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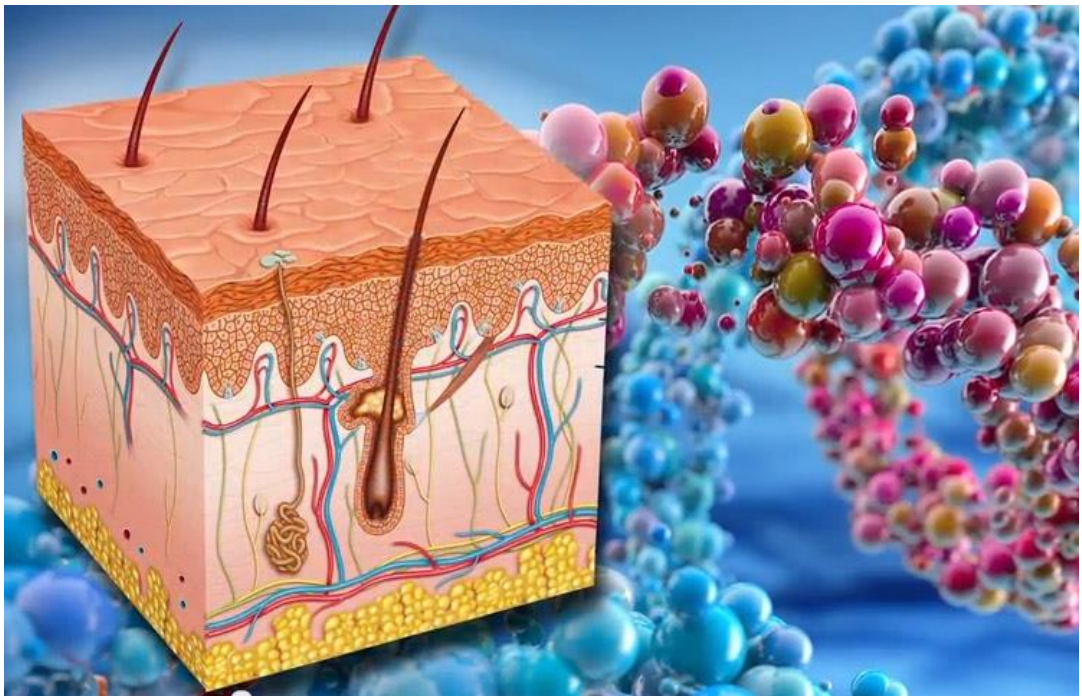

KAFOLAT TAFAKKUR

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THE MINISTRY OF HEALTH CARE OF REPUBLIC OF UZBEKISTAN

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THE DEPARTMENT OF DERMATOLOGY AND VENEREOLOGY

ADKHAMJON PAKIRDINOV

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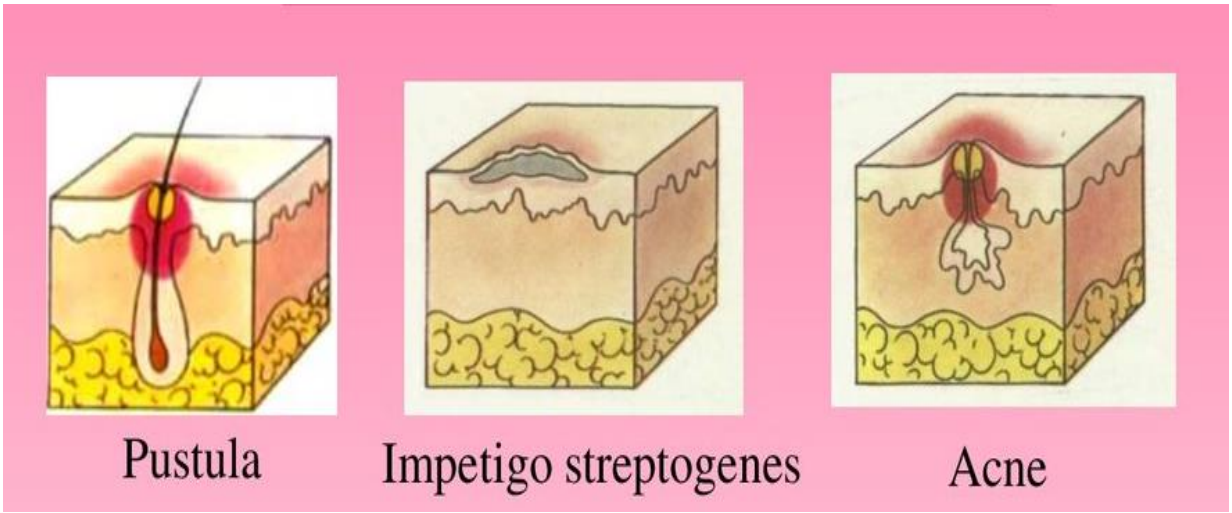
(FOR RESIDENTS, CLINICAL INTERNS, TREATMENT AND PEDIATRICS STUDENTS)



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LICHEN PLANUS.

Lichen planus

Lichen planus (LP) is a pruritic, inflammatory disease of the skin, mucous membranes, and hair follicles. It occurs throughout the world, in all races. It is a common disorder, comprising more than 0.5% of all dermatological visits. It may be familial in 1-2% of cases. The pattern of LP detected and the age distribution vary among various genetic and geographic groups. In persons of European descent, it appears largely after the age of 20, and peaks between 40 and 70 years. Very few cases appear after age 80. Childhood LP typically accounts for 5% or less of cases. However, in some regions, childhood cases are responsible for more than 10% of all LP cases. These areas include the Indian subcontinent, Arab countries, and Mexico. Race appears to be the critical factor, since in the UK 80% of childhood LP is seen in Indians.

The primary lesions of LP are characteristic, almost patho- gnomonic, small, violaceous, flat-topped, polygonal papules (Fig. 1). The color of the lesions initially is erythematous. Well-developed lesions are violaceous, and resolving lesions are often hyperpigmented, especially in persons of color. The surface is glistening and dry, with scant, adherent scales. On the surface, gray or white puncta or streaks (Wickham striae) cross the lesions. Dermoscopy may enhance the visualization of this critical diagnostic element. Lesions begin as pinpoint papules and expand to 0.5-1.5 cm plaques. Infrequently, larger lesions are seen. There is a predilection for the flexor wrists, trunk, medial thighs, shins, dorsal hands, and glans penis (Fig. 2). The face is only rarely involved, and when it is, lesions are usually confined to the eyelids and/or lips. The palms and soles may be affected with small papules or hyperkeratotic plaques (Fig. 3). Certain morphologic patterns favour certain locations, e.g. annular lesions favoring the penis (Fig. 4), and keratotic lesions favoring the anterior shins. The Koebner phenomenon occurs in LP.

Pruritus is often prominent in LP. The pruritus may precede the appearance of the skin lesions, and, as with scabies, the intensity of the itch may seem out of proportion to the amount of skin disease. It may be almost intolerable in acute cases.

Most patients react to the itching of LP by rubbing rather than scratching, and consequently scratch marks are usually not present.

The natural history of LP is highly variable and dependent on the site of involvement and the clinical pattern. Two-thirds of patients with skin lesions will have LP for less than 1 year and many patients spontaneously clear in the second year. Mucous membrane disease is much more chronic. Recurrences are common.

Nail changes are present in approximately 5-10% of patients. Involvement of the nail can occur as an initial manifestation, especially in children. Longitudinal ridging and splitting are most common. Onycholysis may be present and the lunula may be red. Involvement of the entire matrix may lead to obliteration of the whole nail plate (idiopathic atrophy of the nail). Yellow nail syndrome may be simulated by LP of the nails. Pterygium formation is very characteristic of LP of the nails (Fig. 5). The nail matrix is destroyed by the inflammation and replaced by fibrosis. The proximal nailfold fuses with the proximal portion of the nailbed. LP may be a cause of some cases of twenty-nail dystrophy of childhood. Twenty-nail dystrophy in the absence of periungual lesions or pterygium formation usually resolves spontaneously

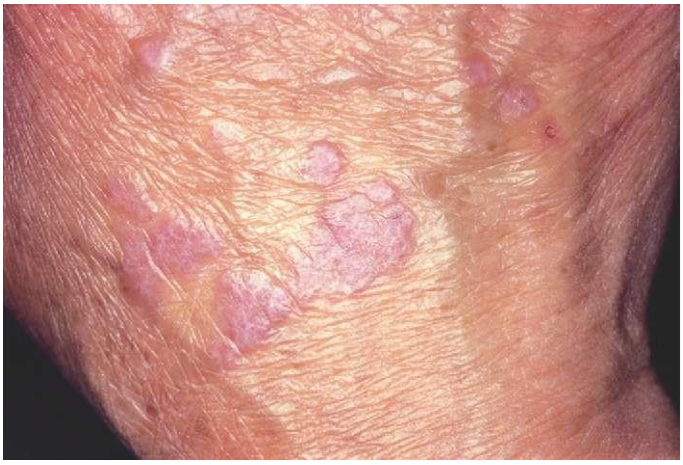


Fig. 1 Lichen planus, violaceous, flat-topped papules with minimal scale.

and frequently in these cases, no other stigmata of cutaneous or mucosal LP are found. Rarely, nailbed LP can result in onychopapilloma, a localized distal subungual hyperkeratosis.

Involvement of the genitalia, with or without lesions at other sites, is common. On the glans or shaft of the penis the lesions may consist of flat, polygonal papules, or these may be annular. Erosive LP can occur on the glans. Simultaneous involvement of the gingival and penile mucosa may occur. On the labia and anus similar lesions are observed; they are generally whitish, owing to maceration. In the vulvovaginal areas, erosive or ulcerative disease is common and may coexist with typical reticulate lesions. Vulval splitting may be caused by LP.

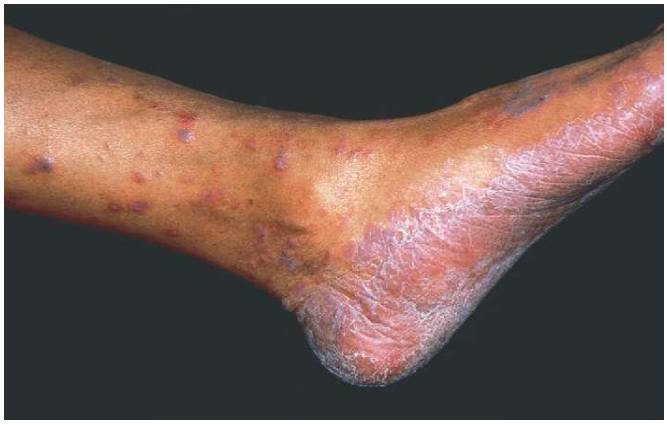


Fig. 3 Lichen planus of the soles.

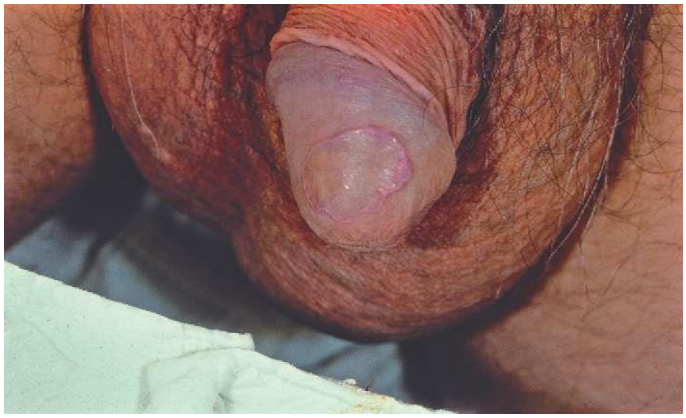


Fig. 4 Annular lichen planus of the penis.

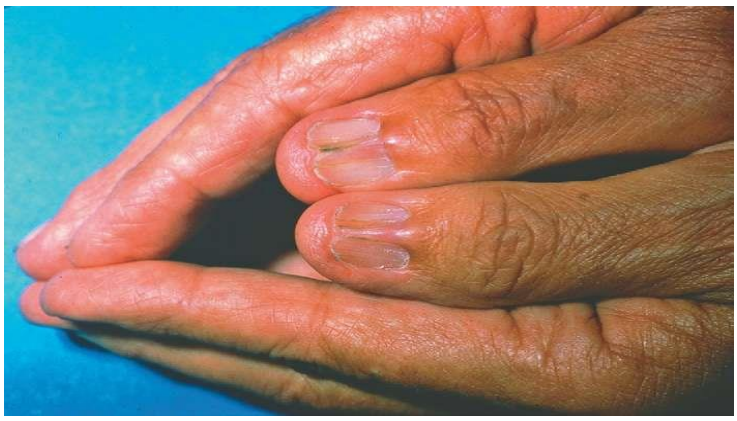


Fig. 5 Lichen planus, nail involvement with pterygium.

Conjunctival involvement is a very rare complication of LP. It occurs in patients with oral and gingival involvement. Cicatrization and subepithelial scarring can occur, as well as keratitis. It may closely simulate mucous membrane pemphigoid. Routine histology and direct immunofluorescence (DIF) may be required to confirm the diagnosis.

LP of the esophagus is increasingly being recognized, but still occurs in only 1% of cases of LP. The diagnosis is frequently delayed. Dysphagia, odynophagia, and weight loss are typical manifestations. The mid-esophagus is primarily affected. Virtually all the patients have coexistent oral disease. Esophageal involvement is much more common in women with vulvovaginal and oral disease, in whom 15% develop esophageal lesions. Stricture formation occurs in 80% of esophageal LP and may require frequent dilatations. Esophageal squamous cell carcinoma may complicate esopha- geal LP, suggesting that, once this diagnosis is made, routine gastrointestinal evaluation is required.

There are many clinical variants of LP. Whether these represent separate diseases or part of the LP spectrum is unknown. They all demonstrate typical LP histologically. They are described separately, since their clinical features are distinct from classic LP. Some patients with these clinical variants may have typical skin lesions of classic LP as well. The more common or better-known variants are described below.

Linear lichen planus

Small linear lesions caused by the Koebner phenomenon often occur in classic LP. Limitation of LP to one band or streak has also been described in less than 1% of patients, except in Japan, where up to 10% of reported cases are linear. Although originally described as following dermatomes (zosteriform), the lesions actually follow lines of Blaschko. It is more common in children, but also occurs in adults. Papules with varying degrees of overlying hyperkeratosis, or simple hyperpigmentation may be the presenting manifestations. There are often skip areas of normal skin between the individual lesions.

Annular/annular atrophic lichen planus

Men represent 90% of patients with annular LP. Lesions with this configuration favour the axilla, penis/scrotum, and groin. LP lesions of the mucosae, scalp, and nails are rare in patients with annular LP. Patients usually have fewer than 10 lesions. Most patients with annular LP are asymptomatic. The ringed lesions are composed of small papules and measure about 1 cm in diameter. Central hyperpigmentation may be the dominant feature. They may coalesce to form polycyclic figures. Annular lesions may also result from central involution of flat papules or plaques, forming lesions with violaceous, elevated borders and central hyperpigmented macules.

Hypertrophic lichen planus (lichen planus verrucosus)

Hypertrophic LP occurs most commonly on the shins, although it may be situated anywhere. The typical lesions are verrucous plaques with variable amounts of scale. At the edges of the plaques, small, flat-topped, polygonal papules may at times be discovered. Superficial inspection of the lesion often suggests psoriasis or a keratinocytic neoplasm rather than LP, but the typical appearance resembling rapidly cooled igneous rock (igneous rock sign) may be useful in suspecting LP over keratinocytic neoplasms. The lesions are of variable size, but are frequently several centimeters in diameter

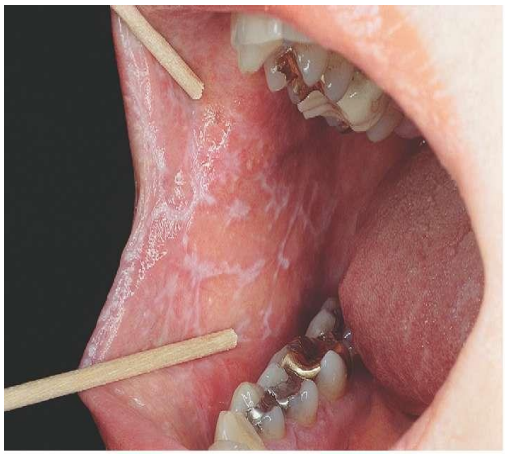
and larger than the lesions of classic LP. The anterior lower leg below the knee is the sole area of involvement in the majority of patients. Clinical diagnosis may be difficult and biopsy is often required. Histologically, the pseudoepitheliomatous keratinocyte hyper- plasia may be marked, leading to the erroneous diagnosis of squamous cell carcinoma. True squamous cell carcinoma may also evolve from longstanding hypertrophic LP, and over 50% of cutaneous squamous cell carcinoma arising in LP occurs below the knee in lesions of hypertrophic LP. In addition, keratoacanthoma-like proliferations may occur in lesions of hypertrophic LP. This has also been called "hypertrophic lichen planus-like reactions combined with infundibulocystic hyperplasia." Hypertrophic LP is chronic and often refractory to topical therapy. Hypertrophic lupus erythematosus resembles hypertrophic LP both clinically and histologically. Hypertrophic lupus tends to affect the distal extremities, face, and scalp. The finding of continuous granular immunoglobu- lin on DIF strongly suggests a diagnosis of hypertrophic lupus erythematosus rather than LP.

Ulcerative/mucosal lichen planus

Ulcerative LP is rare on the skin but common on the mucous membranes. Typical skin lesions of LP rarely ulcerate. A rare ulcerative variant of cutaneous LP, or lupus erythematosus/ LP overlap syndrome, affects the feet and toes, causing bullae, ulcerations, and permanent loss of the toenails. These chronic ulcerations on the feet are painful and disabling. Cicatricial alopecia may be present on the scalp and the buccal mucosa may also be affected. Skin grafting of the soles has produced successful results.

Oral mucosal LP is the most common form of mucosal LP, and it is usually chronic. Between 10 and 15% of patients with oral LP will also have skin lesions. Women represent 75% of patients with oral LP. Oral LP in women begins 10 years later than in men (57 years vs 47 years). Oral lesions may be reticulate (reticular)

(Fig. 6), erythematous (atrophic), or ulcera- tive (erosive). The most common pattern in oral LP is the ulcerative form (40% of patients). Usually, reticulate and erythematous lesions are found adjacent to the ulcerative areas. The erythematous pattern is the predominant pattern in 37% of patients, but almost always reticulate lesions are also seen in these patients. In oral LP the "classic" reticulate lesions are most prominent in 23% of patients. Symptoms are least common in patients with reticulate lesions; 23% are symptomatic and then only when the tongue is involved. All patients with erosive lesions are symptomatic, usually with burning or pain. Patients may simultaneously have several patterns, so patients are characterized by the primary form they exhibit. Lesions appear on any portion of the mouth, and multisite involvement is common. The buccal mucosa is involved in 90%, the gingiva in more than half, and the tongue in about 40%. On the gingiva, LP may produce desquamative gingivitis (Fig. 7). Oral LP may involve any portion of the mouth. The buccal mucosa is involved in 90% of cases, and the gingiva in more than 50%. Gingival involvement is particularly hard to diagnose, and often requires biopsy for both histology and DIF to confirm the diagnosis and exclude autoimmune causes of desquamative gingivitis. Gingival involvement is associated with accelerated gingival recession and aggressive management of oral hygiene, and control of candidal overgrowth is critical in the management of oral LP patients. Mechanical injury from dental procedures and poor-fitting appliances, as well as increased plaque from an inability to clean teeth due to pain, may trigger or exacerbate gingival LP. On the tongue and palate, lesions are often mistaken for leukoplakia (Fig. 8). The lower lip is involved in 15% of oral LP patients, but the upper lip in only 2%. Oral LP is stable but chronic, with less than 3% of patients having a spontaneous remission in an average 5-year follow-up. Aggressive oral hygiene plays an important role in the management of gingival LP.



