Chapter 26
Mycobacterial Infections

Mycobacteria, which stain well in the Ziehl-Neelsen, are acid-fast bacteria that causes mycobacterial infection. Of species in the genus Mycobacterium, three are the main pathogens to human skin: *Mycobacterium* (M.) *tuberculosis*, the nontuberculous (atypical) *M. marinum*, and *M. leprae*. Diseases caused by these mycobacteria are introduced in this chapter.

A. *Mycobacterium tuberculosis* infections

**Outline**
- Skin lesions are caused by *M. tuberculosis* complex.
- The main type is tuberculosis of the skin (true cutaneous tuberculosis), in which *M. tuberculosis* causes lesions directly in the skin. Tuberculid is allergic skin reaction to *M. tuberculosis*.
- Tuberculosis of the skin is further classified into subtypes by clinical features and mechanisms (Table 26.1). Most cases of tuberculosis of the skin are secondary infection in those who have a history of extracutaneous tuberculosis.

**a. Tuberculosis of the skin**

1. **Lupus vulgaris**

**Outline**
- This was once the most common type of tuberculosis of the skin. It rarely occurs today.
- Reddish-brown papules appear on the face and neck, coalescing into elevated, infiltrative plaques.
- It is caused by *M. tuberculosis* that disseminates hematogenously or lymphogenously from a focus of infection.

Clinical images are available in hardcopy only.

**Classification of mycobacterial infections**

Mycobacteria include tuberculosis bacteria (*M. tuberculosis*), nontuberculosis (atypical) bacteria, and leprosy bacilli (*M. leprae*). These are the pathogens of diseases listed below.

<table>
<thead>
<tr>
<th>Causative Mycobacteria</th>
<th>Diagnostic name</th>
<th>Bacterial culture</th>
<th>Examination</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>M. tuberculosis</em></td>
<td>Tuberculosis of the skin</td>
<td>+</td>
<td>+</td>
<td>Tuberculin reaction (+)</td>
</tr>
<tr>
<td></td>
<td>Tuberculid</td>
<td>-</td>
<td>-</td>
<td>Tuberculin reaction (+++)</td>
</tr>
<tr>
<td><em>M. marinum</em> and other nontuberculous mycobacteria</td>
<td>Nontuberculous mycobacterial infection</td>
<td>-+-+</td>
<td>+</td>
<td>DNA homology probing</td>
</tr>
<tr>
<td><em>M. leprae</em></td>
<td>Leprosy</td>
<td>-+-+</td>
<td>-</td>
<td>Skin smear test (-+-+)</td>
</tr>
</tbody>
</table>
extracutaneous tuberculosis.

- It progresses slowly, and may progress to squamous cell carcinoma in rare cases.

**Clinical features**

A single or several, unilateral, reddish-brown papules first appear on the face, neck or arms, coalescing into erythematous plaques. The surface of the papules exfoliates, and the centers scar. Papules recur on the scarred areas, gradually and repeatedly enlarging and coalescing. This leads to the formation of large, firm, elevated plaques (Figs. 26.1-1 to 26.1-3). At the periphery are small reddish-yellow or brown nodules. Yellowish-brown papules resembling apple jelly are observed by diascopy. Lupus vulgaris progresses extremely slowly over the course of many years. In addition to preexisting lesions, ulceration and atrophy occur, sometimes leading to squamous cell carcinoma. Lupus vulgaris is classified by clinical course into flat macular, ulcerative, and proliferative hypertrophic.

**Pathogenesis**

*M. tuberculosis* is thought to disseminate hematogenously or lymphogenously from a focus of tuberculosis in extracutaneous organs, such as lungs and lymph nodes. In lupus vulgaris, a tubercle forms by hematogenous dissemination at the first infection of tuberculosis reactivates.

**Pathology**

A tubercle consisting of epithelioid cells and Langerhans giant cells accompanied by caseous necrosis appears in the dermis.

**Diagnosis**

Lupus vulgaris is diagnosed by the clinical features, pathology, and strong positive in tuberculin skin test. Identification of *M. tuberculosis* is thought to disseminate hematogenously or lymphogenously from a focus of tuberculosis in extracutaneous organs, such as lungs and lymph nodes. In lupus vulgaris, a tubercle forms by hematogenous dissemination at the first infection of tuberculosis reactivates.

