CHAPTER 8

VIRAL DERMATOSES

Three main groups of cutaneous viral infections may be distinguished according to the etiology:

Poxvirus (DNA, 250-300 nm)

- **Molluscum contagiosum**

Herpesvirus (DNA, 90-170 nm)

- **Varicella**
- **Herpes zoster**
- **Herpes simplex**

Papillomavirus (DNA, 46-52 nm)

- **Common warts (verruca vulgaris)**
- **Flat warts (verruca plana)**
- **Anogenital warts**

(condylomata acuminata are described in the sexually transmitted diseases section)

In the following chapter we will also examine:

- **HIV cutaneous manifestations**

STATE OF THE ART

By Stefania Jablonska

The cutaneous viral and bacterial infections are especially frequent in human mobile populations since often linked with poor economico-social conditions and malnutrition. Particularly the prevalence of herpesvirus and papillomavirus infections and their extent depend on the immune status of the people.

Molluscum contagiosum. Molluscum contagiosum is induced by a virus which escapes from the surveillance mechanisms, and therefore up to now only destructive measures or removal by curettage were effective. Infection occurs often in immunocompetent population, frequently in children. However a very widespread involvement is always associated with immunosuppression, and the best results have been achieved by the treatment with immune modifier, 5% imidazoquinoline cream imiquimod (Aldara®).

Varicella. Varicella-zoster virus is extremely contagious, thus over 90% of adult population is infected and develop immunity. Therefore varicella does not show recurrences. In adults the disease is extremely rare and the cases, recognized as varicella in immunosuppressed patients are in essence zoster disseminatus. Differentiation between recurrent varicella and zoster disseminatus caused by the same viruses and having quite similar clinical presentation, is of minimal practical significance since both are associated with immunosuppression.

In varicella with no complications the symptomatic management for secondary infection is usually quite sufficient, in more severely ill adult patients acyclovir is indicated for 5 days in similar dosages as in zoster.

Zoster

The disease , although occurring at any ages in immunocompetent people, is much more frequent and much more severe in immunosuppressed population due to activation of the persistent latent varicella-zoster viruses in neural ganglions. In HIV-infected patients zoster might be disseminated, hemorrhagic and necrotic.

The diagnosis in atypical generalized or recurrent cases may require confirmation of the virus, best by PCR, immunofluorescence or culture. The histopatholgy and smears are not useful for differentiation from herpes simplex since multinucleated giant cells are characteristic for both diseases. The therapy of not complicated cases, with no associated neuralgia, could be only symptomatic with antibiotics and anti-bacterial ointments in case of secondary infection and drying lotions topically on blisters. Acyclovir in high doses, 800 mg 5 times a day for 7 days, enhances clearing and reduces, at least partly, neuralgia. We found that for prophylaxis of neuralgia most effective are small doses of corticosteroids (about 20-30 mg/day), started at

5th-7th day of the disease, after the bullous lesions have regressed.

Herpes simplex (HSV)

This is a world-wide infection, usually remaining latent in the nerves for a lifetime, with periodic recurrences in facio-oral and anogenital areas. The primary infection with HSV type 1 usually occurs in early childhood and very rarely is associated with severe symptoms (meningitis, gingivostomatitis etc.), type 2 is mostly sexually transmitted. The lesions localized on fingers, ears, elsewhere on the skin are not infrequently difficult to recognize, and by linear distribution may be misdiagnosed as zoster. The type of HSV is best established by PCR, indirect immunofluorescence, ELISA and Westernblot. If these techniques are not available, the smears disclosing multinucleated giant cells may be of some diagnostic significance, although the similarity to zoster and varicella could be the cause of errors. The acantholytic cells in pemphigus vulgaris also may mimic the abnormal giant cells in oral HSV infection. The serology is not useful for diagnosis since all adult persons have anti-HSV antibodies. However, it could be helpful in primary infection of small children, and , to some extent, in adults if the antibody titres rapidly increase. The circulating antibodies are only the marker of infection, and thus of some significance mainly for epidemiologic studies. The cellular immunity appears to play a most important role in the pathogenesis since in the immunosuppressed population the infection is usually very widespread and severe.

Of great interest is detection (with the use of PCR technique) of HSV-1 in 50% of active cases of erythema multiforme. Interestingly, DNA HSV-1 can be detected in the epidermis even one to three months after regression of cutaneous lesions, although the virus is no longer active. The alleged relationship of HSV-1 with pemphigus vulgaris was not confirmed on a large series of patients. Thus HSV, as various other infectious agents, might be just contamination in the denuded skin.

The therapy of recurrent herpes simplex with specific anti- HSV DNA compounds is very expensive. The topical application of acyclovir or its analogue 1% pencyclovir is much less effective than oral use, and the results are equal to those achieved with drying gels. Acyclovir infusions are the best therapeutic modality for very severe cases. In recurrent cases high oral doses 200-400 mg 5 times/day for 5 days, are usually effective. For prophylaxis of relapses the doses of 400 mg, twice daily, applied for several months to two years, proved to be efficacious, decreasing significantly the number of recurrences.

Resiquimod. The newest development is introduction of this very strong immune response modifier for the therapy of HSV-2 infection. Topically applied 0,01% Resiquimod gel induced – similarly as imiquimod – interferon and interleukin 2. It was found to delay significantly recurrences of herpes simplex by enhancing local cellular immunity.

The role of HSV-2 in genital cancerogenesis. The presumed cancerogenic activity was not confirmed on a large series of patients with genital malignancies. Although HSV-2 has not been proved a causative factor of genital cancers, it is probably an important co-cancerogen in cases associated with high risk human papillomaviruses (HPVs). The problem of vertical transmission of HSV during the pregnancy is not entirely clear, although transmission through the placenta has been documented in single cases. However, this is a very rare event, and the women infected with HVS-2 can deliver by natural ways since the antibodies of the mothers are limiting or inhibiting the spread of viruses.

Cutaneous warts (verrucae). Warts induced by human papillomaviruses (HPVs) are extremely widespread in nature, with highest incidence in school children between ages of 12 and 16 years. Distinct types of HPVs have been found associated with cutaneous and genital warts. There is a preferential association of cutaneous HPVs with skin warts differing in morphology and location, classified as common, plane and plantar warts. The recognition of the types of warts is important because of differences in immune responses, course of the disease and mode of regression. Not infrequently, the removal of one lesion induces regression of surrounding warts. This could be explained as immunological booster since in consequence of excision the viral particles, present exclusively in the epidermis and therefore separated from circulation, penetrate into the blood inducing formation of antibodies. A similar mechanism is probably involved in clearance of warts by hypnosis (involuntary scratching, touching, etc.).

Plane warts. These warts, more frequent in children, young adults and immunosuppressed persons, are usually multiple and, after several months, tend to disappear simultaneously with an oedematous and erythematous reaction on all of them. This phenomenon is due to the cell mediated immunity, with consecutive invasion of mononuclear cells into the epidermis, its destruction and eradication of the viruses. Such mode of regression is highly characteristic of plane warts induced by HPV-3 and 10. In case of deficient immunity the warts persist for several months or years, and plane warts are the most frequent HPV infection in immunosuppressed population. Since there are no specific kits for typing cutaneous warts, the histopathologic pattern, especially cytopathic effect, may be helpful in recognizing HPV-3/10 type: characteristic perinuclear vacuolization of the granular and spinous cells, with small pyknotic nuclei, mimicking “bird eyes”. Somewhat more elevated multiple warts, with prominent hyperkeratosis, similar to verrucae vulgares in clinical presentation, are referred to as intermediate warts. These warts, associated mainly with HPV-10 and 28, have structure similar to the common warts, induced mainly by HPV-2, but the “bird eye”- like cytopathic effect is of HPV-3 type and natural history, immune responses and mode of regression is characteristic for plane warts. Although plane warts are not associated with oncogenic HPVs , they appear not infrequently in epidermodysplasia verruciformis in coexistence with lesions induced by potentially oncogenic EV-specific HPVs

Common warts. Verrucae vulgares. The recognition of typical common wart is usually easy. Only differentiation from intermediate wart may be difficult, but the histology is of diagnostic significance. Parakeratosis in common wart has a characteristic columnar arrangement, and vacuolized cytoplasm of the granular cells contains numerous condensed kerathyaline granules of various sizes, shapes and stainability.

Common warts have a wide spectrum of clinical morphology - from deep endophytic, filiform to highly proliferative and/or confluent lesions. The clinical presentation depends partly on the type of evoking HPVs (endophytic warts, especially palmar, are often associated with HPV-4 and highly proliferative lesions-mainly in butchers- with HPV-7). Despite specific association of common warts of different morphology with distinct HPVs , in immunosuppressed population could be detected all types of HPVs including even genital HPV types 6 and 11.

Plantar warts. Plantar warts are of two types: mostly single, endophytic myrmecia warts induced by HPV-1, and more superficial, multiple, confluent with polygonal outlines mosaic warts associated with HPV-2. Plantar myrmecia warts appear most often between 12 and 15 years of age, but not infrequently also in smaller children. The plantar warts are often contracted at the swimming pools and public baths, and are not associated with defect of cell mediated immunity. The plantar mosaic warts appear mostly in adults, the course is more chronic due to decreased immune responses. Both types differ in pathologic pattern, myrmecia HPV-1 _ induced wart has a highly characteristic histology, while mosaic warts have cytopathic effect of HPV-2.

The treatment of warts depends on their morphology, extent and duration. The treatment modalities are similar for all types of warts, and there is no specific anti-HPV DNA compound. The single warts are eradicated by various destructive procedures, for multiple plane and common warts may be envisaged imiquimod - imidazoquinoline – an immune system modifier for topical application. Although this drug has no direct anti-HPV properties, it upregulates immune responses increasing local levels of interferons, especially interferon alfa, tumor necrosis factor, interleukin 2 and others. The 1% imiquimod cream is applied once daily two- three times a week for two or more months. The therapy might produce mild irritation, however is safe and in many cases proved to be very effective. The limitation of this treatment is a high cost of the product. Therefore in cases of widespread recalcitrant plane warts might be tried immunomodulation with the oral use of cimetidine (30 mg/kg/day) combined with levamisole 2,5 mg/kg on two consecutive days per week. Significant improvement to complete clearance was achieved in 80% patients within 8 weeks. Levamisole, found to increase cell mediated immunity, applied alone did not improve the treatment of warts, however combination with cimetidine was reported as highly effective, safe and not very expensive.

