**LICHEN PLANUS**

**Synonym**
- Lichen ruber planus

**Key features**
- Idiopathic inflammatory disease of the skin, hair, nails and mucous membranes, seen most commonly in middle-aged adults
- Flat-topped violaceous papules and plaques favor the wrists, forearms, genitalia, distal lower extremities and presacral area
- Clinical variants include annular, bullous, hypertrophic, linear, ulcerative and lichen planopilaris
- Histologically, there is a dense, band-like lymphocytic infiltrate with destruction of the epidermal basal cell layer
- In this T cell-mediated autoimmune disorder, basal keratinocytes express altered self-antigens on their surface

**Introduction**

Lichen planus (LP), the prototype of lichenoid dermatoses, is an idiopathic inflammatory disease of the skin and mucous membranes. It is characterized by pruritic violaceous papules that favor the extremities. Histologically, a dense, band-like lymphocytic infiltrate is seen underlying an acanthotic epidermis with destruction of the basal cell layer and hypergranulosis. Although its etiology and pathogenesis are not fully understood, LP has been associated with multiple disease processes and agents, such as viral infections, autoimmune diseases, medications, vaccinations and dental restorative materials. LP-like lesions indistinguishable from idiopathic LP also develop in chronic graft-versus-host disease (GVHD) where alloreactive T cells that recognize foreign major histocompatibility complex (MHC) molecules are central effectors. This lends support to the hypothesis that an autoimmune reaction against epitopes on lesional keratinocytes that have been modified by viral or drug antigens may be responsible for this disorder.

Lichenoid eruptions represent a heterogeneous group of conditions that resemble idiopathic LP in terms of their clinical appearance and demonstrate a lichenoid tissue reaction. The latter (as defined by Pinkus) is a histologic pattern characterized by epidermal basal cell damage that is intimately associated with a massive infiltration of mononuclear cells in the papillary dermis. Many clinically distinct inflammatory dermatoses have in common varying elements of lichenoid histologic features, and these are referred to as lichenoid dermatoses (Table 12.1).

**History**

<table>
<thead>
<tr>
<th>LICHENOID DERMATOSES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lichenoid dermatoses</td>
</tr>
</tbody>
</table>

**Table 12-1. Lichenoid dermatoses.**
The term *lichen planus* was initially introduced by Erasmus Wilson in 1869 to describe the condition that had been previously named *leichen ruber* by Hebra.

**Epidemiology**

Although its incidence varies depending upon geographic locale, cutaneous LP has been reported to affect from 0.22 to 1% of the adult population, whereas oral lesions have been observed in up to 1-4% of the population. There is no overt racial predisposition. The onset of LP occurs most commonly during the fifth or sixth decade, with two-thirds of patients developing the disease between the ages of 30 and 60 years. Only 1-4% of patients are children and the elderly are rarely affected. Oral LP is also very uncommon in young patients and appears most often in middle-aged to elderly individuals (mean age at diagnosis being 52 years). Although LP is frequently thought to have no gender predilection, some studies have found that women were affected approximately twice as often as men.

Mucosal involvement, including oral lesions, may be observed in up to 75% of patients with cutaneous LP, and in approximately 25% of cases it can be the only manifestation of the disease. Conversely, only 10-20% of patients whose initial presentation is oral LP will develop cutaneous LP. Although reports of familial LP are rare, it may occur more frequently than previously thought; for example, LP occurs in up to 10% of first-degree relatives of affected patients; cases of familial LP had an earlier onset and the relapse rate was higher. Nonetheless, reports of concurrent LP in monozygotic twins who were living together suggest an infectious or other environmental trigger.

**Pathogenesis**

There is a growing body of evidence that LP represents T cell-mediated autoimmune damage to basal keratinocytes that express altered self-antigens on their surface.

**Target antigens**

Clinical observations and anecdotal evidence have long suggested a relationship between...
exposure to a number of exogenous agents (e.g. viruses, medications and contact allergens) and the development of LP. A critical component for the generation of effector T cells with cytotoxic potential is the presentation of these exogenous antigens in the context of antigen-presenting cells.

Hepatitis C virus

Of the many potential exogenous antigens, attention has recently been focussed on the possible role of viruses, in particular hepatitis C virus (HCV). In several case-control studies, the prevalence of HCV (3.4-38%) was 2- to 13.5-fold higher in patients with LP than in controls. This association seems to be strongest in Japanese and Mediterranean populations, probably due to the high prevalence of HCV infection in these countries. In the US, one case-control study found that 12 (55%) of 22 patients with LP had anti-HCV antibodies, and this was significantly higher than the 25% of 40 psoriatic patients or the 0.17% of blood donors who tested positive; however, not all investigators have confirmed this association. Of note, an association between either hepatitis A virus (HAV) or hepatitis B virus (HBV) and LP has never been well demonstrated.

Of the various types of LP, it is the oral form that is most commonly viewed as a manifestation of HCV infection. The polymerase chain reaction (PCR) technique (see Fig. 4.3) detected HCV RNA in 93% of oral LP lesions; however, this result was not confirmed by a less sensitive immunoperoxidase staining procedure or by other PCR studies. Possible explanations for these conflicting results include: (1) the detection of HCV RNA could simply reflect the absorption of viral particles onto the cellular surface membrane via Fc-receptor-mediated binding of antibody-coated viral particles; (2) there is a scarcity of active viral replication, as evidenced by the inability to constantly detect HCV genomic sequences in LP lesions of most patients with HCV-associated LP; (3) HCV itself may not be of pathologic importance in the skin and it only represents a triggering factor necessary for immune system alterations; (4) an interaction with other factors (e.g. genetic, infectious and/or environmental agents) is required (e.g. HCV infection might only cause LP in patients with a predisposing HLA haplotype); and (5) there are technical limitations in viral detection due to the well-described genomic diversity of HCV, which makes it particularly difficult to develop equally sensitive and specific experimental conditions for all the existing genotypes. Of note, increased frequency of the HLA-DR6 allele has been reported in Italian patients with HCV-associated oral LP, raising the possibility that CD4+ T cells activated upon recognition of HCV-encoded peptides bound to HLA-DR6 molecules could be directly involved in the pathogenesis of LP.

Other viruses

With regard to the role of other viruses in LP, investigations have examined TT virus (TTV), because TTV is highly prevalent in patients with liver diseases including those with chronic hepatitis C infection. In situ hybridization was positive in the oral mucosa biopsy specimens from all patients with TTV DNA in their serum, irrespective of whether they had oral LP or not. The hybridization signals were localized exclusively within the cytoplasm of the basal keratinocytes, indicating that epithelial cells represent a site of TTV replication. However, the results did not support a direct role for TTV in causing oral LP. In contrast, human herpesvirus-6 (HHV-6) was detected in 67-100% of oral LP lesions by in situ hybridization and immunohistochemical techniques and it was absent from normal oral tissues. However, PCR detected HHV-6 in only 22-23% of specimens from normal oral tissue.