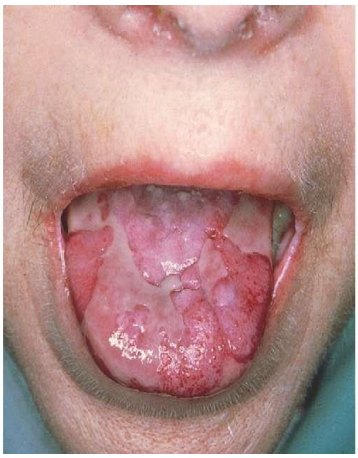


Fig. 6. Lichen planus reticulate white Lesions of the buccal mucosa

Fig. 8. Lichen planus of the tongue

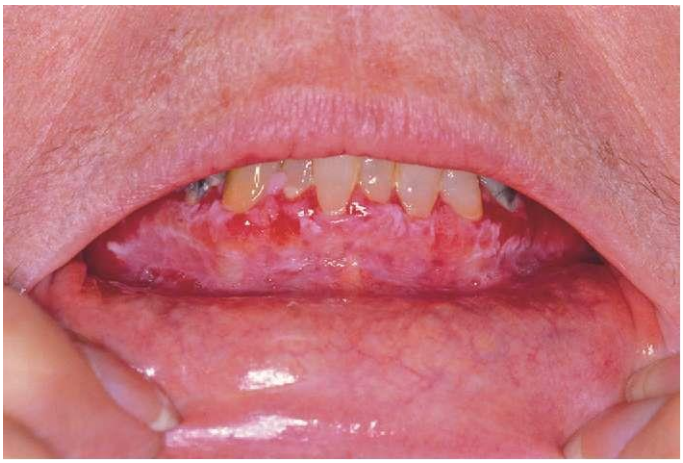


Fig. 7 Desquamative gingivitis secondary to lichen planus.

Mercury, gold, cobalt, indium, manganese, chromate, nickel, or palladium sensitivity may be found by patch testing in up to 60-75% of patients with oral LP or oral lichenoid reactions. In patients with positive patch tests to metals, these tests appear relevant in at least 44% of patients, and removal of the offending amalgam leads to improvement of the oral lichenoid process in 60-100% of patch test-positive patients (more than 60% of patients who did not remove their amalgam also improved). Patch testing, however, may not identify all patients whose oral lichenoid lesions improve with removal of the oral metal. Neither can histopathological evaluation

identify the metal-induced patients. This has made the role of metals in the induction of oral lichenoid lesions and oral LP very controversial. Rarely, patients with metal sensitivity will also have skin and nail lesions that improve with removal of the oral metal. Metal sensitivity as a cause of an oral lichenoid reaction should be considered, especially in those patients whose oral involvement is directly adjacent to amalgam fillings. If patch testing is positive for amalgam or metals, removal of the amalgam should be considered. Oral lichenoid reactions to cinnamates and spearmint have also been reported.

Involvement of the vulva and vagina with LP, along with the gingiva, has been called the vulvovaginal-gingival (VVG) syndrome. Although all three of these mucous membranes may be involved, only one or two sites may be involved at any one time. The prevalence of erosive vulvar LP has been underappreciated until recently, simply because many women with LP will not volunteer their vulvovaginal complaints unless specifically asked. Women affected with vulvar LP have vulvar pain or burning. Vulvar LP produces lesions very similar to oral lichen planus, with erythema, leukokeratosis, and erosion. Surrounding the red or eroded lesions is a narrow rim of white reticulation. This rim is the most fruitful area to biopsy in order to confirm the diagnosis. Scarring (Fig. 9) of the vagina and vulva with adhesions, vestibular bands, and atrophy of the labia minora or prepuce occurs, making the morphology similar to vulvar lichen sclerosus. In one-third, typical reticulate buccal LP is seen, and in up to 80% the oral mucosa is also involved. Cutaneous lesions occur in between 20% and 40% of VVG patients. The course of the vulvovaginal syndrome is protracted and patients frequently have sequelae, including chronic pain, dyspareunia, and even scarring of the conjunctiva, urethra, and oral, laryngeal, pharyngeal, and esophageal mucosae. Nails are involved in about 15% of patients with VVG (as compared to only 2% of patients with oral

LP). The VVG syndrome is now considered to be a separate subgroup of mucosal LP that is particularly disabling, scarring, and refractory to therapy.

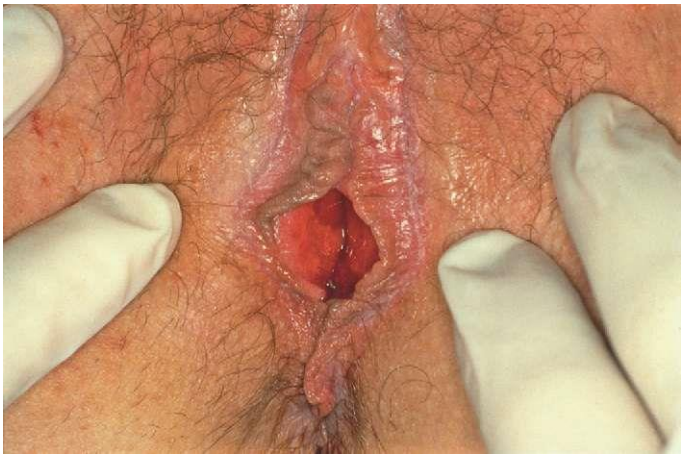


Fig. 9 Scarring and erosions in the vulvovaginal-gingival syndrome.

While the pathogenesis of LP is unknown, there is evidence that erosive LP of the vulva (and lichen sclerosus) may have an autoimmune basis. A personal and family history of autoimmune disorders (usually thyroid disease) is present in up to 30% of patients with vulvar LP, and up to 40% have circulating autoantibodies. The prevalence of autoimmune phenomena is NOT increased in patients with classic cutaneous LP. The autoantibodies do not appear to be pathogenic, as the disease seems to be caused by cytotoxic T cells. Erosive LP has significant impact on quality of life, and patients with erosive LP have high levels of depression, anxiety, and stress.

Cancer risk and lichen planus

Rare cases of squamous cell carcinoma of the skin occurring on the lower leg in lesions of hypertrophic LP have been reported. There is no statistical increase in cutaneous or visceral carcinoma in patients with cutaneous LP, and cutaneous LP alone is not considered to be a condition with increased cancer risk. Oral and vulvovaginal LP does appear, however, to increase the risk of developing squamous cell carcinoma. Between 0.4%

and 5% (on average about 1-2%) of patients with oral LP will develop oral squamous cell carcinoma. Squamous cell carcinoma only occurs in patients with ery- thematous or ulcerative LP, not in patients with only the reticulate pattern. Of the oral LP patients who develop oral squamous cell carcinomas, about 45% have only one cancer. The majority develop multiple cancers, and close vigilance is recommended in these patients. LP patients with erosive penile and vaginal disease also have developed squamous cell carcinoma. The number of penile cases is too low to determine the frequency of this consequence, but in the case of vulvar LP, the frequency of development of SCC may be as high as 3%. Clinicians should have a low threshold to biopsy fixed erosive or leukokeratotic lesions in patients with mucosal LP. The use of oral and topical calcineurin inhibitors for LP has been associated with the appearance of squamous cell carcinoma on the genitalia. There is no evidence that the medications caused the neoplasia, but if these agents are used, regular follow-up and careful examination are required.

Hepatitis-associated lichen planus

Three liver conditions have been associated with LP: hepatitis C virus (HCV), HBV immunization, and primary biliary cirrhosis. HCV infection was found in proportionately more patients with LP than in controls in 20 of 25 studies. The prevalence of HCV infection in patients with LP varies from 1.6% to 20%. There is an association with the human leukocyte antigen (HLA)-DR6 allele. The association of HCV infection and LP has been questioned. In a large series of patients with oral LP from the US, none of the 195 patients was infected with HCV, while 29% of patients with oral LP from Italy had HCV. Twenty percent of patients infected with HCV in Scotland had oral LP, as compared to 1% of seronegative patients. Although the data are conflicting, screening for HCV appears appropriate in persons from a geographic region or population in which HCV infection is commonly associated with LP. The clinical features of LP in patients with hepatitis C infection are identical to classic LP, but LP patients with HCV infection are reported as being more likely to have erosive mucous membrane

disease. The existence of underlying hepatitis cannot be predicted by clinical pattern or the results of liver function tests. Treatment of hepatitis C with interferon-a may be associated with the initial appearance of LP or exacerbation of preexisting LP. LP may occur at the sites of interferon injections, and skin testing may reproduce LP-like lesions. LP may improve or not change with interferon and ribavirin treatment for hepatitis C. Improvement is usually seen towards the end of the treatment course. Most patients do not completely clear their LP. The HCV genome is not found in lesions of LP associated with HCV infection.

HBV immunization may be associated with the appearance of LP in both children and adults. More than 30 cases have been reported. Lesions are typical of LP and the oral mucosa may be affected. Most typically, the first lesions of LP appear about 1 month after the second dose of vaccine. Lesions typically resolve after some time.

Primary biliary cirrhosis and LP may coexist. Patients with this liver abnormality, in addition, have a marked propensity to develop a lichenoid eruption while on d-penicillamine therapy. Xanthomas in patients with primary biliary cirrhosis may appear initially in lesions of LP, and the infiltrate, while lichenoid, may contain xanthomatous cells. Primary sclerosing cholangitis has been associated with oral LP in at least five patients.

Bullous lichen planus

Two forms of LP may be accompanied by bullae. In classic LP, usually on the lower extremities, individual lesions will vesic- ulate centrally (Fig. 10). This represents macroscopic exaggeration of the subepidermal space formed by the lichenoid interface reaction destroying the basal keratinocytes. These lesions often spontaneously resolve.

Lichen planus pemphigoides describes a rare subset of patients who usually have typical LP, then develop blistering on their LP lesions and on normal skin. Less commonly, the blistering antedates the LP. Clinically, they appear to be a combination of LP and bullous pemphigoid.

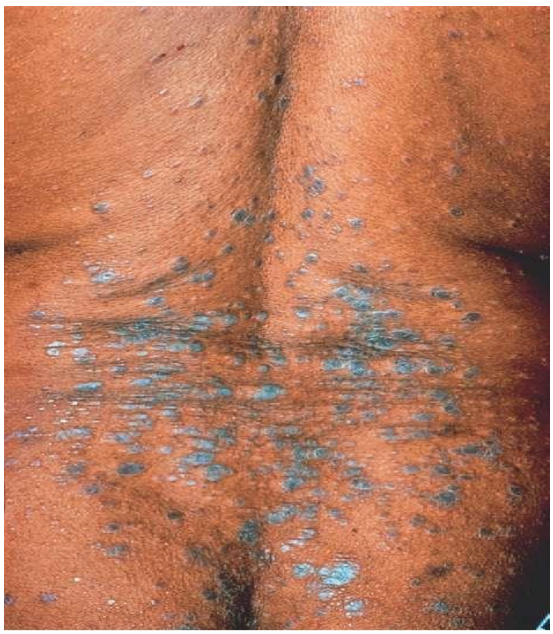


Fig. 10 Generalized lichen planus.

Oral disease may occur and resemble either LP or mucous membrane pemphi- goid. Lichen planus pemphigoides has been triggered by medications and PUVA. Pruritus may be severe and lesions may evolve to resemble pemphigoid nodularis. Bullous pem- phigoid affects an older age group than lichen planus pemphi- goides (typical onset for lichen planus pemphigoides is between age 30 and 50). Histologically, the LP lesions show LP and the bullous lesions show the features of bullous pem- phigoid. DIF is positive in a linear pattern, with IgG and C3 along the basement membrane zone, at the roof of saline split skin. The antigen targeted by the autoantibody in lichen planus pemphigoides is located in the same region as the bullous pemphigoid antigen (at the basal hemidesmosome). Antibodies from patients with lichen planus pemphigoides typically bind the 180 kD bullous pemphigoid antigen, but in a different region from bullous pemphigoid sera. Lichen planus pemphi- goides tends to follow a benign and chronic course, even when compared to bullous pemphigoid. Treatment is similar to bullous pemphigoid, with potent topical steroids, systemic steroids, tetracycline, nicotinamide, intravenous immunoglob- ulin, and immunosuppressives all being variably effective.

Pathogenesis and histology

LP is characterized by an immunologic reaction mediated by T cells. These cells induce keratinocytes to undergo apoptosis by an unknown mechanism. Recently, there have been reports of insulin resistance and frank type 2 diabetes mellitus being increased in patients with LP compared to controls.

Lichen planus pemphigoides is hypothesized to result from exposure to the immune system of epitopes in the BP180 antigen as keratinocytes are destroyed by the lichenoid inflammation. Epitope spreading can occur, and lichen planus pemphigoides patients may also have autoantibodies to the same epitopes as bullous pemphigoid patients.

The histologic features of LP are distinctive and vary with the stage of the lesion. In early lesions there is an interface dermatitis along the dermoepidermal junction. As the lesion evolves, the epidermis takes on a characteristic appearance. There is destruction of the basal layer with a "saw-tooth" pattern of epidermal hyperplasia, orthokeratosis, and beaded hypergranulosis. The basal cells are lost, so the basal layer is described as "squamatized." In the superficial dermis there is a dense, bandlike infiltrate composed of lymphocytes and melanophages. "Civatte bodies" (cytoid bodies, colloid bodies) represent necrotic keratinocytes in the superficial dermis. Hypertrophic LP shows marked epidermal hyperplasia (pseudoepitheliomatous hyperplasia). Old lesions of LP show effacement of the rete ridge pattern, melanophages in the upper dermis, and occasional Civatte bodies. LP rarely demonstrates parakeratosis or eosinophils. The presence of either of these suggests a different cause of lichenoid tissue reaction, such as lichenoid drug eruption.

Lichen planopilaris, frontal fibrosing alopecia, and Graham- Little-Piccardi-Lassueur syndrome show the findings of LP, centered on the superficial follicular epithelium. On DIF, clumps of IgM, and less frequently IgA, IgG, and C3, are commonly present subepidermally, corresponding to the colloid bodies. Dense shaggy staining for fibrinogen along the basement membrane zone is characteristic of LP. A

lichenoid drug eruption may be difficult to differentiate from LP. The presence of eosinophils or parakeratosis supports the diagnosis of lichenoid drug eruption. Although LP virtually never has eosi- nophils or parakeratosis, they are not universally present in other lichenoid eruptions such as lichenoid drug eruption. Graft versus host disease tends to have a sparser infiltrate. Hypertrophic lupus may be histologically identical to LP, and the diagnosis is best made by clinical correlation and DIF. In most other forms of lupus erythematosus, there is a greater tendency for epidermal atrophy with parakeratosis, dermal mucin is found, and follicular plugging is more prominent. The infiltrate in lupus tends to surround and involve deep portions of the appendageal structures, such as the follicular isthmus and eccrine coil. Deep nodular perivascular lympho- plasmacytic infiltrates and necrosis of the fat lobule with fibrin or hyalin rings are also findings characteristic of lupus erythematosus.

Differential diagnosis

Classic LP displays lesions that are so characteristic that clinical examination is often adequate to lead to suspicion of the diagnosis. Lichenoid drug eruptions may be difficult to distinguish. A lichenoid drug reaction should be suspected if the eruption is photodistributed, scaly but not hypertrophic, and confluent or widespread—clinical features that are unusual for idiopathic LP. The presence of oral mucosa involvement may prompt suspicion of LP, but oral lesions may occasionally occur in lichenoid drug eruptions as well. Pityriasis rosea, guttate psoriasis, the small papular or lichenoid syphilid, and pityriasis lichenoides et varioliformis acuta are dermatoses that may resemble generalized LP. Mucous membrane lesions may be confused with leukoplakia, lupus erythematosus, mucous patches of syphilis, candidiasis, cancer, and the oral lesions of autoimmune bullous diseases, such as pemphigus or cicatricial pemphigoid. On the scalp the atrophic lesions may be mistaken for other cicatricial alopecias, such as lupus erythematosus, folliculitis decalvans, and pseudopelade of Brocq. Hypertrophic LP type may simulate psoriasis and squa- mous cell carcinoma in situ. Isolated patches of LP may resemble lichen simplex chronicus or, if heavily pigmented, may suggest a fixed drug eruption.

Treatment

Limited lesions may be treated with superpotent topical steroids or intralesional steroid injections. In patients with widespread disease, these treatments are usually unsatisfactory. Widespread lesions respond well to systemic corticosteroids but tend to relapse as the dose is reduced. Monthly pulse dosing has been championed by dermatologists in India. Phototherapy may be effective for cutaneous LP, including narrow-band ultraviolet (UV) B, UVA1, and PUVA. Topical cream PUVA has been used effectively in genital LP. Isotretinoin and acitretin, in doses similar to or slightly lower than those used for psoriasis, may also be useful and avoid the long-term complications of systemic steroids. They are especially helpful in cases of hypertrophic LP. Retinoid therapy may be combined with phototherapy in refractory cases. Photodynamic therapy with topical 5-aminolevulinic acid can be effective in penile LP. Low molecular weight heparin (enox- aparin), 3 mg injected subcutaneously once a week, led to remission of cutaneous and reticulate oral LP in 61% of patients and improvement in 11%. Erosive oral LP responded variably and lichen planopilaris not at all. For erosive skin lesions topical tacrolimus or pimecrolimus can be effective. Oral immunosuppressive agents may be effective for cutaneous LP, but their potential toxicity limits use to the most severe cases. Cyclosporine in typical psoriasis doses is very beneficial. Similarly, mycophenolate mofetil can induce remission in severe cases of cutaneous and oral LP.

For oral lesions, superpotent steroids in Orabase or gel form are useful. Vinyl dental trays may be used to apply steroid ointments to the gingiva. Begin with 30 min applications three times a day and reduce to maintenance of 20 min every evening. Addition of nystatin to clobetasol in Orabase may be especially effective. Overall, more than 70% of patients with vulvar LP have their symptoms relieved with topical clobetasol. Intralesional injections may be used for focal unresponsive lesions. Topical tacrolimus 0.1% ointment has become standard treatment in erosive LP of the oral and genital mucosa. While burning may occur initially, this can be reduced by concomitant use of topical steroids or initial use of a lower strength. Higher

concentrations, up to 0.3%, may be used. Most patients have a partial but significant response, with increased ability to eat with much less pain. Blood levels can be detected, independent of area of involvement, but tend to decrease over time as the oral erosions heal. Pimecrolimus can be used successfully in patients intolerant of topical tacrolimus. Sustained remissions are rare, and chronic use is usually required to maintain remission. Topical cyclosporine is ineffective. Topical isotretinoin, in concentrations up to 0.18%, can be effective. PUVA, photodynamic therapy, and 308 nm excimer laser have been effective in oral LP. Hydroxychloroquine, 200-400 mg/day for 6 months, was reported to produce an excellent response in 9 of 10 patients with oral LP. Thalidomide has also proven effective in doses of 50-150 mg/day. The systemic agents recommended above to treat cutaneous LP may also improve oral disease. For VVG syndrome, corticosteroids topically and systemically are beneficial. Topical therapy with corticosteroids may be enhanced by mixing the steroid in vaginal bioadhesive moisturizer (Replens). Iontophoresis may improve delivery. Methotrexate, mycophenolate mofetil, and cyclosporine are usually effective in the most refractory cases. Extracorporeal photochemotherapy (photopheresis) has proven effective in refractory oral LP.

