

Chapter 178: Donovanosis

Chapter 178 | Part 5: Infectious Diseases | Part 5 – Infectious Diseases: Bacterial | DETAILED EDITION

KEY CLINICAL POINTS

1. Donovanosis is a chronic, progressive bacterial infection that usually involves the genital region.
2. The condition is generally regarded as a sexually transmitted infection of low infectivity.
3. Also known as granuloma inguinale.
4. Causative organism: *Klebsiella granulomatis* (formerly *Calymmatobacterium granulomatis*).
5. Characteristic Donovan bodies measure $1.5 \times 0.7 \mu\text{m}$ and are found in macrophages.
6. Classic lesion is a beefy red ulcer that bleeds readily when touched.
7. Genitals are affected in 90% of patients; inguinal region in 10%.
8. Donovanosis is a risk factor for HIV infection.
9. Diagnosis is confirmed by microscopic identification of Donovan bodies in tissue smears.
10. Extragenital lesions occur in 6% of cases and may involve lip, gums, cheek, palate, pharynx, larynx, and chest.

FIGURES IN THIS CHAPTER

1. CHAPTER 178 FIGURE 178-2 Pund cell...
2. CHAPTER 178 FIGURE 178-2 Pund cell...

1. DEFINITION & OVERVIEW

- 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.
- 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.
- The organism was not reproducibly cultured until the mid-1990s, when its isolation in peripheral-blood monocytes and human epithelial cell lines was reported.
- He identified the characteristic Donovan bodies, measuring $1.5 \times 0.7 \mu\text{m}$, in macrophages and the stratum malpighii.

2. 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.
- 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.

Geographic Distribution

- Papua New Guinea
- Parts of southern Africa
- India
- The Caribbean
- French Guyana
- Brazil
- Aboriginal communities in Australia

Risk Factors

- Poor hygiene
- Lower socioeconomic groups
- Men more than women
- Risk factor for HIV infection

3. ETIOLOGY & PATHOPHYSIOLOGY

- 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.
- The organism was not reproducibly cultured until the mid-1990s, when its isolation in peripheral-blood monocytes and human epithelial cell lines was reported.
- He identified the characteristic Donovan bodies, measuring $1.5 \times 0.7 \mu\text{m}$, in macrophages and the stratum malpighii.

4. CLINICAL FEATURES

- A lesion starts as a papule or subcutaneous nodule that later ulcerates after trauma.

- 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.
 - (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.
- Polyarthritits 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.
- Complications include neoplastic changes, pseudoelephantiasis, and stenosis of the urethra, vagina, or anus.

Lesion Types

- Classic ulcerogranulomatous lesion: Beefy red ulcer that bleeds readily when touched.
- Hypertrophic or verrucous ulcer: Raised irregular edge.
- Necrotic ulcer: Offensive-smelling ulcer causing tissue destruction.
- Sclerotic or cicatricial lesion: Fibrous and scar tissue.

Anatomic Distribution

- Genitals: 90% of patients.
- Inguinal region: 10% of patients.
- Most common sites in men: Prepuce, coronal sulcus, frenum, glans.
- Most common sites in women: Labia minora, fourchette.
- Extragenital: Lip, gums, cheek, palate, pharynx, larynx, chest (6% of cases).
- Hematogenous spread: Liver and bone (reported).

Special Populations

- Pregnancy: Lesions develop more quickly and respond more slowly to treatment.
- Newborn infants: May present with ear infection.
- Children: Cases attributed to sitting on the laps of infected adults.

5. DIFFERENTIAL DIAGNOSIS

- 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.

6. INVESTIGATIONS & 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 (Pund) 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.
- A diagnostic polymerase chain reaction (PCR) test was based on the observation that two unique base changes in the *phoE* gene eliminate *HaeIII* 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.

Microscopy

- Direct microscopy with rapid Giemsa or Wright's stain.
- Granulation tissue crushed and spread between two slides.
- Donovan bodies in large, mononuclear (Pund) cells.
- Gram-negative intracytoplasmic cysts filled with deeply staining bodies.
- Safety-pin appearance of Donovan bodies.
- Cysts rupture and release infective organisms.

Molecular & Serology

- PCR based on two unique base changes in the *phoE* gene.
- Elimination of *HaeIII* restriction sites.
- Differentiation of *K. granulomatis* from related *Klebsiella* species.
- Colorimetric detection system for routine use.
- Genital ulcer multiplex PCR including *K. granulomatis*.
- Serologic tests: Poorly specific, not currently used.

7. MANAGEMENT & TREATMENT

- Many patients with donovanosis present quite late with extensive hypertrophic features.
- They may be embarrassed and have low self-esteem related to their disease.
- Reassurance that they have a treatable condition is important.

Clinical Approach

- Patients often present late with extensive hypertrophic features.
- Reassurance regarding treatability is important.
- Patient counseling on embarrassment and low self-esteem.

8. PROGNOSIS & COMPLICATIONS

- Complications include neoplastic changes, pseudoelephantiasis, and stenosis of the urethra, vagina, or anus.
- Polyarthritis and osteomyelitis are rare complications.
- Hematogenous spread with involvement of liver and bone has been reported.