A number of reports have described the appearance of LP after administration of the HBV vaccination. The time interval between the initial dose and the development of cutaneous or mucosal lesions has varied from 2 weeks to 5 months. It is possible that HBV-reactive T cells cross-react with epitopes expressed on keratinocytes.

Bacteria
Studies investigating a possible bacterial connection with LP have been limited and have not supported a definitive etiologic role for *Helicobacter pylori* in LP.

**Contact allergens**

The role of contact allergy to a variety of metals in the exacerbation or induction of oral LP has been well described, based on exposure to metallic dental restorations or constructions, positive patch test results, and regression or complete clearing after removal of the sensitizing metal and replacement with other materials. The metals that aggravate oral LP include amalgam (mercury), copper and gold. Although approximately 94% of patients had improvement after the removal of the sensitizing metal, 75% of patients with negative patch test results also reported clearing of oral LP after removal of the metal and replacement with other materials. Such results indicate that spontaneous remissions may occur and draw into question the importance of contact allergy to metals in the pathogenesis of LP. The development of contact allergy to metals within dental restorations in patients with LP could be explained by easy penetration of the metal through damaged mucosa.

**Autoantigens**

In occasional patients, LP has been reported as an autoimmune reaction triggered by an underlying neoplasm. In addition, a lichenoid tissue reaction is seen in patients with paraneoplastic pemphigus. The temporal relationship between LP and the underlying neoplasm in the reported patients suggests that the neoplasms may have stimulated a cell-mediated immune response against tumor antigens that led to the generation of autoreactive T cells that cross-reacted against antigens expressed on epidermal cells.

Many investigators have described a significant association between specific HLA antigens and LP, for example, an increased frequency of HLA-B27, HLA-B51, HLA-Bw57 (oral LP in English patients), HLA-DR1 (cutaneous and oral LP) and HLA-DR9 (oral LP in Japanese and Chinese patients) has been reported in patients with LP. However, a true association with a particular HLA allele has been difficult to establish because of the significant geographic heterogeneity and clinical patient selection. Patients with LP often relate the onset and aggravation of symptoms to increased levels of stress, but no conclusive data have been published. Finally, a variety of drugs have been implicated in the pathogenesis of LP or lichenoid dermatitis (see below).

---

**Figure 12.1 Mouse model for the lichenoid tissue reaction.** Because in humans all the analyses are performed on existing skin lesions (after the inflammatory response is underway), it is difficult to provide insight into initiating events and to establish whether the T cells present are indeed relevant to the pathogenesis. This experimentally induced animal model has the advantage that the orchestrated series of events resulting in epidermal injury can be examined from the onset and over time.

A murine model of LP has been established by employing autoreactive T cells (Fig. 12.1). Intradermal inoculation of CD4+ autoreactive T-cell clones into the footpads of syngeneic mice can induce local histologic changes similar to LP or lichenoid skin diseases. In this model, the autoreactive T cells can respond to self MHC class II antigens constitutively expressed on...
macrophages and Langerhans cells, and they migrate into the epidermis, resulting in epidermal injury. These T cells, therefore, can induce LP-like lesions without any alteration in the antigenicity of the epidermis. In the natural disease process, however, alterations in the antigenicity of epidermal cells induced by exogenous agents such as infections (see above) could be a prerequisite for triggering the activation of these T cells. Of note, such autoaggressive reactions could function to eliminate abnormal keratinocytes altered by these exogenous agents. However, in the situation where T cells initially responding to self-antigens modified by exogenous agents subsequently become cross-reactive with some self-epitopes, these T cells would chronically respond to the previously ignored self-epitopes, leading to perpetuation of an autoimmune attack by these T cells rather than elimination of the abnormal keratinocytes.

**Effector cells**

There are conflicting data regarding the phenotype of the inflammatory infiltrate in LP lesions. Although initial immunohistochemical studies showed that the cellular infiltrate contained an increased ratio of CD4+ to CD8+ T cells, other investigators found a predominance of CD8+ T cells, particularly in older lesions. Evidence to support the crucial role of CD8+ T cells in autoimmune damage to basal keratinocytes has been provided by CD8+ T cells isolated from lesional skin; these T cells exhibited specific cytotoxic activity against autologous lesional and normal keratinocytes. Further investigations found that T-cell lines derived from lesional skin contained a distinct population of T cells that was rarely present in the lines derived from normal skin. In addition, Schiller et al. demonstrated that of 36 patients with LP, 9 (25%) had monoclonal rearrangements of the TCR-β chain gene in the biopsy specimens of their skin lesions. One caution is that these CD8+ T-cell lines and clones could represent an in vitro selection and/or expansion of autoreactive T cells during their culture with autologous antigen-presenting cells.

Basal cell damage as evidenced by apoptotic DNA fragments is greatest in the epidermis closely associated with areas of CD8+ T-cell invasion of the epidermis. Therefore, keratinocytes are likely to be killed via cross-linking of the Fas receptor expressed on the keratinocytes by its ligand (Fas L) expressed by CD8+ T cells and possibly NK cells. This interaction triggers a cascade of intracellular enzymatic reactions resulting in DNA fragmentation (see Chapter 108). In addition to Fas, death receptor-induced apoptosis involves signaling processes via TNF-R1, TRAIL-R1 and 2, and DR3 or DR6. Because Th1 T cells (see Chapter 5), like the autoreactive CD4+ T cells in the murine model (see Fig. 12.1), can produce large amounts of IFN-γ and lymphotoxin-α (LT-α, known as TNF-β) upon activation and thereby induce or enhance the expression of apoptosis-associated proteins such as Fas and TRAIL, they may also have a role in extensive epidermal damage by promoting apoptotic death of keratinocytes.

In addition, IFN-γ and TNF-α released by both CD4+ T cells and CD8+ T cells can induce keratinocyte expression of ICAM-1, thereby rendering these T cells more adhesive to the keratinocytes and thus facilitating granular exocytosis mediated by perforin/granzymes. Of note, these cytokines have been shown to be present at high concentrations in LP lesions and these proinflammatory cytokines can also be produced by altered keratinocytes. Recent studies have shown that granule exocytosis rather than the Fas/Fas L system is the main pathway of cytotoxicity mediated by CD4+ and CD8+ T cells in humans. Thus, the effector mechanism(s) for epidermal damage by T cells could be far more complex than originally thought, and further studies are needed to define the complex interplay among these T cells.

