

61 - 178 Donovanosis

178 Donovanosis

B. henselae) and avoidance and treatment of body louse infestation (for prevention of *B. quintana*). Primary prophylaxis is not recommended, but suppressive therapy with a macrolide or doxycycline is indicated in HIV-infected patients with bacillary angiomatosis or bacillary peliosis until CD4+ T-cell counts are $>200/\mu\text{L}$. Relapse may necessitate lifelong suppressive therapy in individual cases.

CARRIÓN'S DISEASE (OROYA FEVER AND VERRUGA PERUANA) ■ ■ DEFINITION AND ETIOLOGY

Carrión's disease is a biphasic disease caused by *B. bacilliformis*. Oroya fever is the initial, bacteremic, systemic form, and verruga peruana—or "Peruvian warts"—is its late-onset, eruptive manifestation. ■ ■ EPIDEMIOLOGY AND PREVENTION Infection is endemic to the geographically restricted Andes valleys of Peru, Ecuador, and Colombia (~500–3200 m above sea level). Sporadic epidemics occur. The disease is transmitted by the phlebotomine sandfly *Lutzomyia verrucarum*. Maternal-fetal transmission as well as transmission by blood transfusion have been reported. Humans are the only known reservoir of *B. bacilliformis*. Sandfly control measures (e.g., insecticides) and personal protection measures (e.g., repellents, screening, bed nets) may decrease the risk of infection. ■ ■ PATHOGENESIS After inoculation by the sandfly, bacteria invade the blood vessel endothelium and proliferate; the reticuloendothelial system and various organs also may be involved. Upon reentry into blood vessels,

B. bacilliformis invades, replicates, and ultimately destroys erythrocytes, with consequent massive hemolysis and sudden, severe anemia. Microvascular thrombosis results in end-organ ischemia. Survivors sometimes develop cutaneous hemangiomatous lesions characterized by various inflammatory cells, endothelial proliferation, and the presence of *B. bacilliformis* (verruca peruana). PART 5 Infectious Diseases ■ ■ CLINICAL MANIFESTATIONS The incubation period is 3 weeks (range, 2–14 weeks). Oroya fever may present as a nonspecific bacteremic febrile illness without anemia or as an acute, severe hemolytic anemia with hepatomegaly and jaundice of rapid onset leading to vascular collapse and clouded sensorium. Myalgia, arthralgia, lymphadenopathy, and abdominal pain may develop. Temperature is elevated but not extremely so; high fever may suggest intercurrent infection. Subclinical asymptomatic infection also occurs. Secondary infection with *Salmonella* (typhi and non-typhi) is common, though other secondary infections have been reported and should be suspected when fever persists or recurs after defervescence. In verruga peruana, red, hemangioma-like, cutaneous vascular lesions of various sizes appear either weeks to months after systemic illness or with no previous suggestive history. These lesions persist for months up to 1 year. Mucosal and internal lesions also may develop. ■ ■ DIAGNOSIS AND APPROACH TO THE PATIENT Systemic illness (with or without anemia) or the development of cutaneous lesions in a person who has been to an endemic area raises the possibility of *B. bacilliformis* infection. Severe anemia with exuberant reticulocytosis—and sometimes

thrombocytopenia—can occur. In systemic illness, Giemsa-stained blood films may show typical intraerythrocytic bacilli. Blood and bone marrow cultures may be positive, but growth is slow (1–6 weeks) and requires lower incubation temperature. Serologic assays may be helpful. Diagnosis of verruga peruana is largely clinical, although biopsy may be required to confirm the diagnosis. Several PCR assays have been described; however, their role in diagnosis remains to be clinically validated. Differential diagnosis includes coendemic systemic febrile illnesses (e.g., typhoid fever, malaria, brucellosis) and diseases producing cutaneous vascular lesions (e.g., hemangiomata, bacillary angiomatosis, Kaposi's sarcoma).