Follicular lichen planus (lichen planopilaris)

Lichen planopilaris is lichen planus involving the follicular apparatus (Fig. 11). Most cases involve the scalp and it is an important cause of cicatricial alopecia (see Chapter 33). Seventy to 80% of affected patients are women, usually around the age of 50. The oral mucosa is involved, with reticulate lichen planus in 7-27% of patients, and between 20% and 40% of patients have cutaneous involvement. Graham-Little- Piccardi-Lassueur syndrome describes patients with lichen planopilaris of the scalp with coexistent keratosis pilaris-like lichen planopilaris lesions and nonscarring alopecia of the eyebrows, axillae, and pubic area. Thalidomide and cyclosporine have been reported to be effective.

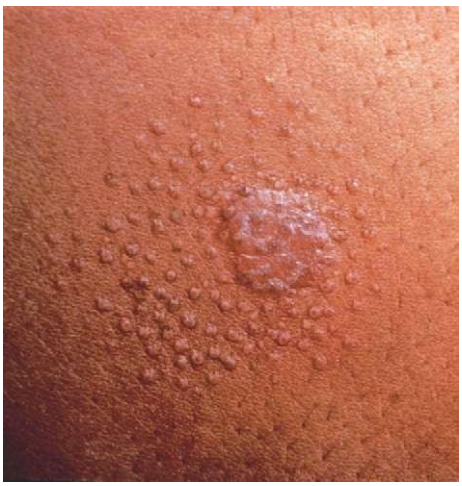


Fig. 11 Follicular lichen planus surrounding a classic lichen planus papule.

Lichen planus pigmentosus/actinicus

Lichen planus pigmentosus is seen primarily in Central America, the Indian subcontinent, the Middle East, and Japan. It appears to be a form of LP restricted to certain racial groups. The persons from these genetic groups can develop the condition when they move to North America and Europe, but Caucasians from Europe and North America do not develop lichen planus pigmentosus when they move to tropical areas where the disease is common. Lichen planus pigmentosus patients are young (between 20 and 45 in most cases), and men and women are equally represented. Men present a decade earlier (mean age 26 vs 34). The face and neck are primarily involved, but the axilla, inframammary region, and groin may also be affected. Lesions may be unilateral. The condition is usually mild (<10% body surface area), and while patients may have associated pruritus, it is usually much milder than in patients with classic LP. Sometimes classic LP papules occur at other sites or at the periphery of the lesions. In the US, persons of color may demonstrate this pattern of LP. Individual lesions are typically several millimeters to several centimeters in size, are oval in shape, and may follow lines of Blaschko. Some patients with lichen planus pigmentosus may have lesions predominantly in sun-exposed areas, and the diagnosis of lichen planus actinicus can be used in these cases. Lichen planus actinicus is reported most frequently in Africa, the Middle East, and the Indian subcontinent, and represents a substantial proportion of LP diagnosed in these geographic areas (36% of all LP patients in a recent Egyptian series). Most cases

reported as lichen planus actinicus occur in childhood through young adulthood, 20-30 years being the primary decade of presentation. The disease presents in the spring or summer, and is frequently quiescent during the winter. Lesions favor the sun-exposed parts of the body, especially the face, which is almost always the most severely affected site. Most lesions occur on the forehead, cheeks, eyelids, and lips. Outside the face, the V area of the chest, the neck, the backs of the hands, and the lower extensor forearms are involved. Associated pruritus, the hallmark of LP, is usually described as mild or absent. Lesions are usually annular but may be reticulate or diffuse. Individual lesions are often macular but may be plaques with peripheral violaceous papules. Characteristically, lesions are hyperpigmented, sometimes with the blue-gray tinge of dermal melanin. They may resemble melasma. Since overlap cases between lichen planus pig- mentosus and lichen planus actinicus do occur, it is best to think of these conditions as a single disorder that may or may not be photoexacerbated. It is important to recognize the lichen planus actinicus variant of lichen planus pigmentosus, as these patients do respond to sun protection, with gradual fading of their hyperpigmentation. Mucous membrane disease is significantly less common in patients with lichen planus pigmentosus/ actinicus. Histologically, any papular element will usually show features of LP. Even macular areas may show subtle evidence of an interface dermatitis, with prominent dermal melanophages.

Erythema dyschromicum perstans

Erythema dyschromicum perstans is also known as ashy der- matosis or dermatosis cinicienta. The age of onset is virtually always before 40, but since it is a chronic disease, patients of all ages have been described. Prepubertal children have been reported. Lesions are typically several centimeters in size and affect primarily the trunk. A characteristic very fine (several millimeters), erythematous, palpable, nonscaling border is seen at the periphery of the lesions. This is described as feeling like a small cord. Unfortunately, this leading edge (and diagnostic feature) of the disorder is only present early in the disease course (a few months). Pruritus is not reported, and typical lichenoid papules are said not to occur. Nail and mucosal

involvement is not found. An association with HLA-DR4 has been suggested for Mexican patients. Unfortunately, erythema dyschromicum perstans became a wastebasket term for the panoply of dermatological disorders that heal with prominent postinflammatory change in persons of color. It is now believed that most cases previously called erythema dyschromicum perstans are actually cases of lichen planus pigmentosus. Childhood cases may represent idio- pathic eruptive macular pigmentation. True erythema dys- chromicum perstans, if it exists, is quite rare, and largely restricted to certain geographic regions.

At the active border the characteristic histologic features of erythema dyschromicum perstans are those of a lichenoid dermatitis. In the centers of the lesions, the histologic changes are those of postinflammatory pigmentation. Therapeutic agents used for LP may benefit the acute inflammatory stage, but have limited effect on the pigmented lesions. Clofazimine, 100 mg/day for patients over 40 kg, and every other day for patients under 40 kg, has been reported to induce clearing in approximately 50%, but clofazimine pigment may complicate prolonged treatment. Dapsone has also been reported as effective. In some affected children, spontaneous improvement has occurred, leading some to suggest that no treatment is reasonable.

Idiopathic eruptive macular pigmentation

Although rarely reported, this condition is not rare. Young persons (mean age 11 years) in one study presented with asymptomatic widespread brown to gray macules of up to several centimeters in diameter on the neck, trunk, and proximal extremities. Lesions are not confluent and there is no history of preceding inflammation. Lesions may spontaneously involute. Some cases reported as erythema dyschromi- cum perstans in childhood may actually represent this entity.

Keratosis lichenoides chronica

This very rare dermatosis is characterized by its chronicity. In adults the disease begins in the late twenties. Typical lesions are papulonodular, hyperkeratotic, and covered with gray scales. These lesions favor the extremities and buttocks.

Although initially discrete, the lesions frequently coalesce to form linear and reticulate arrays of warty lichenoid lesions (Fig. 12). Lesions are infundibulocentric and acrosyringo- centric. Keratotic plugs and prominent telangiectasia may be present. The palms and soles have discrete hyperkeratotic papules.

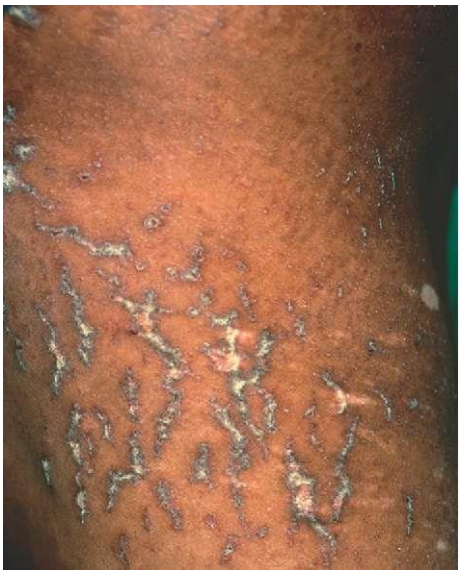


Fig. 12 Keratosis lichenoides chronica.

There is an associated sharply marginated erythema, scaling, and telangiectasia of the face, superficially resembling seborrheic dermatitis or rosacea. Nail changes, including thickening of the nail plate, yellowing, longitudinal ridging, onycholysis, hyperkeratosis of the nailbed, paronychia, and warty lesions of the periungual areas, have been described. In addition, painful oral aphthae-like lesions often occur. Other findings include hoarseness due to vocal cord edema, and involvement of the eyelids (one-third of patients), conjunctiva, iris, or anterior chamber. Topical calcipotriol, PUVA, re-PUVA, bath PUVA, photodynamic therapy, and oral retinoids (isotretinoin and acitretin) may all prove beneficial. Keratosis lichenoides chronica rarely responds to topical or systemic steroids. Childhood cases are rare and differ from adult cases. They start in the first year of life, and have prominent facial purpura and erythema, especially on the cheeks. There are familial associations in more than half of childhood cases, suggesting an autosomal-recessive inheritance.

Histologically, there is irregular acanthosis or epidermal atrophy with hyperkeratosis and zones of parakeratosis. A lichenoid infiltrate, consisting primarily of lymphocytes, and vacuolar alteration at the basal cell layer, but concentrated around the infundibular and acrosyringia. Marked follicular plugging and plugging of the acrosyringia are characteristic.

Lichen nitidus Clinical features

Lichen nitidus (LN) is a chronic inflammatory disease characterized by minute, shiny, flat-topped, pale, exquisitely dis crete, uniform papules, rarely larger than 1-2 mm. Children and young adults are primarily affected.

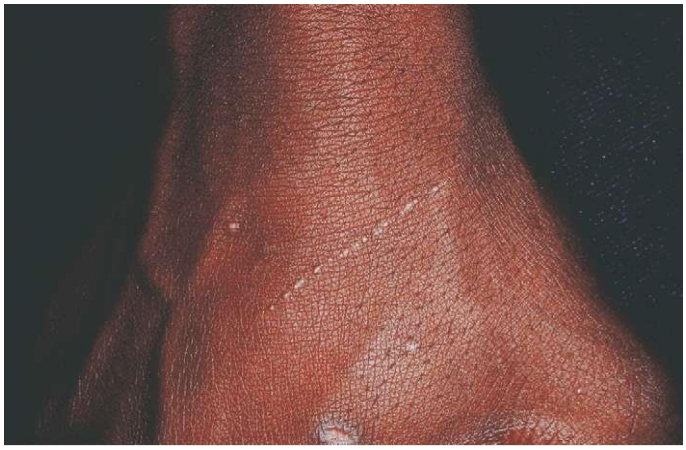


Fig. 13 Lichen nitidus, linear lesion from trauma.

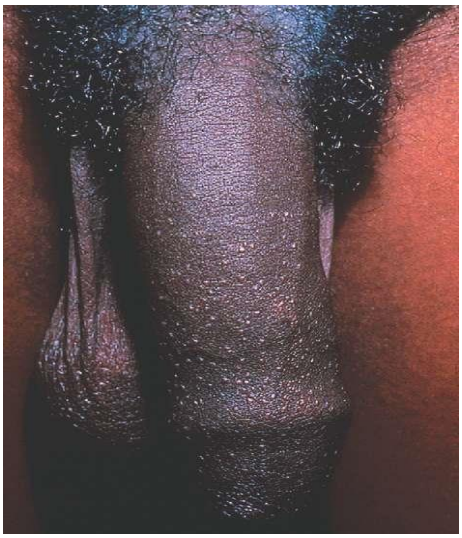


Fig. 14 Lichen nitidus, characteristic lesions of the penile shaft.

Pruritus is usually minimal or absent, but may be more prominent in more generalized cases. Linear arrays of papules (Koebner phenomenon) are common,

especially on the penis, forearms, and dorsal hands. Initially, lesions are localized and often remain limited to a few areas, chiefly the penis and lower abdomen, the inner surfaces of the thighs, and the flexor aspects of the wrists and dorsal hands/forearms (Figs 13 and 14). In other cases, the disease assumes a more widespread distribution, and the papules fuse into erythematous, finely scaly plaques. The reddish color varies with tints of yellow, brown, or violet. Unusual variants of LN include vesicular, hemor- rhagic, linear, purpuric (resembling a pigmented purpuric dermatosis), and spinous follicular (resembling lichen spinulosus).

Palm and sole involvement may occur in LN, and the disease may be restricted to these areas. It presents with multiple, tiny, hyperkeratotic papules. The papules may coalesce to form diffuse hyperkeratotic plaques that fissure. The differentiation of LN from hyperkeratotic hand eczema and lichen planus of the palms is aided by the presence of a keratotic plug in the center of lesions of palmoplantar LN. Nail involvement with pitting; beaded, longitudinal ridging; and nailfold inflammation have been reported. Oral involvement, with gray-yellow papules or petechiae of the hard palate, is rare.

A variant of LN, termed actinic lichen nitidus, has been reported in dark-skinned patients from the Middle East and Indian subcontinent. Cases seen in African Americans have also been termed "pinpoint, papular polymorphous light eruption (PMLE)," or known by the older term "summer actinic lichenoid eruption." These cases all have lesions clinically and histologically identical to LN, which are limited to the sun-exposed areas of the dorsal hands, brachioradial area, and posterior neck. The LN histology may represent subacute or chronic lesions of pinpoint PMLE. Actinic LN/pinpoint papular PMLE usually responds to sun protection, with or without topical steroids.

The course of LN is slowly progressive, with a tendency for remission. The lesions may remain stationary for years but eventually they often disappear spontaneously and entirely. The cause of LN is unknown. Rare familial cases do occur. It is clinically and histologically distinct from lichen planus, and immunohistochemical studies also suggest they are distinct disorders. However,

patients have been reported who have had both disorders, suggesting some common pathogenic basis. Both LP and LN have been reported as being secondary to hepatitis B immunization, and during treatment of hepatitis with interferon-a. There are also reports of patients with both LN and Crohn's disease, another condition with granuloma- tous inflammation. LN has a characteristic histologic appearance. Dermal papillae are widened and contain a dense infiltrate composed of lymphocytes, histiocytes, and melano- phages. Multinucleate giant cells are often present, imparting a granulomatous appearance to the infiltrate. The epidermal rete ridges on either side of the papilla form a clawlike collarette. The overlying epidermis is attenuated, and there is usually vacuolar alteration of its basal layer. At times the infiltrate may extend down adjacent hair follicles and eccrine ducts, making distinction of LN from lichen scrofulosorum and lichen striatus difficult.

Because LN is usually asymptomatic, treatment is often not necessary. Topical application of high or superpotent topical corticosteroids or topical calcineurin inhibitors may suppress pruritus and lead to resolution of skin lesions. Narrow-band UVB and PUVA could be considered in more generalized and symptomatic cases. Anecdotal reports suggest therapeutic benefit from oral retinoids (etretinate and acitretin). As in lichen planus, refractory cases requiring aggressive therapy may respond to cyclosporine A.

Lichen striatus

Lichen striatus is a fairly common self-limited eruption that is seen primarily in young children (mean age 3 years). Girls are affected 2-3 times more frequently than boys. Lesions begin as small papules that are erythematous and slightly scaly (Fig. 15). In more darkly pigmented persons, hypopigmentation is prominent and may be purely macular. The 1-3 mm papules coalesce to form a band 1-3 cm wide, either continuous or interrupted, which over a few weeks progresses down the extremity or around the trunk, following lines of Blaschko. An extremity is more commonly involved, but trunk lesions, or lesions extending from the trunk on to an extremity, can also occur. About 10% of cases occur on the head. Multiple bands can

uncommonly occur. Lesions are usually asymptomatic but pruritus may occur, especially in patients who are also atopic.

Nail involvement can occur if the process extends down the digit to the nail. Most commonly, the lichen striatus appears first on the skin, but the skin and nail abnormality may appear simultaneously. Uncommonly, only the nail may be involved for months, with later appearance of the band on the skin, or the nail may remain the sole area of involvement throughout the course of the disease. Nail-plate thinning, longitudinal ridging, splitting, and nailbed hyperkeratosis may be seen. Often only a part of the nail is involved. The histology of involved nails is identical to that of the skin lesions.

The active lesions of lichen striatus last for an average of 1 year, but may persist for up to 4 years. Eventually, all the lesions, including dystrophic nails, spontaneously resolve without scarring. Hypopigmentation may persist for several years. Hyperpigmentation is uncommon (<5%) and should suggest a diagnosis of linear lichen planus instead. Relapses can occur in up to 5% of cases, either in the same distribution or in a different anatomic region.

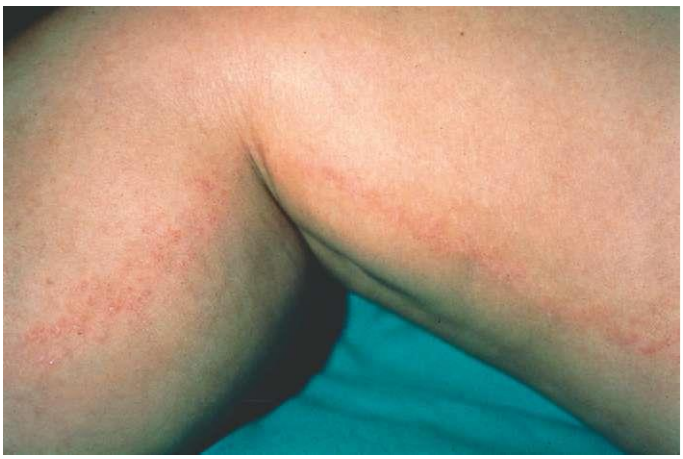


Fig. 15 Lichen striatus.

The histologic features of lichen striatus vary, partly reflecting the stage of evolution of the lesion. There may be a spon- giotic dermatitis, but most frequently a lichenoid component is present. There is a bandlike infiltrate with necrotic keratino- cytes at the dermoepidermal junction. Granulomatous inflammation may occasionally be present. Typically there is a dense lymphoid infiltrate around the

eccrine sweat glands and ducts. This helps to distinguish lichen striatus from lichen planus.

Multiple reports exist of simultaneous cases in siblings. There is also a seasonal variation, with most cases occurring in the spring and summer. Epidemic outbreaks have been reported. These suggest a viral etiology or trigger. Trauma has also been reported to precipitate an outbreak of lichen striatus.

Adult cases of lichen striatus differ from those in childhood, being rarer and more papulovesicular, affecting multiple regions, resolving more rapidly (less than 2 months), and relapsing more frequently (up to one-third of cases). Histologically, they show more spongiotic and less lichenoid features. This has led some authors to call these cases "adult Blaschkitis" or "Grosshans-Marot disease." This splitting is probably not of any clinical utility.

Usually the diagnosis is straightforward in the setting of a young child, with the sudden onset of an eruption following the lines of Blaschko. The differential diagnosis could include linear lichen planus, linear psoriasis, inflammatory linear ver- rucous epidermal nevus, epidermal nevus, linear cutaneous lupus erythematosus, and verruca plana. Histologic evaluation will usually distinguish these entities, but is rarely required.

Treatment is usually not necessary. Parents may be reassured of the uniformly excellent prognosis. Topical steroids and topical tacrolimus or pimecrolimus may accelerate the resolution of lesions. In children with an acquired nail dystrophy of one or two digits, this diagnosis must be considered, and watchful waiting might be considered before biopsying the nail.

Lichen sclerosus (lichen sclerosus et atrophicus)

Lichen sclerosus is a chronic disease of the skin and mucosa. The terms lichen sclerosus et atrophicus, kraurosis vulvae, and balanitis xerotica obliterans are synonymous but have been replaced by the single term lichen sclerosus (LS). LS can present from childhood to old age. Although it occurs in all races, whites appear to be preferentially affected. Both sexes are affected both before and after puberty, with

females predominating at all ages. The prevalence is about 1.7% in the general female population.