**Effector T cells' access to the epidermis**

A critical event in the initiation of immune responses in LP lesions is for T cells to migrate from the circulation into a particular skin site. Large amounts of proinflammatory and type 1 cytokines, such as TNF-α and IFN-γ, released by activated T cells induce or upregulate E-selectin and subsequently ICAM-1 and skin-associated chemokines, such as CCL27, on the endothelium and this sequential expression of adhesion molecules is important for facilitating the
transmigration of specific T cells across the endothelium and into the interstitial space of the dermis (see Chapter 5). With regard to migration of T cells towards the epidermis, keratinocytes have been shown to secrete a variety of lymphocyte-attractant chemokines upon stimulation with cytokines. A set of chemokines composed of IP-10, MCP-1, RANTES and MIG are produced by basal keratinocytes in LP lesions, in particular early lesions, and would serve to attract T cells to the dermo-epidermal junction.

CXC chemokine receptor 3 (CXCR3) is expressed by memory T cells (preferentially by the Th1 subset) and by NK cells. Flier et al. demonstrated that CXCR3 was consistently expressed by the majority of both CD4+ and CD8+ dermal T cells in LP lesions and that CXCR3-targeting chemokines CXCL10, CXCL9 and CXCL11, which are all induced by IFN-γ, were expressed at the dermo-epidermal junction and adjacent papillary dermis at sites where lymphocytes were in close contact with the epidermis. These findings indicate that these CXCR3-activating chemokines play an important role in the recruitment and maintenance of the band-like T-cell infiltrates seen in LP.

Clinical Features

The characteristic primary lesion of LP is a small, polygonal-shaped, violaceous, flat-topped papule; some papules are umbilicated. The surface is slightly shiny or transparent, and a network of fine white lines called ‘Wickham’s striae’ or small gray-white puncta are also seen. The latter correspond histologically to focal thickening of the granular layer. The papules may be widely dispersed or they may cluster or coalesce into larger plaques. Although LP is usually pruritic, secondary excoriations and impetiginization are unusual.

The Koebner phenomenon (i.e. isomorphic response) is commonly seen. LP may present initially as linear papules presumably reflecting koebnerization into sites of previous trauma. Such lesions need to be distinguished from the linear variant of LP which follows the lines
of Blaschko (see below). The most frequently involved sites are the flexor surfaces of the wrists and forearms; the dorsal surfaces of the hands, anterior aspect of the lower legs, neck and presacral area are also common sites. The mucous membranes, especially the oral mucosa (see below), are affected in more than half of patients, and this is often the only site of involvement. Lesions are also commonly seen on the glans penis, where they can have an annular configuration (Fig. 12.7A) or become erosive. Several of the distinctive variants of LP are discussed separately. The duration of the disease is dependent on the LP variant. Spontaneous remission is infrequent, particularly in hypertrophic, oral and nail LP; most patients will have oral LP for the duration of their lives.

**Actinic LP**

This variant is reported under a variety of names, including LP actinicus, LP subtropicus, LP tropicus and lichenoid melanodermatitis. Although the majority of cases have been reported from Middle Eastern countries, it is has been observed worldwide. Most patients are young adults or children. There is no predilection for either sex. The onset of this variant is during the spring and summer, and the lesions primarily involve sun-exposed skin of the forehead and face, followed by the dorsal surfaces of the arms and hands and the neck. The lesions usually consist of red-brown plaques with an annular configuration, but melasma-like hyperpigmented patches have been observed. In the literature, summertime actinic lichenoid eruption has sometimes been regarded as a variant or synonymous with actinic LP, but in our opinion they are two separate entities with different histologic features. However, it appears uncertain whether actinic LP could represent a photolocalized variant of LP or an intermediate form between LP and photoallergic dermatitis.

**Acute LP**

Because lesions are usually widely distributed and disseminate rapidly, this form is also known as exanthematous or eruptive LP. The commonly affected areas include the trunk (Fig. 12.8), the inner aspects of the wrists and the dorsae of the feet. Reports of this form in the literature probably include lichenoid drug eruptions. The clinical course is usually self-limited and, in general, lesions resolve with hyperpigmentation within 3 to 6 months.

**Annular LP**

This form is thought to occur when papules spread peripherally and the central area becomes inactive (Fig. 12.7). Annular lesions occur in about 10% of patients with LP and are usually scattered amongst more typical lesions. A predominance of annular lesions is unusual and case...
with a few large annular lesions are rare.

Figure 12.4 Lichen planus on the dorsal surface of the hand. Wickham’s striae can be easily identified in the upper right lesion. Note the flat-topped nature of the lesions.

Figure 12.5 Lichen planus. Violaceous papules and plaques with white scale and Wickham's striae.

Atrophic LP

Atrophic LP may represent a resolving phase of LP, given the history of the lesions: papules coalesce to form larger plaques that often, over time, become centrally depressed and atrophic with residual hyperpigmentation. The clinical appearance of atrophic LP is likely a result of thinning of the epidermis rather than degeneration of elastic fibers. The most common site of involvement is the lower leg. This form closely resembles lichen sclerosus clinically; it may even mimic the early phase of morphea. Occasionally, morphea of the trunk has been reported in association with oral LP, as has the simultaneous occurrence of LP and lichen sclerosus, as well as the combination of LP, morphea and lichen sclerosus, the latter reflecting the well-known relationship between morphea and lichen sclerosus. Pseudopelade has been observed in patients with atrophic LP.

Figure 12.6 Koebnerization of lichen planus into the site of the excision of the saphenous vein. Lesions also appeared where steri-strips® had been supplied.
Figure 12.7 Annular lichen planus of the glans penis (A) and the trunk (B).

Figure 12.8 Papulosquamous lesions of exanthematous LP on the back.

Figure 12.9 Bullous lichen planus on the shin.

Bullous LP and LP pemphigoides
Bullous or vesiculobullous lesions can develop either within pre-existing LP lesions or in previously uninvolved skin. The former is often called bullous LP (Fig. 12.9), while the latter is referred to as LP pemphigoides. There has been considerable confusion regarding terminology in the dermatologic literature: while some authors have used the term ‘LP pemphigoides’ to describe bullous LP, others believe that LP pemphigoides represents the coexistence of LP and bullous pemphigoid (BP). As a result of more recent studies, a consensus has emerged that LP pemphigoides can be differentiated from bullous LP. In the latter, blisters occur in long-standing lesions of LP as a result of an intense lichenoid infiltration of lymphocytes and extensive epidermal damage, i.e. exaggerated Max-Joseph spaces. In contrast, in LP pemphigoides there are circulating IgG autoantibodies directed against the 180 kDa BP antigen (BPAG2, type XVII collagen), as in idiopathic BP. These findings suggest that damage to the basal layer by a lichenoid infiltrate may expose hidden antigens to the autoreactive T cells, leading to the formation of autoantibodies and subepidermal bullae. No reactivity against the 230 kDa BP antigen, type VII collagen or the laminin-5 subunits has been detected.

