powders are helpful treatments. The family members and sexual partners are also treated to avoid “ping-pong” infestation, in which the disease repeatedly rebounds from untreated to treated persons.

7. Tick bite

Clinical features

Tick bite is caused by ixodid (hard) ticks. Because ticks of the family Ixodidae tend not to be felt when crawling on human skin, they are able to attach insidiously to the face, arms or even the trunk or genitals of humans (Figs. 28.8-1 and 28.8-2). The bite tends to be painless. The main symptoms are inflammation around the bite, erythema, edematous swelling, bleeding and blistering. The mouthpart is firmly fixed in the skin while sucking blood; a tick bite is often found when the complaint has been a wart or skin tumor. A tick that has sucked its fill of blood falls naturally from the skin. *Borrelia* spirochetes may be transmitted by a tick bite, leading to Lyme disease (described later).

Pathogenesis

Ixodidae are 2 mm to 8 mm long (Fig. 28.9) and tend to inhabit grasslands or woods. They burrow into the skin of humans and animals to suck blood.

Treatment

If a tick is forcefully pulled while sucking blood, it may tear, leaving the mouthpart in the skin. This can lead to foreign-body granuloma. The whole tick, including the mouthpart, should be removed by either inserting scissors into the bite spot or punching the site out with the tick attached. Oral administration of tetracycline 1 week after removal is advised as a prophylactic against Lyme disease.

B. Skin diseases transmitted by insects and other animals

1. Lyme disease

Outline

- It is an infection caused by the spirochete bacteria *Borrelia burgdorferi sensu lato*, transmitted by ticks of the family Ixodidae.
- It occurs most frequently in USA, Scandinavia and central Europe, during spring and summer.
- It begins as erythema chronicum migrans (first stage) and progresses to arthritis and cerebral meningitis (second stage) and then to dysfunction of the joints and central nervous system.

<table>
<thead>
<tr>
<th>Table 28.1 Classification of <em>Borrelia</em> species.</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>B. burgdorferi</em></td>
</tr>
<tr>
<td>Other <em>Borrelia</em> species</td>
</tr>
</tbody>
</table>

Clinical images are available in hardcopy only.

Fig. 28.8 A tick bite.
- c: A tick on the neck.

Fig. 28.9 An ixodid tick removed from human skin.
- It is generally 5 mm to 8 mm long.
Skin Diseases Caused by Arthropods and Other Noxious Animals

Lyme disease occurs from Borrelia (B.) burgdorferi (Table 28.1) infection caused by the bite of ixodid ticks. The course follows repeated remissions and recurrences. It is divided into three stages. Besides the typical courses shown in Table 28.2, courses with localized scleroderma, lichen sclerosus et atrophicus, and B-cell lymphoma have been reported.

First stage (erythema period): After an incubation of 3 to 40 days, an erythema or papule occurs at the bite in about half of all cases. Ixodid ticks tend to bite the thighs, groin and axillary fossae. The skin lesion enlarges within several days, forming a characteristic ring-shaped lesion (erythema chronicum migrans, ECM) (Figs. 28.10-1 and 28.10-2). The periphery is vivid red and sometimes elevated. There is discoloration at the center. It is asymptomatic and may become as large as 40 cm in diameter. Influenza-like symptoms such as fever, headache and general malaise, and cerebral meningitis-like symptoms are often present. These subside in several weeks. Secondary multiple annular erythema occurs in about 30% of all cases.

Second stage (dissemination period): One to three months after infection, B. burgdorferi spread to the whole body and cause various organ symptoms, such as arthritis, peripheral neuritis, meningitis and dysfunctional transmission of cardiac muscle impulse. Multiple erythema chronicum migrans occurs on the whole body. Dome-shaped tumors may appear on the face (pseudolymphoma, also called lymphadenosis benigna cutis; Chapter 21).

Third stage (chronic period): Several months to several years after onset, lesions develop in the joints and central nervous system. Acrodermatitis chronica atrophicans, which is characterized by the insidious onset of painless, dull-red nodules or plaques on the extremities leaving central areas atrophy, occurs as a late skin trauma. Asymptomatic, infiltrative, edematous erythema occurs and enlarges. The skin atrophies and becomes so thin that subcutaneous vessels can be seen.

Epidemiology

Lyme disease was first recognized in 1975 from a study of epidemic infections whose main symptoms were erythema and arthritis, made in Lyme, Connecticut (USA). Lyme disease occurs worldwide, especially in the U.S.A., Scandinavia and central Europe.

Clinical features

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Epidemiology

Lyme disease was first recognized in 1975 from a study of epidemic infections whose main symptoms were erythema and arthritis, made in Lyme, Connecticut (USA). Lyme disease occurs worldwide, especially in the U.S.A., Scandinavia and central Europe.