The pathogenesis of LS is poorly understood. Autoimmune diseases (thyroid disease, vitiligo, alopecia areata, and pernicious anemia) occur in between one-fifth and one-third of women with LS, but are much less common in men. Psoriasis is increased in women with LS, reported to occur in 7.5-17% of patients. Autoantibodies to extracellular matrix protein (ECM) 1 are found in 80% of LS patients (as compared to 4% of controls and 7-10% of patients with other autoimmune diseases). The titer of the ECM 1 autoantibody correlates with the disease severity. The importance of this humoral autoim- munity in the pathogenesis of LS is currently unclear.

In females, there is a bimodal age distribution—prepubertal and postmenopausal. The initial lesions of LS are white, polygonal, flat-topped papules, plaques, or atrophic patches (Fig. 16). Lesions may be surrounded by an erythematous to violaceous halo. In atrophic lesions, the skin is smooth, slightly wrinkled, soft, and white (Fig. 17). Bullae, often hemor- rhagic, telangiectasias, and fixed areas of purpura may occur on the patches. About 40% of women with LS are asymptomatic. However, when women referred to specialists are questioned, virtually 100% are symptomatic. Itching is frequently severe, especially in the anogenital area. In the genital area, fissuring and erosion may occur. This may result in dysuria, urethral and vaginal discharge, dyspareunia, and burning pain. Normal anatomic structures may be obliterated, with loss of the labia minora, clitoral hood, and urethral meatus. In women, this perineal involvement typically affects the vulvar and perianal areas, giving a "figure-eight" or "hourglass" appearance. Introital stenosis or fusion may occur.

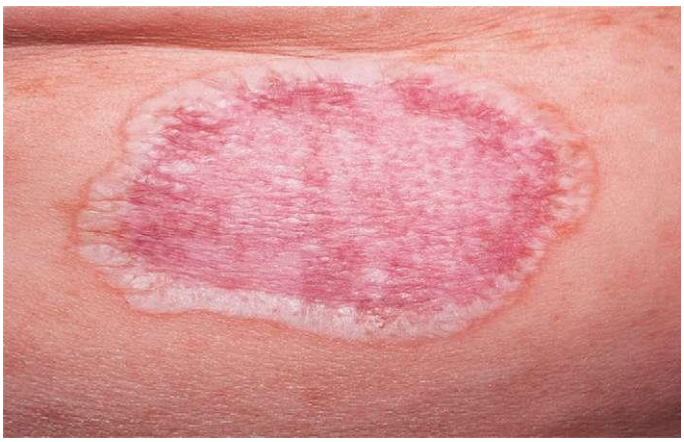


Fig. 16 Lichen sclerosus of the glabrous skin.

The vaginal and cervical mucosa are not involved by LS (in contrast to lichen planus). Prepubertal girls may also be affected and usually have vulvar and perianal lesions. Vulvar disease is associated with similar skin changes to those in adult women, and pruritus may be a prominent symptom. Perianal involvement may produce significant symptomatology of constipation, stool holding, and rectorrhagia due to rectal fissures. Infantile perineal protrusion refers to a pyramidal soft-tissue swelling covered by red or rose-colored skin along the median perineal raphe (the skin between the posterior fourchette and the anus).

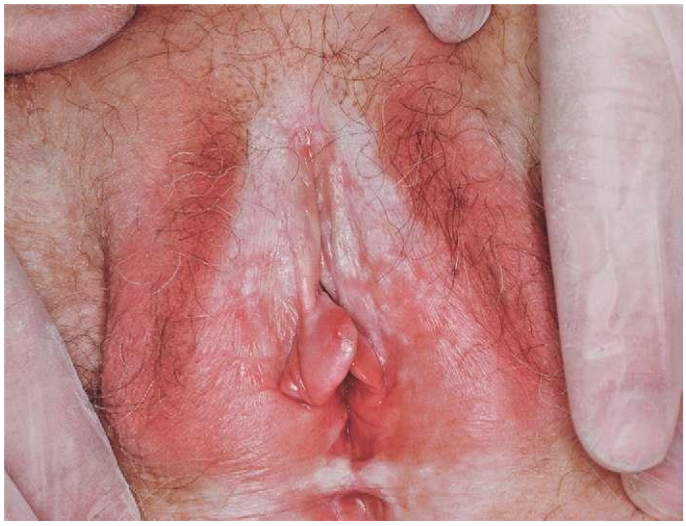


Fig. 17 Lichen sclerosus, white atrophic lesions with loss of normal tissue markings.

This occurs only in girls and appears to be a manifestation of LS in some prepubertal girls. Two-thirds of girls with LS have been evaluated for sexual abuse, largely due to the ecchymoses that accompany the lesions. If risk of sexual abuse is suspected, appropriate investigations must be performed.

There is clearly a relationship between the hormonal milieu and LS. Postmenopausal women are preferentially affected. Pregnancy leads to improvement, and often complete resolution. Oral contraceptive pill (OCP) use is common in premeno- pausal women with LS. These OCPs are often anti-androgenic. Stopping these agents and treating with standard topicals leads to significant improvement, suggesting that the anti- androgen OCPs may have accelerated the appearance of the LS. However, treatment of postmenopausal women with estrogen supplementation does not alter the incidence or course of their LS.

In males, lesions are atrophic and may be markedly hypo- pigmented or depigmented, resembling vitiligo. Lesions usually involve only the glans penis, but may extend on to the penile shaft and scrotum. If the glans is involved, hemorrhage is common, and shallow erosions may occur. LS of the glans does not usually lead to nonhealing erosions of the glans, but rather simply skin fragility. Phimosis and paraphimosis are common complications of LS in men (Fig. 18). Between 15% and 100% of circumcision specimens from prepubertal boys show features of LS. Sixty percent of acquired phimosis in boys and at least 10% in adult men are associated with LS. Most men with LS are uncircumcised. However, circumcision does not universally "cure" LS in boys or men, with at least 50% of men so treated continuing to have lesions of LS. Urethral meatal stenosis may occur and requires surgical

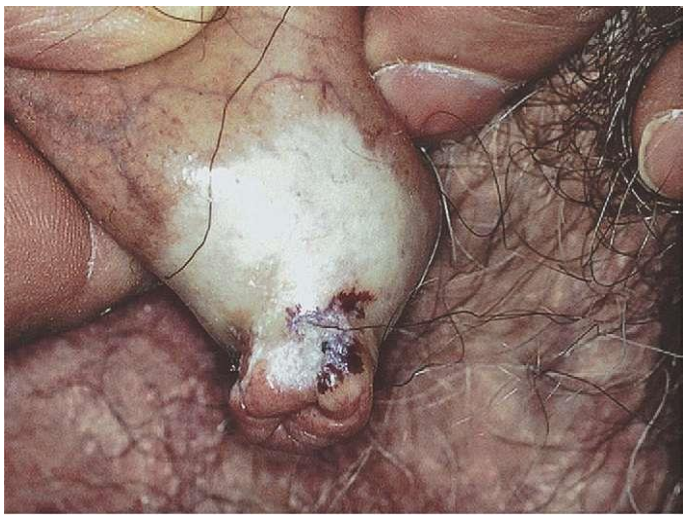


Fig. 18 Lichen sclerosus, phimosis; note the hemorrhagic macule.

correction. Perianal involvement by LS is much less common in men and boys.

Extragenital lesions are most frequent on the upper back, chest, and breasts, and are usually asymptomatic. The tongue and oral mucosa may also be involved, either alone or with lesions elsewhere. Peristomal involvement around colostomy sites may occur. Patients having only extragenital lesions with histologic features of both LS and morphea have been reported. They may simultaneously have other cutaneous lesions of morphea or atrophoderma of Pasini and Pierini. These patients are best viewed as having morphea with overlying LS-like changes, rather than a form of LS. Rarely, in Europe, *Borrelia* has been reported to cause extragenital LS, and treatment with antibiotics has arrested the progression of the lesions.

Lichen sclerosus and cancer

Although the risk is not as high as was proposed early in this century, LS of the genitalia is a condition with increased risk for genital squamous cell carcinoma (SCC) in both women and men. The lifetime risk for women who are carefully followed appears to be 5% or less, but is clearly higher than for the general population. In one study, 14 of 23 (60%) anogenital SCCs in women arose on a background of LS. Human papillomavirus (HPV) appears to be associated with only about 15% of SCCs arising in women with LS. Hypertrophic vulvar lesions and age beyond 60 are clear risk factors for the development of SCC in women with LS. Such lesions and patients should be evaluated carefully. In men with LS the risk for genital SCC is less than in women with LS. However, between 44% and 55% of cases of penile SCC are associated with LS. Oncogenic HPV types do not appear to be associated with LS-associated penile cancer.

The use of potent topical steroids and calcineurin inhibitors can be associated with activation of latent HPV infection and is of theoretical concern.

Histopathology

Early lesions are characterized by an interface dermatitis with vacuolar alteration of keratinocytes. With evolution the epidermis is thinned and the rete

ridges are effaced. Compact orthokeratosis and follicular and eccrine plugging are present. The upper dermis is edematous, with the upper dermal collagen homogenized. Immediately beneath the altered papillary dermis there is a sparse bandlike and perivascular lymphoid infiltrate. In pruritic lesions, coexistent changes of lichen simplex chronicus may be seen, with acanthosis rather than atrophy of the epidermis.

Differential diagnosis

Extragenital LS must be differentiated from guttate morphea and lichen planus, especially of the atrophic type. Anogenital LS must be distinguished from genital lichen planus, lichen simplex chronicus, vulvar intraepithelial neoplasia (SCC in situ), and extramammary Paget's disease. The white color and atrophic surface are characteristic, and such areas are most fruitful if biopsied to confirm the diagnosis.

Treatment

The use of superpotent topical steroids has dramatically changed the management of anogenital LS. They are universally accepted as the treatment of choice for all forms of genital LS. Most patients will respond to once daily application of these agents and can subsequently be tapered to less frequent applications (once or twice a week) or to lower-strength steroids. In general, weekend application of an ultrapotent steroid is more effective than daily application of a mild steroid. Generally, the untreated lesions are atrophic, and pulsed weekend applications of a potent topical steroid treatment are associated with clinical and histologic reversal of the epidermal atrophy as the inflammatory process is controlled. Coexistent candidiasis may be present or appears with this treatment, and can be managed with topical or oral agents. Penile, vulvar, and prepubertal LS in girls have all been documented to respond to this form of treatment. Phimosis in young boys should be treated initially with potent topical steroids. The degree of symptomatic improvement far exceeds the objective improvement. The majority of patients have dramatic reduction in their itching and burning with topical clobetasol.

However, the visible white, atrophic, scarred vulvar skin is often only minimally improved. It is unclear if aggressive topical therapy of LS reduces the risk of cancer development. Vulvar pain associated with LS may have a neuropathic component (as in vulvodynia), and treatment with tricyclic antidepressants (amitriptyline, for example), gabapentin, and duloxetine hydrochloride may be tried.

Topical tacrolimus 0.1% and 0.03% ointments and pime- crolimus 1% cream have also been demonstrated to be effective in genital LS. However, since superpotent steroids have proven so effective in genital LS, topical calcineurin inhibitors should be reserved for patients in whom topical steroids are ineffective or not tolerated. Close clinical follow-up is recommended, since the long-term risk of applying topical calcineurin inhibitors to skin predisposed to malignant degeneration is not known. Topical calcipotriol may also be of benefit. Topical testosterone was no more effective than emollient and in one trial was worse than emollients as maintenance therapy. It is no longer recommended. Hydroxychloroquine, calcitriol, topical 8% progesterone cream, topical calcipotriol, topical tretinoin, cyclosporine, and hydroxyurea can be considered in refractory cases. UVA-1 phototherapy led to moderate improvement in 3 out of 7 patients unresponsive to topical steroids. Some patients responded to topical corticosteroids following the UV treatment. Surgical treatments can be effective, starting with cryo- therapy, which has been reported as helpful in three-quarters of patients with severe vulvar itch. Carbon dioxide ablation in male patients led to long-term remissions. Photodynamic therapy has brought significant improvement in multiple reports and can be considered in refractory cases. Extragenital LS is very difficult to treat. If superpotent topical steroids are ineffective, potassium p-aminobenzoic acid, PUVA, UVA-1, narrow-band UVB, calcipotriol, or antimalarials may be tried.

PSORIASIS

Psoriasis Clinical features

Psoriasis is a common, chronic, and recurrent inflammatory disease of the skin characterized by circumscribed, erythema- tous, dry, scaling plaques of various sizes. The lesions are usually covered by silvery white lamellar scales. The lesions have a predilection for the scalp, nails, extensor surfaces of the limbs, umbilical region, and sacrum. The eruption is usually symmetrical. It usually develops slowly but may be exanthema- tous, with the sudden onset of numerous guttate (droplike) lesions (Fig. 19). Subjective symptoms, such as itching or burning, may be present and may cause extreme discomfort.

The early lesions are small erythematous macules, which from the beginning are covered with dry, silvery scales. The lesions increase in size by peripheral extension and coalescence. The scales are micaceous, meaning that they peel in layers. They are looser toward the periphery and adherent centrally. When removed, bleeding points appear (Auspitz sign). Although plaques typically predominate, lesions may be annular or polycyclic. Old patches may be thick and covered with tough lamellar scales like the outside of an oyster shell (psoriasis ostracea). Various other descriptive terms have in the past been applied to the diverse appearances of the lesions: psoriasis guttata, in which the lesions are the size of water drops; psoriasis follicularis, in which tiny, scaly lesions are located at the orifices of hair follicles; psoriasis figurata, psoriasis annulata, and psoriasis gyrata, in which curved linear patterns are produced by central involution; psoriasis discoi- dea, in which central involution does not occur and solid patches persist; and psoriasis rupioides, in which crusted lesions occur, resembling syphilitic rupia. The term chronic plaque psoriasis is often applied to stable lesions of the trunk and extremities. Inverse psoriasis predominates in intertrigi- nous areas. Pustular variants of psoriasis may be chronic on the palms and soles (Fig. 20), or may be eruptive and accompanied by severe toxicity and hypocalcemia.

Involved nails (Fig. 21) can demonstrate distal onycho- lysis, random pitting (the result of parakeratosis from the proximal matrix), oil spots (yellow areas of subungual parakeratosis from the distal matrix), or salmon patches (nailbed psoriasis). Thick subungual hyperkeratosis may resemble onychomycosis.

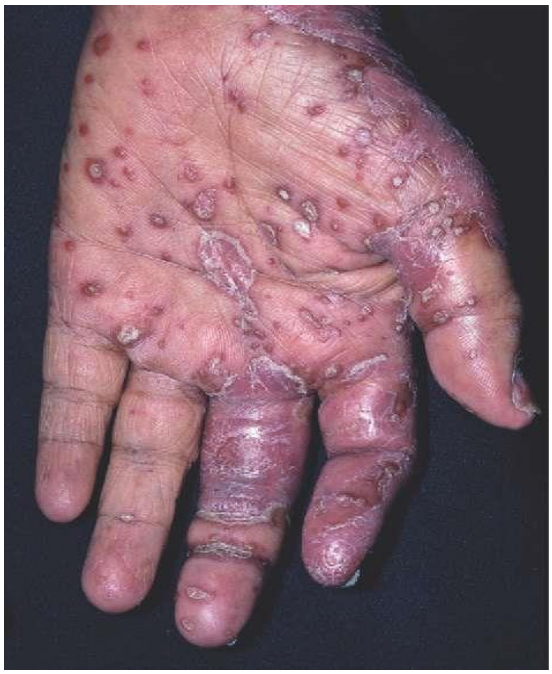


Fig. 21 Pustular psoriasis of the hand.

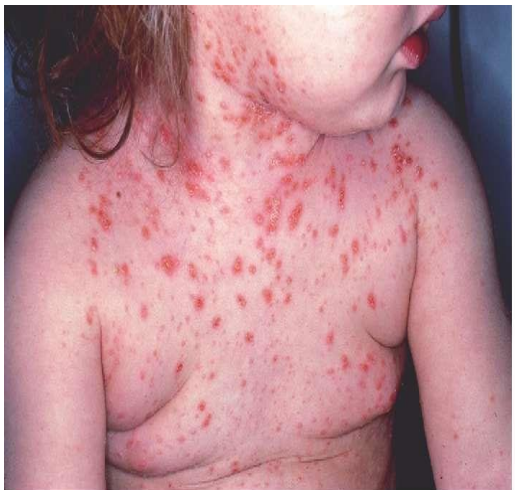


Fig. 19 **Psoriasis**

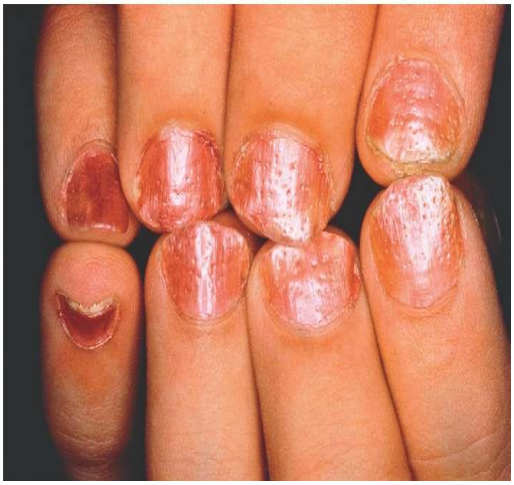


Fig. 20 **Nail pitting and distal onycholysis In psoriasis**

Types

Seborrheic-like psoriasis

Some cases of psoriasis overlap with seborrheic dermatitis. Seborrheic lesions may predominate on the face, under the breasts, and in the scalp, flexures, and axillae. Lesions in these areas are moist and erythematous, with yellow, greasy, soft scales, rather than dry and micaceous scales. Terms such as sebopsoriasis and seborrhiasis may be used to describe the condition of such patients.

Inverse psoriasis

This form selectively and often exclusively involves folds, recesses, and flexor surfaces such as the ears, axillae, groins, inframammary folds, navel, intergluteal crease, penis (Fig. 22), lips, and web spaces. Other areas, such as the scalp and nails, may be involved.

"Napkin" psoriasis

Napkin psoriasis, or psoriasis in the diaper area, is characteristically seen in infants between 2 and 8 months of age. Lesions appear as brightly erythematous, sharply demarcated patches of skin involving much of the diaper area. The lesions typically clear with topical therapy, but psoriasis may reappear in adulthood.

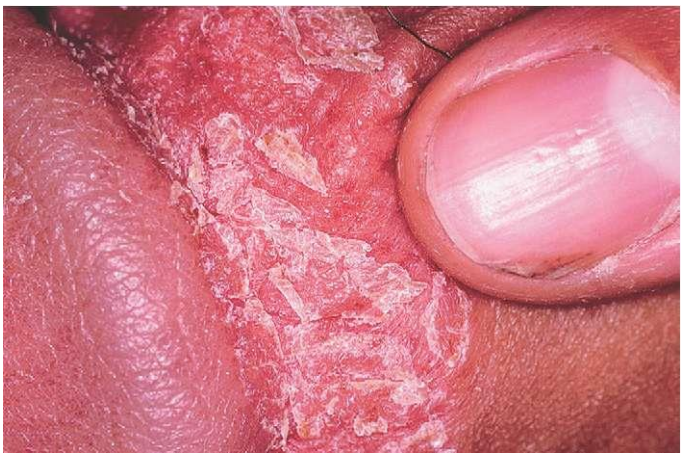


Fig. 22 Penile psoriasis with erythema and silver scale.

Psoriatic arthritis

1. Five clinical patterns of arthritis occur: asymmetrical distal interphalangeal joint involvement with nail damage (16%) arthritis mutilans with osteolysis of phalanges and metacarpals (5%) (Fig. 23).
2. symmetrical polyarthritis-like rheumatoid arthritis, with claw hands (15%).
3. oligoarthritis with swelling and tenosynovitis of one or a few hand joints (70%).
4. ankylosing spondylitis alone or with peripheral arthritis (5%).

