**Viral Skin Diseases**

**Warts (verrucae).**

Warts are benign epidermal neoplasms that are caused by human papillomaviruses (HPVs). There are more than 100 different types of HPVs. HPVs infect epithelial cells of the skin, mouth, esophagus, larynx, trachea, and conjunctiva and cause both benign and malignant lesions. Warts commonly occur in children and young adults, but they may appear at any age. Warts are transmitted simply by touch. Warts commonly appear at sites of trauma, on the hands, in periungual regions as a result of nail biting, and on plantar surfaces. Their course is highly variable; most resolve spontaneously in weeks or months, and others may last years or a lifetime. HPVs induce hyperplasia and hyperkeratosis.

Immunologic response. The regression of virus-infected cells involves a multifactorial response that includes cell-mediated immunity and induction of interferons. Individual variations in cell-mediated immunity may account for differences in severity and duration. Warts develop on many immunosuppressed patients.

Warts obscure normal skin lines; this is an important diagnostic feature. When skin lines are reestablished, the warts are gone. Warts vary in shape and location and are managed in several different ways.

Viral warts are tumors initiated by a viral infection of keratinocytes. The cells proliferate to form a mass but the mass remains confined to the epidermis. There are no “roots” that penetrate the dermis. Several types of warts form cylindrical projections. These projections are clearly seen in digitate warts that occur on the face. The projections become fused together in common warts on thicker skin; this produces a highly organized mosaic pattern on the surface. This pattern is unique to warts and is a useful diagnostic sign. Thrombosed black vessels become trapped in these projections and are seen as black dots on the surface of some warts. The wart is confined to the epidermis, but it expands and displaces the dermis, giving the impression that it extends into the dermis or subcutaneous tissue.

Common warts.

Common warts (verruca vulgaris) begin as smooth, flesh-colored papules and evolve into dome-shaped, gray-brown, hyperkeratotic growths with black dots on the surface. The black dots, which are thrombosed capillaries, are a useful diagnostic sign and may be exposed by paring the hyperkeratotic surface with a surgical blade. The hands are the most commonly involved areas, but warts may be found on any skin surface.

Treatment. Topical salicylic acid preparations, liquid nitrogen cryotherapy, and very light electrocautery are the best methods of initial therapy. Blunt dissection is used for resistant or very large lesions. Nightly application of the immunomodulatory drug imiquimod (Aldara cream) may be effective.

Filiform and digitate warts.

These growths consist of a few or several fingerlike, flesh-colored projections emanating from a narrow or broad base. They are most commonly observed about the mouth, beard, eyes, and ala nasi.

Treatment. Curettage or light electrocautery.

Flat warts

Flat warts (verruca plana) are pink, light brown, or light yellow and are slightly elevated, flat-topped papules that vary in size from 0.1 to 0.5 cm. There may be only a few, but in general they are numerous. Typical sites of involvement are the forehead, around the mouth, the backs of the hands, and shaved areas such as the beard area in men and the lower legs in women. A line of flat warts may appear as a result of scratching these sites (Koebner’s phenomenon).

Treatment. Imiquimod 5% cream or cryotherapy or light touch electrocautery or 5-fluorouracil cream.

Planter warts.

Warts of the soles are called so. Plantar warts frequently occur at points of maximum pressure, such as over the heads of the metatarsal bones or on the heels. A thick, painful callus forms in response to pressure and the foot is repositioned while walking. A cluster of many warts that appears to fuse is referred to as a mosaic wart.

Differential diagnosis.

Corns are a mechanically induced lesion that forms over or under a weight-bearing surface or structure. Corns over the metatarsal heads are frequently mistaken for warts. The two entities can be easily distinguished by paring the callus with a surgical blade. Warts lack skin lines that cross their surface and have centrally located black dots that bleed with additional paring. Corns also lack skin lines crossing the surface, but they have a hard, painful, well-demarcated, translucent central core. Lateral pressure on a wart causes pain, but pinching a plantar corn is painless.

Warts in the process of undergoing spontaneous resolution, particularly on the plantar surface, may turn black and feel soft when pared with a blade. Cell-mediated immunity against virus-infected keratinocytes may take place in the process of regression of some warts.

Treatment. The options are 40% salicylic acid plasters or imiquimod 5% cream or blunt dissection. Cryotherapy on the sole may produce a deep, painful blister and interfere with mobility.

