



### Diagnosis, Differential diagnosis

*M. marinum* infection is suspected when skin lesions in patients whose occupation involves fish are examined. Mycobacteria are detected from the pus, biopsy tissue, or cultured fish tank water. Cutaneous mycosis such as sporotrichosis, various forms of cutaneous tuberculosis, and foreign-body granuloma should be differentiated from *M. marinum* infection. *M. marinum* is detected by PCR or cultured pus.

### Treatment

*M. marinum* infection heals in 2 to 3 months with the administration of tetracycline antibiotics or rifampicin. Since *M. marinum* is active in the temperature range of 25 to 33°C, local thermotherapy is helpful. Antibiotics and rifampicin are helpful.

### 2. *Mycobacterium avium* intracellular complex ★

Nodules, ulcers and subcutaneous induration occur on areas subjected to pressure. The extremities and buttocks are most commonly involved. Antituberculosis drugs are used in combination with either macrolide or new quinolone drugs for most cases. Surgical removal may be helpful for localized skin lesions.

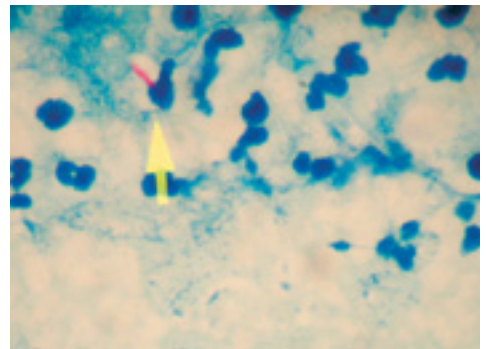
### 3. *Mycobacterium fortuitum* infection, *Mycobacterium chelonae* infection

A cold abscess, fistula, ulcer or nodule occurs (Fig. 26.3). Antituberculosis agents are often ineffective. Incision, drainage of pus, debridement or excision is often conducted.

### 4. *Mycobacterium kansasii* infection

A verrucous plaque, nodule or ulcer occurs. Antituberculosis drugs, new quinolone drugs and macrolide drugs are useful.

Clinical images are available in hardcopy only.



**Fig. 26.3** *Mycobacterium fortuitum* infection on a woman in her 20s. Pulsating nodules and abscesses occurred in a large area of the trunk. Pus was discharged in large amounts by puncture.

## C. *Mycobacterium leprae* infection

### Leprosy ★★

Synonym: Hansen's disease

### Outline

- It is a chronic infection caused by *M. leprae*. The skin and peripheral nerves are mainly involved.
- It is classified into tuberculoid leprosy (TT), lepromatous leprosy (LL), borderline leprosy, and indeterminate leprosy (IL), according to the cellular immunity against *M. leprae*. In TT, there are few erythema, papules, and

slightly reduced sensory perception. In LL, *M. leprae* proliferate in the entire body to form lepromas.

- Multidrug therapy including DDS (dapsons) is the main treatment.

### Pathogenesis, Epidemiology

Leprosy is an infection caused by *Mycobacterium leprae*. The mechanism of infection has not been fully clarified. Because the pathogenicity of *M. leprae* is extremely low, the natural immune response usually eliminates the infection. The incubation period is usually 3 to 5 years. This makes the disease rare. Leprosy occurs worldwide, with half of the world's roughly 12 million cases occurring in Asia and Africa.