**Hypertrophic LP**

This variant is also referred to as LP verrucosus (Fig. 12.10). Extremely pruritic, thick hyperkeratotic plaques are seen primarily on the shins or dorsal aspect of the foot. The lesions are usually symmetric and tend to be chronic because of repetitive scratching. The average duration of hypertrophic lesions in patients whose lesions had cleared was reported to be 6 years. Chronic venous stasis frequently contributes to the development of this condition. Squamous cell carcinoma, which must be distinguished from pseudoepitheliomatous hyperplasia, has been reported to arise within these lesions.

**Lichen planopilaris**

In lichen planopilaris, involvement of the hair follicle is observed, both clinically and histologically. This variant is also called follicular LP and LP acuminatus. Multiple, keratotic plugs surrounded by a narrow violaceous rim are observed primarily on the scalp, although other hair-bearing areas can also be affected (Fig. 12.11). The inflammatory process may result in scarring and loss of follicular structure, i.e. a permanent alopecia. Over time, the central areas of the scalp often 'burn out' and are indistinguishable from pseudopelade of Brocq. However, examination of the periphery may reveal the primary lesions (Fig. 12.11C). Women are more frequently affected than men, and this form may occur alone or with typical LP lesions elsewhere. A variant of lichen planopilaris known as Graham Little-Piccardi-Lassueur syndrome is characterized by the triad of (1) spinous or acuminated follicular lesions (Fig. 12.11B); (2) typical cutaneous or mucosal LP; and (3) alopecia of the scalp with or without atrophy (Fig. 12.11C). These features need not be present simultaneously.
Figure 12.11 **Lichen planopilaris.** A Keratotic spines surrounded by a violaceous rim in a linear variant and B scattered on the trunk. C Scarring alopecia with pseudopelade-like changes centrally, but perifollicular inflammation at the margins.

**Linear LP**

Although linear lesions frequently occur in patients with LP as a result of the Koebner phenomenon in sites of scratching or trauma, the term linear LP ([Fig. 12.12](#)) is usually reserved for lesions that appear spontaneously within the lines of Blaschko ([Fig. 12.11A](#)). This form has also been referred as zosteriform but the distribution pattern is not dermatomal (with the rare exception of the koebnerization of LP into the site of a previous herpes zoster infection). Although linear LP is usually seen in patients in their late 20s or early 30s, the initial presentation can be in the first to eighth decades. Presumably this pattern reflects somatic mosaicism (see [Chapter 62](#)), but how the involved and uninvolved skin differ is not known.

**LP-lupus erythematous overlap syndrome**

Patients whose lesions have overlapping features of both LP and lupus erythematous (LE) have been reported. These lesions are preferentially located in acral sites. Whether systemic immunologic abnormalities such as high titers of ANA are present in these patients is controversial.

Figure 12.12 **Linear lichen planus.** Discrete lesions along the lines of Blaschko on the lower extremity of a child.
Nail LP

The nails are affected in approximately 10% of patients with LP; usually several nails are affected. The characteristic nail abnormalities include lateral thinning, longitudinal ridging and fissuring or dorsal pterygium formation (Fig. 12.13); these are manifestations of matrix damage which can lead to scarring if left untreated. Non-specific changes in the nail bed may include yellow discoloration, onycholysis and subungual hyperkeratosis. In some patients, twenty-nail dystrophy may represent a variant of LP.

Oral LP

Oral LP can appear in at least seven forms that occur separately or simultaneously: atrophic, bullous, erosive, papular, pigmented, plaque-like and reticular. The most common and characteristic form of oral LP is the reticular pattern (Fig. 12.14A). It is characterized by slightly raised whitish linear lines in a lace-like pattern or in rings with short radiating spines. This form is usually asymptomatic and the most common site of involvement is the buccal mucosa; lesions are often bilateral and symmetric. Gingival involvement is common and oral LP affecting the gingivae exclusively is seen in approximately 10% of cases. It typically presents as chronic desquamative gingivitis.

Atrophic, erosive (Fig. 12.14B) and bullous lesions are associated with symptoms ranging from mild discomfort to severe pain. There is a higher incidence of plaque-like lesions amongst tobacco smokers. For unknown reasons, oral LP is very uncommon in young patients and, in some studies, women have been affected about twice as often as men.

Several studies have reported a relationship between oral LP and chronic liver disease, particularly that due to hepatitis C viral infection. Some authors found that in patients with the reticular and plaque forms, there were statistically significant differences between those with and those without HCV infection, whereas others authors reported an association of HCV with the erosive type. In the HCV+ oral LP group, oral lesions were more frequently located on the tongue, labial mucosa and gingiva.

Ulcerative LP

Ulcerations can occur within palmoplantar lesions of LP, particularly those on the soles. This form of LP is not as rare as it was once thought to be and usually appears between the third and fifth decade of life. Although palmoplantar LP is more common in men than in women, ulcerative LP prevails in female patients. More typical LP lesions may be present on other parts of the body. The ulcers are intensely painful and often recalcitrant to conventional therapy. Chronic ulcerative lesions are at risk of developing squamous cell carcinoma.
Figure 12.13 **Nail lichen planus.** A Thinning of the nail plate with lateral loss. B Violaceous discoloration of the periungual area with pterygium formation.

Figure 12.14 **Oral lichen planus.** A White lacy pattern on the buccal mucosa, the most common location for this form. B Multiple erosions on the tongue.

**Pathology**

Despite its different clinical manifestations, the histopathology of LP is fairly uniform. The primary features are hyperkeratosis without parakeratosis, focal increases in the granular cell layer, irregular acanthosis with a 'sawtooth' appearance, liquefactive degeneration of the basal cell layer, and a band-like lymphocytic infiltrate at the dermo-epidermal junction (Fig. 12.15). Colloid bodies representing apoptotic or dyskeratotic keratinocytes (also referred to as Civatte, hyaline or cytoid bodies) are usually present in the lower levels of the epidermis and the superficial dermis. Vacuolar changes within the basal cell layer may become confluent and result in small separations between the epidermis and the dermis (called 'Max-Joseph spaces'). There is often incontinence of pigment with multiple dermal melanophages.

Epidermal Langerhans cells are usually increased in active lesions. The majority of cells in the inflammatory infiltrate are lymphocytes, mainly CD3+ T cells (see Pathogenesis, above). However, exocytosis by lymphocytes into the epidermis is usually not abundant in LP. Plasma cells, macrophages or eosinophils may be seen within the dermis but not frequently; neutrophils are also not commonly seen in LP.
Add to lightbox

Figure 12.15 Histopathologic features of lichen planus. Hyperkeratosis, focal increase in the granular layer, saw tooting of the epidermis and a lichenoid infiltrate.