Subungual and periungual warts.

A wart next to the nail may simply be the tip of the iceberg; much more of the wart may be submerged under the nail.

Treatment options are salicylic acid plasters application, blunt dissection.

Genital warts (condylomata acuminata or venereal warts) are pale pink with numerous, discrete, narrow-to-wide projections on a broad base. The surface is smooth or velvety and moist, and lacks the hyperkeratosis of warts found elsewhere. The warts may coalesce in the rectal or perineal area to form a large, cauliflower-like mass. Perianal warts may be present in persons who do not practice anal sex.

They are effectively treated with light electrodesiccation, cryosurgery, or scissor excision. Imiquimod 5% cream, podophyllotoxin 0.5% gel, trichloroacetic acid solution, or 5-fluorouracil cream are also effective.

**Herpes simplex.**

Skin infection caused by herpes simplex virus (HSV). HSV-1 is generally associated with oral infections, and HSV-2 is associated with genital infections. HSV infections have two phases: the primary infection, after which the virus becomes established in a nerve ganglion; and the secondary phase, characterized by recurrent disease at the same site. Lesions are intraepidermal and usually heal without scarring.

Many primary infections are asymptomatic. The virus may be spread via respiratory droplets, direct contact with an active lesion, or contact with virus-containing fluid such as saliva or cervical secretions in patients with no evidence of active disease. Symptoms occur from 3 to 7 days after contact. Tenderness, pain, mild paresthesias, or burning occurs before the onset of lesions at the site of inoculation. Localized pain, tender lymphadenopathy, headache, generalized aching, and fever are characteristic prodromal symptoms. Clinically, grouped vesicles on an erythematous base appear and subsequently umbilicate. The vesicles in primary herpes simplex are more numerous and scattered than those in the recurrent infection where they are small in number and more grouped. The vesicles of herpes simplex are uniform in size in contrast to the vesicles seen in herpes zoster, which vary in size. Mucous membrane lesions accumulate exudate, whereas skin lesions form a crust. Lesions last for 2 to 4 weeks unless secondarily infected and heal without scarring. The virus replicates at the site of primary infection. Virons are then transported by neurons via retrograde axonal flow to the dorsal root ganglia, and latency is established in the ganglion.

Recurrent infection. Local skin trauma (e.g., ultraviolet light exposure, chapping, abrasion) or systemic changes (e.g., menses, fatigue, fever) reactivate the virus, which then travels down the peripheral nerves to the site of initial infection and causes the characteristic focal, recurrent infection. Recurrent infection is not inevitable. Many individuals have a rise in antibody titer and never experience recurrence. The prodromal symptoms of itching or burning, lasting 2 to 24 hours, resemble those of the primary infection. Within 12 hours, a group of lesions evolves rapidly from an erythematous base to form papules and then vesicles. The dome-shaped, tense vesicles rapidly umbilicate. In 2 to 4 days, they rupture, forming aphthaelike erosions in the mouth and vaginal area or erosions covered by crusts on the lips and skin. Crusts are shed in approximately 8 days to reveal a pink, reepithelialized surface. In contrast to the primary infection, systemic symptoms and lymphadenopathy are rare unless there is secondary infection.

Treatment of primary and recurrent herpes simplex is acyclovir 400mg three times daily for 10 days. Treatment is of benefit only if initiated early in course of the disease.

There are several clinical forms of herpes simplex infection: oral labial herpes simplex, cutaneous herpes simplex, herpetic whitlow, and eczema herpeticum.

Oral labial herpes simplex

Primary infection. Transmission is dependent on intimate, personal contact with someone excreting HSV. Gingivostomatitis and pharyngitis are the most frequent manifestations of first-episode HSV-1 infection. Infection occurs most commonly in children between ages 1 and 5 years. The incubation period is 3 to 12 days. Although most cases are mild, some are severe. Sore throat and fever may precede the onset of painful vesicles occurring anywhere in the oral cavity or on the face. The vesicles rapidly coalesce and erode with a white, then yellow, superficial, purulent exudate. Children are unable to swallow liquids because of the edema, ulcerations, and pain. Tender cervical lymphadenopathy develops. Fever subsides in 3 to 5 days, and oral pain and erosions are usually gone in 2 weeks; in severe cases, they may last for 3 weeks.