### Clinical features, Classification

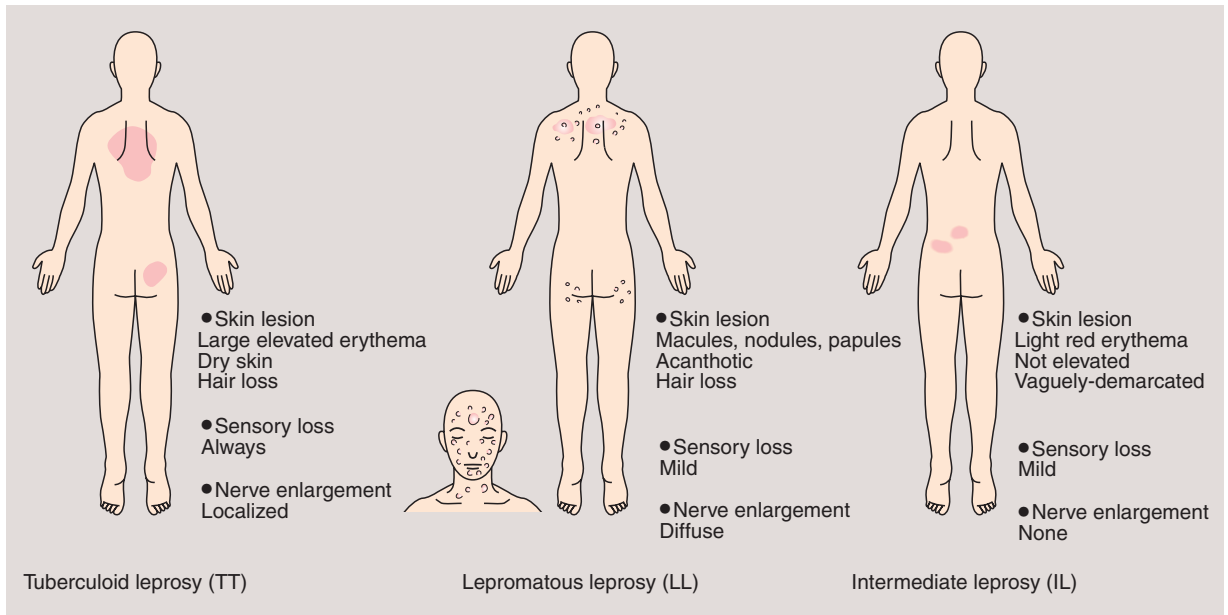
Leprosy is divided by the strength of the host's cellular immunity against *M. leprae* into the subtypes listed below (Ridley-Jopling classification, **Table 26.3**). The severity of the skin lesions and peripheral nerve symptoms varies by subtype (**Fig. 26.4**).

**Tuberculoid leprosy (TT):** This type is mildest. It occurs in hosts with strong cellular immunity. Sharply demarcated, localized, patchy erythema or papules appear singly or multiply. Faded patches also appear. Alopecia and reduced sensation and

**Table 26.3 Ridley-Jopling classification of leprosy.**

Disease type	Clinical findings				Pathological findings	Lepromin test
	Number and distribution of eruptions	Clinical features of eruptions	Sensation abnormality	Peripheral nerve hypertrophy		
<b>Indeterminate leprosy (IL)</b>	A few	Vaguely demarcated, flat, macular, light pink	Mild	None	Slight, lymphocytic, perivascular infiltration, perineural cellular infiltration	-- ~ +
<b>Tuberculoid leprosy (TT)</b>	A few	Elevated erythema with dry surface. Alopecia is present.	Reduced sensation, paralytic	Irregular and marked in adjacent areas of the eruptions.	Epithelioid cells, giant cells, and the lymphocyte in the dermis.	++ ~ +++
<b>Borderline leprosy that is close to tuberculoid leprosy (BT)</b>	Relatively many	Smaller eruptions than those of TT. Macular or plate-like. Vaguely demarcated. Satellite eruptions are present.	Paralytic	Multiple and regular in adjacent areas of the eruptions.	Epithelioid cells enclosed by lymphocyte	+ ~ ++
<b>Borderline leprosy (BB)</b>	Multiple	① Elevated, sharply demarcated erythema. ② Vaguely outlined erythema with a delle-like center. Satellite eruptions may be present.	Mild	Multiple, mild	Diffuse epithelioid cells	± ~ +
<b>Borderline leprosy that is close to lepromatous leprosy (BL)</b>	Multiple/Asymmetrical distribution	Macular or plate-like erythema, papules, or nodules. The eruptions are less glossy than those of LL.	Mild	From the early stages onward.	① Absent of foamy changes; few lymphocytes ② Histiocytes with foamy changes. (Globi are not produced.)	-- ~ ±
<b>Lepromatous leprosy (LL)</b>	Multiple/Symmetrical distribution	Multiple, macular changes from diffuse infiltration to small nodules. Erythema nodosum leprosum is present. The lesion is glossy and accompanied by alopecia.	Mild. Paralytic when the course is prolonged.	Systemic. Occurs at late stages.	Collagen layer is present between a leprous granuloma and epidermis. Foamy structure is present in old leproma.	--