Cutaneous manifestations of HIV infection. Cutaneous infections in HIV/AIDS patients are extremely variable, induced by different microbes, viruses, fungi and protozoa. The infections are more extensive than in immunocompetent population and their course, as well as that of induced autoimmune connective tissue and hematologic disorders, psoriasis and other diseases, much more severe. Characteristic for HIV is Kaposi sarcoma found to be associated with human herpes simplex virus type 8 and present almost exclusively in homosexual AIDS patients (extremely rare in hemophiliacs and females with HIV/AIDS). HSV type 8 was also disclosed in patients with endemic or East-European sarcoma Kaposi without HIV/AIDS, and the latent infection with this virus was not infrequently disclosed in some endemic areas. Lymphoma type B, associated with Epstein-Barr virus, is a more rare complication in AIDS patients. Very frequent in HIV-positive patients occur infections with genital human papillomaviruses of low risk HPV 6-11 inducing condylomata or genital oncogenic HPV-16,18,31 and others associated with anogenital malignancies.

The cutaneous involvement, skin warts and hyperkeratotic lesions, could also be very widespread and resistant to therapy. Worth noticing that combination of antiretroviral drugs, through improvement of the general condition of patients, a decrease in viral load and increase of cell mediated immunity not infrequently produce clearance of HPV-associated warts.

8.1
Molluscum Contagiosum

Synonyms: molluscum sebaceum, dellwarzen
Definition: the molluscum contagiosum is a cutiqueous infectious disease, caused by a DNA virus of the Poxvirus group, characterized clinically by a papular umbilicated lesion.
Distribution: ubiquitous infection, very frequent in children as well as in HIV infected patients. In the latter case it can assume very diffused and large- dimensioned clinical characteristics.
Incubation period: varies from 2 to 8 weeks. In some cases it can reach 3-4 months.
Clinical Features: the lesion manifests itself with small hemispherical reliefs, umbilicated in the centre, of milky white colour, sometimes pink, with a smooth surface and well delimited borders, of variable dimensions from a pinhead to a pea; some forms can reach greater dimensions, longer or pedunculated (in the giant forms). The umbilicated centre is the characteristic that can be observed particularly in the bigger elements. It can manifest itself with only one element, but more often we can observe multiple elements, up to more than ten. Preferred zones are the face, torso and, in adults, the genitals.
Diagnosis: the clinical aspect of the lesion is characteristic and indicative for the diagnosis. If needed, histological examination may be performed.
Differential diagnosis: must be made in confrontation with colloid milia, syringoma, the keratoacanthoma, verruca vulgaris and granuloma pyogenicum.
Histopathology: intracytoplasmic bodies (Patterson corpuscles).
Therapy: in many cases lesions resolve spontaneously within 8 months without scarring. Nevertheless, even if molluscum contagiosum is self-limiting and asymptomatic in healthy individuals, the correct therapeutic decision is crucial, in order to prevent autoinoculation or transmission of the virus via close contact, to relieve symptoms and, sometimes, for cosmetic considerations. The single elements can be removed with the use of a surgical spoon, or by producing an epidermal injury and subsequent desquamation of the molluscum and surrounding uninvolved skin. The treatment should be chosen considering the age and immunocompetence of the patient, and the extent of the areas involved as well. Patients should be advised to avoid swimming pools, communal baths, shared towels, etc., until cleared. Sexual partners should be examined and treated to prevent reinoculation

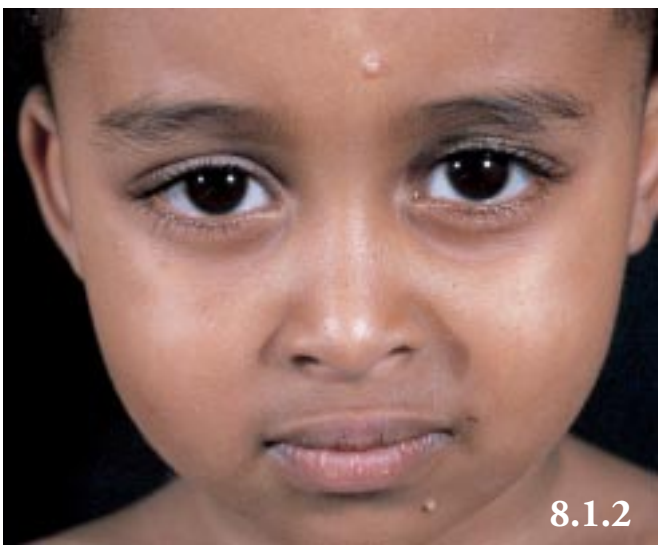
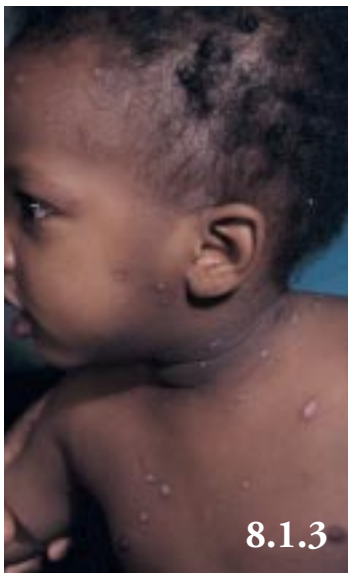


Figure 8.1.1 Molluscum contagiosum in a girl from Eritrea: multiple papulae, hemispheric, of translucent aspect, characteristic umbilicated centre.
Figure 8.1.2 Molluscum contagiosum on the face of a girl from Somalia.



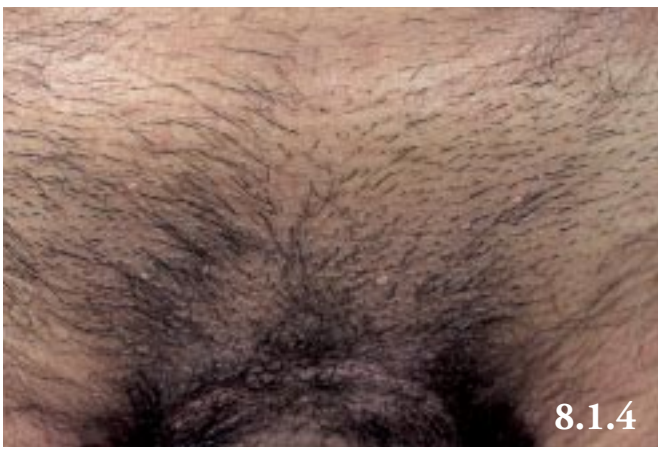


Figure 8.1.3 Molluscum contagiosum on the face of a girl from Zaire.
Figure 8.1.4 Molluscum contagiosum on the pubic area in a man from Morocco.

8.2
Varicella

Synonyms: chickenpox, varicelle, petite vérole volante, windpocken

Definition: a generalized acute viral infection, with sudden onset, caused by the varicella-zoster virus, accompanied by a light general symptomatology and a generalized eruption of cutaneous lesions in different evolutionary phases: blisters, papules, crusts and scars.

Distribution: the disease is universally distributed, very common in childhood, but not rare in adults from the tropical regions.

Incubation period: varies between 14 and 18 days, up to a maximum of 3-4 weeks.

Clinical features: the general symptomatology is usually light, there can be fever associated with a transitory maculated rash, asthenia, headache. The cutaneous lesion appears progressively as a papule, and a blister that can be umbilicated and thus leading to a pustule.

At early stages it is possible to observe crusty lesions as well. The oral mucosa, the cunnus and the conjunctiva can be affected very early on in the disease; the lesions are distributed in a centripetal way. The multiform eruption of the lesions in different sizes and in different evolutionary phases, affecting the head and scalp, is very characteristic.

Itching is usually present and can be very severe. In tropical regions, due to the lack of sufficient hygienic conditions, a secondary bacterial infection is very frequent.

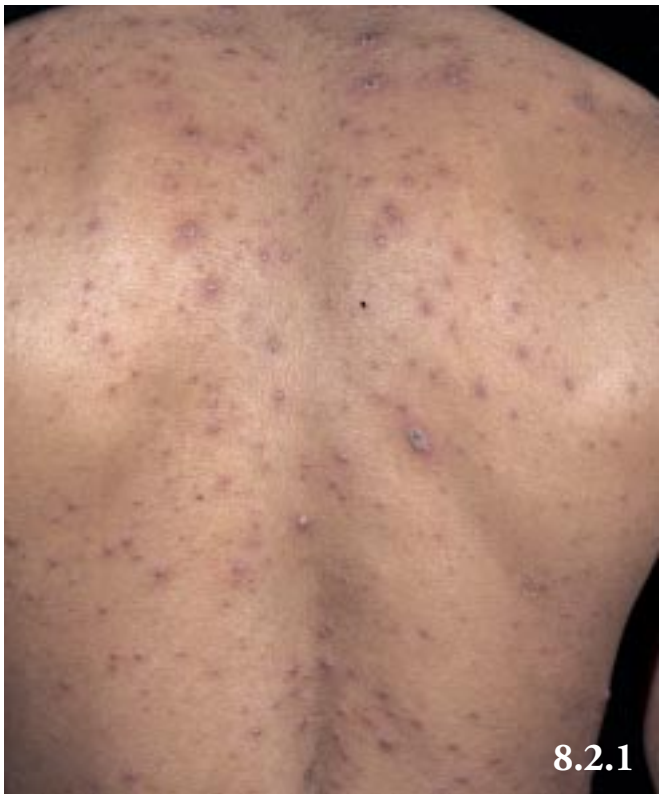
Diagnosis: characteristic appearance of lesions in different evolutionary phases, smear from the floor of the blister, microscopic Giemsa staining examination; isolation of the virus, electronic microscopy, biopsy.

Differential diagnosis: with herpes simplex, disseminated exanthema in secondary syphilis, impetigo, epizoonosis, microbic eczema, multiform drug erythema, hidroa aestivalis and scabies.

Histopathology: intraepidermal blister, acantholysis.

Therapy: the treatment of varicella consists in symptomatic treatment (mainly against pruritus and fever) and aetiologic (antiviral) therapy.