Most radiographic findings resemble those in rheumatoid arthritis, but certain findings are highly suggestive of psoriasis. These include erosion of terminal phalangeal tufts (acrosteo- lysis), tapering or "whittling" of phalanges or metacarpals with "cupping" of proximal ends of phalanges (pencil in a cup deformity), bony ankylosis, osteolysis of metatarsals, predilection for distal interphalangeal and proximal interphalangeal joints, relative sparing of metacarpal phalangeal and metatar- sal phalangeal joints, paravertebral ossification, asymmetrical sacroiliitis, and rarity of "bamboo spine" when the spine is involved. Nearly half the patients with psoriatic arthritis have type human leukocyte antigen (HLA)-B27.

Rest, splinting, passive motion, and nonsteroidal anti- inflammatory drugs (NSAIDs) may provide symptomatic relief but do not prevent deformity. Methotrexate, cyclosporine, tacrolimus, and biologic agents are disease-modifying drugs that prevent deformity.

Guttate psoriasis

In this distinctive form of psoriasis typical lesions are the size of water drops, 2-5 mm in diameter. Lesions typically occur as an abrupt eruption following some acute infection, such as a streptococcal pharyngitis.

Guttate psoriasis occurs mostly in patients under age 30. This type of psoriasis usually responds rapidly to broad-band ultraviolet (UV) B at erythemogenic doses. Suberythemogenic doses often have little impact on the lesions. This is one of the few forms of psoriasis where broadband UVB may have an advantage over narrow-band UVB. Minimal erythemogenic dose (MED) testing is recommended to allow for appropriately aggressive treatment. Recurrent episodes may be related to pharyngeal carriage of the responsible streptococcus by the patient or a close contact. A course of a semisynthetic penicillin (such as dicloxacillin, 250 mg four times a day for 10 days) with rifampin (600 mg/day for an adult) may be required to clear chronic streptococcal carriage.

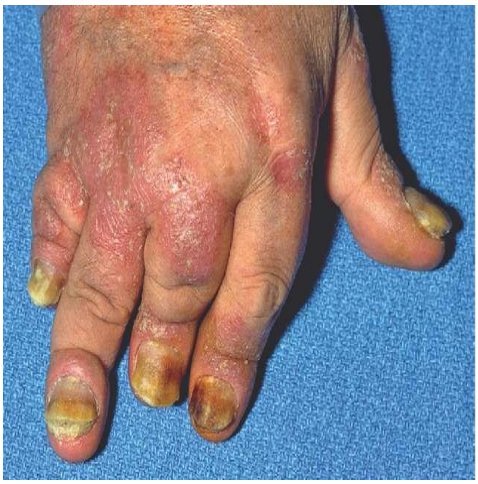


Fig. 23 Psoriasis arthritis

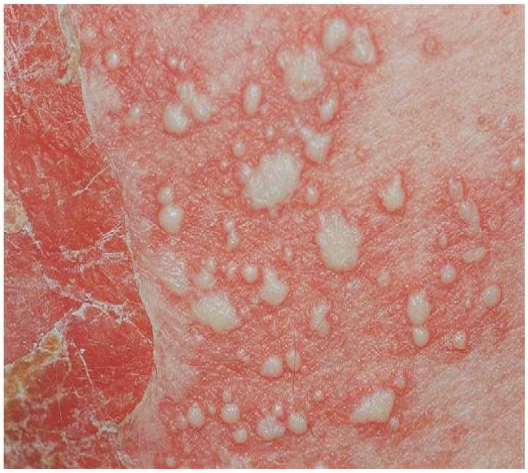


Fig. 24 Pustular psoriasis

Generalized pustular psoriasis (von Zumbusch)

Typical patients have had plaque psoriasis and often psoriatic arthritis. The onset is sudden, with formation of lakes of pus periungually, on the palms, and at the edge of psoriatic plaques. Erythema occurs in the flexures before the generalized eruption appears. This is followed by a generalized erythema and more pustules (Fig. 24). Pruritus and intense burning are often present. Mucous membrane lesions are common.

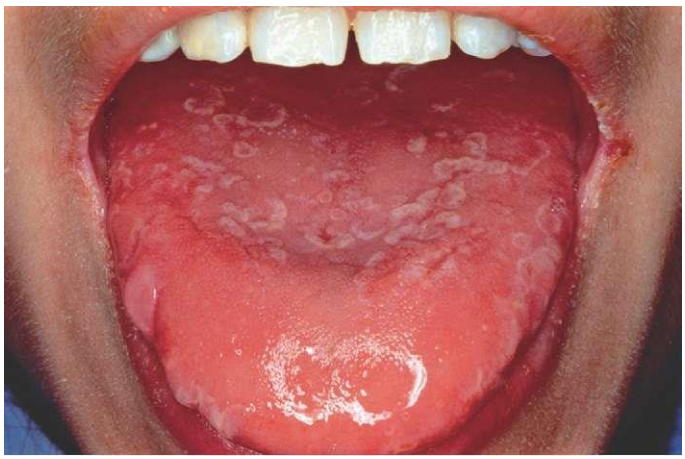


Fig. 25 Geographic tongue in pustular psoriasis.

The lips may be red and scaly, and superficial ulcerations of the tongue and mouth occur. Geographic or fissured tongue frequently occurs (Fig. 25).

The patient is frequently ill with fever, erythroderma, hypocalcemia, and cachexia. A number of cases of acute respiratory distress syndrome associated with pustular and erythroder- mic psoriasis have been reported. Other systemic complications include pneumonia, congestive heart failure, and hepatitis.

Episodes are often provoked by withdrawal of systemic corticosteroids. The authors have also observed generalized pustular psoriasis as the presenting sign of Cushing's disease. Other implicated drugs include iodides, coal tar, terbinafine, minocycline, hydroxychloroquine, acetazolamide, and sali- cylates. There is usually a strong familial history of psoriasis. Generalized pustular psoriasis may occur in infants and children with no implicated drug. It may also occur as an episodic event punctuating the course of localized acral pustular psoriasis.

Acitretin is the drug of choice in this severe disease. The response is generally rapid. Isotretinoin is also effective. Cyclosporine, methotrexate, and biologicals are alternatives. Sometimes dapsone is effective in doses of 50-100 mg/day.

Acrodermatitis continua of Hallopeau

Typical patients develop acral erythematous plaques studded with pustules. The nailbeds are heavily involved, and the fingernails float away on lakes of pus, resulting in anonychia. Hyperkeratosis often ensues, and the fingertips become

increasingly painful, tapering to long keratotic points. Occasionally, patients may develop generalized pustular flares (Fig. 26). Acrodermatitis continua is discussed in more detail below.

Impetigo herpetiformis

This term has been applied to generalized pustular psoriasis of pregnancy. Flexural erythema, studded with pustules, often occurs initially, followed by a generalized pustular flare and increasing toxicity. As the patients are pregnant, systemic retinoids are not appropriate. Many patients only respond to delivery, and early delivery should be strongly considered as soon as it is safe for the infant. Alternatively, patients may respond to prednisone at a dose of 1 mg/kg/day. The cortico- steroid can also contribute to neonatal lung maturity.

Keratoderma blennorrhagicum (Reiter syndrome)

Keratoderma blennorrhagicum resembles psoriasis both histologically and clinically, except for its tendency for thicker keratotic lesions. Patients are often positive for HLA-B27 and develop reactive arthritis and skin disease after a bout of ure- thritis or enteritis.

Erythroderma psoriasis

Patients with psoriasis may develop a generalized erythro- derma (Fig. 27). Erythrodermic psoriasis is covered in greater detail under exfoliative dermatitis.

Course

The course of psoriasis is unpredictable. It usually begins on the scalp or elbows, and may remain localized in the original region for years. Chronic disease may also be almost entirely limited to the fingernails. Involvement over the sacrum may easily be confused with candidiasis or tinea. Onset may also be sudden and widespread.

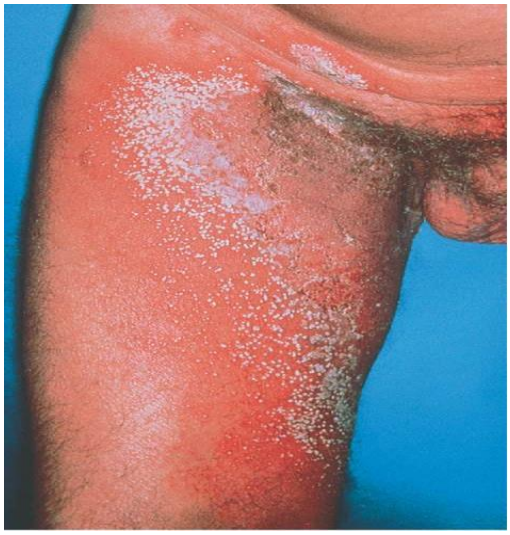


Fig. 26 Generalized pustular flare in a patient with acrodermatitis continua.

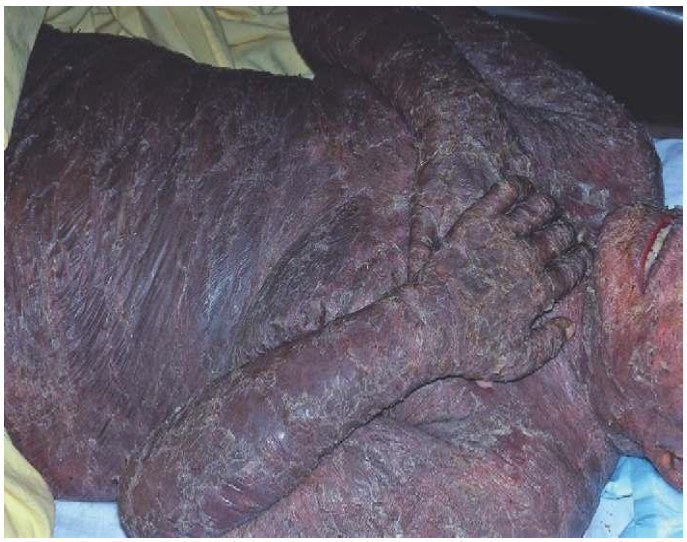


Fig. 27 Erythroderma psoriasis.

Two of the chief features of psoriasis are its tendency to recur and its persistence. The isomorphic response (Koebner phenomenon) is the appearance of typical lesions of psoriasis at sites of even trivial injury (Fig. 28). Lesions may occur at sites of scratches, incisions, and burns. Lesions may first appear after a viral exanthema or following pityriasis rosea. The isomorphic response may occur if psoriatic lesions are severely burned during phototherapy. With a reduction in light dosage, the erythema and burning resolve, and the plaques begin to clear. Woronoff's ring is concentric blanching of the erythematous skin at or near the periphery of a healing psoriatic plaque. It is often the first sign that the patient's psoriasis is responding to phototherapy.

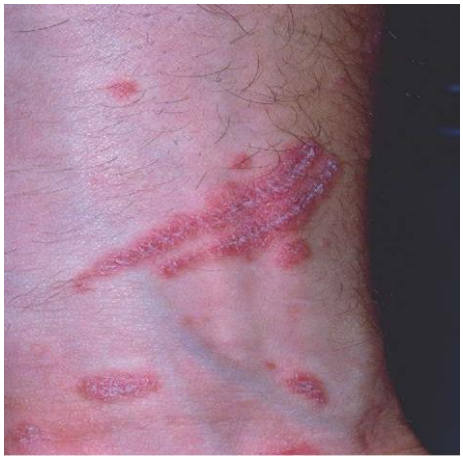


Fig. 28 Koebner phenomenon in psoriasis.

The palms and soles are sometimes exclusively affected, showing discrete erythematous dry scaling patches, circumscribed verrucous thickenings, or pustules on an erythematous base. The patches usually begin in the mid-portions of the palms or on the soles, and gradually expand. Psoriasis of the palms and soles is typically chronic and extremely resistant to treatment.

Many studies report an association between hepatitis C and psoriasis, and hepatitis C has also been implicated in psoriatic arthritis. If treatment of psoriasis is to include a potentially hepatotoxic drug, such as methotrexate, a hepatitis C serology should be obtained. It should also be noted that interferon treatment of the hepatitis can further exacerbate or induce psoriasis. Anti-tumor necrosis factor (TNF)-a therapy shows promise in the treatment of psoriasis, even in the setting of chronic hepatitis C infection.

Inheritance

In a large study of psoriasis in monozygotic twins, heritability was high and environmental influence low. Patients with psoriasis often have relatives with the disease, and the incidence typically increases in successive generations. Multifactorial inheritance is likely. Analysis of population-specific HLA hap- lotypes has provided evidence that susceptibility to psoriasis is linked to the class I and II major histocompatibility complex (MHC) on human chromosome 6. A number of genetic loci are linked to psoriasis, including *PSORS1* on chromosome 6 and within the MHC, and *PSORS2* on chromosome 17q. It has also been shown that there are two subsets that differ in age of onset and in the frequency of HLA associations. Early onset is type I psoriasis and is associated mostly with Cw6, B57, and DR7. Late onset is type II and this predominantly features Cw2. *PSORS9* has also been confirmed as a susceptibility locus for psoriasis.

A variety of other HLA associations have been reported. It is believed that any individual who has B13 or B17 carries a five-fold risk of developing psoriasis. In pustular psoriasis HLA-B27 may be seen, whereas B13 and B17 are increased in

guttate and erythrodermic psoriasis. In palmoplantar pustulo- sis, there is an association with HLA-B8, Bw35, Cw7, and DR3. HLA typing is a research tool for population-based studies, but is of limited value in assessing an individual patient.

Epidemiology

Psoriasis occurs with equal frequency in both sexes. Between 1 and 2% of the US population has psoriasis. It occurs less frequently in the tropics. It is less common in North American and West African black persons. Native Americans and native Fijians rarely have psoriasis. The onset of psoriasis is at a mean age of 27 years, but the range is wide, from the neonatal period to the seventies. Severe emotional stress tends to aggravate psoriasis in almost half of those studied.

In pregnancy there is a distinct tendency for improvement or even temporary disappearance of lesions in the majority of women studied. After childbirth there is a tendency for exacerbation of lesions. Paradoxically, pregnancy is also the milieu for impetigo herpetiformis, and psoriasis may behave differently from one pregnancy to another in the same patient.

A high prevalence of celiac disease has been noted in patients with psoriasis. Lymphoma also has an increased incidence in these patients, and psoriasis has been linked to the metabolic syndrome and a higher risk of cardiovascular disease.

Pathogenesis

Psoriasis is a hyperproliferative disorder, but the proliferation is driven by a complex cascade of inflammatory mediators. Psoriasis appears to represent a mixed T-helper (Th)1 and Th17 inflammatory disease. Th17 cells appear to be more prox- imal in the inflammatory cascade. T cells and cytokines play pivotal roles in the pathophysiology of psoriasis. Overexpression of type 1 cytokines, such as IL-2, IL-6, IL-8, IL-12, IFN-y and TNF-a, has been demonstrated, and overexpression of IL-8 leads to the accumulation of neutrophils. The main signal for Th1 development is IL-

12, which promotes intracellular IFN-y production. In animal models, shifting from Th1 to Th2 responses improves psoriasis. IL-4 is capable of inducing Th2 responses and improving psoriasis. Reduced expression of the anti-inflammatory cytokines IL-1RA and IL-10 has been found, and polymorphisms for IL-10 genes correlate with psoriasis. IL-10 is a type 2 cytokine with major influences on immuno- regulation, inhibiting type 1 proinflammatory cytokine production. Patients on established traditional therapies show rising levels of IL-10 mRNA expression, suggesting that IL-10 may have antipsoriatic capacity.

The response to biologic agents has demonstrated that CD2+ lymphocytes, CD-11a and TNF-a are important in the pathogenesis of psoriasis. IL-15 triggers inflammatory cell recruitment, angiogenesis, and production of inflammatory cytokines, including IFN-y, TNF-a, and IL-17, all of which are upregu- lated in psoriatic lesions. The interplay is complex, but IL-17 appears to be proinflammatory, while IL-22 may serve to retard keratinocyte differentiation. IL-23 stimulates survival, as well as proliferation of Th17 cells. Circulating NK cells are reduced in psoriasis.

Specific targets for therapy include TNF-a, leukocyte function-associated antigen-1 (LFA-1)/intercellular adhesion molecule-1 (ICAM-1) binding, and LFA-3/CD2 binding. An IL-15 monoclonal antibody has been shown to be effective in a mouse model of psoriasis.

Streptococci

Streptococci play a role in some patients. Patients with psoriasis report sore throat more often than controls. Beta-hemolytic streptococci of Lancefield groups A, C, and G can cause exacerbation of chronic plaque psoriasis. Th1 cells recognize cell- wall extract isolated from group A streptococci. HLA variation has a significant effect on the immune response to group A streptococci.

Stress

Various studies have shown a positive correlation between stress and severity of disease. In almost half of patients studied, stress appears to play a significant role.

Drug-induced psoriasis

Psoriasis may be induced by P-blockers, lithium, antimalarials, terbinafine, calcium channel blockers, captopril, glyburide, granulocyte colony-stimulating factor, interleukins, interfer- ons, and lipid-lowering drugs. Systemic steroids may cause rebound or pustular flares. Antimalarials are associated with erythrodermic flares, but patients traveling to malaria-endemic regions should take appropriate prophylaxis. Often, drugs such as doxycycline or mefloquine are appropriate for the geographic area, but when a quinine derivative offers the best protection, it is generally better to take the prophylactic doses of a quinine derivative than to risk disease and full-dose treatment.

Pathology

Histologically, all psoriasis is pustular. The microscopic pustules include spongiform intraepidermal pustules, and Munro microabscesses within the stratum corneum. In early guttate lesions, focal parakeratosis is noted within the stratum corneum. The parakeratotic focus typically has an outline resembling a child's rendition of a seagull. Neutrophils are generally noted immediately above the focus of parakeratosis, but in some sections, the neutrophils will not be visible as a result of sampling error. In plaque psoriasis, neutrophilic foci are so numerous that they are rarely missed. Neutrophilic microabscesses are generally present at multiple levels in the stratum corneum, usually on top of small foci of parakeratosis. These foci generally alternate with areas of orthokeratotic stratum corneum, suggesting that the underlying spongiform pustules arise in a rhythmic fashion. The granular layer is absent focally, corresponding to areas producing foci of para- keratosis. In well-developed plaques, there is regular epidermal acanthosis with long, bulbous rete ridges, thinning over the dermal papillae, and dilated capillaries within the dermal

papillae. The last two findings correlate with the Auspitz sign. The stratum corneum may be entirely parakeratotic but still shows multiple small neutrophilic microabscesses at varying levels. Spongiosis is typically scant, except in the area immediately surrounding collections of neutrophils.

In pustular psoriasis, geographic tongue, and Reiter syndrome, intraepidermal spongiform pustules tend to be much larger. Grossly pustular lesions often have little associated acanthosis. In Reiter syndrome, the stratum corneum is often massively thickened, with prominent foci of neutrophils above parakeratosis, alternating with orthokeratosis.

Acral lesions often demonstrate nondiagnostic features his- tologically. Spongiosis is typically prominent in these lesions and often leads to a differential diagnosis of psoriasis or chronic psoriasiform spongiotic dermatitis. Foci of neutrophils often contain serum and may be interpreted as impetiginized crusting.

On direct immunofluorescence testing, the stratum corneum demonstrates intense fluorescence with all antibodies, complement, and fibrin. This fluorescence may be partially independent of the fluorescent label, as it has been noted in hematoxylin and eosin (H&E)-stained sections and frozen unstained sections. The same phenomenon of stratum corneum autofluores- cence has been noted in some cases of candidiasis that demonstrate a psoriasiform histology.