(Based on; Ridley DS, Jopling WH. Classification of leprosy according to immunity: a five-group system. Int J Leprosy 1966; 54: 255-73).



**Fig. 26.4** Comparison between lepromatous leprosy, tuberculoid leprosy and indeterminate leprosy.

perspiration are found.

**Lepromatous leprosy (LL):** *M. leprae* proliferates systemically in hosts with cellular immunodeficiency. A leproma, a mass of histiocytes containing large quantities of *M. leprae*, forms in the peripheral nerves, eyes and lymph nodes. Multiple nodules appear on the skin. As the infection progresses, visual impairment, neuralgia, and deformity of the face and extremities occur (facies leontina).

**Borderline leprosy (BT, BL and BB):** The clinical condition is intermediate in severity between those of TT and LL (Fig. 26.5). The number of patients with borderline leprosy has been increasing in recent years. Intricate clinical features of TT and LL are observed.

**Indeterminate leprosy (IL):** This type easily escapes diagnosis as leprosy. Two or three flat, poorly demarcated, light pink patches appear. Peripheral nerve symptoms are mild or absent. Characteristic findings of leprosy are not found in a skin biopsy.

The WHO classification published in 1995 subdivided indeterminate leprosy into multibacillary (MB) and paucibacillary (PB) subtypes according to the results of skin smear examination, cutaneous symptoms and nervous symptoms.

Nervous symptoms tend to precede eruptions. During the course of LL and BL, the symptoms rapidly aggravate in some cases (lepra reaction). Multiple, nodular, erythema-like eruptions accompanied by perspiration and arthralgia may occur on the whole body during the leprosy reaction (erythema nodosum leprosum).

Clinical images are available in hardcopy only.

**Fig. 26.5** Borderline leprosy.

### Pathology

In tuberculoid leprosy (TT), epithelioid granuloma and Langerhans giant cells surrounded by infiltration of multiple lymphocytes are observed. In lepromatous leprosy (LL), lymphocytes are not fully responsive to *M. leprae*, and there are few inflammatory lymphocytes. *M. leprae* proliferates in macrophages.

### Laboratory findings, Diagnosis

Leprosy is diagnosed by skin lesions that are accompanied by reduced sensation, thickening of peripheral nerves, and neurological disorders. *M. leprae* is detected from the tissue fluid or pathological tissue of the lesion by acid-fast stain. Lepromin test (see Chapter 5) may be used for classification of leprosy: It is strongly positive in TT and weakly positive in BB, BL and LL. However, diagnostic value of lepromin test is limited because the test may be false positive under normal conditions. When direct detection of *M. leprae* is difficult, such as for the TT type, PCR is performed.

Serological anti-PGL-1 assay, a peripheral blood test, has diagnostic value. There are elevated levels of human immunoglobulin and biological false positive (BFP) for syphilis in serological reaction.

### Differential diagnosis

Leprosy should be differentiated from tuberculosis, syphilis, cutaneous mycosis, diseases that are accompanied by peripheral nerve impairment including diabetes and syringomyelia, and mycosis fungoides.

### Treatment

Multidrug therapy of DDS, rifampicin and clofazimine is recommended by WHO. The therapy should be continued for 6 months in mild cases and 2 years in severe cases, until the cure is complete. In recent years, new quinolone antibiotics have also been used. NSAIDs are administered when leprosy reaction causes sharp pain.