Pathogenesis

Lyme disease is caused by spirochete bacteria B. burgdorferi sensu lato, mainly by B. burgdorferi, a tick-borne spirochete bacterium, most frequently transmitted by the ixodid tick Ixodes ovatus. B. burgdorferi inhabits the midgut of the ticks, which
burrow into human skin. The bacteria spread hematogenously, causing systemic lesions.

**Laboratory findings**

Detection of specific antibody: IgM-specific antibodies are detected at the early stage; IgG-specific antibodies are detected later. The specific antibodies may be false positive in patients with systemic lupus erythematosus or rheumatoid arthritis.

Detection of *B. burgdorferi sensu lato*: The bacteria are isolated from blood, cerebrospinal fluid or skin lesion for culturing. *Borrelia* proteins can be detected by Western blot, and *Borrelia* DNA can be identified by nested PCR.

**Diagnosis, Differential diagnosis**

Diagnosis can be made by the tick bite and by erythema chronicum migrans (ECM). To confirm the diagnosis, an antibody test is conducted.

**Treatment**

Doxycycline, penicillin or cefoxime is orally administered for 20 days. Cefem drugs are used at the second and third stages of the disease because they are transported to the nerves in sufficient concentrations.

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2. Leishmaniasis

**Definition**

Leishmaniasis is a parasitic infection caused by protozoa of the genus *Leishmania*. Several species in the genus cause leishmaniasis, and each species tends to occupy a particular zoogeographical zone. *Leishmania* protozoa are transmitted to humans by bloodsucking sand flies. Human leishmaniasis is usually classified as cutaneous or visceral. Leishmaniasis is endemic in 88 countries, occurring most frequently in Brazil, Iran, Afghanistan and Sudan. Leishmaniasis is classified into three subtypes by *Leishmania* species. The distribution and clinical features differ for each type.

**Clinical features, Classification**

1. **Cutaneous leishmaniasis**

   The causative protozoan of cutaneous leishmaniasis is *Leishmania tropica*, which is predominantly distributed in Africa. The main parasite hosts are dogs and rodents. A painless papule appears at the bite and progresses to an ulcer that is accompanied by induration and enlargement. The skin lesion heals with scarring. The patient obtains permanent immunity.

2. **Mucocutaneous leishmaniasis**

   The causative protozoan of mucocutaneous leishmaniasis is *Leishmania braziliensis*, which inhabits South America, is carried by dogs and rodents, and is transmitted to humans by sand
flies. Tumors and odorous ulcers form. For decades after an infection, secondary ulceration involving the skin, mucosa and bones occurs in the ears, nasal cavity, oral cavity, pharynx and esophagus.

3. Visceral leishmaniasis

The causative protozoan of visceral leishmaniasis is *Leishmania donovani*, which inhibits many countries, particularly India and parts of South America and Africa. It parasitizes human liver, spleen, bone marrow and leukocytes. After an incubation period of several months, remittent fever, anemia and splenomegaly occur. At the terminal stages, black pigmentation appears in the skin of the abdomen, hands and feet.

**Examination, Treatment**

History of sandfly bites or exposure to an endemic area is important for diagnosis. The causative protozoan of Leishmaniasis is detected from skin lesions, blood or bone marrow. Amastigotes are observed in Gimza-stained smears from skin lesion by direct microscopy. Leishmanial DNA is found by PCR. Pentostam, a pentavalent antimony drug, is the first-line treatment.

3. Cat scratch disease, Cat scratch fever

Infection is caused by *Bartonella henselae*, a gram-negative bacillus, after a cat scratch or bite. Among cats, the bacillus is transmitted by fleas. After a latency of several days to 2 weeks, a red papule and crust appear at the inoculated site. One to three weeks later, painful swelling accompanied by systemic symptoms including fever and headache occurs in the regional lymph node. It resolves spontaneously in several weeks to several months. In persistent cases, trimethoprim, ciprofloxacin, cefem regimen, tetracycline or macrolide antibiotics are administered orally.

4. Tsutsugamushi disease

Synonym: Scrub typhus

**Outline**

- It is a rickettsial infection caused by the obligate intracellular bacterium *Orientia tsutsugamushi* and transmitted by the mite *Leptotrombidium akamushi*.
- It is characterized by high fever and light pink eruptions 2 mm to 5 mm in diameter on the trunk and extremities.
- Careful observation may reveal the bite of the mite *Leptotrombidium akamushi*.
- Tetracycline and chloramphenicol are effective treatments.

**Clinical features**

Five to fourteen days after a bite by the mite *Leptotrombidium*...
akamushi, a fever of about 40 °C occurs, accompanied by sudden chills and headache (Fig. 28.11). A bite can be found by careful examination of the trunk, genitalia and axillary fossa. The bite presents infiltrative erythema 1 to 2 cm in diameter with black crusts at the center. Two to three days after the onset, light pink eruptions appear on the trunk and extremities, disappearing in 7 to 10 days. There is systemic painful swelling of lymph nodes, conjunctival congestion, pharyngeal reddening, splenomegaly and hallucinations from high fever.