Recurrent infection. The most common manifestation consists of eruptions on the vermilion border of the lip (recurrent herpes labialis). Recurrent herpes begins with a prodrome of itching or burning. A group of vesicles appears on an erythematous base. Previous episodes in the same area are typical.

Herpetic whitlow.

It is the cutaneous herpetic infection of the pulp of the distal phalanx of the hand. It results from direct inoculation of the involved digit through the abraded skin by HSV.

Eczema herpeticum.

It is the association of two common conditions: atopic dermatitis and HSV infection. Certain atopic infants and adults may develop the rapid onset of diffuse cutaneous herpes simplex. The severity of infection ranges from mild to fatal. The disease is most common in areas of active or recently healed atopic dermatitis, particularly the face. The disease in most cases is a primary HSV infection. Secondary staphylococcal infection commonly occurs. High fever and adenopathy occur 2 to 3 days after the onset of vesiculation. Recurrent disease is milder and usually without constitutional symptoms. Treatment: Eczema herpeticum of the young infant is a medical emergency, treated by acyclovir 5-10mg/kg 8 hourly IV. In adult, acyclovir 800mg 3 times daily for 10 days.

Genital herpes simplex.

Genital herpes simplex virus (HSV) infection is primarily a disease of young adults. It is a recurrent, lifelong infection. There are two serotypes: HSV-1 and HSV-2. Most genital cases are caused by HSV-2. Vesicles appear approximately 6 days after sexual contact. Vesicles become depressed in the center (umbilicated) in 2 or 3 days, and then erode. Crusts form and the lesion heals in the next week or two. Scars form if the inflammation has been intense. Discharge, dysuria, and inguinal lymphadenopathy are common. Systemic complaints, including fever, myalgias, lethargy are more common in women. The virus ascends the peripheral sensory nerves after the primary infection and establishes latency in the nerve root ganglia. Intercourse, skin trauma, cold or heat, stress, concurrent infection, and menstruation can trigger reactivation. Itching or pain may precede the recurrent lesion. A small group of vesicles appears, umbilicates in 1 or 2 days, and then erodes and crusts.

Treatment is acyclovir 400mg 3 times daily for 10 days.

**Varicella.**

Varicella (chickenpox) is a highly contagious viral infection. Transmission occurs via airborne droplets or vesicular fluid. Patients are contagious from 2 days before onset of the rash until all lesions have crusted. An attack of chickenpox usually confers lifelong immunity. After it has produced chickenpox, varicella-zoster virus (VZV) becomes latent in ganglia along the entire neuraxis. The incubation period averages 14 days, with a range of 9 to 21 days. The prodromal symptoms in children are absent or consist of low fever, headache, and malaise, which appear directly before or with the onset of the eruption. Symptoms are more severe in adults. Fever, chills, malaise, and backache occur 2 to 3 days before the eruption.

On the skin, lesions of different stages are present at the same time in any given body area. New lesion formation ceases by day 4 and most crusting occurs by day 6. The lesion starts as a 2- to 4-mm red papule that develops an irregular outline (rose petal) as a thin-walled clear vesicle appears on the surface (dewdrop). This lesion, “dewdrop on a rose petal,” is highly characteristic. The vesicle becomes umbilicated and cloudy and breaks in 8 to 12 hours to form a crust as the red base disappears. Fresh crops of additional lesions undergoing the same process occur in all areas at irregular intervals during the following 3 to 5 days, giving the characteristic picture of intermingled papules, vesicles, pustules, and crusts. Pruritus is usually present during the vesicular stage. The degree of temperature elevation parallels the extent and severity of the eruption. The temperature returns to normal when the vesicles have disappeared. Crusts fall off in 7 days (with a range of 5 to 20 days) and heal without scarring. Secondary infection or excoriation extends the process into the dermis, producing a craterlike, pockmark scar. Vesicles often form in the oral cavity and vagina and rupture quickly to form multiple, aphthaelike ulcers. The rash begins on the trunk (centripetal distribution) and spreads to the face and extremities (centrifugal spread).

The complication of varicella are secondary bacterial infection, encephalitis, Reye’s syndrome, and pneumonia.

Treatment. Antipyretic like paracetamol (excluding aspirin because of its association with Reye’s syndrome). Antihistamines like hydroxyzine may help control excoriation. Oral antibiotic active against *Streptococcus* and *Staphylococcus* like cephalexin is indicated for secondarily infected lesions.

