Leprosy
Leprosy is caused by *M. leprae* and predominantly affects the skin and peripheral nerves.
Immunopathologic Spectrum of Leprosy
The sequence of disease pathogenesis is complex, very chronic, and depends on host-parasite immunologic responses. The leprosy spectrum is a continuum, ranging from a cellular immune response to M. leprae antigens and few bacilli in tissues; at the opposite pole, lepromatous leprosy indicates an absent cellular immune response to M. leprae antigens, with no macrophage activation and abundant bacilli in tissues. The term "borderline" is used to denote patterns that share some features of both tuberculoid and lepromatous leprosy.
TT and LL patients are stable, the former often self-healing and the latter remaining heavily infected unless given appropriate chemotherapy.
Leprosy = اﻠﺠذاﻢ
Leprosy = اﻠﺠذاﻢ

absence of treatment. The central point of the spectrum (BB) is the most unstable, with most patients downgrading to LL if not treated. The term indeterminate leprosy is used to describe patients presenting with very early leprosy lesions that cannot be categorized definitely along the immunopathologic spectrum (e.g., cannot be determined as BT or LL).

It is likely that in endemic zones, a high proportion of people are infected by M. leprae, a high proportion be people are infected by M. leprae, and no disease or have developed disease.
Staining of *Mycobacterium leprae* Bacilli
The classical method for demonstrating leprosy bacilli in lesions is a modified Ziehl-Neelsen stain, where the degree of bacterial index follows Ridley’s logarithmic scale (which applies to both skin biopsies and slit skin smears).

\[
\text{BI} = 0: \text{no bacilli observed}
\]
<table>
<thead>
<tr>
<th>BI</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:10</td>
<td>1 to 10 bacilli in 10 to 100 hpf (oil immersion)</td>
</tr>
<tr>
<td>2:10</td>
<td>1 to 10 bacilli in 1 to 10 hpf</td>
</tr>
<tr>
<td>3</td>
<td>1 to 10 bacilli per hpf</td>
</tr>
<tr>
<td>4</td>
<td>10 to 100 bacilli per hpf</td>
</tr>
<tr>
<td>5</td>
<td>100 to 1,000 bacilli per hpf</td>
</tr>
<tr>
<td>6</td>
<td>&gt;1,000 bacilli per hpf</td>
</tr>
</tbody>
</table>
Solid-staining bacilli indicate that the organisms are capable of multiplication. Fragmented (beaded) and granular acid-fast bacilli indicate that they are dead. Patients with no bacilli detectable in lesions are termed *paucibacillary*; those with some or many bacilli are *multibacillary* (this distinction is important in determining the duration of chemotherapy). Immunocytochemical methods for demonstrating mycobacterial antigens have a limited role. The most frequently used is a...
Clinical Pathology of Leprosy

For general discussions of clinical leprosy and leprosy pathology, the reader is referred to Job (147) and
Many patients present with obvious or advanced skin and peripheral nerve lesions (the latter are primarily nerve involvement)....
Histopathology

There is mild lymphocytic and macrophage accumulation around neurovascular bundles, the superficial and deep dermal vessels, sweat glands, and erector pili muscle; focal lymphocytic invasion in
A distinctive variant of lepromatous leprosy, the histoid type, first described in 1963 (149), is characterized by the presence of dermatofibromas. It frequently follows incomplete chemotherapy or acquired drug resistance, leading to bacterial relapse.

Rarely, lepromatous leprosy can present as a single lesion rather than as multiple lesions (150).
Leprosy = اﻠﺠذاﻢ

Histopathology.

Lepromatous leprosy, in the usual macular or infiltrative-nodular lesions, exhibits an extensive cellular infiltrate that may show a variety of patterns. The macrophages have abundant eosinophilic cytoplasm and contain a mixed population of solid and fragmented bacilli (Bl = 4 or 5) (Figs. 21-33). The bacilli can be seen to measure about 5.0 by 0.5 μm and if solid may form epithelioid cell granulomas. Lymphocyte infiltration is not prominent, but there may be many plasma cells.
In time, and with antimicrobial chemotherapy, degenerate bacilli accumulate in the macrophages—the so-called lepra globi. In lepromatous leprosy, in contrast to tuberculoid leprosy, the nerves in the skin may contain considerable numbers of leprosy bacilli but remain well preserved for a long time and slowly become fibrotic.
Leprosy
Leprosy = اﻠﺠذاﻢ
Histoid Leprosy

Histoid leprosy shows the highest loads of bacilli (frequently, the Bl is 6), and the majority are solid staining.
Histopathology

The important difference between LL and BL leprosy histology is that in BL, the lymphocytes are more prominent and there is less epidermal involvement. Foamy cells are not prominent, and globi do not usually accumulate; the Bl ranges from 4 to 5.
In midborderline (BB) leprosy, the skin lesions are irregularly dispersed and shaped erythematous plaques.
Histopathology. In BB leprosy, the macrophages are uniformly activated to epithelioid cells but are not focalized into distinct granulomas. There are no Langhans giant cells. The Bl ranges from 3 to 4. Dermal edema is prominent between the inflammatory cells.