TREATMENT Carrion's Disease (Table 177-2) Antibiotic therapy for systemic *B. bacilliformis* infection usually results in rapid defervescence. Additional antibiotic treatment of intercurrent infection is often required. Blood transfusion may be necessary. Treatment of verruga peruana is not always required. Patients with numerous lesions, especially lesions that have been present for only a short period, may respond well to antibiotic therapy. ■

■ **COMPLICATIONS AND PROGNOSIS** Mortality rates associated with Oroya fever have been reported to be as high as 40% without treatment but are considerably lower (~10%) with treatment. Complications such as bacterial superinfection and neurologic and cardiac manifestations occur frequently. Generalized massive edema (anasarca) and petechiae are associated with poor outcome. Permanent immunity usually develops. ■

■ **FURTHER READING** Fournier PE et al: Epidemiologic and clinical characteristics of *Bartonella quintana* and *Bartonella henselae* endocarditis: A study of 48 patients. *Medicine (Baltimore)* 80:245, 2001. Gomes C, Ruiz J: Carrion's disease: The sound of silence. *Clin Microbiol Rev* 31:e56, 2018. Koehler JE et al: Molecular epidemiology of *Bartonella* infections in patients with bacillary angiomatosis-peliosis. *N Engl J Med* 337:1876, 1997. Landes M et al: Cat scratch disease presenting as fever of unknown origin is a unique clinical syndrome. *Clin Infect Dis* 71:2818, 2020. Rolain JM et al: Recommendations for treatment of human infections caused by *Bartonella* species. *Antimicrob Agents Chemother* 48:1921, 2004. Rose SR, Koehler JE: *Bartonella* including cat scratch disease, in *Principles and Practice of Infectious Diseases*, 9th ed, GL Mandell et al (eds). Philadelphia, Elsevier, Inc. 2020, pp 2824–2843. Wagner A, DeHio C: Role of distinct type-IV-secretion systems and secreted effector sets in host adaptation by pathogenic *Bartonella* species. *Cell Microbiol* 21:e13004, 2019. Nigel O'Farrell

Donovanosis Donovanosis is a chronic, progressive bacterial infection that usually involves the genital region. The condition is generally regarded as a sexually transmitted infection of low infectivity. This infection has been known by many other names, the most common being granuloma inguinale. ■ **ETIOLOGY** The causative organism has been reclassified as *Klebsiella granulomatis* comb nov on the basis of phylogenetic analysis, although there is ongoing debate about this decision. Some authorities consider the original nomenclature (*Calymmatobacterium granulomatis*) to be more appropriate in light of analysis of 16S rRNA gene sequences. Donovanosis was first described in Calcutta in 1882, and the causative organism was recognized by Charles Donovan in Madras in 1905. He identified the characteristic Donovan bodies, measuring

1.5 × 0.7 μm, in macrophages and the stratum malpighii. The organism was not reproducibly cultured until the mid-1990s, when its isolation in peripheral-blood monocytes and human epithelial cell lines was reported.

■ ■ **EPIDEMIOLOGY** Donovanosis has an unusual geographic distribution that has included Papua New Guinea, parts of southern Africa, India, the Caribbean, French Guyana, Brazil, and Aboriginal communities in Australia. In Australia, donovanosis has been almost entirely eliminated through a sustained program backed by strong political commitment and resources at the primary health care level. In South Africa, donovanosis is also very close to elimination. Although few cases are now reported in the United States, donovanosis was once prevalent in this country, with 5000–10,000 cases recorded in 1947. The largest epidemic recorded was in Dutch South Guinea, where 10,000 cases were identified in a population of 15,000 (the Marind-anim) between 1922 and 1952. Donovanosis is associated with poor hygiene and is more common in lower socioeconomic groups than in those who are better off and in men than in women. Infection in sexual partners of index cases occurs to a limited extent. Donovanosis is a risk factor for HIV infection (Chap. 208). Globally, the incidence of donovanosis has decreased significantly in recent times. This decline probably reflects a greater focus on effective management of genital ulcers because of their role in facilitating HIV transmission.