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**Table 26.1 Classification of cutaneous tuberculosis (TB).**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Mechanism of skin infection</th>
<th>Frequent site</th>
<th>Lesion of other organs (e.g., lungs)</th>
<th>Caseous necrosis in pathological tissue</th>
<th>Tubercle bacillus in cutaneous tissue</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tuberculosis of the skin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Lupus vulgaris</td>
<td>Exogenous infection / endogenous spread</td>
<td>Face</td>
<td>+/−</td>
<td>+</td>
<td>+</td>
<td>Differentiate from DLE and sarcoidosis.</td>
</tr>
<tr>
<td>2. Scrofuloderma</td>
<td>Endogenous spread</td>
<td>Neck</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
<td>Cold abscess</td>
</tr>
<tr>
<td>3. Warty TB</td>
<td>Exogenous infection</td>
<td>Extremities</td>
<td>+/−</td>
<td>+</td>
<td>+</td>
<td>Affects those who have a history of tuberculosis.</td>
</tr>
<tr>
<td><strong>Tuberculid</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Papulonecrotic</td>
<td></td>
<td>Extensor surfaces of the extremities</td>
<td>+/−</td>
<td>+</td>
<td>−</td>
<td>Multiple, contralateral eruptions</td>
</tr>
<tr>
<td>3. Lichen scrofulosorum</td>
<td></td>
<td>Trunk</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>Most frequently occurs after BCG vaccination.</td>
</tr>
</tbody>
</table>

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**Lupus**

Lupus is a general term for diseases in which erosive, erythematous ulceration occurs on the face. The name is Latin for wolf, and it comes from the facial appearance that was thought to resemble the bites of a wolf. Until the 19th century lupus was most commonly caused by cutaneous tuberculosis. In recent years, the prevalence of lupus vulgaris has drastically decreased. The term lupus now almost always refers to lupus erythematosus (Chapter 12).

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**MEMO**

Lupus is a general term for diseases in which erosive, erythematous ulceration occurs on the face. The name is Latin for wolf, and it comes from the facial appearance that was thought to resemble the bites of a wolf. Until the 19th century lupus was most commonly caused by cutaneous tuberculosis. In recent years, the prevalence of lupus vulgaris has drastically decreased. The term lupus now almost always refers to lupus erythematosus (Chapter 12).
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**tuberculosis** is made by PCR or culture.

**Differential diagnosis**

Chronic discoid lupus erythematosus, cutaneous sarcoidosis, tertiary syphilis and sporotrichosis should be differentiated from lupus vulgaris.

**Treatment**

Lupus vulgaris responds well to antitubercular drugs. Although the prognosis is good, it leaves distinct scarring.

### 2. Scrofuloderma

**Outline**

- This is the most common tuberculosis of the skin. The neck and trunk are most frequently involved.
- It begins as painless subcutaneous nodules. It is characterized by fistula formation and pus discharge from cold abscesses.
- It is caused by *M. tuberculosis* disseminated from extracutaneous tuberculosis throughout to the skin.
- Cordlike scars form in most cases.

**Clinical features, Pathogenesis**

Scrofuloderma, tuberculosis of the skin, is caused by a lesion in the lung, lymph node, bone, muscle or tendon that continuously spreads to the skin. A painless light pink subcutaneous nodule called a cold abscess first appears. It softens and forms a fistula in the skin, from which pus discharges. At a previously formed scrofuloderma, ulceration and characteristic cordlike scarring occur. There is slight localized fever and pain for the entire course of the disease.

**Diagnosis, Treatment**

Large quantities of *M. tuberculosis* are seen in the pus and tissue of the lesion. The treatments for scrofuloderma are the same as for lupus vulgaris. Identification of *M. tuberculosis* is made by PCR or culture.

### 3. Warty lupus

**Synonym:** Tuberculosis verrucosa cutis

**Clinical features, Pathology**

Warty lupus occurs most frequently at the ends of the extremities, dorsal surfaces of joints, and buttocks, after subjection to external stimulation or injury (Fig. 26.2). Several small, asymptomatic, indurated wart-like papules with a slight inflammatory edge coalesce and enlarge, forming erythematous plaques with
verrucous periphery. The lesions enlarge centrifugally and tend to heal in the center. Warty tuberculosis is an infection of the superficial layers of the skin. There is inflammation with histopathological atypism. Ulceration does not occur.

**Pathogenesis**

Warty lupus is a tuberculosis of the skin caused by *M. tuberculosis*. It occurs from inoculation of organisms into the skin of a previously infected patient who usually has a moderate or high degree of immunity.

**Diagnosis, Differential diagnosis**

Identification of *M. tuberculosis* is made by PCR or culture. Strong positive in tuberculin skin test and pathological findings of the skin are diagnostic. Lupus vulgaris, chromomycosis, viral warts and tinea cruris should be differentiated from warty tuberculosis.