9. SPECIAL CONSIDERATIONS

- Pregnancy: Lesions tend to develop more quickly and respond more slowly to treatment.
- Children: Cases attributed to sitting on the laps of infected adults.
- Newborn infants: May present with ear infection.

Pregnancy

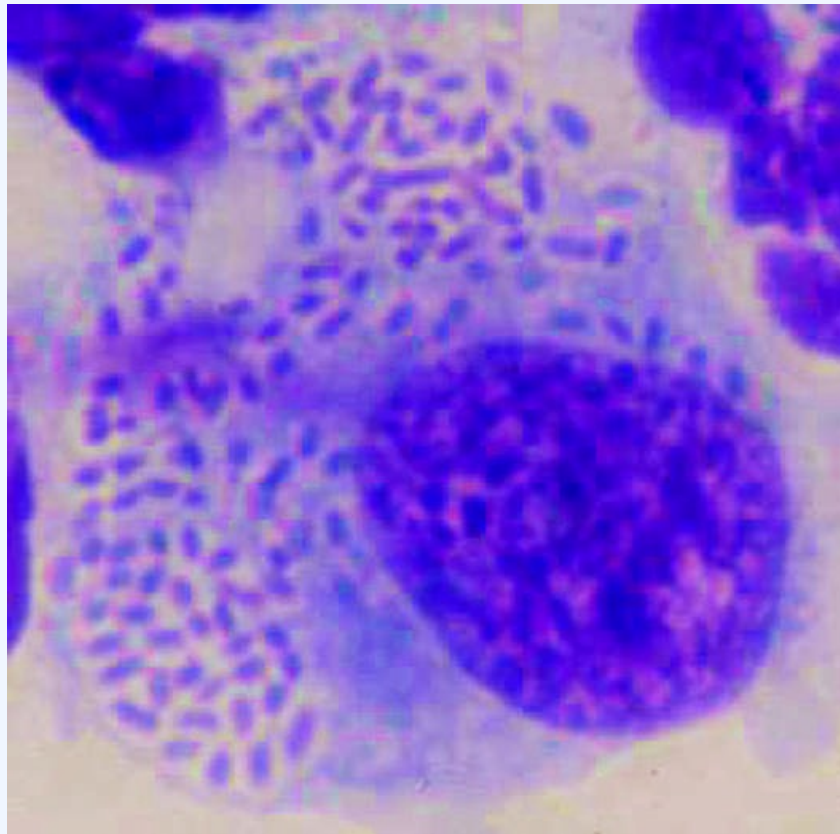
- Lesions develop more quickly.
- Response to treatment is slower.

Pediatrics

- Cases attributed to sitting on the laps of infected adults.
- Newborn infants may present with ear infection.

10. KEY PEARLS & CLINICAL TRAPS

- Donovanosis is a chronic, progressive bacterial infection of the genital region.
- Known as granuloma inguinale.
- Causative organism: *Klebsiella granulomatis* (formerly *Calymmatobacterium granulomatis*).
- Characteristic Donovan bodies measure $1.5 \times 0.7 \mu\text{m}$ and are found in macrophages.
- Classic lesion is a beefy red ulcer that bleeds readily when touched.
- Genitals are affected in 90% of patients; inguinal region in 10%.
- Donovanosis is a risk factor for HIV infection.
- Diagnosis is confirmed by microscopic identification of Donovan bodies in tissue smears.
- Extragenital lesions occur in 6% of cases and may involve lip, gums, cheek, palate, pharynx, larynx, and chest.



Harrison's 22e · Figure 1

CHAPTER 178 FIGURE 178-2 Pund cell stained by rapid Giemsa (RapiDiff) technique. Numerous after trauma. The incubation period is uncertain, but experimental Donovan bodies are visible. 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 clinical diagnosis of donovanosis made by an experienced practitioner—necrotic, offensive-smelling ulcer causing tissue destruction; and (4) a nodule on the basis of the lesion's appearance usually has a high positive sclerotic or cicatricial lesion with fibrous and scar tissue. The diagnosis is confirmed by microscopic identification of Donovan bodies (Fig. 178-2) in tissue smears. Preparation — Figure 178-1: Ulcerogranulomatous penile lesion of donovanosis, with some ulceration.



Harrison's 22e · Figure 2

CHAPTER 178 FIGURE 178-2 Pund cell stained by rapid Giemsa (RapiDiff) technique. Numerous after trauma. The incubation period is uncertain, but experimental Donovan bodies are visible. 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; DIAGNOSIS (2) a hypertrophic or verrucous ulcer with a raised irregular edge; (3) a A clinical diagnosis of donovanosis made by an experienced practitio- necrotic, offensive-smelling ulcer causing tissue destruction; and (4) a ner on the basis of the lesion's appearance usually has a high positive sclerotic or cicatricial lesion with fibrous and scar tissue. predictive value. The diagnosis is confirmed by microscopic identifi- The genitals are affected in 90% of patients and the inguinal region cation of Donovan bodies (Fig. 178-2) in tissue smears. Preparation — Figure 178-2: Pund cell stained by rapid Giemsa (RapiDiff) technique. Numerous Donovan bodies are visible.