Itching may be alleviated by application of antipruritic lotions, e.g., calamine alone or with 0,25% menthol and/or phenol. Cool water compresses and tepid baking soda baths may also offer relief. Oral antihistamines may be effective in controlling generalized pruritus. Mouth and perineal regions can be treated using saline or 1.5% hydrogen peroxide rinses or compresses. Fever can be controlled by antipyretics, aspirin excluded because of its association with Reye's syndrome. Topical corticosteroids should be avoided in any case. Bacterial superinfections of the skin can be treated using topical antibiotics (mupirocin ointment or bacitracin-polymyxin), while systemic antibiotics should be administered in case the infection is widespread (erithromycin, dicloxacillin or cephalexin). Aetiologic therapy includes several chemotherapeutic agents, mostly nucleoside analogues, that interfere with viral replication thus exerting a virostatic effect but not eradicating viral latency. In cases of disseminated or complicated varicella acyclovir (ACV), a guanosine analogue, is the drug of choice. ACV must be initiated within 24-48 hours of the outbreak of the rash. It may be administered orally



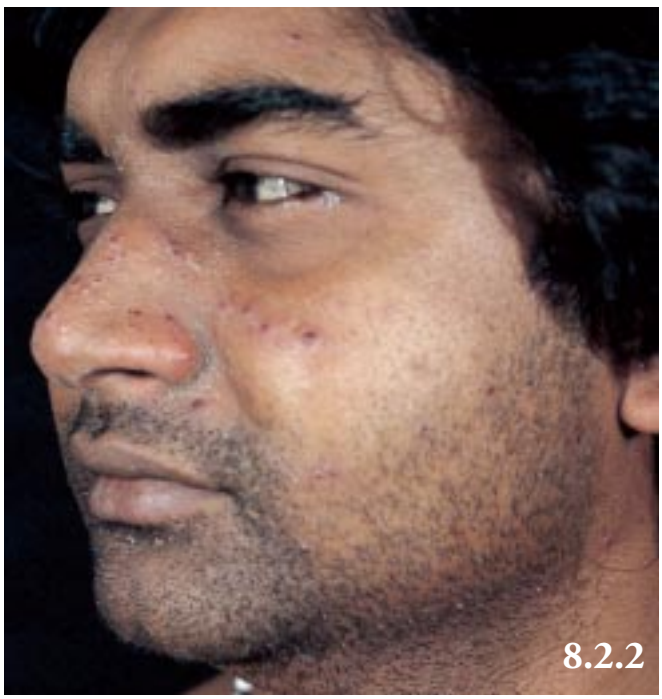


Figure 8.2.1 Chickenpox in Bangladesh immigrant patient: papulo-blistering lesions, with limpid serous content, others with subsequent crusty evolution.
Figure 8.2.2 Chickenpox in young boy from Somalia: characteristic face lesion.

8.2 Varicella

(20mg/kg, maximum 800mg, 4 times a day for 5 days in children, or 800mg, 5 times daily for 5 days in adults), or intravenously (500mg/m2 or 10mg/kg every 8 hours for 8-10 days or until no new lesions have appeared for 48 hours) . Resistance to ACV is very rare among immunocompetent individuals. In case of drug resistance or in immunocompromised patients, the use of Foscarnet (40mg/kg i.v. every 8 hours) is indicated.
Another antiviral drug, Vidarabine, represents a valid but far more toxic alternative to ACV in case of severe varicella (10mg/kg i.v. over 12 hours for 5 days). Human interferon-a (3.5 C 105 U/kg daily for 2 days, followed by 1,75C 105 U/kg daily for 3 days), or infusion of irradiated lymphocytes from healthy donors recovering from VZV infection, have been used with satisfactory results.
Several new antiviral agents have been developed lately, but are still under evaluation. Oral penciclovir (and its prodrug famciclovir) and oral valacyclovir have not been approved yet, while oral sorivudune has proved to be superior to ACV and is administered daily at a dose of 40 mg for 5 days.

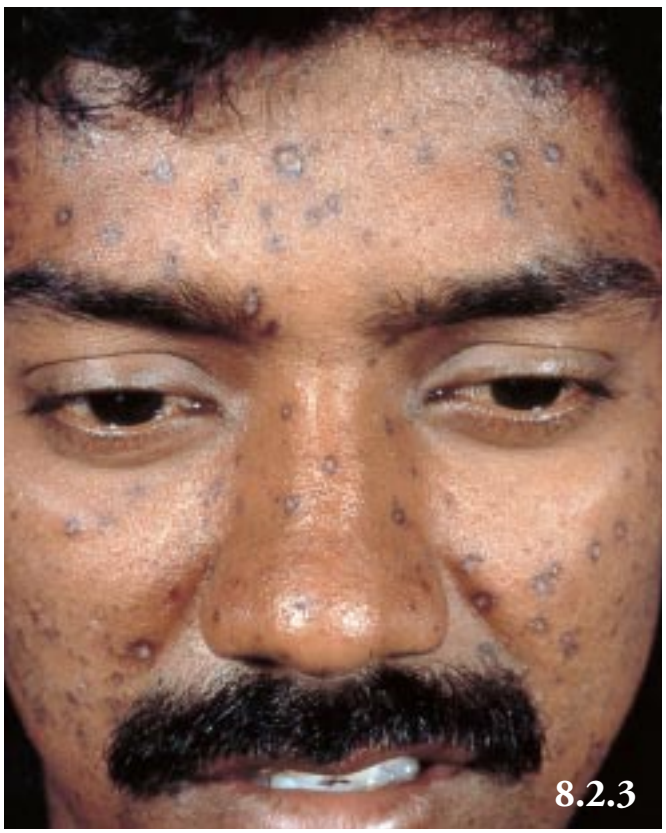


Figure 8.2.3 Chickenpox dyschromic effects in African man.

8.3 Herpes Zoster

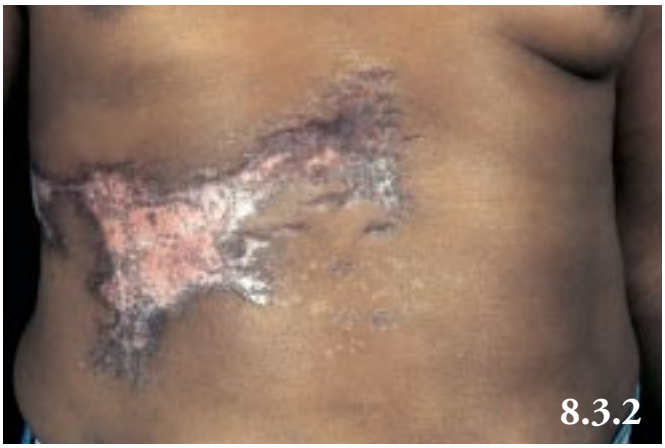
Synonyms: zona, shingles, zoster, gurtelrose.
Definition: herpes zoster is a neuro-cutaneous disease, generated by the varicella-zoster virus (VZV), with an acute inflammation course characterized by a ganglioneuritis, by a vesicular manifestation with a metameric distribution, and by regional adenopathy and neuritic pains. It is believed to be caused by a violent virulence of the silent virus located in the ganglia (back root) after chickenpox.
Distribution: the disease is generally diffused, more frequent in the elderly population, but not rare in childhood. It is generally sporadic, but can present a greater incidence in spring and autumn.
Incubation period: varies from 1 to 3 weeks.
Clinical features: the cutaneous manifestations appear in an acute form and can be preceded by a slight fever, asthenia, indisposition. Initially erythematous patches appear, disposed along the route of a nervous trunk; after a few hours on these patches appear big hemispheric pearly blisters, with a limpid content, disposed in clusters, that in some points are confluent with big phlyctenas. The blisters vary in number from few to many; after a few days, such blisters become dark, and desiccate and turn into yellow-brown crusts. Regional early reactive adenopathy is present, causing slight pain. The zosterian neuritis is characterized by two principal forms of pain: a deep severe pain, involving muscles and ligaments, and a superficial burning pain with great hyperaesthesia of the affected areas. The dermatosis topography coincides with a nervous metamere; the most frequent locations are in the intercostal, loin-groin-femoral, cervical and cephalic regions. Particular interest arises from the cephalic zosters due to the possible serious complications they can provoke, particularly when the ophthalmic area is involved. Different variations of the zoster eruption exist: absence of exanthema (zoster sine herpete), with haematic content (haemorrhagic zoster) and necrotic forms (gangrenous zoster).
Recovery can be observed after 3-4 weeks, usually without scars, which can be present in the necrotic-haemorrhagic forms, in dark-skinned subjects, and particularly in the regions of Central-Africa. In immunodepressed subjects generalized dissemination is possible.
Diagnosis: the pattern is quite characteristic, with the classical symptomatological triad: blistery eruptive lesions, segmental and radicular disposition, neuritic pains; electron microscope observation of the virus, biopsy, and virus cultivation.
Differential diagnosis: has to be made in confrontation with herpes simplex, chickenpox, and in the initial phase, with erysipelas
Histopathology: presence of giant epithelial cells, multinucleated, located at the blister.
Therapy: symptomatic therapy aims at alleviating acute pain and itching and at promoting healing. Cool compresses with tap water, saline solution or Burow's solution seve-

Herpes Zoster

ral times a day may have a soothing, drying effect. Flexible collodion tincture, lotions containing alcohol, menthol and/or phenol, baking soda solutions and calamine lotion may also be beneficial. Olive oil may help in the case of crusted lesions. Warm soaks and topical antibiotics should be applied in the case of secondary infected lesions. Oral antihistamines, e.g. hydroxyzine, may relieve pruritus. Analgesics (e.g. oxycodone with acetaminophen) are often necessary to relieve pain. Topical corticosteroids are contraindicated.

In immunocompetent individuals under 50, only symptomatic measures are necessary. In elderly immunocompetent individuals, oral antivirals should be administered (Acyclovir 800mg 5 times a day for 5-10 days). Immunocompetent and immunocompromised patients of any age with cutaneous dissemination or evidence of visceral or CNS involvement, should receive with no delay antiviral therapy with intravenous ACV (500mg/m2 or 10mg/kg every 8 hours for 7 days or until there is no evidence of VZV replication). Antiviral therapy should also be considered in ophthalmic herpes zoster, due to the increased risk for ocular or CNS complications. Resistance to ACV is very rare; Foscarnet (40mg/kg i.v. every 8 hours) is the drug of choice in this case.