Adult chickenpox, in addition to above, should be treated with oral acyclovir 800mg 5 times daily for 7 days.

**Herpes zoster (shingles)**

A cutaneous viral infection caused by varicella-zoster virus (VSV) generally involving the skin of a single dermatome. Zoster results from reactivation of varicella zoster virus that entered the cutaneous nerves during an earlier episode of chickenpox, traveled to the dorsal root ganglia, and remained in a latent form. Age, immunosuppressive drugs, lymphoma, fatigue, emotional upsets, and radiation therapy have been implicated in reactivating the virus, which subsequently travels back down the sensory nerve, infecting the skin. Virus reactivation usually occurs once in a lifetime; the incidence of a second attack is less than 5%. The elderly are at greater risk to develop segmental pain(postherpetic neuralgia), which can continue for months after the skin lesions have healed.

Preeruptive pain (preherpetic neuralgia), itching, or burning, generally localized to the dermatome, precedes the eruption by 4 to 5 days. The eruption begins with red, swollen plaques of varying sizes and spreads to involve part or all of a dermatome. The vesicles arise in clusters from the erythematous base and become cloudy with purulent fluid by day 3 or 4. The vesicles vary in size, in contrast to the cluster of uniformly sized vesicles noted in herpes simplex. Successive crops continue to appear for 7 days. Vesicles either umbilicate or rupture before forming a crust, which falls off in 2 to 3 weeks. The elderly or debilitated patients may have a prolonged and difficult course. For them, the eruption is typically more extensive and inflammatory, occasionally resulting in hemorrhagic blisters, skin necrosis, secondary bacterial infection, or extensive scarring, which is sometimes hypertrophic or keloidal. Approximately 50% of patients with uncomplicated zoster have a viremia, with the appearance of 20 to 30 vesicles scattered over the skin surface outside the affected dermatome.

Ophthalmic zoster.

Headaches, nausea, and vomiting are prodromal symptoms. Ipsilateral preauricular and, sometimes, submaxillary nodal involvement is a common prodromal event. Reactive lymphadenopathy can occur later with secondary infection of vesicles. The ophthalmic branch of the fifth cranial nerve sends branches to the tentorium and to the third and sixth cranial nerves, which may explain the meningeal signs. The rash extends from eye level to the vertex of the skull but does not cross the midline. The tip and side of the nose and eye are innervated by the nasociliary branch of the trigeminal nerve. Vesicles on the side or tip of the nose (Hutchinson’s sign) that occur during an episode of zoster are associated with the most serious ocular complications.

Treatment of herpes zoster: is acyclovir 800mg 5 times daily for 7 days.

Complications of herpes zoster:

* Ramsay Hunt syndrome.

Ramsay Hunt syndrome (geniculate ganglion zoster) is peripheral facial nerve palsy accompanied by a vesicular rash on the ear (zoster oticus) or in the mouth. It is caused by zoster of the geniculate ganglion. Other frequent signs and symptoms include tinnitus, hearing loss, nausea, vomiting, vertigo, and nystagmus. These eighth cranial nerve features are caused by the close proximity of the geniculate ganglion to the vestibulocochlear nerve within the bony facial canal.

There is involvement of the sensory portion and motor portion of the seventh cranial nerve. There may be unilateral loss of taste on the anterior two thirds of the tongue as well as vesicles on the tympanic membrane, external auditory meatus, concha, and pinna. Involvement of the motor division of the seventh cranial nerve causes unilateral facial paralysis. Auditory nerve involvement occurs in 37.2% of patients, resulting in hearing deficits and vertigo. Recovery from the motor paralysis is generally complete. Treatment is with acyclovir and prednisone within 7 days of onset.

* Sacral zoster (S2, S3, or S4 dermatomes).

A neurogenic bladder with urinary hesitancy or urinary retention has reportedly been associated with zoster of the sacral dermatome S2, S3, or S4.

* Postherpetic neuralgia (PHN).

It is the persistence of pain in affected dermatome after all lesions of herpes zoster have healed. PHN occurs especially in patients older than 50 years. Pain can persist in a dermatome for months or years. Pathophysiology of pain: Postherpetic neuralgia is associated with scarring of the dorsal root ganglion and atrophy of the dorsal horn on the affected side. These changes are caused by the extensive inflammation that occurs during the active infection.