In oral LP, lesions often show parakeratosis rather than hyperkeratosis, and the epidermis frequently becomes atrophic. Lesions of lichen planopilaris are characterized by an inflammatory cell infiltrate around the hair follicles even at an early stage. Most of the inflammation involves the upper half of the follicle with the isthmus affected in one-third of patients. Destruction of the follicles represents a later stage. In LP pemphigoides, a primary histologic feature of the bullous lesions is a subepidermal separation with an abundance of eosinophils (occasionally neutrophil-rich infiltrates), whereas the papular lesions have the usual features of LP. Direct immunofluorescence microscopy of peribullous skin shows linear deposition of IgG and C3 along the dermo-epidermal junction, similar to BP. This pattern of immunoreactant deposition may occasionally be seen in typical LP lesions, but a higher percentage of cases with linear deposition will prove to be LP pemphigoides.

Apoptotic cells, as evidenced by Civatte bodies, tend to remain in the lower levels of the epidermis in idiopathic LP; in contrast, they are found in the spinous or granular layer in lichenoid drug eruptions (LDE). In a non-specific 'sponge-like' manner, colloid bodies often stain with IgM, IgA, or C3. In lichen planopilaris lesions, IgM, IgG, or IgA are found in varying combinations along the follicle-dermal interface. Although the band-like inflammatory infiltrate is usually restricted to the papillary dermis in LP and involvement of the deep vascular plexus suggests LDE, inflammation and destruction of the distal and proximal ends of the sweat ducts is also seen in some cases with LP; however, the secretory glands are unaffected.

**Differential Diagnosis**

LP can be viewed as one of the major reaction patterns in response to various exogenous agents such as drugs and contact allergens. Before labeling patients as having 'idiopathic LP', an in-depth search should be undertaken to identify any such inducing factors. There are no definite criteria (either clinical or histologic) for differentiating drug-induced LP from idiopathic LP. Some differences do exist, however, including a more eczematous and/or psoriasiform appearance and a predilection for the sun-exposed areas in patients with LDE (see Table 12.5). Histopathologic features seen more commonly in LDE include focal parakeratosis and eosinophilia (see Pathology). Despite these differences, the histologic changes in photodistributed, drug-induced LP can be indistinguishable from those of idiopathic LP. Because some studies have suggested that nearly 40% of patients with a diagnosis of oral LP may have a contact hypersensitivity that exacerbates or causes the disease, patients with oral LP lesions in apposition to metallic dental restorations should undergo patch testing with relevant metals (see Chapter 15). These metals include amalgam (mercury), copper and gold.

Other inflammatory conditions that are in the clinical differential diagnosis are lupus erythematosus (LE), lichen nitidus, lichen striatus, lichen sclerosus, pityriasis rosea, erythema dyschromicum perstans (ashy dermatosis), pсорiasis and secondary syphilis. In paraneoplastic...
pemphigus, a disease characterized by autoantibodies directed against plakin proteins and desmogleins 1 and 3, patients can have clinical features of LP or lichenoid eruption. The possibility of paraneoplastic pemphigus should be considered when the presumptive diagnosis is pemphigus vulgaris, erythema multiforme/Stevens-Johnson syndrome or erosive LP, but there are atypical features or a lack of response to appropriate therapy.

The disease most difficult to differentiate from LP is LE, particularly in patients with oral or scalp lesions alone. In these patients, the diagnosis of LE may only be made after additional biopsies are performed or other signs of LE appear. Direct immunofluorescence studies are helpful: granular or homogeneous bands of immunoglobulin in the basement membrane zone have been demonstrated in lesional and non-lesional mucosa in SLE (100% and 71%, respectively) and in lesional mucosa in DLE (73%), but only rarely in LP (4%).

Treatment

It is difficult to evaluate the efficacy of different forms of therapy in LP, because the majority of reports regarding its treatment consist of small series of patients or anecdotes (Table 12.2). In addition, spontaneous remission of cutaneous and oral LP can occur after varying amounts of time. For example, spontaneous remission of cutaneous LP has been observed in up to two-thirds of patients after 1 year, whereas the reported mean duration of oral LP is about 5 years; the erosive form rarely spontaneously resolves.

The standard therapies for LP include topical, intralesional and systemic corticosteroids, retinoids, psoralen plus ultraviolet A (PUVA) and, for severe or treatment-resistant cases, cyclosporine. In mild cases, symptomatic treatment includes topical corticosteroids and oral antihistamines for reducing pruritus. Topical corticosteroids are particularly popular in children. Hypertrophic LP lesions may benefit from intralesional corticosteroids or class I corticosteroids under occlusion. It should be noted, however, that despite their worldwide use the efficacy of topical corticosteroids in LP has not been systematically evaluated. Inhaled forms of corticosteroid are sometimes used for oral LP.

<table>
<thead>
<tr>
<th>Table 12-2. Therapeutic ladder for lichen planus.</th>
</tr>
</thead>
<tbody>
<tr>
<td>THERAPEUTIC LADDER FOR LICHEN PLANUS</td>
</tr>
<tr>
<td>Topical corticosteroids (2)</td>
</tr>
<tr>
<td>Superpotent topical corticosteroids (2)</td>
</tr>
<tr>
<td>Topical immunomodulators (e.g. tacrolimus; in oral LP (2), in other forms (3))</td>
</tr>
<tr>
<td>Intraleisional corticosteroids (2)</td>
</tr>
<tr>
<td>Griseofulvin (2)</td>
</tr>
<tr>
<td>Narrowband UVB (2)</td>
</tr>
<tr>
<td>Oral metronidazole (3)</td>
</tr>
<tr>
<td>Antimalarials (2)</td>
</tr>
<tr>
<td>Systemic retinoids (1)</td>
</tr>
<tr>
<td>PUVA (2)</td>
</tr>
<tr>
<td>Low-dose weekly methotrexate (3)</td>
</tr>
<tr>
<td>Systemic corticosteroids (2)</td>
</tr>
<tr>
<td>Cyclosporine (3)</td>
</tr>
<tr>
<td>Extracorporeal photophoresis (2)</td>
</tr>
</tbody>
</table>
Systemic treatments are usually reserved for more severe disease. Key to evidence-based support: 1, double-blind studies; 2, clinical series; 3, anecdote.

In severe, acute cases, systemic corticosteroids remain a commonly employed intervention. Although different dosage regimens have been proposed, the minimal effective daily dose of prednisone for treating LP is usually 15 to 20 mg; treatment is continued for 2-6 weeks and then gradually tapered over several weeks. Rebound and relapses may occur, but long-term maintenance therapy with systemic corticosteroids should be avoided. One study demonstrated that the median time to clearing was 18 weeks in the corticosteroid-treated group and 29 weeks in the placebo group.