**Treatment**

Warty lupus responds well to antituberculosis drugs.

**b. Tuberculid**

Tuberculid is a disorder that is associated with a focus of internal tuberculosis. The cutaneous symptoms are thought to be immune reactions in the skin resulting from hematogenous dissemination of *M. tuberculosis* or its antigens from a primary infection. Individuals with strong antituberculous cell-mediated immunity are affected.

**1. Papulonecrotic tuberculid**

This is thought to be vasculitis caused by allergic reaction to *M. tuberculosis*. It occurs in young people, most frequently on the extensor surfaces of extremities, particularly on the elbows and popliteal fossae. Multiple, contralateral dark red papules with a diameter of 1 cm or less appear and necrotize, forming pustules and ulceration. They heal with scarring. These eruptions occur in succession and progress slowly, presenting new eruptions mixed with old ones. Antituberculosis drugs are useful.

**2. Lichen scrofulosorum**

Lichen scrofulosorum most frequently occurs after the initial infection of *M. tuberculosis* or BCG vaccination. Scattered or aggregated, red follicular papules of 1 mm to several millimeters in diameter appear on the trunk or extremities. Histopathologically, epithelial cells and Langerhans giant cells are found in the dermis. There is granulomatous formation; nevertheless, necrosis is not present nor is *M. tuberculosis* detected. Therefore, lichen scrofulosorum is considered tuberculid, an allergic reaction
against fungal compounds. Antituberculosis drugs and minocycline are useful. Most cases heal in several months. See Chapter 18 for erythema induratum.

**B. Nontuberculous mycobacterial infections**

Nontuberculous (atypical) mycobacteriosis is a general term for infections caused by nontuberculous mycobacteria other than *M. tuberculosis* and *M. leprae*. The term “nontuberculous mycobacteria” has become more commonly used than “atypical mycobacteria” in recent years. There are about 30 nontuberculous mycobacteria that are pathogenic to humans. The main nontuberculous mycobacteriosis and the number of reported cases are shown in Table 26.2.

**Table 26.2 Nontuberculous mycobacterioses in Japan (1969-1996).**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th># of reported cases</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>M. marinum</em></td>
<td>161</td>
<td>64.1</td>
</tr>
<tr>
<td><em>M. fortuitum</em></td>
<td>26</td>
<td>10.4</td>
</tr>
<tr>
<td><em>M. avium-intracellulare</em> complex</td>
<td>19</td>
<td>7.6</td>
</tr>
<tr>
<td><em>M. chelonae</em></td>
<td>18</td>
<td>7.2</td>
</tr>
<tr>
<td><em>M. abscessus</em></td>
<td>11</td>
<td>4.4</td>
</tr>
<tr>
<td><em>M. kansasi</em></td>
<td>9</td>
<td>3.6</td>
</tr>
<tr>
<td><em>M. gordonae</em></td>
<td>2</td>
<td>0.8</td>
</tr>
<tr>
<td><em>M. peregrinum</em></td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td><em>M. scrofulaceum</em></td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td><em>M. smegmatis</em></td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td><em>M. ulcerans</em>-like organism</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td><em>M. vaccae</em></td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>251</strong></td>
<td></td>
</tr>
</tbody>
</table>


**1. Mycobacterium marinum infection**

Synonyms: Fish tank granuloma, Swimming pool granuloma

- Aquarium staff and tropical fish breeders are most commonly affected.
- Contaminated water from a swimming pool or tropical fish tank enters a minor injury, causing infection. Nodules, exfoliation and ulceration occur.
- Tetracyclines and rifampicin are effective.

**Clinical features**

Aquarium staff and tropical fish breeders are commonly infected with *M. marinum*. The onset is after a 2-week incubation period of infection in an external injury. Areas that are subjected to external friction such as the dorsum of fingers and joints are most commonly involved. Skin lesions accompanied by central reddening and crusting progress to nodular plaques. Scaling and verrucous plaques occur later on. The eruptions are solitary in most cases. However, *M. marinum* may be disseminated by lymph flow or spread systemically in immunodepressed patients.

**Pathogenesis**

Among nontuberculous mycobacteria, *M. marinum* is the most common cause of skin disease. Because *M. marinum* favors freshwater environments, most cases of infection are caused by water from swimming pools or fish tanks.

**Pathology**

There are findings of pustular inflammation and epithelial cell granuloma in *M. marinum* infection. It is difficult to detect the mycobacteria from a pathologic specimen.