Psoriasis can generally be distinguished from dermatitis by the paucity of edema, the relative absence of spongiosis, the tortuosity of the capillary loops, and the presence of neu- trophils above foci of parakeratosis. Neutrophils in the stratum corneum are commonly seen in tinea, impetigo, candidiasis, and syphilis, but rarely are found atop parakeratosis alternating with orthokeratosis in a rhythmic fashion. In psoriasiform syphilis the rete are typically long and slender, a vacuolar interface dermatitis is commonly present, dermal blood vessels appear to have no lumen because of endothelial swelling, and plasma cells are present in the dermal infiltrate. About one- third of biopsies of syphilis lack plasma cells, but the remaining characteristics still suggest the correct diagnosis. Psoriasiform lesions of mycosis

fungoides exhibit epidermo- tropism of large lymphocytes with little spongiosis. The lymphocytes are typically larger, darker, and more angulated than the lymphocytes in the dermis. There is associated papillary dermal fibrosis, and the superficial perivascular infiltrate is asymmetrically distributed around the postcapillary venules, favoring the epidermal side (bare underbelly sign).

Clinical differential diagnosis

Psoriasis must be differentiated from dermatomyositis, lupus erythematosus, seborrheic dermatitis, pityriasis rosea, lichen planus, eczema, and psoriasiform syphilid. The distribution in psoriasis is on the extensor surfaces, especially of the elbows and knees, and on the scalp; dermatomyositis shares this distribution, whereas lupus erythematosus generally lacks involvement of the extensor surfaces. Patients with dermato- myositis may exhibit a heliotrope sign, atrophy, poikiloderma, and nailfold changes. Advanced lesions of discoid lupus ery- thematosus often demonstrate follicular hyperkeratosis (carpet tack sign). Seborrheic dermatitis has a predilection for the eyebrows, nasolabial angle, ears, sternal region, and flexures. The scales in psoriasis are dry, white, and shiny, whereas those in seborrheic dermatitis are greasy and yellowish. On removal of the scales in psoriasis there is an oozing of blood from the capillaries (Auspitz sign), whereas this does not occur in seb- orrheic dermatitis.

In pityriasis rosea the eruption is located on the upper arms, trunk, and thighs, and the duration is a matter of weeks. Lesions are typically oval and follow skin tension lines. Individual lesions show a crinkling of the epidermis and collarette scaling. A herald patch is frequently noted. Lichen planus chiefly affects the flexor surfaces of the wrists and ankles. Often the violaceous color is pronounced. In darker-skinned individuals, the lesions have a tendency to pronounced hyperpigmentation. The nails are not pitted as in psoriasis, but longitudinally ridged, rough, and thickened. Pterygium formation is characteristic of lichen planus.

Hand eczema may resemble psoriasis. In general, psoriatic lesions tend to be more sharply marginated, but at times the lesions are indistinguishable. Psoriasiform

syphilid has infiltrated copper-colored papules, often arranged in a figurate pattern. Serologic tests for syphilis are generally positive, but prozone reactions may occur, and the serum may have to be diluted in order to obtain a positive test. Generalized lymph- adenopathy and mucous patches may be present.

Treatment

Topical therapy is generally suitable for limited plaques. Localized treatments, such as the excimer laser or other forms of intense pulsed light, may be suitable for limited plaques. Phototherapy remains highly cost-effective for widespread psoriasis. Cyclosporine has a rapid onset of action, but is generally not suitable for sustained therapy. Methotrexate remains the systemic agent against which others are compared. Biologic agents can produce dramatic responses at dramatic expense. Rotating therapeutic agents that have varying toxicities have conceptual appeal, and combination therapy may reduce tox- icity and reduce the incidence of neutralizing antibodies to agents such as infliximab. Attention should be paid to comorbidities including metabolic syndrome, cardiac risk, and joint manifestations.

Topical treatment

Corticosteroids

Topical application of corticosteroids in creams, ointments, lotions, foams, and sprays is the most frequently prescribed therapy for psoriasis. Class I steroids are suitable for 2-week courses of therapy on most body areas. Therapy can be continued with pulse applications on weekends to reduce the incidence of local adverse effects. On the scalp, corticosteroids in propylene glycol, gel, foam, and spray bases are preferred by most white patients. Black patients may find them drying, and may prefer oil and ointment preparations. Low to mid- strength creams are preferred in the intertriginous areas and on the face. To augment effectiveness of topical corticosteroids in areas with thick keratotic scale, the area should be hydrated prior to application, and covered with an occlusive dressing of a polyethylene film (Saran wrap) or a sauna suit. Unfortunately, there is typically a rapid recurrence of disease

when topical corticosteroid therapy is discontinued. Side effects include epidermal atrophy, steroid acne, miliaria, and pyoderma.

Intralesional injections of triamcinolone are helpful for refractory plaques. Triamcinolone acetonide (Kenalog) suspension, 10 mg/mL, may be diluted with sterile saline to make a concentration of 2.5-5 mg/mL. Good results are also obtained in the treatment of psoriatic nails by injecting triamcinolone into the region of the matrix and the lateral nailfold. A digital block can be performed prior to injection to provide anesthesia. Injections are given once a month until the desired effect is achieved.

Tars

Crude coal tar, and tar extracts such as liquor carbonis detergens, can be compounded into agents for topical use. Tar bath oils and shampoos are readily available. Oil of cade (pine tar) or birch tar in concentrations of 5-10% may also be incorporated into ointments. The odor of all tars may be offensive.

Anthralin

Anthralin is effective, but is irritating and stains skin, clothing, and bedding. To avoid these drawbacks, short-contact anthra- lin treatment (SCAT) can be helpful, with anthralin washed off after 15-30 min. In warmer climates, SCAT is often done outdoors to keep the mess out of the house.

Anthralin exerts a direct effect on keratinocytes and leukocytes by suppressing neutrophil superoxide generation and inhibiting monocyte- derived IL-6, IL-8, and TNF-a.

Tazarotene

Tazarotene is a nonisomerizable retinoic acid receptor-specific retinoid. It appears to treat psoriasis by modulating keratino- cyte differentiation and hyperproliferation, as well as by suppressing inflammation. Combining its use with a topical corticosteroid and weekend pulse therapy can decrease irritation.

Calcipotriene

Vitamin D_3 affects keratinocyte differentiation partly through its regulation of epidermal responsiveness to calcium. Treatment with the vitamin D analog calcipotriene (Dovonex) in ointment, cream, or solution form has been shown to be very effective in the treatment of plaque-type and scalp psoriasis. Combination therapy with calcipotriene and high- potency steroids may provide greater response rates, fewer side effects, and steroid-sparing. Calcipotriene is unstable in the presence of many other topical agents and degrades in the presence of UV light. Monitoring of serum calcium levels in adults is not required. Calcipotriene plus betamethasone dipropionate (Taclonex) is more effective than either agent alone.

Macrolactams (calcineurin inhibitors)

Topical macrolactams such as tacrolimus and pimecrolimus are especially helpful for thin lesions in areas prone to atrophy or steroid acne. The burning commonly associated with these agents can be problematic, but may be avoided by prior treatment with a corticosteroid, and by application to dry skin, rather than after bathing.

Salicylic acid

Salicylic acid is used as a keratolytic agent in shampoos, creams, and gels. It can promote the absorption of other topical agents. Widespread application may lead to salicylate toxicity manifesting with tinnitus, acute confusion, and refractory hypoglycemia, especially in patients with diabetes and those with compromised renal function.

Ultraviolet light

Phototherapy is a cost-effective and underutilized modality for psoriasis. In most instances sunlight improves psoriasis. However, severe burning of the skin may cause the Koebner phenomenon and an exacerbation. Artificial UVB light is produced by fluorescent bulbs in broad-band or narrow-band spectrums. Maximal

effect is usually achieved at MEDs. Although suberythemogenic doses can be effective, the response is slower than with erythemogenic regimens. With treatment, a tanning response occurs, and the dose must be increased to maintain efficacy. Maintenance UVB phototherapy after clearing contributes to the duration of remission and is justified for many patients.

Using a monochromator, it has been shown that wavelengths of 254, 280, and 290 nm are ineffective; at 296, 300, 304, and 313 nm there is clearing. Narrow-band UVB (peak emission around 311 nm) has been shown to be more effective in treating psoriasis than broad-band UVB. Erythemogenic doses are not required in order to achieve a response. The response rates are better than 70% and close to those achievable with PUVA therapy.

Goeckerman technique

The Goeckerman technique remains an effective and cost- effective method of treatment. In its modern form, a 2-5% tar preparation is applied to the skin, and a tar bath is taken at least once a day. The excess tar is removed with mineral or vegetable oil, and UV light is given. In psoriasis daycare centers, patients clear in an average of 18 days, and 75% remain free of disease for extended periods. The addition of a topical corticosteroid to the Goeckerman regimen shortens the time required for remission. Phototoxic reactions (tar smarts) may occur as a result of UVA generated by the predominantly UVB bulbs.

Ingram technique

The Ingram technique consists of a daily coal tar bath in a solution such as 120 mL liquor carbonis detergens to 80 L of warm water. This is followed by daily exposure to UV light for increasing periods. An anthralin paste is then applied to each psoriatic plaque. Talcum powder is sprinkled over the lesions and stockinette dressings are applied. Modern versions of the technique employ SCAT.

PUVA therapy

High-intensity longwave UV radiation (UVA) given 2 h after ingestion of 8-methoxypsoralen (Oxsoralen-Ultra), twice a week, is highly effective, even in severe

psoriasis. Most patients clear in 20-25 treatments, but maintenance treatment is needed.

Although PUVA therapy is highly effective, in patients with less than 50% of the skin surface affected, UVB may be as good. Polyethylene sheet bath PUVA is another therapeutic alternative to oral psoralen-UVA. The patient is immersed in a psor- alen solution contained in plastic sheeting that conforms to the patient's body.

Oral psoralen can produce cataracts, and protective eyewear must be used. PUVA therapy is a risk factor for skin cancer, including squamous cell carcinoma and melanoma. Arsenic exposure is a more significant cofactor than prior exposure to methotrexate, UVB, or concomitant use of topical tar. Men treated without genital protection are at an increased risk of developing squamous cell carcinomas of the penis and scrotum. Although the risk of cancer is dose-related, there is no definitive threshold dose of cumulative PUVA exposure above which carcinogenicity can be predicted.

Surgical treatment

In patients with pharyngeal colonization by streptococci, an excellent response has been reported after tonsillectomy. More effective antibiotic regimens, such as a 10-day course of dicloxacillin combined with rifampin (600 mg/day for an adult), have largely replaced tonsillectomy.

Hyperthermia

Local hyperthermia can clear psoriatic plaques, but relapse is usually rapid. Microwave hyperthermia may produce significant complications, such as pain over bony prominences and tissue destruction.

Occlusive treatment

Occlusion with surgical tape or dressings can be effective as monotherapy or when combined with topical drugs.

Systemic treatment

Corticosteroids

The hazards of the injudicious use of systemic corticosteroids must be emphasized. There is great risk of "rebound" or induction of pustular psoriasis when therapy is stopped.

Corticosteroid use is generally restricted to unique circumstances, such as impetigo herpetiformis when expeditious delivery is not possible.

Methotrexate

This folic acid antagonist remains the standard against which other systemic treatments are measured. Methotrexate has a greater affinity for dihydrofolic acid reductase than has folic acid. The indications for the use of methotrexate include psoriatic erythroderma, psoriatic arthritis, acute pustular psoriasis (von Zumbusch type), or widespread body surface involvement. Localized pustular psoriasis or palmoplantar psoriasis that impairs normal function and employment may also require systemic treatment.

It is important to make sure that the patient has no history of liver or kidney disease. Methotrexate can be toxic to the liver and decreased renal clearance can enhance toxicity. Other important factors to consider are alcohol abuse, cryptogenic cirrhosis, severe illness, debility, pregnancy, leukopenia, thrombocytopenia, active infectious disease, immunodeficiency, anemia, colitis, and ability to comply with directions. Hepatic enzymes, bilirubin, serum albumin, creatinine, alkaline phosphatase, complete blood count (CBC), platelet count, hepatitis serology (B and C), HIV antibody, and urinalysis should all be evaluated before starting treatment. Patients with hypoalbuminemia have a higher risk of developing pulmonary complications.

The need for liver biopsy remains controversial. Biopsy is not without risks and is not commonly performed in the setting of methotrexate therapy for rheumatic disease. However, patients with psoriasis have a greater risk of liver disease than

other patient populations. In most patients with no risk factors for liver disease, the first liver biopsy is commonly obtained at approximately 1.0-1.5 g of cumulative methotrexate and repeated every subsequent 1.5-2.0 g until a total of 4.0 g is reached. The frequency then changes to every 1.0-1.5 g cumulative intervals. These recommendations are likely to change as more data are evaluated. Weekly blood counts and monthly liver enzyme assessment are recommended at the onset of therapy or when the dosage is changed. Monitoring of aminoterminal procollagen III peptide and metabolic panels that predict the risk of fibrosis (NASH Fibrosure) may reduce the need for liver biopsy.

Numerous treatment schedules have evolved. The authors recommend either three divided oral doses (12 h apart) weekly, weekly single doses orally, or single weekly subcutaneous injections. The weekly dose varies from 5 mg to more than 50 mg, with most patients requiring 15-30 mg a week. Once a single dose exceeds 25 mg, oral absorption is unpredictable and subcutaneous injections are recommended. Mid-week doses can result in severe toxicity and must be avoided. Oral or cutaneous ulceration may be a sign that the patient has taken a mid-week dose. Oral folic acid has been reported to decrease side effects, especially nausea, and doses of 1-4 mg/day are used. Oral folic acid is not adequate for the treatment of overdosage and leukovorin must be used in such cases.

Cyclosporine

1-The therapeutic benefit of cyclosporine in psoriatic disease may be related to downmodulation of proinflammatory epidermal cytokines. The microemulsion formulation Neoral has greater bioavailability and is now standard. Doses of 5 mg/kg/day generally produce rapid clearing of psoriasis. Unfortunately, the lesions recur rapidly as well, and transition to another form of therapy is required. Treatment durations of up to 6 months are associated with a low incidence of renal complications, but blood pressure and serum creatinine must be monitored and doses adjusted accordingly. Usually, the dose is reduced if the baseline creatinine increases by onethird.

Diet

The anti-inflammatory effects of fish oils rich in n-3 polyun- saturated fatty acids have been demonstrated in rheumatoid arthritis, inflammatory bowel disease, psoriasis, and asthma. n-3 and n-6 polyunsaturated fatty acids affect a variety of cytokines, including IL-1, IL-6, and TNF. Herbal remedies have also been used with variable effects. Many of these products are unpalatable, and their efficacy does not compare favorably to pharmacologic agents.

Oral antimicrobial therapy

The association of streptococcal pharyngitis with guttate psoriasis is well established. *Staphylococcus aureus* and streptococci secrete exotoxins that act as superantigens, producing massive T-cell activation. Oral antibiotic therapy for patients with psoriasis infected with these organisms is imperative. The efficacy of antimicrobial agents in other subsets of psoriasis is unclear. Oral bile acid supplementation has been shown to improve psoriasis, presumably by affecting the microflora and endotox- ins in the gut. Oral ketoconazole, itraconazole, and other anti-biotics have shown efficacy in a limited number of patients with psoriasis.

Retinoids

Oral treatment with the aromatic retinoid ethylester, etreti- nate, was effective in many patients with psoriasis, especially in pustular disease. Because of its long half-life, the drug has been replaced by acitretin. Alcohol ingestion can convert acitretin to etretinate and is strongly discouraged. 13-G's- retinoic acid can also produce good results in some patients with pustular psoriasis. All of these drugs are potent tera- togens and elevations in triglycerides may complicate therapy. Combinations of retinoic acids with photochemotherapy can be effective in chronic plaque psoriasis, resulting in lowered cumulative doses of light.

Dapsone

Dapsone use is limited largely to palmoplantar pustulosis or other variants of pustular psoriasis. Even in this setting, it is a second- or third-line agent with limited efficacy.

Biologic agents

A number of biologic agents are available that can produce dramatic responses in some patients with psoriasis; all are expensive. Three agents block TNF-a. Infliximab is a chimeric monoclonal antibody to TNF-a and requires intravenous infusion; etanercept is a fusion protein of human TNF type II receptor and the Fc region of IgG1; and adalimumab is a recombinant, fully human IgG1 monoclonal antibody to TNF- a. Alefacept is a fusion protein of the external domain of LFA-3 and the Fc region of IgG1; it blocks T-cell activation and triggers apoptosis of pathogenic T cells. Efalizumab, a humanized monoclonal antibody to the CD11a portion of LFA-1, has been withdrawn from the market. Ustekinumab, a human monoclonal antibody against IL-12 and 23, is the first of a new class of agents that appear highly effective. They block the inflammatory pathway at a more proximal point than TNF agents. Neutralizing antibodies may decrease the effectiveness of many of the biologic agents.

Percentage of patients clearing with each drug

Published data allow for various comparisons between biologic agents, but as trials are designed by the manufacturer to demonstrate the efficacy of the agent, the endpoints of some trials differ. In controlled trials of infliximab, the percentage of patients reaching at least 75% improvement from baseline in the psoriasis area and severity index (PASI 75) at week 10 is about 70% with infliximab 3 mg/kg and 90% with 5 mg/ kg, as compared to 6% with placebo. About 35% of patients receiving etanercept, 25 mg subcutaneously twice a week, achieve PASI 75 at 12 weeks and 45% at 24 weeks. With the 50 mg induction dose administered twice a week, about 46% of patients achieve PASI 75 at 12 weeks and 50% at 24 weeks. About 14% of

patients receiving 12 weekly intramuscular or intravenous injections of alefacept will achieve PASI 75, and about 38% PASI 50. After two 12-injection courses, about 26% of patients reach PASI 75 and 55% PASI 50. The onset of action is somewhat slower than with other agents, but ultimate clearing can be excellent. The data available suggest that about 53% of patients taking 40 mg of adalimumab every other week achieve PASI 75 by week 12, and about 80% of those taking 40 mg a week achieve PASI 75. An analysis of 24 randomized controlled trials including 9384 patients suggested that infliximab was superior to the other agents studied, and that adalimumab was superior to etanercept, 50 mg twice weekly, and cyclosporine. Ustekinumab was included in the study.

A phase III, parallel, double-blind, placebo-controlled study of ustekinumab for moderate to severe psoriasis (45 mg or 90 mg at weeks 0 and 4, and then every 12 weeks) showed that 67.1% of those who received 45 mg and 66.4% receiving 90 mg achieved PASI 75 at week 12. In a second multicenter, phase III, double-blind, placebo-controlled trial of ustekinu- mab in patients with moderate to severe psoriasis, 66.7% of patients receiving 45 mg and 75.7% receiving 90 mg achieved PASI 75.

Rapidity of clearing and relapse

The effects of infliximab are rapid and similar to those achieved with cyclosporine. In contrast to cyclosporine, clinical improvement after three intravenous infusions of infliximab is maintained for as long as 6 months in approximately half the patients. Adalimumab is also rapid in onset, with many patients demonstrating a response within the first week of treatment. About 15% of patients treated with alefacept will maintain benefits for more than 6 months.