Recently new antiviral drugs have been approved for the treatment of herpes zoster, such as Valacyclovir (1g 3 times a day for 7 days), Famciclovir (500mg 3 times a day for 7 days, starting within 72 hours of the onset of the rash), with satisfactory results and minor side effects. Experimental treatments with Vidarabine (10mg/kg over 12 hours for 7 days), human interferon-a (1,7or 1,5 U/kg per day for 7 days) and Soriduvine have shown good results but high toxicity. One of the major problems in patients with herpes zoster is the management of the postherpetic neuralgia (PHN). Once instituted, PHN is refractory to treatment. Emotional support and various therapeutic modalities with encouraging results are crucial for improving the patient's quality of life. Carbamazepine, an antiepileptic drug, is particularky effective for shooting pain. Neurosurgical intervention (rhizotomy or surgical separation of pain fibers) should be considered for patients with intolerable pain.



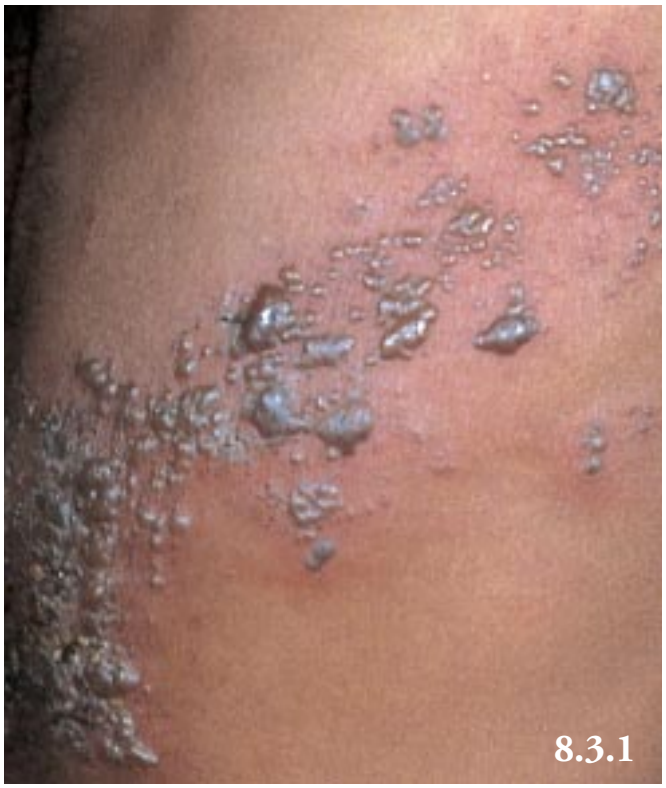


Figure 8.3.1 Herpes zoster in patient from Uganda: clear erythematous-blistering lesion, in "clusters" in a metameric torso disposition.

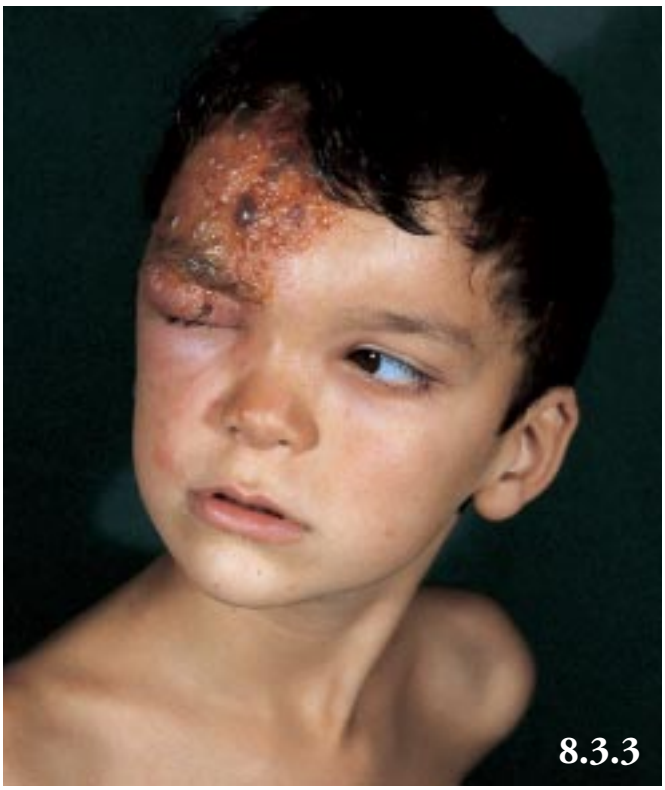


Figure 8.3.2 Torso-abdominal herpes zoster, in an Indian female patient with a clear keloid reaction.
Figure 8.3.3 Trigeminal herpes zoster in an immigrant child.

8.4

Herpes simplex

Synonyms: herpes febrilis, herpetic fever, fever blister, cold sore, herpes, fieberblashen.
Definition: herpes simplex is an erythemato-vesicular dermatitis, with an acute course, and with a characteristic cluster formation of the blister lesion.
It is caused by the herpes virus, of which two varieties are known: type 1 that causes lip herpes, and type 2 that causes genital herpes.
Distribution: universal; genital herpes is more common in adolescents and young adults, while lip herpes is diffused in all age groups.
Incubation period: can vary from 2 to 8 days, but most frequently between 3 and 5 days.
Clinical features: initial contact with the organism leads to the appearance of acute lesions, (gingivostomatitis, balanoposthitis, vulvovaginitis). The virus is located in the sensitive ganglia from where, as a result of immunodepression and consequent virulence episodes, it transfers to the cutis and mucous membranes. The appearance of the eruption is usually preceded by a burning or localized painful feeling, subsequently a turgid, erythemato-oedematous patch appears, on which blisters with a serous content, in variable dimensions and number, rapidly come up in clusters. The lip and genital regions are the most frequently affected areas, but any body part can be involved. Precipitating factors may include: fever, sun exposure, mechanical irritation, and gastrointestinal problems. The type 1 virus is responsible for eruptions in the mouth, on the lips, and on the top part of the body; type 2 causes genital lesions, lesions in the gluteal region, and, by inoculation, on the hands and feet. Herpes can be episodic, but more often is recurrent, with differently distanced crises, but always localized in the same areas (herpes recidivans in loco). Lip herpes is the most frequent and commonly recurrent clinical form. When the blisters are localized to the mouth, to the face, mucous linings, lips, gums and tongue, the herpetic stomatitis clinical pattern manifests itself. In patients with atopic eczema, often recurrent in the first year of life, the herpes simplex virus can determine a blister-pustulous dermatitis with severe evolution, better known as varicelliform Kaposi eruption. In genital herpes, because of the fast breaking of the blisters, we can observe small round superficial erosions, isolated and confluent, with a tendency to form clusters with polycyclic borders.
Diagnosis: anamnesis and characteristic clinical manifestations, isolation of the virus, and serology for Ig G and Ig M, biopsy.
Differential diagnosis: herpes zoster, chickenpox, herpetiform dermatitis, gingivostomatitis, medicine polymorph erythema .
Histopathology: intraepidermic blister, "ballooning degeneration", numerous leucocytes, and some giant cells at the base of the lesion.
Therapy: primary HSV-1 and 2 infection in immunocompetent adults should be treated with oral aciclovir, 400mg, 5 times a day for 7 days. Any serious disseminated complications, eczema herpeticum included, should be treated in hospital. Initial administration of acyclovir (5mg/kg 3 times a day for 5-7 days), must be followed by oral administration of the new antiviral drugs valaciclovir or famciclovir, until new lesion formation ceases. Local application of acyclovir or 5-ioduridina can be useful, if performed in the initial stages of symptomatology, in case of HSV-1 recurrent disease. Nevertheless systemic treatment seems to be so far the most effective, being suitable for treating multifocal external, as well as intraoral lesions, avoiding viral shedding and virus transmission by saliva. Treatment must be initiated by the patient no later than 1-2 hours after the first prodromal warning sign. The recovery takes usually 5-7 days, without scars. The first episode of HSV-

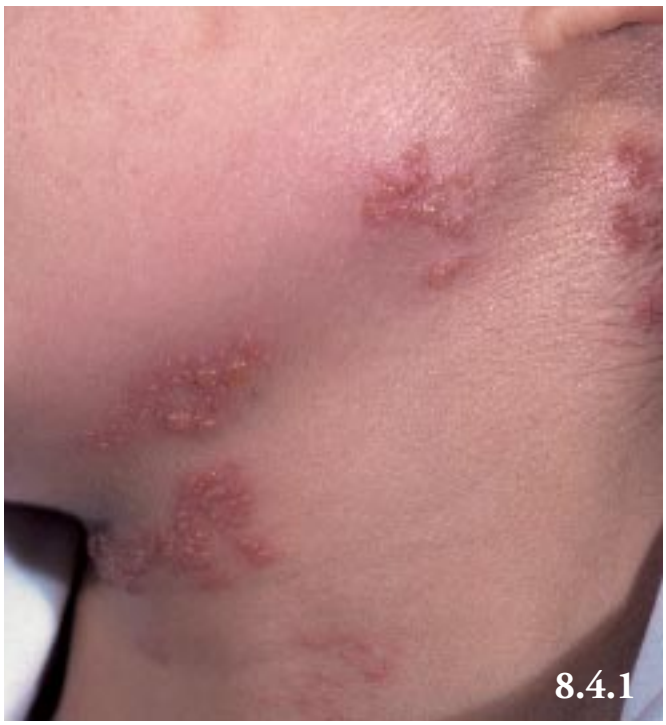


Figure 8.4.1 Herpes simplex in female child from Iran: blistery lesions unified in clusters, on an erythematous basis.

