Leprosy

Diana N J Lockwood

Leprosy is a chronic, granulomatous disease caused by *Mycobacterium leprae*. The principal manifestations are skin lesions and peripheral neuropathy, and medical complications are caused by nerve damage, immunological reactions and bacillary infiltration. Drug treatment is effective in killing bacilli, but does not prevent nerve damage. In the UK, leprosy is a notifiable disease.

Epidemiology

Worldwide, leprosy continues to be a problem. There are about 650,000 new cases per year, 70% of which are in India. In all new cases seen in the UK, infection was acquired overseas. HIV infection is not a risk factor for the development of leprosy, but may worsen leprous neuritis.

Transmission

Untreated lepromatous individuals discharge bacilli from the nose. Infection occurs through the nose followed by haematogenous spread to skin and nerve. The incubation period is 2–5 years in tuberculoid disease and 8–12 years in lepromatous disease.

Pathology

M. leprae cannot be grown *in vitro*; nude mice and nine-banded armadillos are the best animal models. The genome of *M. leprae* has been completely sequenced. Bioinformatic analysis shows 165 unique genes, analysis of which will be vital for the development of new diagnostic tests and increased understanding of the disease.

M. leprae has a predilection for Schwann cells and skin macrophages. The patient's immune response determines the features

What's new ?

- When added to antibacterial therapy, corticosteroids can reverse early nerve damage
- The genome of *M. leprae* has been sequenced

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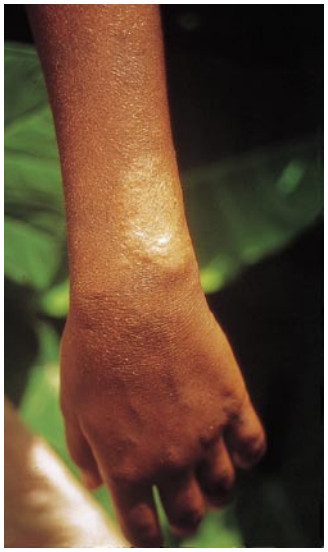
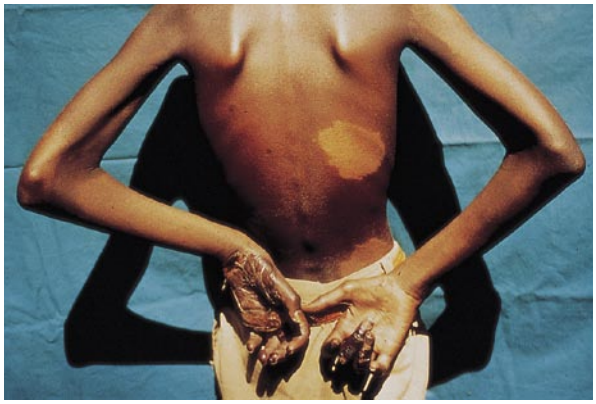
Clinical features of leprosy

Clinical features	Tuberculoid	Borderline tuberculoid	Borderline lepromatous	Borderline	Lepromatous
Skin					
• Infiltrated lesions	Defined plaques, irregular plaques, healing centres	Polymorphic, partially raised edges, satellites	Papules, nodules, punched-out centres	Diffuse thickening	Diffuse thickening
• Macular lesions	Single, small	Several, any size	Multiple, all sizes, bizarre	Innumerable, small	Innumerable, confluent
Peripheral nerve lesions	Solitary, enlarged nerves	Irregular enlargement of several large nerves, asymmetrical pattern	Many nerves involved, symmetrical pattern	Late neural thickening, asymmetrical anaesthesia and paresis	Slow, symmetrical 'glove-and-stocking' anaesthesia

1



2 Tuberculoid leprosy. A typical hypopigmented, anaesthetic tuberculoid lesion with a well-demarcated but active edge.



3 Borderline tuberculoid leprosy with nerve damage. Several hypopigmented patches can be seen. This boy burned his hands as a consequence of anaesthesia caused by bilateral ulnar and median nerve involvement.

of the disease; the two poles are tuberculoid (paucibacillary) and lepromatous (multibacillary) leprosy. At the tuberculoid pole, well-expressed cell-mediated immunity and delayed hypersensitivity control bacillary multiplication. In the lepromatous form, there is cellular anergy towards *M. leprae*, resulting in abundant bacillary multiplication. Between these two poles is a continuum, varying from moderate cell-mediated immunity (borderline tuberculoid), through true borderline, to little cellular response (borderline lepromatous).

Neuropathy – in skin lesions, the small dermal sensory and autonomic nerve fibres are damaged, causing local sensory loss and loss of sweating. Damage to peripheral nerves leads to regional sensory loss and dysfunction of muscles supplied by the affected nerve.

Immunology

Both T cells and macrophages are involved.

Tuberculoid leprosy – in these patients, lymphocytes respond to *M. leprae* antigens *in vitro*. Skin tests with lepromin (a soluble *M. leprae* sonicate preparation) elicit strongly positive responses. Tuberculoid patients have a Th1-type response to *M. leprae*, producing interleukin-2 (IL-2) and interferon-γ (IFNγ). This strong cell-mediated response clears antigen, but with concomitant local tissue destruction.

Lepromatous leprosy – these patients have specific cell-mediated anergy to *M. leprae* and their lymphocytes do not respond to *M. leprae* antigens *in vitro*. They are unresponsive to intradermal challenge with lepromin. Lepromatous patients exhibit specific T cell failure and macrophage dysfunction, with defects in production of IL-2 and IFNγ; they produce Th2-type cytokines.

Immune-mediated reactions: acute immune-mediated reactions are a serious complication of leprosy.

Type 1 reactions are episodes of delayed hypersensitivity occurring at sites of localization of *M. leprae* antigens.

Type 2 reactions – erythema nodosum leprosum results from immune complex deposition.

Clinical features

The signs of leprosy (Figure 1) are:

- skin lesions, typically anaesthetic at the tuberculoid end of the spectrum
- thickened peripheral nerves
- acid-fast bacilli on skin smears or biopsy.