Acitretin is the only systemic retinoid that has a relatively good level of evidence regarding its efficacy in the treatment of cutaneous LP. A therapeutic regimen consisting of 30 mg qd acitretin for 8 weeks resulted in significant improvement or remission in 64% of those in the treatment group, compared with 13% in the placebo group. Retinoids tend to be used for recalcitrant cases and therefore relapses may occur after discontinuation of the drug; as a result, long-term maintenance therapy may be required. We have successfully used etretinate (50 mg qd) to treat patients with the acute, exanthematous form of LP.

Long-term (3 to 6 months) administration of griseofulvin was shown to result in complete improvement in 86% of patients with LP, although the methods used in this study were not completely detailed and do not allow for definitive conclusions. In particular, oral erosive lesions have responded favorably to this drug. As a result, griseofulvin is often tried in such patients. More recently, a complete response or significant improvement (78.9%) of generalized LP (mean duration of disease: 3.5 months) was observed with metronidazole, 500 mg twice daily for 20 to 60 days.

Oral cyclosporine is useful for inducing a remission in severe cases resistant to retinoids and systemic corticosteroid therapy. A complete response was observed with doses of cyclosporine ranging from 1 to 6 mg per kg qd. The majority of patients did not experience a relapse during a follow-up period of several months. Long-term use of cyclosporine can be associated with renal toxicity.

Significant improvement has been observed after bath or systemic PUVA in patients with resistant long-standing LP. However, the risk of promoting carcinogenesis, especially in patients with skin types I and II, has to be balanced against the benefits. The usefulness of PUVA has prompted evaluation of extracorporeal photopheresis (ECP) for recalcitrant LP. One case series demonstrated that erosive oral LP cleared in all seven cases after an average of 24 sessions of ECP (two consecutive days per month) and follow-up at 24 months revealed no recurrences (two consecutive days per month).

Other therapies are often employed when conventional treatments have failed. One of the promising new therapies for LP is topical tacrolimus (see Chapter 129). Therapy with 0.1% topical tacrolimus ointment twice daily for 1 month led to complete resolution of labial ulceration and intraoral ulcerations also resolved after 3 months of daily application; both remained in remission after 1 year without maintenance therapy.

**UPDATE**

Date Added: 24 January 2006

Dr. Adrian B Roberts MB ChB

**Treatment of lichen planus with topical tacrolimus**

New research has been published into the efficacy of topical tacrolimus in treating lichen planus.
Byrd et al\(^1\) have conducted a retrospective postal survey of 37 patients with symptomatic oral lichen planus (OLP), who were treated with either 0.03% or 0.1% tacrolimus. Patients with both erosive and reticulated OLP were represented within the group. The mean duration of disease before initiating treatment with tacrolimus was 4.4 years. Topical tacrolimus was instituted as first-line therapy in two of the patients; prior treatment had proved unsuccessful in the remaining 35 subjects.

Thirty-three (89%) of the patients reported symptomatic improvement, and 31 (84%) reported partial to complete lesion clearance. On average, patients reported an improvement within one month (range, three days to six months\(^1\)). Additional data were available for the 24 patients who had attended a follow-up examination. Fourteen exhibited clinical improvement, and 10 had resolution of their lesions.

Twelve patients (32%) reported adverse effects, although only five discontinued treatment. In the remaining patients, adverse effects resolved with continued use. The most commonly reported problems were burning, irritation, and tingling, while there were infrequent reports of an objectionable taste, bad breath, extra phlegm in the mouth, swelling of the mouth and lips, and problems with the teeth. At the time of the survey, 28 patients were still using the medication. Out of the remaining nine patients who had discontinued treatment, five reported a recurrence.

Thomson et al\(^2\) reported similar results in their retrospective review of 23 patients with erosive OLP who were treated with topical tacrolimus. Physician-observed clinical improvement was found in 21 patients (91.3%) within six weeks. However, 15 of these patients required maintenance therapy to prevent subsequent recurrence.

In another retrospective study, Byrd et al\(^3\) investigated the efficacy of topical tacrolimus in genital lichen planus. Sixteen women with symptomatic vulvar lichen planus received treatment with 0.1% topical tacrolimus. Follow-up data were collected by means of a patient telephone questionnaire.

The mean duration of disease before initiation of therapy with topical tacrolimus was 4.3 years. All patients had previously tried at least one other form of treatment. Of the 16 patients, 15 (94%) experienced a symptomatic response to treatment within three months (mean, 4.2 weeks\(^3\); range, 0.3-12 weeks\(^3\)). These 15 patients also noted partial or complete resolution of the vulvar lesions. A follow-up clinical examination was undertaken in 13 of the women; 10 of them had no clinical evidence of erosions, and three had smaller erosions that were healing.

Six patients (38%) reported minor adverse effects including irritation, burning, and tingling, although these symptoms resolved with continued use. Twelve patients stopped applying topical tacrolimus for various reasons and, in 10 (83%) of these patients, the lesions recurred within six months (median, 1 week; range, 0.3-24 weeks). In six patients, the recurrent lesions were less severe than the pre-treatment lesions.

Byrd et al\(^1\) conclude that treatment with topical tacrolimus appears to be well tolerated with no serious adverse effects noted after more than one year of follow-up. Treatment appears effective for both the erosive and reticulated forms of OLP and also for recalcitrant vulvar lichen planus. However, treatment with topical tacrolimus rarely seems to result in complete remission, and most patients require maintenance therapy.


LICHEN STRIATUS

Synonyms

- Linear lichenoid dermatosis
- Blaschko linear acquired inflammatory skin eruption (BLAISE)

Key features

- An asymptomatic, linear dermatosis that primarily affects children
- The primary lesion is a small flat-topped papule that ranges in color from pink to skin-colored to tan
- Multiple lesions appear over the course of days to weeks among the lines of Blaschko and usually on an extremity
- Spontaneously resolves over months to a few years
- Digital involvement may result in nail dystrophy

Introduction

Lichen striatus (LS) is an asymptomatic, uncommon, self-limited, linear dermatosis of unknown etiology that generally affects children. The diagnosis of LS is usually made clinically based on the appearance of the primary lesions and the distinct developmental pattern. Its distribution along Blaschko's lines plus the age of the patient usually narrows the differential diagnosis rather quickly. Occasionally, there is overlap with linear lichen planus and 'Blaschkitis' (see Chapter 62).

History

In 1898, Balzer & Mercier first described a peculiar linear papular eruption that they termed lichenoid trophoneurosis. Forty years later Senear & Caro proposed the name lichen striatus. Since the condition was first described, the pathogenesis of its linearity has been the subject of debate. Regarding its distribution pattern, Brocq proposed the hypothesis that it represented a locus minoris resistentiae, but we now know that it is a manifestation of mosaicism (see Chapter 62).