Treatment is gabapentine 1800-3600mg/day in 3 divided doses, if not effective, tricyclic antidepressants nortriptyline or desipramine can be used. Opioid analgesics can be added like codeine.

* Necrosis, infection, and scarring.

Elderly, malnourished, debilitated, or immunosuppressed patients tend to have a more virulent and extensive course of disease. The entire skin area of a dermatome may be lost after diffuse vesiculation. Large adherent crusts promote secondary bacterial infection and increase the depth of involvement. Scarring, sometimes hypertrophic or keloidal, follows.

* Dangerous eye involvement from ophthalmic zoster.

Differential diagnosis

Herpes simplex.

Herpes simplex can be extensive, particularly on the trunk. It may be confined to a dermatome and possess many of the same features as zoster (zosteriform herpes simplex). The vesicles of zoster vary in size, whereas those of simplex are uniform within a cluster. An early or later recurrence proves the diagnosis of herpes simplex.

Zoster sine herpete.

It is neuralgia within a dermatome without rash, which can be confusing.

**Molluscum contagiosum****.**

It is a poxvirus infection of the skin characterized by discrete, 2- to 5-mm, slightly umbilicated, flesh-colored, dome-shaped papules. It spreads via autoinoculation, scratching, or touching a lesion and fomites. The areas most commonly involved are the face, trunk, axillae, extremities in children, and the pubic and genital areas in adults. Lesions are frequently grouped. Unlike warts, the palms and soles are not involved. It is not uncommon to see erythema and scaling at the periphery of a single lesion or several lesions. This may be the result of inflammation from scratching or may be a hypersensitivity reaction. The individual lesion begins as a smooth, dome-shaped, white- to flesh-colored papule. With time, the center becomes soft and umbilicated. Most lesions are self-limiting and clear spontaneously in 6 to 9 months; however, they may last 2 to 4 years or longer.

Treatment. Curettage, cryosurgery, or topical imiquimod. Topical corticosteroids like hydrocortisone cream are used to treat dermatitis near or involving the lesions.

**Pityriasis rosea.**

Pityriasis rosea (PR) is a common, benign, usually asymptomatic, self-limiting skin eruption of unknown etiology. Human herpesvirus 6 (HHV-6) may be involved. The incidence of disease is higher during the colder months. Twenty percent of patients have a recent history of acute infection with fatigue, headache, sore throat, lymphadenitis, and fever.

Typically, the herald patch, a single 2- to 10-cm round-to-oval lesion, abruptly appears in 17% of patients. It may occur anywhere, but is most frequently located on the trunk or proximal extremities. The herald patch retains the same features as the subsequent oval lesions. Within a few days to several weeks (average, 7 to 14 days) the disease enters the eruptive phase. Smaller lesions appear and reach their maximum number in 1 to 2 weeks. They are typically limited to the trunk and proximal extremities, but in extensive cases they develop on the arms, legs, and face. An inverse distribution (inverted PR) involving mainly the extremities is seen in 6% of cases. Lesions are typically benign and are concentrated in the lower abdominal area. Individual lesions are salmon pink in whites and hyperpigmented in blacks. Many of the earliest lesions are papular (papular PR common in children, pregnant women, and blacks), but in most cases the typical 1- to 2-cm oval plaques appear. A fine, wrinkled, tissue-like scale remains attached within the border of the plaque, giving the characteristic ring of scale, called collarette scale. The long axis of the oval plaques is oriented along skin lines. Numerous lesions on the back, oriented along skin lines, give the appearance of drooping pine-tree branches, which explains the designation “Christmas-tree distribution.” The number of lesions varies from a few to hundreds. Most lesions are asymptomatic, but many patients complain of mild transient itching. Severe itching may accompany extensive inflammatory eruptions. The disease clears spontaneously in 1 to 3 months.

The differential diagnosis is secondary syphilis, guttate psoriasis, viral exanthems, tinea, nummular eczema, and drug eruptions.

Treatment: Topical steroids like betamethasone and oral antihistamines like hydroxyzine may be used for itching. The extensive case with intense itching responds to a 1- to 2-week course of prednisone (20 mg twice a day). Oral acyclovir (800 mg five times daily) may be of benefit because of the possible association of the disease with HHV-6 and HHV-7.

**Reference:**

Thomas P. Habif. Clinical Dermatology, A Color Guide to Diagnosis and Therapy. 5th edition, 2010. Elsevier Inc.