Risks

TNF agents may induce flares of psoriasis through upregulation of plasmacytoid dendritic cells. This may be a class effect. The biologic agents all suppress the normal immune response. Infliximab has been associated with

reactivation of tuberculosis, demyelinating disease, and serious systemic opportunistic infection. It may also lose its effect because of neutralizing antibodies. Methotrexate or azathioprine may be needed as concomitant therapy to reduce the incidence of neutralizing antibodies and infusion reactions. Even though adalimumab is a fully human antibody, it may also induce an antibody response. Serious infections have been reported in patients with rheumatoid arthritis treated with this agent. Etanercept has been associated with infection, onset, or exacerbation of multiple sclerosis, vasculitis, and lupus erythematosus-like manifestations. All these manifestations are rare, and may not be statistically increased from the general population. A single 12-week course of alefacept does not appear to impair primary or secondary antibody responses to a neoantigen or memory responses to a recall antigen, but roughly 10% of patients have to interrupt therapy because CD4 counts fall below 250/mm^3, and CD4 counts must be monitored with this agent. Many of the reported complications, such as lymphoma, demyelinating disease, and infection, are not unique to any one biologic agent.

The National Psoriasis Foundation has endorsed a recommendation that all patients be screened for latent tuberculosis infection prior to any immunologic therapy. They recommend delaying immunologic therapy until prophylaxis for latent tuberculosis infection is completed, although they note that patients with severe disease may be treated after 1-2 months of prophylaxis. IFN-y assays have greater specificity than tuberculin skin tests and are being used along with imaging studies to confirm tuberculosis in patients with positive skin tests.

Combination therapy

In more severe forms of psoriasis a combination of treatment modalities may be employed. In treating patients with metho- trexate, for example, concomitant topical agents may be used to minimize the dose. Methotrexate has been combined with infliximab to reduce the incidence of neutralizing antibodies, and has been used with acitretin in managing patients with severe, generalized pustular psoriasis. The use of PUVA and retinoids is called Re-PUVA and has been studied extensively.

Acitretin has been combined with biologic agents to treat refractory psoriasis. Combination systemic therapy has the potential to reduce overall toxicity if the toxicities of each agent are different. However, new regimens should be used with caution because the potential for cumulative toxicity or drug interaction exists.

Alternative therapies

Alternative therapies for psoriasis include mycophenolate mofetil, sulfasalazine, paclitaxel, azathioprine, fumaric acid esters, climatotherapy, and Grenz ray therapy. Nail disease can respond to systemic agents, topical retinoids, local triamcinolone injections, and topical 5-fluorouracil. The latter agent can cause onycholysis if applied to the free edge of the nail.

Reactive arthritis with conjunctivitis/urethritis/diarrhea (Reiter syndrome)

Reiter syndrome is a characteristic clinical triad of urethritis, conjunctivitis, and arthritis. The disease occurs chiefly in young men of HLA-B27 genotype, generally following a bout of urethritis or diarrheal illness. Systemic involvement can include the gastrointestinal tract, kidneys, central nervous system, and cardiovascular system. As few patients present with the classic triad, the American College of Rheumatology recognizes criteria for limited manifestations of the syndrome, including peripheral arthritis of more than 1 month's duration in association with urethritis, cervicitis, or bilateral conjunctivitis.

Hans Reiter was a Nazi war criminal, involved with or having knowledge of involuntary sterilization, as well as a study of an experimental typhus vaccine that resulted in hundreds of deaths of concentration camp internees. Several authors have suggested that he no longer be afforded the recognition of using his name to designate the syndrome.

Clinical features

Any part of the triad may occur first, often accompanied by fever, weakness, and weight loss. Although the inciting ure- thritis may be bacterial, later

manifestations include a nonbac- terial urethritis with painful urination and pyuria. Cystitis, prostatitis, and seminal vesiculitis may be accompaniments. Vulvar ulceration has been reported. About one-third of patients develop conjunctivitis, which may be bulbar, tarsal, or angular. Keratitis is usually superficial and extremely painful. Iritis is common, especially in recurrent cases. Infrequently, optic neuritis may occur. An asymmetric arthritis affects peripheral joints, especially those that are weight- bearing. Its onset is usually sudden. Pain in one or both heels is a frequent symptom. Sacroiliitis may develop in up to two- thirds of patients, most of whom are of HLA-B27 type.

The skin involvement commonly begins with small, guttate, hyperkeratotic, crusted or pustular lesions of the genitals (Fig. 29), palms, or soles. Involvement of the glans penis (balanitis circinata) occurs in 25% of patients. Lesions on the soles and trunk often become thickly crusted or hyperkeratotic. The eruption on the soles is known as keratoderma blennorrhagi- cum (Fig. 30), and occurs in 10% of patients. The buccal, palatal, and lingual mucosa may show painless, shallow, red erosions. The nails become thick and brittle, with heavy sub- ungual keratosis. Children are much more likely to have the post-dysenteric form, often with conjunctivitis and arthritis as the most prominent complaints.

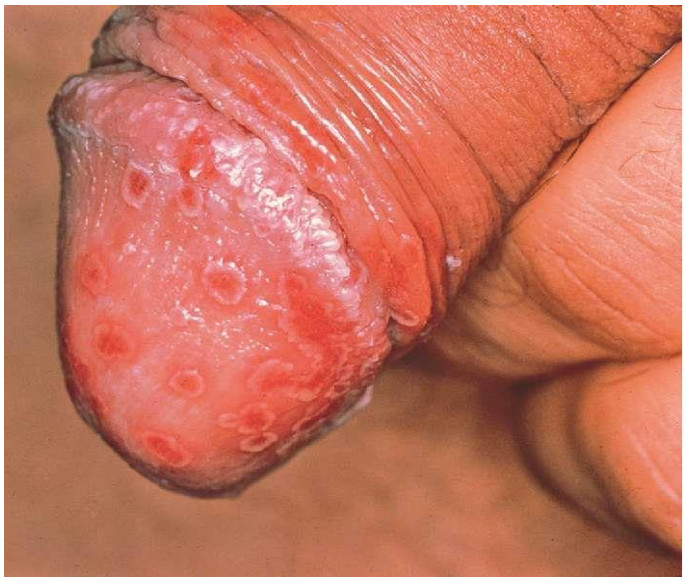


Fig. 29 Genital involvement in reactive arthritis.

The syndrome generally follows an infectious urethritis or diarrheal illness. Implicated organisms include *Chlamydia, Shigella, Salmonella, Yersinia, Campylobacter, Ureaplasma, Borrelia, Cryptosporidium*, gonococci, and bacillus Calmette-Guerin (BCG). *Chlamydia trachomatis* and *Ureaplasma urealyticum* have been isolated from the synovial fluid of affected joints, and some patients respond to antibiotic therapy. Reiter syndrome has also been observed in HIV disease, but may not be directly related to the virus, as it frequently occurs under treatment as the immune response improves. The disease has also been triggered by adalimumab and leflunomide in the setting of ankylosing spondyloarthropathy and Crohn disease.

The syndrome involves both infection and the resulting immunologically mediated tissue injury in a genetically predisposed patient. HLA-B27 is present in about 80% of cases. A positive family history is often noted.

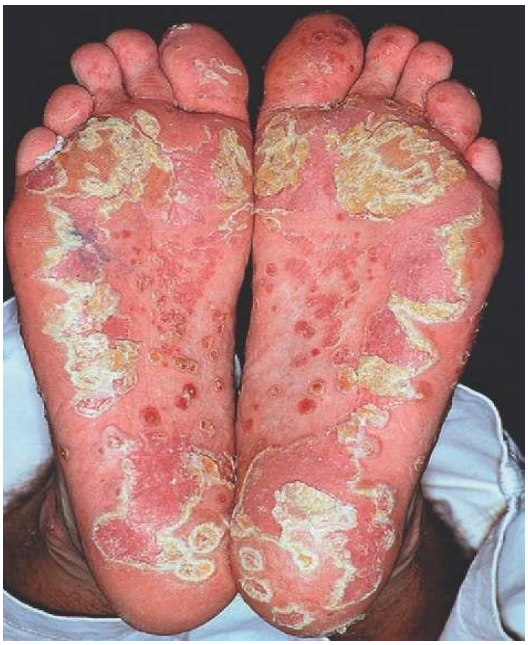


Fig. 30 Keratoderma blennorrhagicum.

Peripheral leukocytosis of 10 000-20 000/mm^3 and elevated sedimentation rate are the most consistent findings. There is no specific test for Reiter syndrome.

The differential diagnosis includes rheumatoid arthritis, ankylosing spondylitis, gout, psoriatic arthritis, gonococcal arthritis, acute rheumatic fever, chronic mucocutaneous can- didiasis, and serum sickness. The presence of associated

mucocutaneous lesions establishes the diagnosis. Some cases of Lyme disease overlap with the syndrome. Individual skin lesions may be indistinguishable from those in psoriasis. Hyperkeratotic lesions generally have a thicker scale crust than most psoriatic plaques, but are otherwise identical.

Mucocutaneous lesions are generally self-limited and clear with topical steroids. Joint disease is managed with rest and NSAIDs. Antibiotics, such as doxycycline, have been effective in some cases. Immunosuppressive agents, such as methotrex- ate, are commonly employed for refractory joint disease. Infliximab has been successful in treating severe disease. Refractory skin lesions are treated like refractory psoriasis, and severely affected patients have responded to acitretin or cyclosporine.

Subcorneal pustular dermatosis (Sneddon-Wilkinson disease)

In 1956, Sneddon and Wilkinson described a chronic pustular disease, which occurred chiefly in middle-aged women. The pustules are superficial and arranged in annular and serpigi- nous patterns, especially on the abdomen, axillae, and groins. Cultures from the pustules are sterile. Oral lesions are rare. Some cases are associated with a monoclonal gammopathy (usually IgA). The condition is chronic, with remissions of variable duration.

Histologically, the pustules form below the stratum corneum, as in impetigo. Acantholysis is absent, but spongiform pustules may be noted in the upper epidermis. The histologic differential diagnosis includes pustular psoriasis, and superficial fungal and bacterial infections. Some cases will show upper epidermal intercellular IgA staining.

IgA pemphigus shows significant overlap with subcorneal pustular dermatosis. Presentations of IgA pemphigus include subcorneal pustular dermatosis and intraepidermal neu- trophilic IgA dermatosis types. Using immunoblotting tech- niques, Hashimoto et al have shown that human desmocollin 1 is an autoantigen for the subcorneal pustular dermatosis type of IgA pemphigus.

Localized cases may respond well to topical corticosteroids. Dapsone, 50-200 mg/day (for an adult), is effective for most of the remaining cases. Some patients have responded better to sulfapyridine therapy. Acitretin, narrow-band UVB photo-therapy, colchicine, azithromycin, biologicals, and tetracycline with niacinamide may also be effective.

Eosinophilic pustular folliculitis

Eosinophilic pustular folliculitis (EPF) was first described in 1970 by Ofuji but is also referred to as sterile eosinophilic pustulosis. It occurs more commonly in males, and is mostly reported in Asia. The mean age of onset is 35. It is characterized by pruritic, follicular papulopustules that measure 1-2 mm. The lesions tend to be grouped and plaques commonly form. New lesions may form at the edges of the plaques, leading to peripheral extension, while central clearing takes place. The most frequent site is the face, particularly over the cheeks. The trunk and upper extremities are commonly affected, and 20% have palmoplantar pustules. The distribution is commonly asymmetrical, and the typical course is one of spontaneous remissions and exacerbations lasting several years. The condition must be distinguished from HIV-associated eosinophilic folliculitis, which is discussed in Chapter 19. A similar condition has occurred in association with hepatitis C virus infection, with allopurinol, and during pregnancy.

Histologically, there is spongiosis and vesiculation of the follicular infundibulum and heavy infiltration with eosino- phils. Follicular mucinosis may be present. There is a peripheral eosinophilia in half the cases, and pulmonary eosinophilia has been described. The cause is unknown; but numerous studies have implicated chemotactic substances, ICAM-1, and cyclooxygenase-generated metabolites. Tryptase-positive and chymase-negative mast cells have also been implicated.

Indomethacin is effective in the vast majority of patients. Topical and intralesional corticosteroids, clofazimine, mino- cycline, isotretinoin, UVB therapy, dapsone, colchicine, cyclosporine, and cetirizine have also been reported as effective.

Childhood cases have been described. This subset differs from the typical cases in Asian males. Pediatric patients develop sterile pustules and papules preferentially over the scalp, although scattered clusters of pustules may occur over the trunk and extremities. Leukocytosis and eosinophilia are often present. Recurrent exacerbations and remissions usually occur, with eventual spontaneous resolution. High- potency topical steroids are the treatment of choice in pediatric patients.

Recalcitrant palmoplanar eruptions Dermatitis repens

Dermatitis repens, also known as acrodermatitis continua and acrodermatitis perstans, is a chronic inflammatory disease of the hands and feet. It usually remains stable on the extremities, but in rare cases generalized pustular flares may occur. The disease usually begins distally on a digit, either as a pustule in the nailbed or as a paronychia. Extension takes place by eruption of fresh pustules with subsequent hyperkeratosis and crusting. The disease is usually unilateral in its beginning and asymmetrical throughout its entire course. As the disease progresses, one or more of the nails may become dystrophic or float away on lakes of pus. Anonychia is common in chronic cases. Some have used the term dermatitis repens to refer to more indolent involvement of the distal fingers.

Involvement of the mucous membranes may occur, even when the eruption of the skin is localized. Painful, circular, white plaques surrounded by inflammatory areolae are found on the tongue and may form a fibrinous membrane. Fissured or geographic tongue may occur.

Histologically, intraepithelial spongiform pustules identical to those of psoriasis are seen in the acute stage. Later stages show hyperkeratosis with parakeratosis or atrophy.

Numerous treatment options have been used, including topical corticosteroids, calipotriene, dapsone, sulfapyridine, methotrexate, PUVA, acitretin, cyclosporine, and topical mechlorethamine. The decision regarding which agent to use should take into consideration the severity of disease, and the patient's age and functional impairment.

Palmoplantar pustulosis (pustular psoriasis of the extremities)

Chronic palmoplantar pustulosis is essentially a bilateral and symmetrical dermatosis (Fig. 31). The favorite locations are the thenar or hypothenar eminences or the central portion of the palms and soles. The patches begin as erythematous areas in which minute intraepidermal pustules form. At the beginning these are pinhead-sized; then they may enlarge and coalesce to form small lakes of pus. As the lesions resolve, denuded areas, crusts, or hyperkeratosis may persist. Palmoplantar pus- tulosis is strongly associated with thyroid disorders and cigarette smoking. Medications such as lithium, which aggravate psoriasis, have also been reported to induce palmoplantar pustular psoriasis.

In 1968, Kato described the first case of bilateral clavicular osteomyelitis with palmar and plantar pustulosis. In 1974, Sonozaki described persistent palmoplantar pustulosis and sternoclavicular hyperostosis. These conditions belong to the spectrum of skin and joint involvement designated by Kahn as the SAPHO syndrome (synovitis, acne, pustulosis, hyper- ostosis, and osteitis). Common features include palmoplantar pustulosis, acneiform eruption, and pain and swelling of a sternoclavicular joint, or sternomanubrial or costochondral junctions. There is shoulder, neck, and back pain, and limitation of motion of the shoulders and neck is common. Brachial plexus neuropathy and subclavian vein occlusion may occur. The lumbar spine and sacroiliac joints are usually spared. Chronic multifocal osteomyelitis in children may be a pediat- ric variant. Others have described an association between palmoplantar pustulosis and arthritis or osteitis.

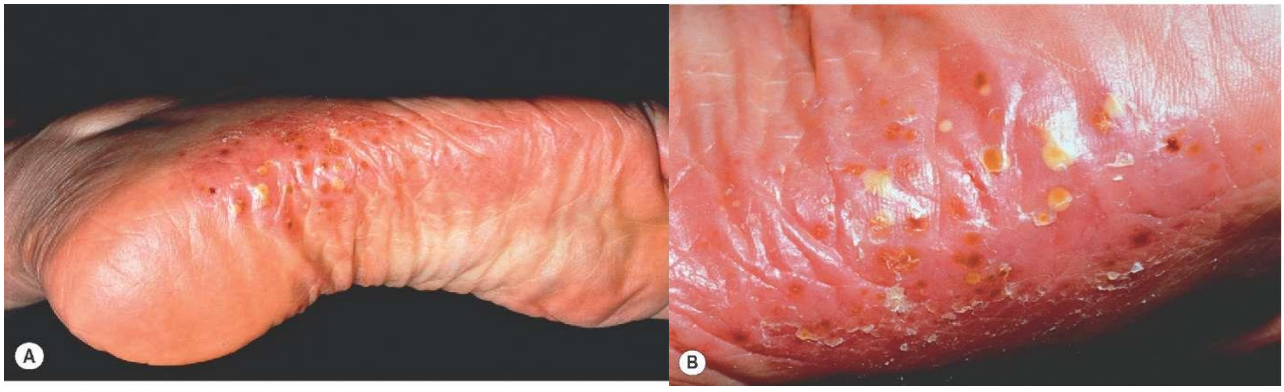


Fig. 32 A.B. Pustular and Plantas pustulosis hyperkeratosis are typical.

SAPHO syndrome may coexist with features of Behcet's disease. The knees, spine, and ankles may be involved. Ivory vertebrae have been described. The disease is commonly resistant to treatment. Topical steroids, retinoids, calcipotriene, or macrolactams are of some benefit. Acitretin is generally extremely effective at a dose of 1 mg/kg/day, although rebound occurs more quickly than with etretinate. Low-dose cyclosporine, in doses ranging from 1.25 to 5 mg/kg/day, has also been very effective, but it is not suitable for long-term treatment. Dapsone, colchicine, leflunomide, and mycophenolate mofetil may be effective. Oral 8-methoxypsoralen and high-intensity UVA irradiation or soak PUVA can both be helpful, and Grenz ray therapy can induce prolonged remissions in some patients. Chronic osteomyelitis in SAPHO syndrome has been reported to respond to bisphosphonates.

Pustular bacterid

Pustular bacterid was first described by George Andrews. It is characterized by a symmetric, grouped, vesicular, or pustular eruption on the palms and soles, marked by exacerbations and remissions over long periods. Andrews regarded the discovery of a remote focus of infection, and cure on its elimination, as crucial to the diagnosis.

The primary lesions are pustules. Tiny hemorrhagic puncta intermingled with the pustules are frequently seen. When lesions are so numerous as to coalesce, they form a honeycomblike structure in the epidermis. The disease usually begins on the mid-portions of the palms or soles, from which it spreads outwardly until it may eventually cover the entire flexor aspects of the hands and feet. There is no involvement of the webs of the fingers or toes, as in tinea pedis.

When the eruption is fully developed, both palms and soles are completely covered, and the symmetry is pronounced. During fresh outbreaks, the white blood count may show a leukocytosis that ranges from 12 000 to 19 000/mm^3 with 6580% neutrophils. As a rule, scaling is present in fully evolved lesions, and the scales are adherent, tough, and dry.

During exacerbations, crops of pustules or vesicles make their appearance, and there is often severe itching of the areas. Tenderness may be present. Many regard this condition as a variant of psoriasis, triggered by infection.

Infantile acropustulosis

Infantile acropustulosis is an intensely itchy vesicopustular eruption of the hands and feet (Fig. 33). Most cases begin by 10 months of age. Lesions often predominate at the edges of the palms and soles. Individual crops of lesions clear in a few weeks, but recurrences may continue for months or years. Scabies, tinea, and herpetic infection can produce similar lesions, and must be excluded.

Histologically, a subcorneal pustule with neutrophils is noted. Eosinophils may be numerous. As the lesions are easily punctured to produce smears of the inflammatory cells, biopsies are seldom employed. Lesions often respond to topical corticosteroids. Refractory lesions may respond to dapsone at doses of 1-2 mg/kg/day.