■ ■ **CLINICAL FEATURES** A lesion starts as a papule or subcutaneous nodule that later ulcerates after trauma. The incubation period is uncertain, but experimental infections in humans indicate a duration of ~50 days. Four types of lesions have been described: (1) the classic ulcerogranulomatous lesion (Fig. 178-1), a beefy red ulcer that bleeds readily when touched; (2) a hypertrophic or verrucous ulcer with a raised irregular edge; (3) a necrotic, offensive-smelling ulcer causing tissue destruction; and (4) a sclerotic or cicatricial lesion with fibrous and scar tissue. The genitals are affected in 90% of patients and the inguinal region in 10%. The most common sites of infection are the prepuce, coronal sulcus, frenum, and glans in men and the labia minora and fourchette in women. Cervical lesions may mimic cervical carcinoma. In men, lesions are associated with lack of circumcision. Lymphadenitis is uncommon. Extragenital lesions occur in 6% of cases and may involve the lip, gums, cheek, palate, pharynx, larynx, and chest. Hematogenous spread with involvement of liver and bone has been reported. During pregnancy, lesions tend to develop more quickly and respond more slowly to treatment. Polyarthritides and osteomyelitis are rare complications. In newborn infants, donovanosis may present with ear infection. Cases in children have been attributed to sitting on the laps of infected adults. As the incidence of donovanosis has decreased, the number of unusual case reports has appeared to be increasing. Complications include neoplastic changes, pseudoelephantiasis, and stenosis of the urethra, vagina, or anus.

FIGURE 178-1 Ulcerogranulomatous penile lesion of donovanosis, with some hypertrophic features.

FIGURE 178-2 Papanicolaou (Pap) smear stained by rapid Giemsa (RapiDiff) technique. Numerous Donovan bodies are visible.

CHAPTER 178 ■ ■ DIAGNOSIS A clinical diagnosis of donovanosis made by an experienced practitioner on the basis of the lesion's appearance usually has a high positive predictive value. The diagnosis is confirmed by microscopic identification of Donovan bodies (Fig. 178-2) in tissue smears. Preparation of a good-quality smear is important. If donovanosis is suspected on clinical grounds, the smear for Donovan bodies should be taken before swab samples are collected to be tested for other causes of genital ulceration so that enough material can be collected from the ulcer. A swab should be rolled firmly over an ulcer previously cleaned with a dry swab to remove debris. Smears can be examined in a clinical setting by direct microscopy with a rapid Giemsa or Wright's stain. Alternatively, a piece of granulation tissue crushed and spread between two slides can be used. Donovan bodies can be seen in large, mononuclear (Papanicolaou) cells as gram-negative intracytoplasmic cysts filled with deeply staining bodies that may have a safety-pin appearance. These cysts eventually rupture and release the infective organisms. Histologic changes include chronic inflammation with infiltration of plasma cells and neutrophils. Epithelial

changes include ulceration, microabscesses, and elongation of rete ridges. Donovanosis A diagnostic polymerase chain reaction (PCR) test was based on the observation that two unique base changes in the *phoE* gene eliminate *Hae*III restriction sites, enabling differentiation of *K. granulomatis* from related *Klebsiella* species. PCR analysis with a colorimetric detection system can now be used in routine diagnostic laboratories. A genital ulcer multiplex PCR that includes *K. granulomatis* has been developed. Serologic tests are only poorly specific and are not currently used. The differential diagnosis of donovanosis includes primary syphilitic chancres, secondary syphilis (condylomata lata), chancroid, lymphogranuloma venereum, genital herpes, neoplasm, and amebiasis. Mixed infections are common. Histologic appearances should be distinguished from those of rhinoscleroma, leishmaniasis, and histoplasmosis. **TREATMENT** Donovanosis Many patients with donovanosis present quite late with extensive ulceration. They may be embarrassed and have low self-esteem related to their disease. Reassurance that they have a treatable

Revision #1

Created 2026-01-06 16:33:15 UTC by Omar Ayman

Updated 2026-01-06 16:33:15 UTC by Omar Ayman