Lepromatous leprosy = اﻠﺠذاﻤﻲ اﻠﺠذاﻢ

Leprosy
Leprosy is caused by *M. leprae* and predominantly affects the skin and peripheral nerves.
Lepromatous leprosy = اﻠﺠذاﻤﻲ اﻠﺠذاﻢ

Immunopathologic Spectrum  Leprosy
The sequence of disease pathogenesis is complex, very chronic, and depends on host-parasite immunologic responses. The disease spectrum is a continuum, ranging from lepromatous leprosy, indicating an absent cellular immune response to M. leprae antigens, with no macrophage activation and abundant bacilli in tissues, to tuberculoid leprosy, indicating strong cellular immune responses against M. leprae antigens and few 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.
Lepromatous leprosy = اﻠﺠذاﻤﻲ اﻠﺠذاﻢ
Lepromatous leprosy

absence of treatment. The central point of the spectrum (BB) is the patient stable with widespread and poorly defined lesions.
Staining of Mycobacterium leprae Bacilli
The classical method for demonstrating leprosy bacilli in lesions is a modified Ziehl-Neelsen stain, where

\[ \text{BI} = 0: \text{no bacilli observed} \]
Lepromatous leprosy

- 1: BI = 1: 1 to 10 bacilli in 10 to 100 hpf (oil immersion)
- 2: BI = 2: 1 to 10 bacilli in 1 to 10 hpf
- 3: BI = 3: 1 to 10 bacilli per hpf
- 4: BI = 4: 10 to 100 bacilli per hpf
- 5: BI = 5: 100 to 1,000 bacilli per hpf
- 6: BI = 6: >1,000 bacilli per hpf
Lepromatous leprosy = لجرم النوبة

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 ...

...the bacilli have fragmented, been partly digested by macrophage enzymes, and lost their acid-fast staining quality.
For general discussions of clinical leprosy and leprosy pathology, the reader is referred to Job (147) and...
Early, Indeterminate Leprosy

Many patients present with obvious or advanced skin and peripheral nerve lesions (the latter are primarily nerve ...
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.

Rarely, lepromatous leprosy can present as a single lesion rather than as multiple lesions (150).
Lepromatous leprosy, in the usual macular or infiltrative-nodular lesions, exhibits an extensive cellular infiltrate that is dominated by lymphocytes and histiocytes; the macrophages have abundant eosinophilic cytoplasm and contain a mixed population of solid and fragmented bacilli ($B_{L} = 4$ or $5$) (Figs. 21-33). The bacilli, on Wade-Fite staining, can be seen to measure about $5.0 \mu m$ by $0.5 \mu m$ and if solid may closely resemble the matrix of the macrophage, thereby contributing to the formation of epithelioid cell granulomas. Lymphocyte infiltration is not prominent, but there may be many plasma cells.
In time, and with anti mycobacterial chemotherapy, granules accumulate in the macrophages—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.
Lepromatous leprosy = اﻠﺠذاﻤﻲ اﻠﺠذاﻢ
Lepromatous leprosy
Histoid Leprosy

Histoid leprosy shows the highest loads of bacilli (frequently, the BI is 6), and the majority are solid staining, similar to those of a fibrohistiocytoma. The epidermis may be stretched over such dermal expansile nodules.
The important difference between LL and BL leprosy histology is that in BL, the lymphocytes are more prominent and there is less of a demarcation between the infiltrate and the epidermis. Foamy cells are not prominent, and globi do not usually accumulate; the Bl ranges from 4 to 5.
Midborderline Leprosy

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 nodular or sheet-like aggregates. 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

**Tuberculoid Leprosy**
The skin lesions of tuberculous (TT) leprosy are scanty, dry, erythematous, hypopigmented papules or plaques. The lesions heal rapidly on chemotherapy.

Histopathology
Primary TT leprosy has large epithelioid cells arranged in compact granulomas and may be associated with demyelination of the nerves.
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.
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 experience serious reactions, which is damaging. At worst, there is caseous necrosis of large peripheral nerves resulting from upgrading reactions.
Lepromatous leprosy = ❪اﻠﺠذاﻤﻲ اﻠﺠذاﻢ❫

Histopathology

The histopathology of type 1 reactions has still not been...
there is edema within and about the granulomas and proliferation of fibrocytes in the dermis. In upgrading reactions, ... who upgrade on therapy show old foamy macrophages and degenerate bacilli admixed with new epithelioid cell granulomas.
type 2 Reaction: Erythema Nodosum Leprosum

Erythema nodosum leprosum (ENL) occurs most commonly in LL leprosy and less frequently in BL leprosy.
Lepromatous leprosy = إلجمي إلجمي

On the skin, tender, red plaques and nodules together with areas of erythema, and occasionally also purpura and vesicles, may appear. These lesions are present for periods of 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 predominate and infective mycobacteria are often found in the dermis. The epidermis becomes thickened and hyperkeratosis is accompanied by a mild lymphocytic infiltrate of the dermis. No bacilli remain 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. Usually occurs in patients who have received either no treatment or inadequate treatment. In contrast to ENL, fever, ... particularly on the legs, 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...
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 is a coating typical of mycobacteria. 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, which prevents the activation of 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 ... 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...
Lepromatous leprosy = اﻠﺠذاﻤﻲ اﻠﺠذاﻢ
In patients with either ENL or the Lucio reaction, deposits of IgG and the third component of complement are found in dermal lesions. This suggests that both reactions are mediated by immune complexes (Gell and Coombes type III reaction).
Lepromatous leprosy = دماغ النحاس

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...