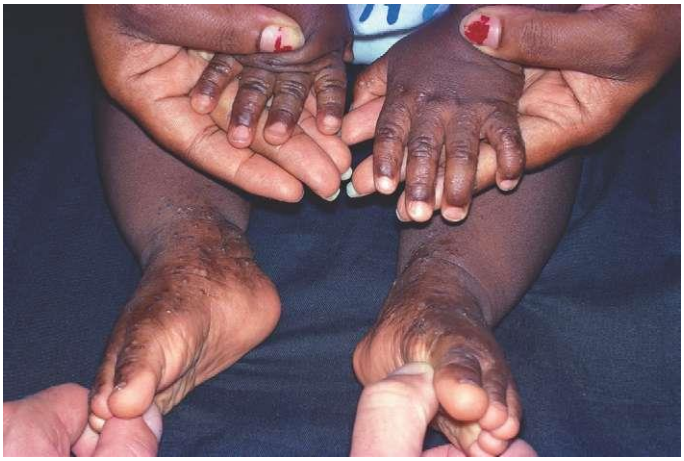


Fig. 33 Acropustulosis of infancy.

TEST

1. The skin is develops from these following germ layers:

* ecto- and mesodermal

mesoderm

enteroderm

ectoderm

2. The weight of the skin without hypodermis is include:

15% of body weight

* 5% of body weight

20% of body weight

There is not correct answer

3. The area of the skin is cover:

* 1.5 - 2 sq. m

3.5 - 4 m

4.5 - 5 m

4. During the day, with the surface of the skin evaporates:

* 600 - 800 ml of water vapor

50 - 100 ml of water vapor

200 - 300 ml of water vapor

1000 - 1500 ml water vapor

5. The sebaceous glands secretes in a week:

* 100 - 200 gr. sebum

10 - 50 gr. sebum

300 - 400 gr. sebum

500 - 600 gr. sebum

6. In the epidermis approximately separates:

* 3 layers

4 layers

5 layers

6 layers

7. In the epidermis layers are distinguished, except:

Basal layer

Suprabasal layer

granular layer

* reticulat layer

8. Proliferative cells of the epidermis are include:

* basal cells

lymphocytes

Macrophages

mastocytes

9.Normal dermographism is:

white

*red

mixed

absent

10. what feels Vater – Paciniand Golgi – Mazzoni bodies:

* feeling of a deep pressure

feeling the heat

feeling cold

pain

11. What feels tactile corpuscle of the Meysner:

* tactile sensitivity

feeling cold

pain

not involved in the perception

12. What feels Ruffini corpuscles:

*heat

pain

sense of balance

feeling cold

13. What feels glomeruli Krause:

* feeling cold

pain

a deep sense of pressure

feeling the heat

14. bristling hair localized everywhere except:

* beard and mustache

field brow

edges of the eyelids

nasal vestibule

15. The outcome of a blister:

erosion

ulcer

spot

* disappears without a trace

16. An ulcer is:

skin defect within the epidermis

* deep skin defect

Changing of the color of the skin

slight thickening of the skin

17. What are the primary morphological elements came from the papillary layer of the dermis:

*blister

epidermal papule

bullas

surface pustule

18. Polymorphic lesions occur in diseases like, except:

* Psoriasis

Lichen planus rubra

molluscum contagiosum

secondary syphilis

19. follicular pustules are listed below, except:

osteofolliculitis

folliculitis

furuncle

*impetigo

20. After opening the vesicules is formed:

vegetation

ulcer

squama

*erosion

21. parakeratosis is typical for:

* Psoriasis

Lichen planus rubra

simple bullas stripping

secondary syphilis

22. acantholysis is typical for:

shingles

scarring pemphigoid

dermatitis Duhring

* acantholytic pemphigus

23. Spongiosis typical for:

* Eczema

pemphigus

simple bullas stripping

skin tuberculosis

24. granulosis typical for:

psoriasis

* lichen planus rubra

true eczema

furuncle

25. papillomatosis is typical for:

molluscum contagiosum

* vulgar warts

Lupus eritramatosis

zoonotic form microsporia

26. Lotions are prescribed for:

Hyperkeratosis

* acute inflammation to get wet

Squamation

itching

27. Disinfectants are:

corticosteroids

*boric acid

zinc oxide

menthol

28. Subcutaneous adiponecrosis is develops from:

* 1-2 weeks of life

1-2 months of life

in the second year of life

after puberty

29. streptoderma affected:

*smooth skin

hair follicles

sebaceous glands

sweat glands

30. hydradenitis cause:

* staphylococci

streptococci

Pseudomonas aeruginosa

mixed infection

31. Vulgar Sycosis differentiate with:

lupus erythematosus

psoriasis

* parasitic sycosis

eczema

32. Gidrodenit - an inflammation:

* apocrine glands

sebaceous follicles volosiny

eccrine glands

Breast

33. Superficial staphilodermatitis is:

* ostiofollikulit

folliculitis

furuncle

hydradenitis

34. The primary lesions of the streptococcal impetigo is:

pustule

* flictenas (flaccid bladder)

blister

nodule

35. vulgar impetigo cause:

streptococci

staphylococci

* mixed infection

viruses

36. What are the morphological lesion is typical for the herpes simplex virus:

* blisters, erosion, crust

nodules, scales

nodules, blisters

abscesses, ulcers

37. primary lesion of the contagious mollusk:

*papule

tubercle

vesicle

blister

38. Ways of infection genital warts:

*sexual

transfusing

close household contact

airborne

39. The infection in a child should take the following actions:

* Isolation of healthy children

Hormone Therapy

Ultrasound of internal organs

Antibiotic treatment

40. Cause of the scabies:

virus

protozoa

* Parasites

bacteria

41. In what layer of the skin the female mite lays itch move:

in shiny

in granular

* in the stratum corneum

in the suprabasal

42. The most frequent length of the incubation period for scabies:

* 5-12 days

21 day

6 weeks

4 months

43. Clinic of the Scabies characterized by the following morphological lesions:

lenticular papules

tubercles

* paired pruritic nodules and blisters

nodule

44. Symptoms Gorchakov-Hardy, Michaelis, Sezary detected in:

Scabies

lice

leishmaniasis

acne vulgaris

45. Symptom Gorchakov-Hardy - is:

* purulent and bloody crusts in the elbow

bloody crusts in the gluteal folds

itchy, worse in the evening

excoriations due to scratching

46. Specify the most frequent complications of scabies:

sepsis

* secondary pyoderma

eczema

dermatitis

47. On the basis of the method of laboratory diagnosis is established the final diagnosis "scabies":

sowing on fertile ground

REEF

PCR

*microscopy

48. Definitive diagnosis of scabies is the main criterion is :

itch

availability scratching

* detect scabies mite

blistering

49. What are the medicines used to treat head lice:

flutsinar

Neo-Penotran

* nittifor

Augmentin

50. Complications of head lice:

* pyoderma

alopecia

allergic reactions

temperature increase

51. Pubic lice can be transmitted in:

in the bath

* during sexual intercourse

when visiting the pool

on the beach

52. The source of infection zoonotic microsporia:

Rodents

* cats, dogs

cows, horses

birds

53. The source of chronic infection trichophytosis:

cats

*people

birds

calves

54. Superfecial trichophytosis common in:

milkmaid

*children

adult men

farm workers

55. rubromikoza causative agent is:

* Trichophyton rubrum

Epidermophyton floccosum

Corynebacteria minutissima

Pityrosporum orbiculare

56. anthroponotic microsporia causative agent is:

* Microsporum ferrugineum

Microsporum lanosum

Trichophyton schonleinii

Trichophyton violaceum

57. The causative agent is Trichophyton antropofilnymi:

* Trichophyton violaceum

Trichophyton rubrum

Trichophyton verrucosum

Microsporum ferrugenii

58 agents of parasitic sycosis is:

Trichophyton rubrum

Trichophyton Schoenleini

* Trichophyton gypseum

Trichophyton violaceum

59. The luminescence in the survey using a Wood's lamp is detected in patients with:

* zoonotic microsporia

surface trichophytosis

crusted ringworm

infiltrative-suppurative trichophytosis

60. At a height of 5 to 8 mm above the hairs break off at the skin:

trihofitii

* microsporia

crusted ringworm

alopecia areata

61. Smooth skin microsporia is not typicalfor:

Presence of the erythematiuos-squamous area

* fuzzy boundaries and fast healing

Squamation

vesicules around the edge of the focus

62. For favus is typical:

the presence of crusts

* brittle hair and papuleformation

scarring

atrophy of the hair

63. For Trichophyton of the Fold are not typical:

infiltration

brick-reddish color

corral-red glow when Luminescence

* papular lesions

64. For Trichophyton Rubra are typical:

acanthosis

* hyperkeratosis

spongiosis

parakeratosis

65. For the topical treatment of fungal infections do not apply:

mikoseptin

Lamisil

clotrimazole

* prednisolone

66. Treatment of the Erythrasma are carry out by:

* erythromycin ointment

oxolinic ointment

toxoids

Oksikort

67. Balzer test is positive for:

candidiasis

athlete's foot

* Tinea versicolor

Trychophyton Rubra

68. Candidiasis of the skin and mucous are causes by:

Trichophyton rubrum

* Candida albicans

Corynebacteria minutissima

Pityrosporum orbiculare

69. The causative agent of tinea versicolor are:

* Pityrosporum orbiculare

Corynebacterium minutissimum

Epidermophyton floccosum

Trichophyton mentagraphytes var interdigitale

70. The main type of allergic response in the skin vasculitis are:

anaphylactoid

cytotoxic

* immunocomplex

and cytotoxic anaphylactoid

71. Vasculitis are divided into:

* to the superfecial and deep

infectious and noninfectious

infectious and medicinal

inherited and acquired

72. In the hemorrhagic vasculitis of the skin, are affected:

nervous system

* vessels of internal organs

articular cartilage

endocrine system

73. itching dermatosis does not include:

hives

neurodermatitis

pruritus of the Gebre

* pink zoster Gibert

74. The morphological lesion that typical for the child pruritus:

blister

nodule

microvesicles

* seropapula

75. What lesions appears in the urticarial:

papules

* blisters

Vesicles

Bulla

76. Location of the primary lesionin the urticaria:

* in the papillary layer of the dermis

in the stratum corneum of the epidermis

in the granular layer of epidermis

in hypodermis

77. What dermographism are investigates urticaria in the patients:

*red

white

mixed

dermogrfizm are not appear

78. Bullous dermatoses does not apply:

pemphigus vulgaris

bullous pemphigoid

herpetiformis dermatosis

* pemphigus of the newborns

79. Bullous dermatosis, in which bulles usually start in the oral mucosa:

* pemphigus vulgaris

familial pemphigus

syphilitic pemphigus

Duhring-Brock disease

80. acantholytic pemphigus group does not include:

vulgar

seborrheic

vegetating

* Familiar

81. Levels of lying of the bulla with respect to the epidermis in the pemphigus are:

* intraepidermal

subepidermal

intradermal

intraepidermal

82. vulgar pemphigus are investigate in the:

* IgG deposition in the intercellular substance and thorny layer cells

IgG deposits in the basal membrane

immune complex deposition beneath the basement membrane

green light (Wood's lamp)

83. The skin around the bullas in the pemphigus:

hyperemic

* is not changed

infiltrated

purplish tone

84. To get the symptoms of asbestos-Hansen should:

* press the bullas

open top of the bullas

Pull top of the bullas

rub between bullas

85. For the treatment of pemphigus apply:

antibiotics

* glucocorticoid hormones

iron supplements

antihistamines

86. Seborrheic pemphigus includes the following symptoms:

* lupus, seborrheic dermatitis and pemphigus

Lichen planus rubra, vasculitis and pemphigus

lupus erythematosus, dermatomyositis, and pemphigus

scleroderma, psoriasis and pemphigus

87. Pemphigus is differentiate from dermatitis Dühring with:

severe itching

tense of the bulla

grouping bullas

* positive sign of Nikolsky

88. Polymorphism of the lesion are typical for:

pemphigus vulgaris

bullous pemphigoid

* Duhring disease

Leaf like-pemphigus

89. dermatosis, which a diagnostic significance with a positive test of iodine:

pemphigus vulgaris

* dermatitis Duhring

bullous pemphigoid

familial pemphigus

90. Laboratory tests for the diagnosis of disease Dühring are:

* eosinophilia in the blood and bullous fluid

Ttsanka cells in smears prints from the bottom of erosions

Sezary cells

a symptom of a ladies' heel

91. Except the skin at the scarring pemphigoid are affected:

skin folds

scalp

* conjunctival mucosa

nail plate

92. What primary lesions observed in psoriasis:

* papule

blister

bullas

tubercle

93. Symptom Pilnova in psoriasis are:

* bright red color of the papules

atrophic ring around papules

isomorphic skin reaction

desquamation in the center of papules

94. When heelpiece (heeling) of the papules in psoriasis are observed:

a symptom of a hidden desquamation

* psoriatic triad phenomena

a symptom of a ladies' heel

symptom "cobblestones"

95. What is the morphological basis of the phenomenon of "terminal membrane":

acantholysis

spongiosis

* acanthosis

ballooned degeneration

96. Positive isomorphic Koebner reaction is:

* the appearance of fresh papules at the site of injury in 7-14 days

the phenomenon of "stearin spot"

the phenomenon of "hidden desquamation"

Voronov rings

97. In the treatment of psoriasis do not apply:

hyposensitizing drugs

sedatives

vitamins

* antivirals

98. Polygon shiny papules with Umbriacal like impression observed at:

*Lichen Planus Rubra

psoriasis

secondary recurrent syphilis

secondary fresh syphilis

99. Pathological changes in lichen planus rubra:

* hypergranulesis

Akantolisis

swelling of the papillary layer of the dermis

endo-, meso-, periarteritis

100. Grid Wickham observed at:

* Lichen planus rubra

discoid lupus erythematosus

psoriasis

centrifugal erythema of Biett

102. lichen rosacea is localized mainly on:

scalp

shins

* the body, along the lines of skin tension

feet

103. For the treatment of lichen rosacea it is advisable to appoint:

* allergen therapy

hormones

antifungal antibiotics

lidase

104. Specify obligate precancerous disease:

Bowen's disease

* xeroderma pigmentosum

leukoplakia

Keira erythroplasia

105. The basal cell carcinoma is more often localized on:

palms

* Facial

trunk

hips

106. In chronic lupus eritematosis affected:

kidneys

liver

C.N.S

*skin

107. centrifugal erythema characterized by:

*erythema

follicular hyperkeratosis

atrophy

108. Currently lupus eritematosis relate to the:

infectious diseases

* autoimmune diseases

viral diseases

sexually transmitted diseases

109. For the topical treatment of lupus eritematosis apply

antibiotic ointments

* steroid ointment

salicylic ointment

antifungal ointment

110. discoid lupus erythematosus ends with:

* scarring

pigmentation spots

pass completely

transformed into lymphoma

111. For dermatomyositis is characterized by:

muscle hypertrophy

hemosiderosis

* kreatinuriya

anemia

112. For the treatment of localized scleroderma are used:

Lotion

UFO

*paraffin

PUVA - therapy

113. plaque of the scleroderma ends with:

* scar atrophy

pigmentation spots

pass completely

joining a secondary infection

114. Primary lesion of the tuberculosous lupus are:

* tuberculums

ulcers

nodules

papules

115. For the treatment of dermatomyositis is used:

* Corticosteroids

calcium supplements

tranquilizers

antistaphylococcal immunoglobulin

116. papule - necrotizing tuberculosis differentiate from:

exudative erythema multiforme

* pruritus

psoriasis

skrofulodermy

117. Skrofuloderma often localized:

* neck area

groin

hips

trunk

118. Verrucose tuberculosis are often localized at:

trunk

* back of the hand

scalp

palms

119. The diagnosis of tuberculosis of the skin is put on the basis of:

tuberculin tests

skin biopsies

fluorography of lungs

* All the above methods are correct

120. Tuberculosis of the skin are treated with:

penicillin

tetracycline

* rifampicin

gerpevir

121. Erythema nodosum of Bazin is localized on:

the face

trunk

* legs

scalp

122. The source of infection of old world type of leishmaniasis are:

sick cats

* Rodents

cattle

sick people

123. The sources of contamination new world leishmaniasis type are:

Rodents

cattle

*sick people

cats, dogs

124. Carriers Leishmania are:

* Mosquitoes

sick animals

sick people

Rodents

125. Leishmaniasis clinic is typical for:

tubercle

ulcer

scar

* All the above mentioned are correct

126. Treatment of leishmaniasis are used:

hormones

* Antibiotics

sulfa drugs

antifungals agents

127. The causative agent of leprosy:

protozoa

* mycobacteria

Spirochetes

Viruses

128. The incubation period for leprosy include:

a few days

a few months

*some years

few hours

129. Mycobacterium leprae looking for:

in sputum

in fecal masses

* in scrapings from the nasal mucosa

urine

130. lepromatous type of leprosy differentiates from:

psoriasis

lichen planus rubra

* gummy syphilides

Lichen rosacea

131. In the base of eczema are highlights histopathological changes:

parakeratosis

* spongiosa

Akantolizis

Vegetation

132. For Vitiligo is typical primary lesions:

papule

blister

* depigmentation spot

Nodule

133. The causative agent of syphilis:

* Treponema pallidum

Treponema balanitidis

Treponema pertenue

Treponema caratea

134. Treponema pallidum has been discovered:

in 1901year

1889 year

* in 1905 year

1926 year

135. The duration of the division of pathogenic Treponema pallidum is including:

6-8 hours

10-12 hours

15-20 hours

* 30-33 hours

136. The length of Treponema pallidum approximately include:

* 6-20 microns

50-60 microns

30-40 microns

40-50 microns

137. The incubation period for syphilis is shortened in:

In drug users (narcomoniac)

* in young, physically healthy people

in individuals with immunodeficiency

after taking antibiotics

138. Headless syphilis is possible in:

* in blood transfusion patient

Late congenital syphilis

indefective preventive treatment

the presence of extragenital chancre

139. After contact with patience syphilis, hard chancre appears within:

1 week

2 weeks

*4 weeks

6-7 weeks

140. What period begins "transfusion" Syphilis:

primary

* with secondary

Tertiary

with congenital

141. The scar after healing of the chancre is called:

Cain printing

* seal the devil

chancre-print

stellate

142. What is the re-infection of syphilis:

* reinfection

superinfection

Jarisch-Herxheimer-Lukashevich response

immunoblotting

143. Wasserman reaction after infection with syphilis will be positive within:

3-4 weeks

* 6-8 weeks

9-12 weeks

24 years

144. The most specific serologic test for syphilis is:

immunofluorescence

* immobilization reaction treponem

Wasserman reaction

microreaction

145. The reaction of immobilization treponema palidium is made purpose of:

confirm the diagnosis of primary syphilis

* confirm the diagnosis of latent syphilis

confirm the diagnosis of secondary syphilis fresh

to monitor of treatment

146. The increase in regional lymph nodes after the appearance of the chancre is usually observed within:

1^{st} -2^{nd} days

* 5^{th}-8^{th} days

9^{th}-12^{th} days

13^{th}-16^{th} days

147. The main drugs for the treatment of patients with syphilis are include:

* penicillin drugs

Tetracycline drugs

drugs erythromycin

macrolides

148. To the side effects in the treatment of syphilis with penicillin are all listed, except:

anaphylactic shock

toksidermia

candidiasis

* alopecia

149. The secondary period of syphilis begins from the moment of infection within:

2 weeks

2 months

*3 months

6 months

150. Secondary syphilides of the mucous membranes:

Occurs rare

* Observed in the form of a papules andspotty rash

Have a fuzzy boundaries

Not very contagious

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CONTENT

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Lichen planus. Psoriasis.
nomli o‘quv qo‘llanmasi
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