Borderline Tuberculoid Leprosy
In borderline tuberculoid (BT) leprosy, the lesions are asymmetrical and may be scanty. They are dry, hairless plaques with central hypopigmentation. Nerve enlargement is usually found, and the lesions are usually anesthetic.

**Histopathology**

Granulomas with peripheral lymphocytes follow the neurovascular bundles and infiltrate sweat glands and erector pili muscles. Langhans giant cells are variable in number.
and are not large in size. Granulomas along the superficial vascular plexus are frequent, but they do not...
The skin lesions of tuberculoid (TT) leprosy are scanty, dry, erythematous, hypopigmented papules or plaques with sharply demarcated borders. They are usually asymptomatic and may ulcerate or involute with healing. The lesions range in size from a few millimeters to a few centimeters. Thickened local peripheral nerves may be found. The lesions heal rapidly on chemotherapy.

**Histopathology**
Primary TT leprosy has large epithelioid cells arranged in compact granulomas and lymphocytic infiltrates.
Peripheral Nerves

In all of these patterns of leprosy, the major peripheral nerves are often undergoing parallel pathologies.
Leprosy Reactions

Leprosy reactions are classified into two main types (1 and 2). A third reaction is specific to Lucio multibacillary leprosy.
Type 1 Reactions
Because the immunopathologic spectrum of leprosy is a continuum, patients may move along it in both directions. Shifts toward the tuberculoid pole are called upgrading reactions; shifts toward the lepromatous pole are termed downgrading reactions. Both are aspects of delayed hypersensitivity, or type 1, leprosy reactions. TT patients are stable. BT patients may suffer irreversible reactions, which is damaging. At worst, there is caseous necrosis of large peripheral nerves resulting from upgrading reactions.
The histopathology of type 1 reactions has still not been well evaluated. The distinction between upgrading and downgrading reactions is difficult to make and may require serial examinations.
there is edema within and about the granulomas and proliferation of fibrocytes in the dermis. In upgrading...
type 2 Reaction: Erythema Nodosum Leprosum

Erythema nodosum leprosum (ENL) occurs most commonly in LL leprosy and less frequently in BL leprosy.
On the skin, tender, red plaques and nodules together with areas of erythema, and occasionally also purpura and vesicles, may appear. This type of reactional leprosy may last for a few weeks and even years in others. This is the only type of reactional leprosy that responds to treatment with thalidomide.

**Histopathology.** In ENL, the lesions are foci of acute inflammation superimposed on chronic multibacillary leprosy. Polymorph neutrophils are present, with areas of acute inflammation in the dermis. There are no bacilli, and macrophages have a granular pink hue on Wade-Fite staining, indicating mycobacterial debris.
anti mycobacterial immunocytochemical stain (e.g., anti-BCG) will indicate abundant antigen. A necrotizing vasculitis affecting arterioles, venules, and capillaries occurs in some cases of ENL; these patients may have superficial ulceration.

Lucio Reaction
The Lucio reaction occurs exclusively in diffuse lepromatous leprosy, in which it is a fairly common complication. It usually occurs in patients who have received either no treatment or inadequate treatment. In contrast to ENL, fever, general malaise, and discomfort are absent. Lesions may appear as greyish plaques, particularly on the legs, or may evolve into ulcers. There may be repeated attacks or continuous appearance of new lesions for years.

**Histopathology.** In the Lucio reaction, vascular changes are critical. Endothelial proliferation leads to luminal obliteration. This is brought on by the vascular occlusion, leads to hemorrhagic infarcts and results in crusted erosions or frank ulcers.
Electron Microscopy of Leprosy
Under electron microscopy, *M. leprae* can be seen to consist of an electron-dense cytoplasm lined by a trilaminal plasma membrane. Outside of this membrane are fibroblasts and collagen fibers. Lepra bacilli are found in the skin, predominantly in macrophages and in Schwann cells.

Pathogenesis of Leprosy
With respect to immunologic reactivity, patients with lepromatous leprosy have a defect in cell-mediated immune responses that allows them to become infected with the tubercle bacillus and thus do not adequately activate macrophages to destroy phagocytosed bacilli. This defect is specific for M. leprae, because patients with lepromatous leprosy show normal immunologic responses to antigens other than lepromin in both in vivo and in vitro testing.
The specific inability of T lymphocytes obtained from patients with lepromatous leprosy to react against lepromin is an increase in the lymphocyte response to lepromin during the reaction and a decrease during the postreaction phase.
Analysis of T-cell subsets in lesions has shown that in tuberculoid leprosy, with its high degree of resistance, the distribution of helper and suppressor T cells is similar to that observed in sarcoidosis.
Leprosy = لجذام
In patients with either ENL or the Lucio reaction, deposits of IgG and the third component of complement (C3) are found in dermal lesions. This suggests that both reactions are mediated by immune complexes (Gell and Coombes type III reaction).
The lepromin skin test, or Mitsuda test, consists of the intradermal injection of a preparation of M. leprae derived from autoclaved infected human tissue. A positive reaction consists of the formation of a nodule measuring...