Epidemiology

LS is seen primarily in children between the ages of 4 months and 15 years, although LS occasionally occurs in adults; the median age of onset is 2 to 3 years and the vast majority of cases occur between 9 months and 9 years. The female: male ratio has varied from 1:1 to 2:1.

Pathogenesis

Although the distribution of LS along Blaschko's lines points to somatic mosaicism (see Chapter 62), neither the gene(s) involved nor the triggering factors are known.

Environmental agents, in particular viruses, have been implicated given the predominance of LS in young children and its seasonal variation (it more commonly appears in spring and summer). However, to date, a viral association has not been proven via serologic testing or cultures.
In theory, during early fetal development an aberrant clone(s) of epidermal cells produced by somatic mutation migrated out along the lines of Blaschko. Exposure to an infectious agent (e.g. virus, BCG vaccine) then breaks previous tolerance to the aberrant clone by inducing a novel membrane antigen. The presence of CD8+ T cells scattered or in clusters around necrotic keratinocytes supports a cell-mediated immunologic reaction by which cytotoxic T cells would attack and eliminate the mutated keratinocyte clones. A similar mechanism has been proposed for linear LP and a post-transplant loss of tolerance could explain linear graft-versus-host disease (GVHD).

LS may represent a manifestation of an atopic diathesis with the abnormal immune responses usually associated with atopy being a predisposing factor for the induction of LS. For example, one study reported that 85% of patients with LS had a positive family history of atopic dermatitis, asthma or allergic rhinitis. Also the timing and relative infrequency of LS suggests a common infectious agent acting on genetically predisposed individuals.

Lastly, there are scattered reports of LS occurring at sites of injury (e.g. the periphery of a burn scar) rather than along Blaschko’s lines, but this could also be explained by a break in tolerance.

**Clinical Features**

The eruption consists of a continuous or interrupted band composed of discrete or clustered pink, skin-colored or tan papules that are flat-topped, smooth or scaly and range in diameter from 2 to 4 mm. Infrequently vesicles may be present. Typically, there is a single streak on an extremity along Blaschko’s lines (Fig. 12.16A); occasionally there is a bilateral distribution and/or multiple parallel bands (Fig. 12.16B). It is uncommon for LS to involve the trunk or head and neck region. There are reports of the eruption spreading distally from the trunk down an extremity, as well as observations of proximal extensions along an extremity.
When lesions involve the nail folds or nail matrix, onycholysis, splitting, fraying and total nail loss may result. The eruption usually appears suddenly, develops fully over days to weeks, and after several months to a year or more undergoes spontaneous resolution, leaving a postinflammatory hypopigmentation, particularly in darkly pigmented persons.

**Pathology**

The histologic features of LS are variable and depend upon the age of the lesion at the time the biopsy is performed. In addition, different areas of the same lesion can have different findings. In general, there is a lichenoid tissue reaction. There are varying degrees of involvement of hair follicles and sweat glands and ducts; lichenoid patterns occasionally present around hair follicles are indistinguishable from that seen in lichen planopilaris.

The alterations in the epidermis are secondary and include intercellular and intracellular edema, exocytosis, parakeratosis, dyskeratosis and focal or diffuse lysis of the basal layer in areas where the lichenoid infiltrate invades the epidermis. Dyskeratotic keratinocytes may be found in the granular and horny layers similar to the corps ronds in Darier's disease and at the dermo-epidermal junction in up to one-half of cases. Older lesions may have features similar to those seen in LP or lichen nitidus. By immunohistochemistry, a CD3+ T-cell infiltrate was seen in which CD8+ T cells surrounded necrotic keratinocytes and infiltrated vesicles filled with Langerhans cells.

**Differential Diagnosis**

Although the differential diagnosis includes other inflammatory diseases that can assume a linear pattern, such as linear porokeratosis, linear psoriasis, linear fixed drug eruption, inflammatory linear verrucose epidermal nevus and linear Darier's disease, the primary differential diagnosis is linear LP, Blaschkitis and linear GVHD. The latter occurs in a specific clinical setting, while Blaschkitis favors the trunk, is usually seen in adults, often consists of multiple streaks and can have features of dermatitis. Although linear LP and LS can occasionally be indistinguishable histologically, the primary lesions usually differ in size and color and hypopigmentation is a frequent sequela of LS while hyperpigmentation appears in the wake of LP. LS is also characterized by minimal, if any, pruritus and spontaneous resolution within a short period of time. In lichen nitidus, linear lesions reflect previous traumatic injury to the skin.

**Treatment**

Treatment of LS is usually not needed, except for the unusual case in which there is significant pruritus. Class I topical corticosteroids under occlusion have been successfully used to hasten spontaneous resolution in some patients.

**LICHEN NITIDUS**

<table>
<thead>
<tr>
<th>Key features</th>
</tr>
</thead>
<tbody>
<tr>
<td>- The eruption consists of multiple, tiny, discrete, shiny papules, often in clusters</td>
</tr>
<tr>
<td>- Favoured sites of involvement include the flexor aspects of the upper extremities, the genitalia and the anterior trunk</td>
</tr>
<tr>
<td>- Linear arrays of papules occur secondary to Koebner phenomenon</td>
</tr>
<tr>
<td>- The histologic correlate of the papule is a well-circumscribed infiltrate</td>
</tr>
</tbody>
</table>
composed of lymphocytes and epithelioid cells confined to the width of two to three dermal papillae

Introduction
Lichen nitidus (LN) is an uncommon chronic eruption consisting of multiple, tiny, discrete, skin-colored papules that are often arranged in large clusters. The papules have a distinctive histology with a dense, well-circumscribed, lymphohistiocytic infiltrate closely apposed to the epidermis. There has been considerable debate, however, as to whether LN represents a distinct and separate entity or should be regarded as an unusual variant of LP. It is generally accepted that LN has no relationship to any systemic illness; only a few authors believe that LN may be a cutaneous manifestation of Crohn’s disease.

History
In 1901, Pinkus first described a peculiar papular eruption termed lichen nitidus. Although he suggested that LN was a distinct entity histologically, a debate has remained as to whether LN represents a variant of LP. Based upon the presence of epithelioid cells within the well-circumscribed inflammatory infiltrate, early authors believed that LN was of tuberculous origin.

Epidemiology
Reliable epidemiologic data are difficult to accumulate because of the relative rarity of LN. In a study of 43 patients, primarily Caucasians and African-Americans, the disorder was not found to be restricted to any specific population group based on race, sex or age. Other authors have reported that LN is more prevalent among children or young adults, and a female predominance has been described in the generalized or confluent type of eruption.

Pathogenesis
Although much attention has been focused on the relationship of LN to LP, there has been limited study of the pathogenesis of LN recently. It was initially thought to represent a tuberculous lesion or tuberculid because of its histologic features. However, no causative (infectious) agents have ever been demonstrated, even by repeated inoculations of tissue into animals.