**Pathogenesis, Epidemiology**

Tsutsugamushi disease is a rickettsial infection caused by the obligate intracellular bacterium *Orientia tsutsugamushi* and transmitted by the mites *Leptotrombidium akamushi*, *Leptotrombidium pallidum*, and *Leptotrombidium scutellare*. These feed on field mice; however, they may attach to humans. *Orientia tsutsugamushi* in the body of *Leptotrombidium akamushi* invades the human body. Fewer than 1% of all *Leptotrombidium akamushi* are thought to carry *Orientia tsutsugamushi*. Tsutsugamushi disease is not transmitted from human to human.

The prevalence of tsutsugamushi disease decreased in the 1960s. Use bans on chloramphenicol initiated in 1976 for its side effects have resulted in increased numbers of cases. There are more than 1,000 new cases annually throughout Japan.

**Diagnosis, Differential diagnosis**

*Leptotrombidium akamushi* bites, eruptions, increased levels of anti-Rickettsial IgM antibodies, and detection of rickettsial DNA are diagnostic for tsutsugamushi disease. Other rickettsial diseases such as *Rickettsia japonica* infection and Rocky Mountain spotted fever should be carefully differentiated from tsutsugamushi disease (Table 28.3).

**Treatment**

Tetracycline or chloramphenicol is administered. With appropriate treatment, the mortality is less than 1%. Without proper

| Table 28.3 Comparisons between tsutsugamushi disease and diseases that resemble it. |
|---------------------------------|-------------------------------|---------------------------------|---------------------------------|
|                                 | Tsutsugamushi disease          | Japanese spotted fever           | Rocky Mountain spotted fever    |
| Rickettsia pathogen             | *Orientia tsutsugamushi*       | *Rickettsia japonica*            | *Rickettsia rickettsii*         |
| Incubation period               | 10-14 days                     | 2-8 days                        | 3-12 days                       |
| Season of common infection      | Autumn, winter, spring (new type); summer (classical type) | April to October                | Early summer                    |
| Erythema                        | Most commonly on the trunk, little subcutaneous bleeding | Extremities tend to be involved. | Most of the body, large ecchymosis |
| Palms and soles are not involved. | Palms and soles are also involved. | Necrosis in the ends of fingers and toes, tip of the nose, and ears |
| Bite                            | Large (about 10 mm in diameter) | Small (about 5 mm in diameter)  | Not found                       |
| Swelling in lymph nodes         | Systemic                      | Localized                       | (−)                             |
| Treatment                       | Tetracycline, chloramphenicol  |                                 |                                 |
treatment, the disease may cause DIC and the mortality is about 30%.

### 5. Lymphatic filariasis

The causative filarial worms of lymphatic filariasis, *Wuchereria bancrofti* and *Brugia malayi*, are carried by mosquitoes. These parasitic nematodes invade the human body and inhabit the lymph system, causing inflammation in lymph nodes and lymph vessels and lymphatic obstruction. They lead to lymphatic edema or testicular hydrocele, progressing to elephantiasis. Diethylcarbamazine and ivermectin are administered.

### C. Diseases caused by parasitic worms

#### Creeping eruption

A cutaneous parasitic larva causes a linear eruption called “creeping eruption” when it moves in the skin (Fig. 28.12). In this textbook two frequent types of creeping eruption are described: cutaneous larva migrans and cutaneous gnathostomiasis.

1. **Cutaneous larva migrans**

   *Ancylostoma braziliense*, a larva of hookworms of dogs and other mammals, mainly causes creeping eruption in tropical/subtropical areas such as southeastern United States. A few days after skin contact with contaminated sand or soil, characteristic pruritic linear or serpentine erythema occurs. Feet, buttocks and genitalia are frequently involved.

2. **Cutaneous gnathostomiasis**

   Cutaneous gnathostomiasis results from ingestion of the third-stage larvae of the nematode *Gnathostoma spinigerum* transmitted by eating raw snakes, freshwater fish or frogs. Several weeks to several months after eating a contaminated animal, localized edema and induration occur. The larva continues to move, causing linear eruptions in the trunk and the thighs. Common endemic areas are Southeast Asia (especially Thailand and Japan) and Latin America (mainly Mexico and Ecuador).

   Other species may cause creeping eruption, such as the larvae of *Spinometra mansoni* (found in amphibian and poultry meat) and nematodes of the superfamily Spiruroidea (found in soft-shelled tortoises and squid). Treatment is removal of the parasite. Oral albendazole and ivermectin are effective.

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Clinical images are available in hardcopy only.

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Fig. 28.12 Creeping eruption: cutaneous gnathostomiasis caused by linear movement of a parasitic larva in human skin.