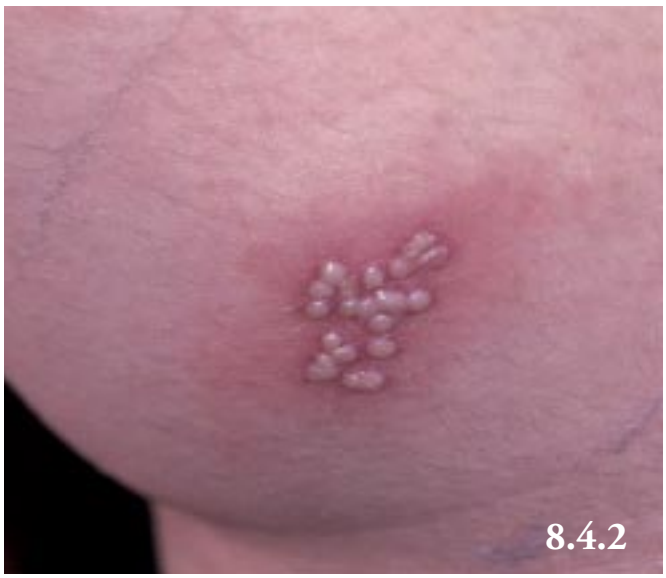
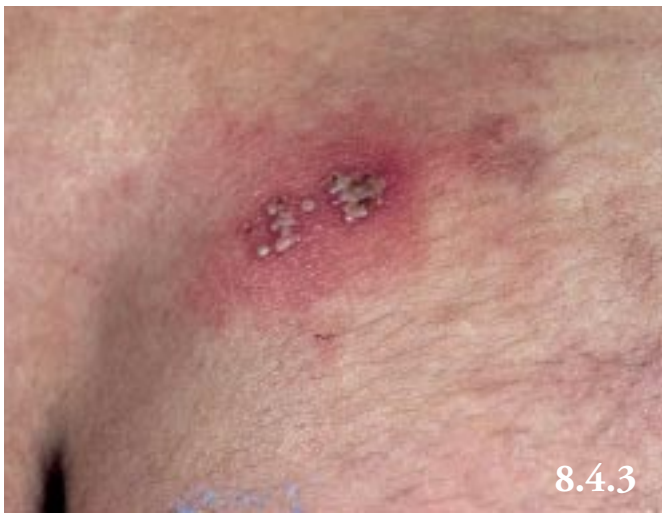


Figure 8.4.2 Blistery lesions by herpes simplex in an African female.

8.4 Herpes simplex

2 infection needs to be promptly treated with oral acyclovir, 200mg, 5 times a day for 10 days. In recurent infections, oral acyclovir offers relative benefit (200mg a day for 5 days), only if taken no later than 48 hours after the onset of symptoms. Because of the increasing resistance to acyclovir, two new antiviral drugs have been introduced (valaciclovir and famciclovir) which are absorbed better and have longer bioavailability.

In HIV-positive subjects we can observe ulcer lesions, with scars. The Kaposi's varicelliform eruption requires hospitalization for the numerous ocular, lung and meningeal complications, and the treatment with systemic antiviral drugs.



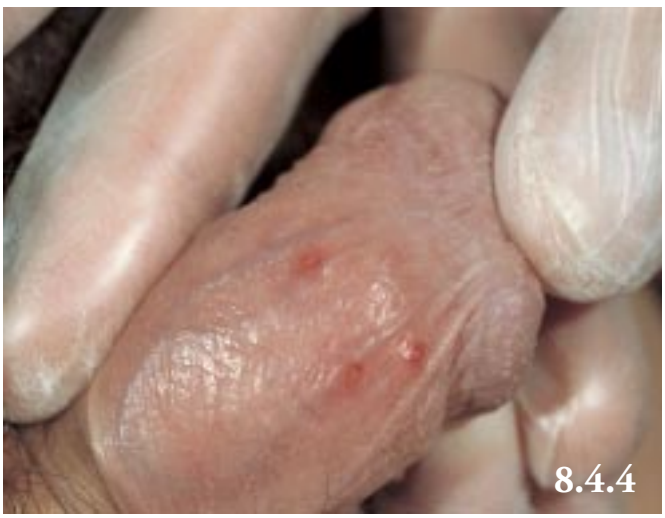


Figure 8.4.3 Herpes simplex: cluster disposition of the blisters.
Figure 8.4.4 Mucous lesions from herpes simplex.

8.5 Flat Warts

Synonyms: verruca plana juvenilis, flat warts, verrugas planas, verrues planes juveniles, Flachwarzen.
Definition: benign papules, autoinoculable, that develop especially in children and young adults. The aetiologic agent belongs to the papillomavirus group, HPV (serotype 3, 10).
Distribution: the dermatosis is diffused all over the world, without any kind of predilection of place.
Incubation period: extremely variable, from a few weeks to many months.
Pattern: the papules can appear isolated or unified. Sometimes they are disposed along cutaneous linear or punctiform excoriations of traumatic origin, revealing an isomorphic irritation effect phenomenon (Koebner's phenomenon). Flat warts usually affect children, but can be observed as well in adults, particularly in females. Clinically they appear as papular flat elements, 3-4 mm in diameter, slightly elevated and thus made visible on the surrounding skin, but neatly delimited, with a smooth surface, of pinky or yellow-brownish colour. They are usually rounded, oval or irregular polygons.
The papules, very numerous (up to hundreds of elements), can be isolated or disseminated. The papules appear in relief, small, of the same colour as the skin, localized principally on the face, particularly on the cheeks, on the forehead, in the areas around the mouth, the chin, and on the back of the hands; rarely they are localized on the wrists and on the knees. Generally they are not accompanied by subjective disturbance, the onset is slow (although we can occasionally observe a sudden appearance) and the course is chronic, often with spontaneous regression. Occasionally they can be disseminated on the extremities. The lesions can appear isolated, unified, or follow a linear direction mainly caused by scratching, like the isomorphic irritation effect phenomenon (Koebner's phenomenon). In general subjective symptoms such as itching and pain are absent.

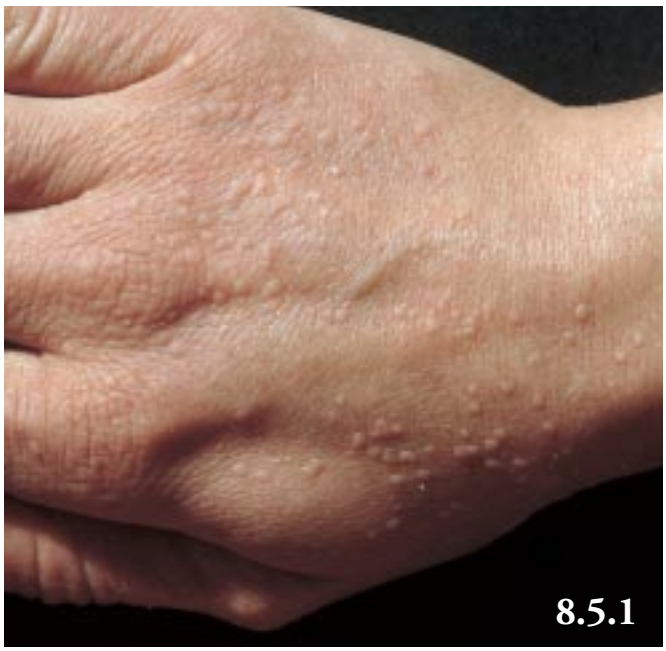


Figure 8.5.1. Flat warts on the back of the hand: small papules in slight relief, with smooth surface.

8.5 Flat Warts

Diagnosis: clinical manifestations are sufficiently typical to perform diagnosis; biopsy and histological examination.
Differential diagnosis: the differential diagnosis has to be made in confrontation with lichen ruber planus, in which the papules are localized on the flexor surface of the wrist and forearms, on the trunk and on the oral mucous membrane: they have polygonal forms, reddish-purple colour, neater margins and a tougher consistency.
Sometimes the flat wart has to be differentiated from the epidermic cyst, or from the Pringle adenoma sebaceum or the tuberous sclerosis. Flat warts also have to be distinguished from lichen nitidus, colloid milia and syringoma.
Histopathology: numerous vacuolated (koilocytes) cells can be seen in the prickle cell layer.
Therapy: often a spontaneous resolution of the pattern is observed. Cryotherapy or a slight localized electrocoagulation can provide good results. Topical retinoids are also often used for flat warts. An excessively destructive method should be avoided as it may be a risk, particularly in the dark-skinned population, for hypertrophic or keloid scars. Hypnosis and autosuggestion have also been proposed.

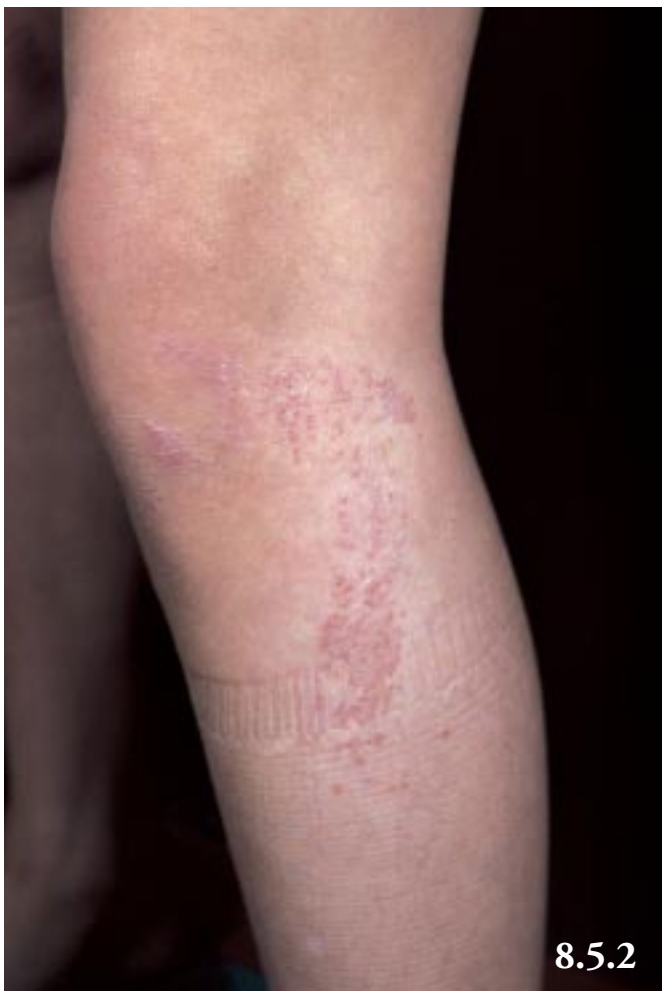


Figure 8.5.2. Flat warts in an unusual location, in a girl from Ethiopia.