Even though LP and LN can coexist in the same patient and they share some similar clinical features (Table 12.3), most authors believe that LN is a separate entity because of its distinct clinical and histologic features. The possibility exists that the two conditions represent different responses to a similar triggering factor. For example, Kano et al. described a patient who had Crohn’s disease in whom LP and LN developed over different time frames. However, in view of the distinct differences in the composition of the respective cellular infiltrates, immunologic mechanisms responsible for the development of LN are likely different from those in LP.

Clinical Features
LN is characterized by asymptomatic, numerous, tiny, discrete, skin-colored, uniform, pinhead-sized papules (Fig. 12.17A) that occasionally exhibit a central depression. Individual papules are usually flat with a shiny surface (Fig. 12.17B). Although most commonly skin-colored, the papules may exhibit a variety of pink, yellow, red-blue or brown hues. The papules in dark-skinned individuals tend to be hypopigmented but sometimes they are hyperpigmented; however, marked hyperpigmentation has rarely been reported.
Table 12-3. Comparison of clinical and histological features of lichen nitidus versus lichen planus.

<table>
<thead>
<tr>
<th>COMPARISON OF CLINICAL AND HISTOLOGICAL FEATURES OF LICHEN NITIDUS VERSUS LICHEN PLANUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lichen nitidus</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
</tr>
<tr>
<td>Size</td>
</tr>
<tr>
<td>Color</td>
</tr>
<tr>
<td>Number</td>
</tr>
<tr>
<td>Distribution</td>
</tr>
<tr>
<td>Oral involvement</td>
</tr>
<tr>
<td>Nail involvement</td>
</tr>
<tr>
<td>Wickham's striae</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
</tr>
<tr>
<td>Hypopigmentation</td>
</tr>
<tr>
<td>Koebner phenomenon</td>
</tr>
<tr>
<td>Pruritus</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
</tr>
<tr>
<td>Parakeratotic cap</td>
</tr>
<tr>
<td>Hypergranulosis</td>
</tr>
<tr>
<td>Dermal infiltrate</td>
</tr>
<tr>
<td>Transepidermal elimination</td>
</tr>
<tr>
<td>Deposits of immunoreactants</td>
</tr>
</tbody>
</table>

* May be underestimated; ** especially darkly pigmented individuals.

The lesions are usually distributed on the flexor aspects of the upper extremities, as well as the genitalia, chest, abdomen and dorsal aspects of the hands. Less commonly, the face, neck, lower extremities, palms, soles and mucous membranes are involved. Oral lesions are thought to be rare but are probably underestimated; they appear as minute, flat, gray-white papules on the soft mucosa or white plaques on the tongue and hard palate. Nail involvement is observed up to 10% of patients (primarily adults) and the changes include pitting, rippling, longitudinal ridging, terminal splitting and increased longitudinal linear striations. Occasionally, the typical papules of LN are seen in the periungual region.

LN is one of several diseases that exhibit the Koebner phenomenon. The latter is especially prevalent in patients with generalized LN. Vesicular and hemorrhagic lesions are found in some patients, and they are often admixed with typical LN papules. A perforating variant has also been reported, usually in association with LP. While grouped papules tend to remain distinct, they may coalesce into plaques (especially in the generalized type) and when this occurs on the elbows...
and knees it can have a psoriasiform appearance. According to the study by Lapins and colleagues\textsuperscript{22}, the duration in 69% of the patients was one year or less; the longest duration was eight years. It is generally accepted that LN is not associated with any systemic diseases or other abnormal laboratory findings.

Pathology

![Figure 12.17 Lichen nitidus. A Numerous tiny flat-topped papules on the hand. B A close-up view shows the shiny surface.](image)

The constellation of histologic features in LN is very distinctive. The clinical diagnosis of LN, therefore, should be confirmed histologically. A well-circumscribed infiltrate composed of lymphocytes, epithelioid cells and occasional Langhans giant cells is typically 'clutched' by the surrounding hyperplastic rete ridges in a 'ball and claw' configuration (Fig. 12.18). In most lesions, the infiltrate is confined to the width of two to three dermal papillae.

The overlying epidermis is usually atrophic and frequently exhibits a parakeratotic 'cap' centrally. Absence or thinning of the overlying granular layer is seen and liquefactive degeneration of the basal layer is constantly observed, often accompanied by incontinence of melanin pigment. Civatte bodies are occasionally seen. A Max-Joseph-like space, i.e. focal separation of the epidermis and dermis, secondary to liquefactive degeneration, is sometimes observed. The lichenoid infiltrate closely apposes the epidermis and is thought to play a role in inducing reactive epidermal proliferation of the surrounding rete ridges and atrophy of the overlying epidermis. In perforating LN, transepidermal elimination is observed (see Chapter 96).
The predominant cell types in the dermal infiltrate are lymphocytes and epithelioid cells, and in some cases epithelioid cells predominate. Immunohistochemical studies have shown a marked predominance of CD4+ T cells over CD8+ T cells and the presence of large numbers of CD1+ Langerhans cells in the dermal infiltrates. Smoller et al. also demonstrated that the pattern of a mixed cellular infiltrate characterized by macrophages and a helper T-cell response with few CLA+ cells in LN lesions is different from that seen in LP, and suggested that LN is not a localized papular variant of LP.

Differential Diagnosis

The differential diagnosis includes LP, guttate lichen sclerosus, lichen spinulosus, lichen scrofulosorum, verruca plana, papular sarcoidosis, lichenoid secondary syphilis, papulonecrotic tuberculid and papular eczema (especially in individuals of African descent). All of these diagnoses (except LP) can usually be excluded relatively easily on the basis of clinical and histologic findings of LN. It is not always easy to differentiate LN from LP, because early tiny LP papules may be clinically and histologically indistinguishable from LN (see Table 12.3). Furthermore, lesions identical with LN can be found in 25 to 30% of patients with LP. In such cases, the lack of variation in size, the absence of a violaceous color or Wickham’s striae, and deposits of immunoglobulin in dermal papillae would suggest the diagnosis of LN.

Treatment

Because the majority of patients experience spontaneous clearing within one or several years, treatment is primarily symptomatic. When significant pruritus is present, topical corticosteroids and oral antihistamines may be helpful in controlling pruritus. Topical tacrolimus has anecdotally proven effective in children with LN. Generalized LN that has failed to respond to topical corticosteroids has been successfully treated with photochemotherapy (PUVA) alone or in combination with low-dose systemic prednisolone. Anecdotally, resolution of LN has also been described with oral etretinate, itraconazole, and astemizole, a selective H1-antagonist. Kano et al. reported a patient with peripheral CD4+ T-cell lymphocytopenia and LN who was treated with topical dinitrochlorobenzene (DNCB). This resulted in the development of a pruritic erythematous eruption followed by resolution of the lesions.