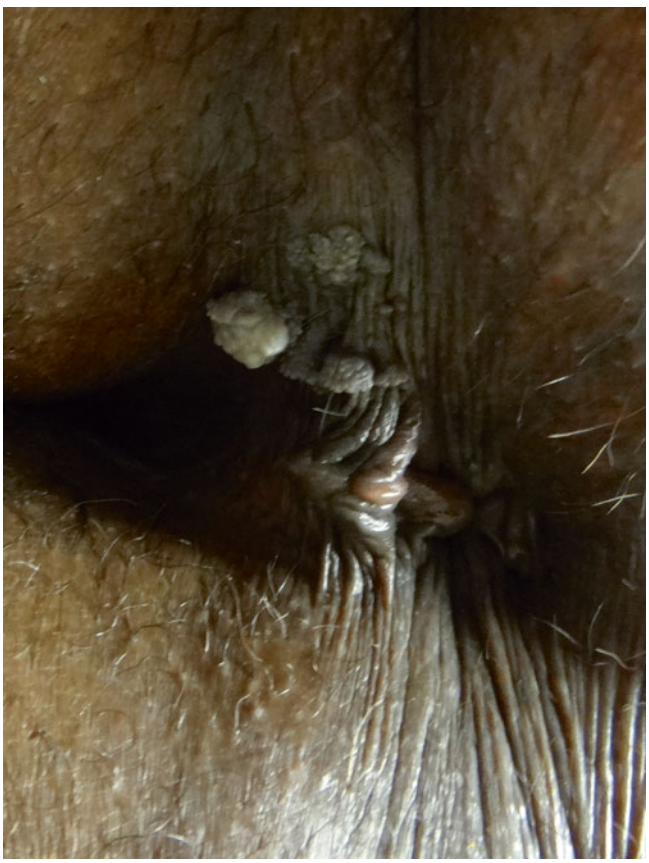

Fig. 34.9 Multiple anogenital warts on the perianal skin of an AA female with HIV infection

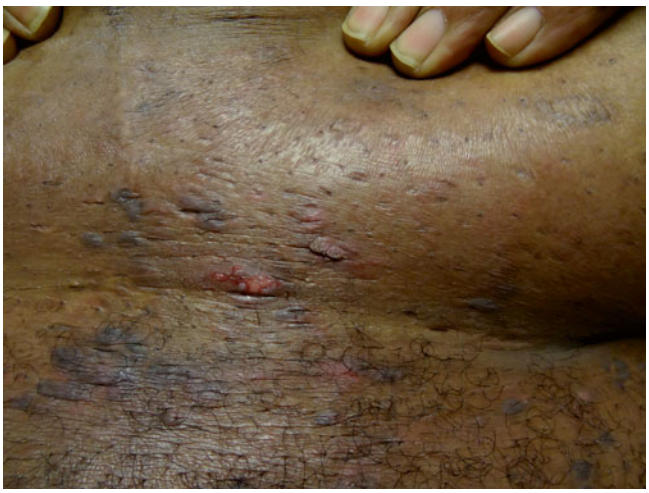

Fig. 34.10 Multiple warts on the abdomen of an AA female with HIV infection

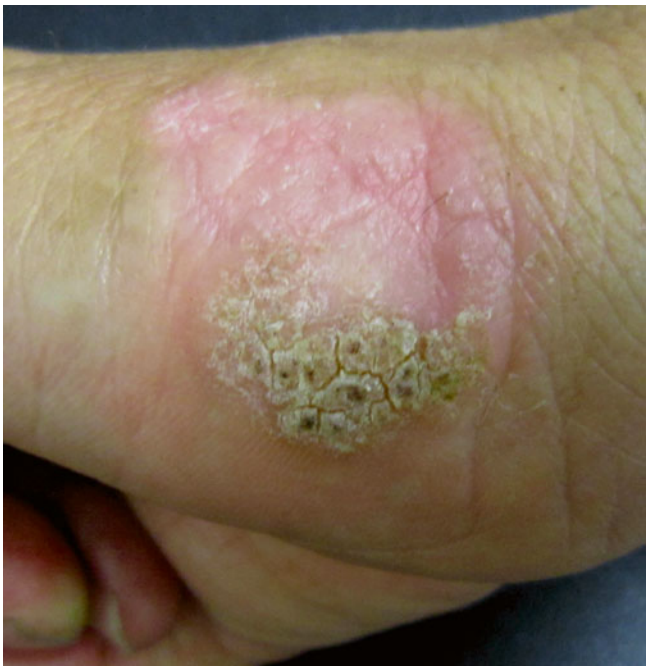

Fig. 34.11 Partially treated mosaic wart on the hand made up of individual small warts

34.4 Associated Symptoms

HPV infections are usually asymptomatic. Pain may or may not be present depending on the location of the wart and HPV type. Genital warts may occasionally cause irritation, pruritus, dysuria, bleeding, or dyspareunia [8]. Plantar warts that occur in pressure point areas can be very painful.

34.5 Systemic Findings

Systemic findings are not usually associated with HPV, except that an immunosuppressed status causes patients to be at higher risk for HPV infection.