8.6 Common wart (verruca vulgaris)

Synonyms: hard wart, verrugas vulgares, skin papilloma, verrues vulgaires.
Definition: warts are papular epidermic reliefs, moderately contagious, benign, autoinoculable. The aetiologic agent is a virus of the papillomavirus group, HPV (serotypes most frequently 2, 6).
Distribution. the dermatosis is ubiquitous and very common.
Incubation period: extremely variable, from a few weeks to many months.
Clinical features: at the beginning, warts manifest themselves as small smooth papular reliefs, pink, irregularly rounded or oval, that appear on normal skin. After a few weeks they grow progressively until reaching the size of a small nut, making new epidermic formations salient and well localized, with a variable colour from greyish-pink to yellowish-brown, and of hard consistency. The dermatosis remains isolated, even for several months. However, often enough, because of autoinoculation of the virus, the warts multiply to dozens or, less commonly, to hundreds. Because of the unifications of viral colonies, sometimes we can observe the formation of large verrucous plaques, with typical characteristics difficult to diagnose at a superficial observation. The areas most frequently involved are the dorsum of the hands and fingers, more rarely the palm and subungual surface. Also the face, scalp, lips, legs and eyelids can be involved, and more often in children elbows and knees. Usually they are not accompanied by a subjective relevant symptomatology. The course is chronic and recurrent; occasionally, especially in the case of only one or just a few viral units, we can observe a spontaneous regression. In other cases, we observe continuous recurrences, in spite of repeated abscissions. Complications are very rare. There can be pyogenic superimposition, with the formation of small abscess groups. In the periungual region, very painful fissures can be formed.
Diagnosis: usually the diagnosis is not difficult; a biopsy can be useful in unclear cases.

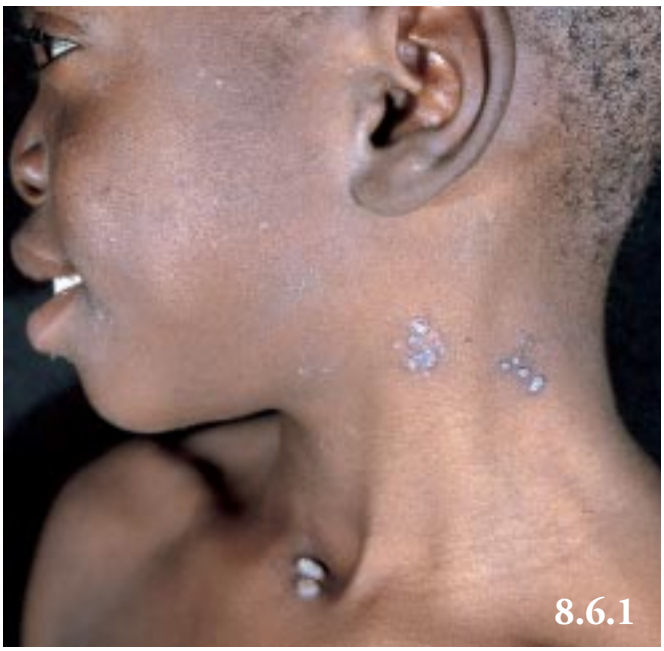
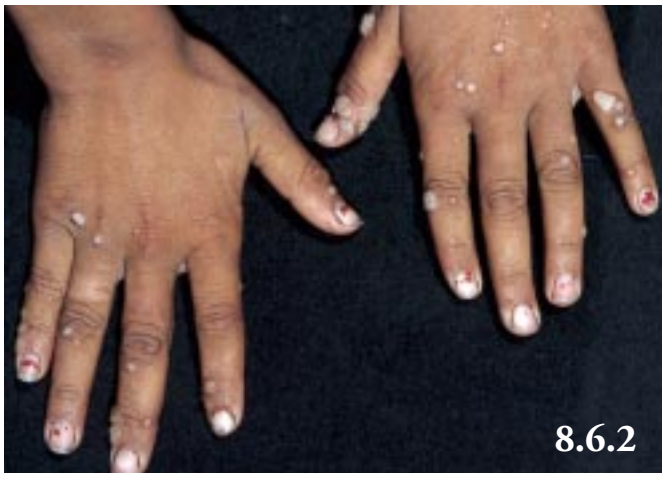


Figure 8.6.1 Common warts in child from Eritrea.

8.6

Common wart (verruca vulgaris)

Differential diagnosis: in the lesion localized on the palms, differential diagnosis must exclude papular secondary syphilis and keratotic elements. The palm and plantar keratoma in small elements (keratoma dissipatum) is distinguished from the verruca vulgaris because it is hereditary and appears in childhood. In the single lesions, which are large and inflamed, present with secondary pyogenic infection, differential diagnosis needs to be made with wart tuberculosis. Finally, it has to be differentiated from Darier's disease, molluscum contagiosum, keratoacanthoma, verrucous lichen and cutaneous corns.
Histopathology: slight parakeratosis, acanthosis, koilocytosis, papillomatosis.
Therapy: spontaneous resolution is possible. Cryotherapy and electrocoagulation are the methods of choice. Podophyllin, phenol and silver nitrate can be used for small lesions. For multiple warts, a topical treatment (keratolytic, vesicant or cytotoxic agent) can be used, sometimes in association with an oral immunomodulatory agent. Cimetidine has been reported to be an effective monotherapy in children. An excessively destructive method must be absolutely avoided given the risk, frequent in dark-skinned people, of hypertrophic or keloid scars formation.



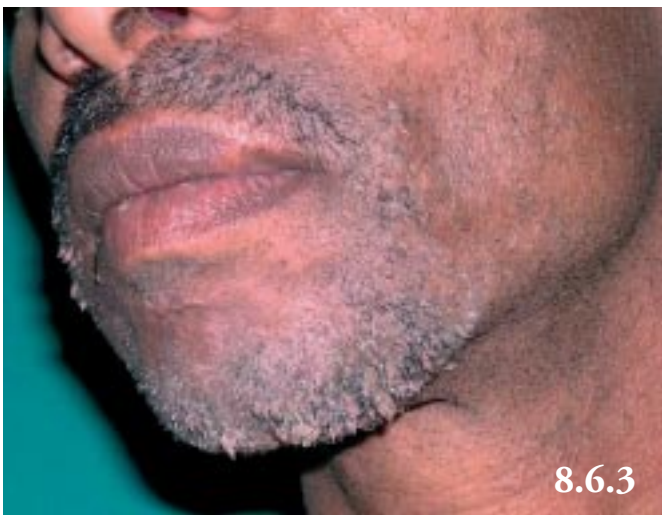


Figure 8.6.2 Warts on the back of the hands of a Serb gypsy woman.
Figure 8.6.3 Filiform warts in a patient from Bangladesh.

8.7

Plantar warts

Synonyms: papilloma of the sole, verrugas plantares, verrues plantarires, Dornwaezen.
Definition: plantar warts are lesions of viral aetiology. Unlike other forms of warts, they can cause considerable pain. The aetiologic agent is the papillomavirus, HPV (prevalently serotype 1).
Distribution: very common with generalized distribution.
Clinical features: a particular morphological aspect can be observed depending on the exact location. On the sole of the foot, in fact, they are under continuous pressure and, instead of proliferating on the surface, they proliferate internally. In this way they can determine plug formations that are able to reach plantar aponeurosis (endophytic development). They are usually located, in particular, on the calcaneum, on the first toe, and in correspondence of the fourth and fifth metatarsus.
Clinically they appear like keratotic flat lesions, of variable dimensions, with a rounded centre part, grey, rough, disseminated with small black dots. The surrounding skin has a normal appearance. They can appear as single or as several units.
The fusion of more plantar warts can lead to the formation of large-sized verrucous plaques (mosaic warts). The pressure on the centre of the wart generates low or intense pain, and can lead to walking difficulties. The plantar warts generally involve adult subjects, but can also be observed in children. Spontaneous regression, although rare, is possible.
Diagnosis: clinical manifestations are very suggestive for the diagnosis; biopsy can be performed in unclear cases.
Differential diagnosis: with the plantar keratoderma (corn), from which the warts are differentiated by a hyperkeratotic edge, and an irregular surface, often disseminated with little black dots. Also it is necessary to differentiate the dystroph-

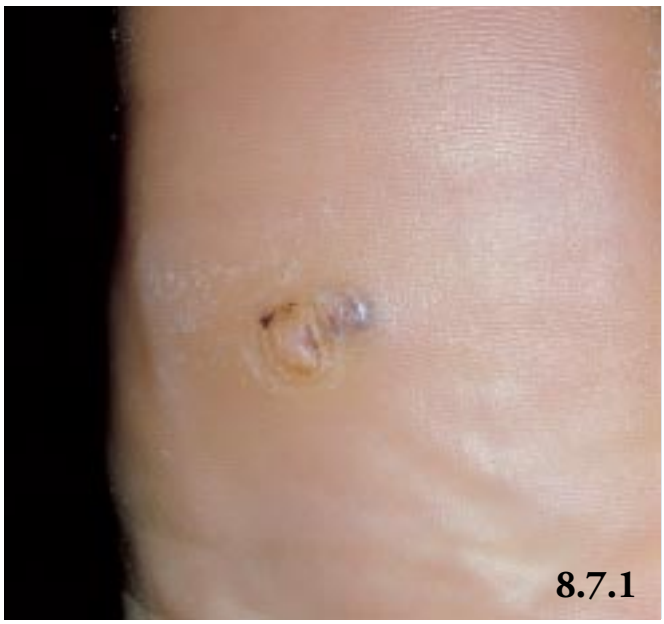
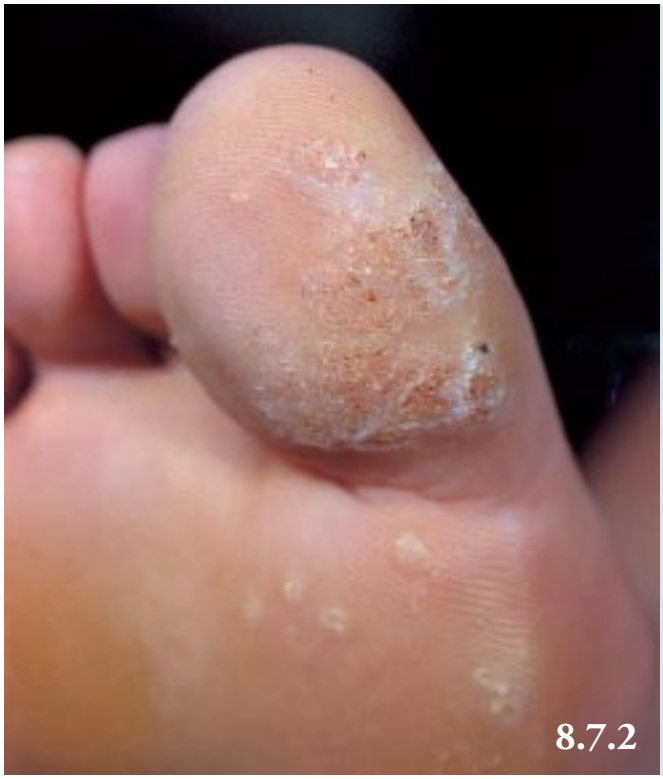


Figure 8.7.1 Plantar wart: endophytic rounded lesion, with a keratotic black dotted surface, corresponding to capillary thrombosis, and corneous collarette.

8.7 Plantar warts

ic lesion from compression or systemic pathologies (diabetes and vasculopathies), and from the foreign body granuloma, particularly the ones generated by sea urchins.
Therapy: cryotherapy with liquid nitrogen or electrocoagulation are the chosen treatments. The application of salicylic creams at 10-20 per cent can be useful too.



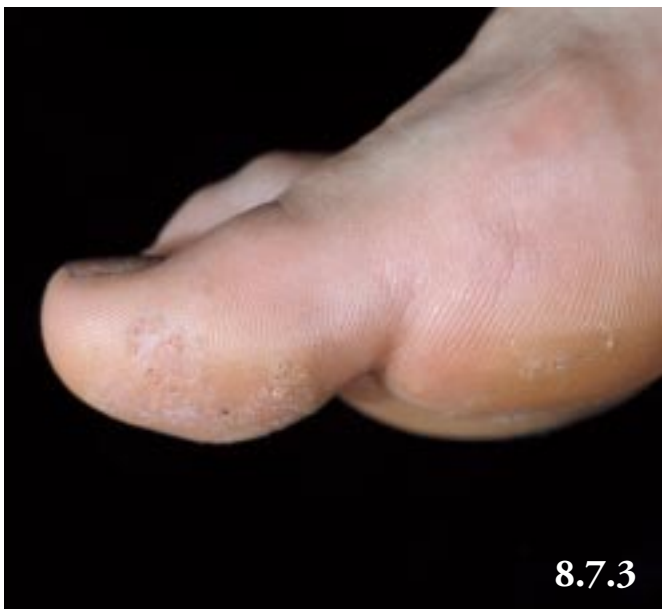


Figure 8.7.2 Plantar mosaic wart.
Figure 8.7.3 Diffused plantar warts.

8.8 Cutaneous manifestations from HIV infections.

Synonyms: Acquired immunodeficiency syndrome, AIDS, syndrome de immunodeficencia adquerida, syndrome de l'immunodeficience acquise, SIDA, erworbene Immunscheache durch, HIV infection.
Definition: AIDS is a multisystemic disease with a high mortality rate. The aetiologic agent is the human immunodeficiency virus (HIV).
The immunodepression state in AIDS causes the onset of opportunistic infectious agents of viral, bacterial, protozoan and fungal nature, and in particular of tumours such as Kaposi's sarcoma and the non-Hodgkin's lymphomas.
Distribution: the infection and the disease are generalized with a dramatic spread in the less developed countries, particularly in the sub-Sahara region, where the number of people infected is more than 20 million. At the end of 1998, according to WHO data, at least 30 million people were infected with HIV or had developed AIDS; in Botswana and Zimbabwe one person out of every four is infected. The infection affects drug addicts, in particular those who have acquired the virus via needle sharing, and is also transmitted through sexual intercourse. According to the WHO and UNAIDS, 16,000 new HIV-infected cases are registered in the world every day.
Incubation period: very variable, from months to years.
Clinical features: cutaneous manifestations from HIV

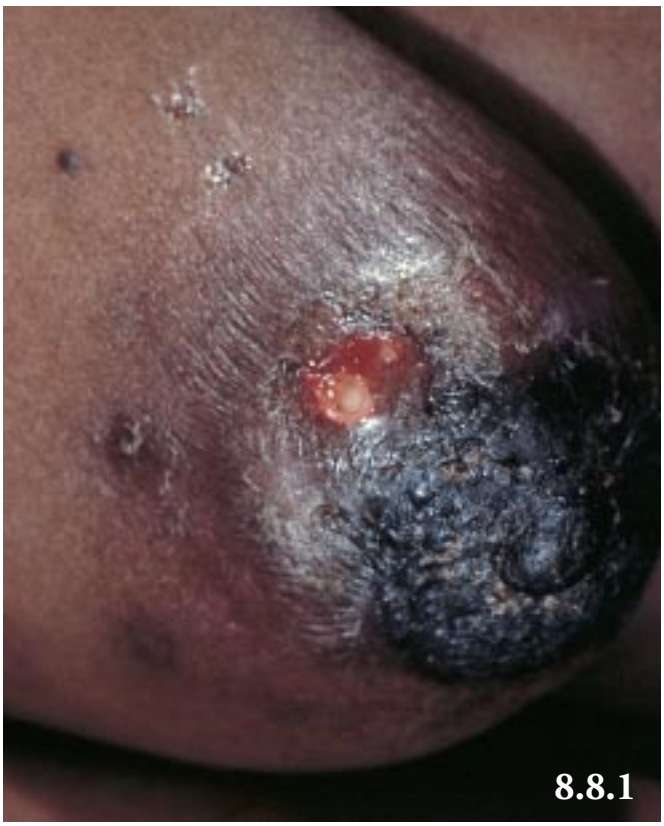
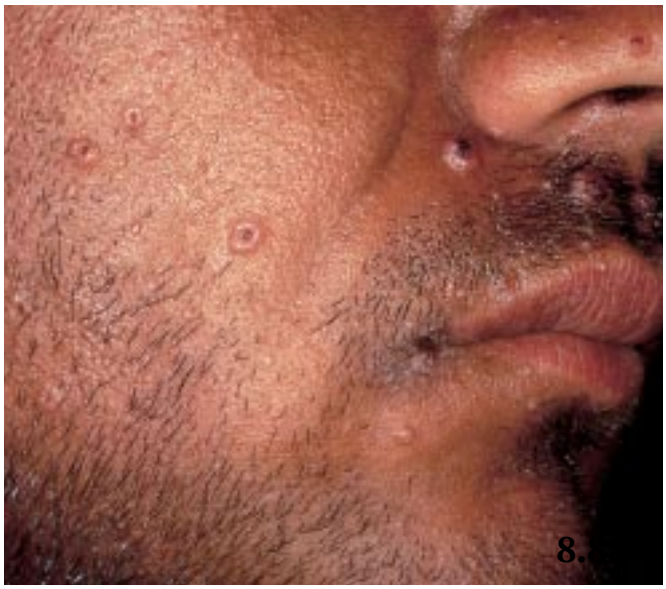


Figure 8.8.1 Unusual localization of primary syphilis in HIV-positive woman.

Cutaneous manifestations from HIV infections

infection are very varied; we can observe opportunistic or infectious diseases, malignant cutaneous neoplasias, vascular and non malignant hyperproliferative dermatoses, cutaneous dystrophic-carential manifestations .
The dermatosis in HIV-positive subjects appears to be usually more diffused and resistant to therapy.
Diagnosis: diagnosis is determined when HIV test is performed.
Differential diagnosis: non-HIV positive cutaneous infections, such as atopic dermatitis, seborrhoeic dermatitis, herpes, and epidermomycosis, should be taken into consideration.
Therapy: the new anti-retroviral and protease inhibitor drugs seem to improve the course and the prognosis of the infection. The nucleoside reverse-transcriptase inhibitors (NRTI), such as zidovudine (AZT, ZDV), were the first drugs approved for treating HIV-infected individuals. Nevertheless, ZDV monotherapy demonstrated modest clinical benefits because of the creation of more virulent HIV strains (due to incomplete viral suppression), and the development of resistance. For that reason, it is commonly used in combination with another antiretroviral agent, i.e. proteinase inhibitors (saquinavir, ritonavir, indinavir) or non-nucleoside reverse transcriptase inhibitors (nevirapine, delavirdine, loviride). The combination of antiretroviral drugs offers a better clinical benefit but implies various toxic effects including CNS toxicity, diabetes mellitus, drug reactions (including the Steven-Johnson syndrome if the drug is not discontinued). These observations underline the necessity for careful monitoring of all patients undergoing multiple antiretroviral therapy. For cutaneous lesions the treatment is similar to the non-HIV manifestations.



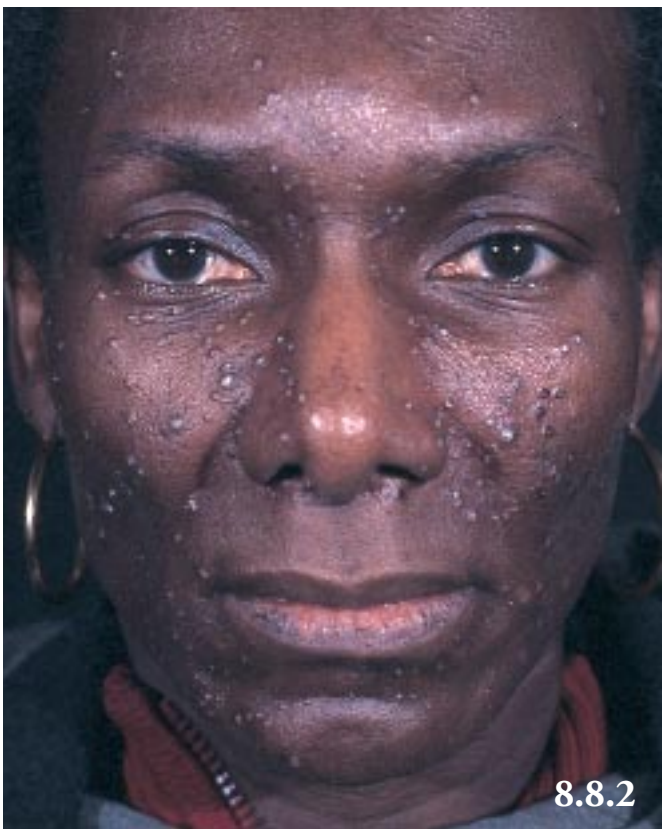


Figure 8.8.2 Multiple lesions of Cutaneous cryptococcosis in HIV-positive patient from Morocco.