34.6 Natural History and Prognosis

Many people infected with HPV are asymptomatic because the immune system tends to eliminate the virus before a wart can form. If a wart does form, the natural history is spontaneous resolution. Lesion regression tends to take place between weeks 8 and 12, and the epithelium resumes a normal appearance by 16 weeks, but many warts last much longer [7]. Reported clearance rates in children are 23 % at 2 months, 30 % at 3 months, 65–78 % at 2 years, and 90 % over 5 years [9]. Immunocompromised patients, such as organ transplant or HIV-infected patients, have a greater predisposition for the development of warts. Because of their impaired immune system, these patients usually have a greater number of warts, which are more challenging to treat and thus have a more protracted course. The distribution, morphology and other findings of warts vary depending on the strain of HPV.

Because most HPV infections go unnoticed or present as benign warts that regress on their own, the prognosis is generally positive. However, HPV in the cervix must be checked with periodic screenings to ensure that neoplasia does not develop.

34.7 Brief Description of Histopathologic Features

Warts have many epidermal changes including parakeratosis and the presence of koilocytes, superficial vacuolated keratinocytes, found in the granular layer [1]. There is also varying degrees of hyperkeratosis, parakeratosis, papillomatosis, acanthosis, and hypergranulosis, depending on the clinical appearance of the warts. Dilated capillaries are found in the dermis.

34.8 Diagnosis and Differential Diagnosis

Diagnosis is usually made by inspection of the affected areas. Condyloma acuminata can also be diagnosed via colposcopy or Pap smear. A biopsy is recommended when the lesions look atypical [8]. DNA testing for the HPV type is usually not indicated because of marginal cost-effectiveness. Differential diagnoses include seborrheic keratosis, actinic keratosis, psoriasis, acrokeratosis verruciformis, angiokeratomas, and Fordyce spots [8]. Other non-HPV-induced cancers can be considered in the differential, including amelanotic melanoma, Bowen's disease, and Paget's disease.

34.9 Treatment

There is no specific antiviral treatment for HPV. Most therapies focus on the local destruction or removal of the wart or induction of cytotoxicity of the infected epithelial cells. Because most warts tend to regress on their own after several months, treatment is usually symptom based [8]. Cryotherapy and curettage is commonly employed, as is treatment with topical creams and gels such as salicylic acid and other keratolytic creams. Cryotherapy in skin of color can lead to prominent hypopigmentation, which is usually transient but can be permanent (Fig. 34.12). It is not clear whether removing the wart reduces infectivity of the patient. Warts in immunosuppressed patients tend to resolve when the immune system is reconstituted, such as with HAART for HIV-positive patients. Plantar warts tend to be more recalcitrant to treatment but usually resolve on their own, though the time course may be longer for adults than children.

It is very difficult to prevent warts, but the best method is generally to avoid skin contact with an infected person. This includes avoiding moist environments where an infected person's skin has had contact, such as in a pool or gym. This also includes sexual intercourse with an individual infected

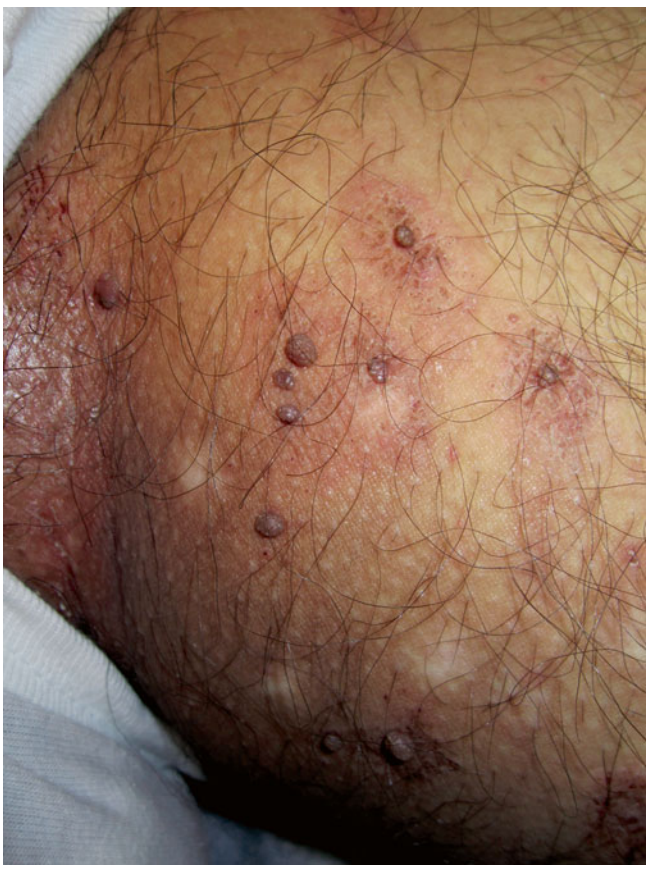

Fig. 34.12 Condyloma acuminata on the thigh of a Hispanic patient with hypopigmentation after cryotherapy

with HPV. Regular Pap smears and limiting sexual partners are important protective measures for genital warts, with a mutually monogamous relationship with a low-risk partner giving the lowest risk. An effective vaccine is available for girls and boys aged 9–26 that protects against the four most common HPV types causing genital warts (HPV types 6, 11, 16, 18), including the two that cause over 90 % of cervical cancers (HPV types 16 and 18).

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