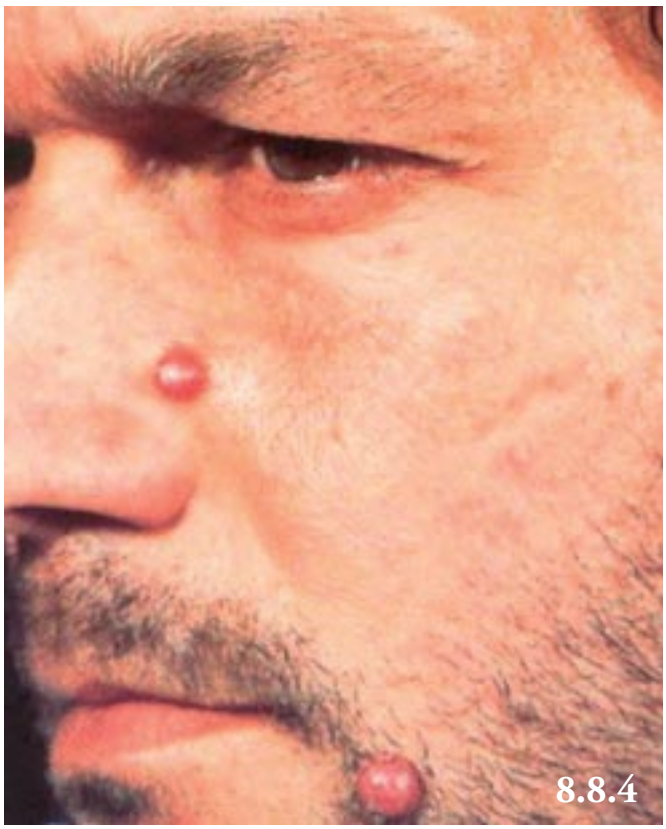
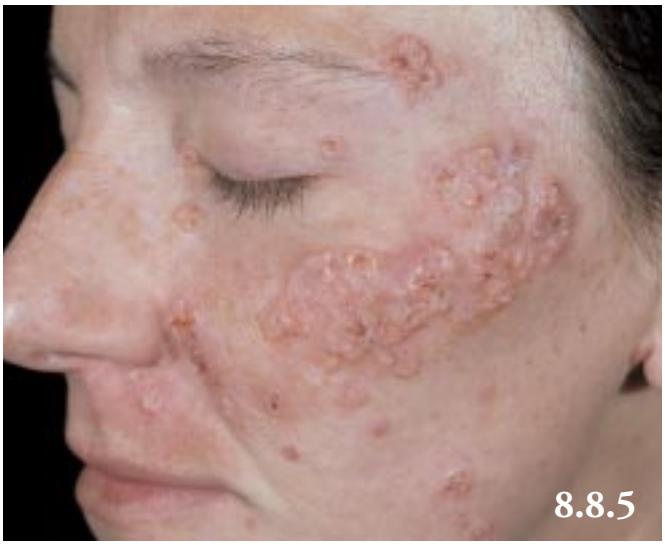
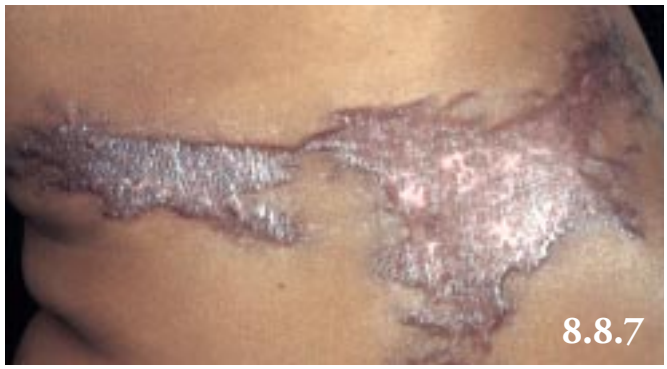
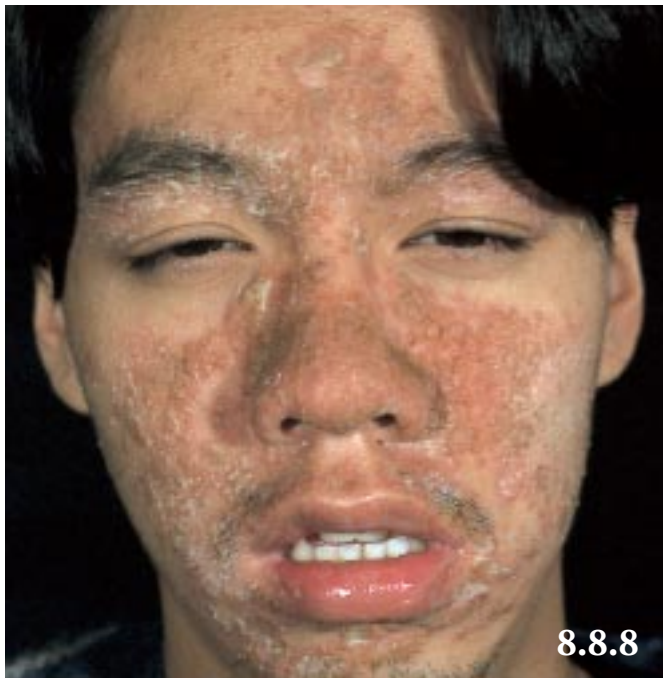


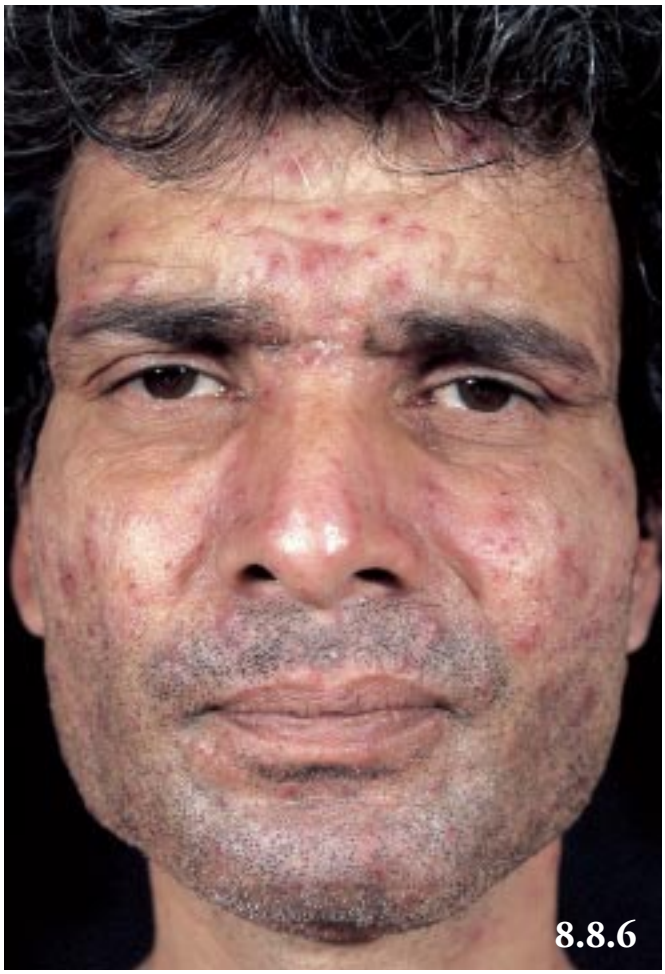
Figure 8.8.3 Cutaneous cryptococcosis with umbilicated aspect in HIV-positive boy from Morocco.
Figure 8.8.4 Kaposi in HIV-positive patient: face nodular lesion.

Cutaneous manifestations from HIV infections









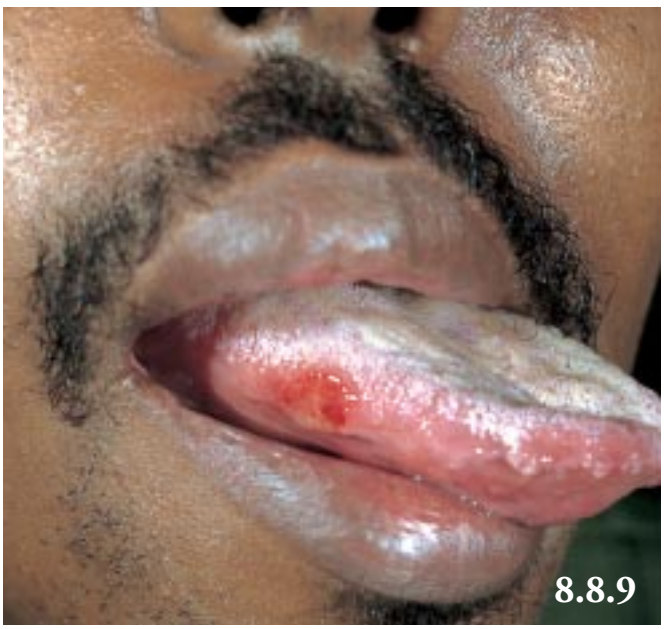


Figure 8.8.5 Molluscum contagiosum diffused and coalescent in plaques on the face of HIV-positive girl from Egypt.
Figure 8.8.6 Chickenpox with severe manifestations in HIV-positive man from Bangladesh.
Figure 8.8.7 Herpes Zoster with keloidal reaction.

Figure 8.8.8 Herpes simplex impetiginized and eczematized on the face of HIV-positive boy from China.
Figure 8.8.9 Recurrent aphthosis of the tongue in HIV-positive subject from Ethiopia.

8

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