



United Kingdom national guideline
for the management of Donovanosis
(Granuloma inguinale)
2011

**Clinical Effectiveness Group
British Association for Sexual Health and HIV**

SCOPE AND PURPOSE

The main objective of BASHH CEG guidelines is to reduce the number of sexually transmitted infections (STIs) and the complications that can arise in people either presenting with signs and symptoms of an STI, or undergoing investigation for possible infection. Specifically, this guideline offers recommendations on the diagnostic tests, treatment regimens and health promotion principles needed for the effective management of Donovanosis (granuloma inguinale) covering, the management of the initial presentation, as well as how to prevent transmission and future infection. It is aimed primarily at people aged 16 years or older (see specific BASHH guidelines for those under 16) presenting to health care professionals, working in departments offering Level 3 care in STI management within the United Kingdom. However, the principles of the recommendations should be adopted across all levels (levels 1 and 2 may need to develop, where appropriate, local care pathways).

What is new in this guidance

An updated literature search has shown that there has been exceedingly little published since the last CEG guideline (2001) concerning this now rare disease, that merits consideration. There have been a handful of case reports of rare (but generally not unknown complications) of the disease and a few observational studies of alternative treatments which would not be seriously considered as rivals to Azithromycin. Therefore this guideline remains essentially unchanged from its 2001 predecessor.

Introduction

Donovanosis is a sexually transmitted infection that usually manifests itself as genital ulceration. It is seen chiefly in small endemic foci in tropical countries. Active foci of disease in recent years have been described in India, Papua New Guinea, the Caribbean, Brazil, the Guyanas, South Africa, Zambia, Vietnam, and in Australian aboriginals.

The causative organism formerly, *Calymmatobacterium granulomatis* has recently been officially redesignated *Klebsiella granulomatis* [1-3].

Clinical features

- At site of primary inoculation: one or more papules/nodules developing into friable ulcers or hypertrophic lesions which gradually increase in size. Lesions tend not to be painful.
- Regional lymph nodes: initially swelling of the nodes, followed particularly in case of inguinal nodes, by spread of infection into overlying tissues, resulting in either abscess formation (pseudobubo) or ulceration of the overlying skin.

Untreated infections may either resolve spontaneously or persist and slowly spread. Primary lesions of mouth and cervix occur and the latter have often been mistaken for malignant lesions. Complications include haemorrhage, genital lymphoedema, genital mutilation and cicatrisation, development of squamous carcinoma and, on rare occasions, haematogenous dissemination to bone and viscera (particularly during pregnancy). The extraordinary range of potential complications is underlined by recent case reports describing manifestations as varied as psoas and perinephric abscess and spinal cord compression. Rare cases of vertical transmission have been reported. Lesions of the ears of infants are characteristic in such cases [4-6].

Diagnosis

The main method of diagnosis is the demonstration of Donovan bodies in either:

- (i) cellular material taken by scraping/impression smear/swab/crushing of pinched off tissue fragment on to glass slide;

or

- (ii) tissue sample collected by biopsy.

Smears can be stained with Giemsa, Wright's stain, or Leishman stain. Biopsies are best stained with silver stains (for example, Warthin-Stary) or Giemsa. Donovan bodies are characterised by :

- (i) location within large (20-90 µm) histiocytes,
- (ii) pleomorphic appearance 1- 2 x 0.5-0.7 µm
- (iii) bipolar densities and a capsule often visible
- (iv) stain Gram negative.

Expert opinion has estimated that in endemic areas identification of Donovan bodies is achievable in 60-80% of patients considered to have Donovanosis on clinical grounds.

Successful culture of the causative organism, *Klebsiella granulomatis*, has recently been reported in human peripheral blood monocytes and in HEp-2 cells [7,8]. Both polymerase chain reaction (PCR) methods [9] and serological tests [10] for Donovanosis have been described but are not yet routinely available.

Management

All patients with active lesions shown to contain Donovan bodies should receive antimicrobial treatment. Patients from areas endemic for Donovanosis with a clinical diagnosis of the disease should be given presumptive treatment.

Treatment options are presented in table 1, which lists drugs shown to be effective in the treatment of Donovanosis in prospective studies. Drugs have been selected on the basis of current availability, lack of major toxicity, and convenient dosage regimens. Older drugs known to be effective but not included are trivalent antimonials, streptomycin, chloramphenicol, thiamphenicol, chlortetracycline, and oxytetracycline. Ampicillin has been omitted because of conflicting data on efficacy. Recent experience with Azithromycin in Australia has been so encouraging in all categories of patient that a proposal to eradicate Donovanosis by the year 2003 in Australia has been formally adopted [11,12,13].

Table 1 Drugs shown to be effective in the treatment of Donovanosis

Drug	Dose	Route	Grading of recommendation	Level of evidence	Reference
Azithromycin	1 g weekly or 500 mg daily	O	B	Ib	Bowden [15]
Ceftriaxone	1 g daily	IM/IV	B	IIb	Merianos [16]
Co-trimoxazole†	160/800 mg twice daily	O	B	IIb	Lal [17]
Doxycycline†	100 mg twice daily	O	C	IV	Greenblatt [18]
Erythromycin†	500 mg four times daily	O	C	IV	Robinson [19]
Norfloxacin	400 mg twice daily	O	B	IIb	Ramanan [20]
Gentamicin†	1 mg/kg every 8 hours	IM/IV	C	III	Maddocks [21]

†Currently recommended by CDC.

Notes on table 1

- Azithromycin is recommended for Donovanosis in the Australian Antibiotic Guidelines.
- CDC recommends ciprofloxacin which has better bioavailability than norfloxacin.
- Gentamicin recommended by CDC as an adjunct to therapy in patients whose lesions do not respond in the first few days to other agents.
- Doxycycline has not been individually assessed prospectively and recommendations are based on trials carried out with older tetracyclines (oxytetracycline, chlortetracycline, etc) which are assumed to be equivalent to doxycycline, which is chosen for more convenient twice daily dosing.
- Duration of treatment should be until lesions have healed. Healing times vary greatly between patients. CDC recommends a minimum of 3 weeks' treatment.

Treatment for pregnant or lactating mothers

Gentamicin, doxycycline, co-trimoxazole, and norfloxacin are not recommended for pregnant or lactating women.

Erythromycin has been used successfully in pregnant women with Donovanosis. Children born to mothers with untreated genital lesions of Donovanosis are at risk of infection and a course of prophylactic antibiotics should be considered.

Partner management

Any person with a history of unprotected sexual contact with a patient with active Donovanosis or within 40 days before the onset of lesions should be assessed clinically for evidence of infection and offered treatment. This recommendation is based on best estimates of the incubation period reported by Clark who studied 60 patients and found an incubation period of between 3 and 40 days in 92% of patients [14].

Follow up

Patients should be followed until symptoms have resolved.

Auditable outcome measures

All cases of Donovanosis should be subjected to clinicopathological review. Target: 100%.

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Conflict of interest

None.

Evidence base

Information was obtained by searching the Cochrane Library and Medline databases and Google Scholar from 1966 up to Feb 2009 using the MeSH heading "granuloma inguinale" and free text searching using "granuloma inguinale," "Donovanosis," and "Calymmatobacterium granulomatis" and "Klebsiella granulomatis." EMBASE was searched from 1980 to Feb 2009. References of all retrieved articles were checked in order to identify additional material. *Index Medicus* from 1879-1965 was hand searched for all articles on granuloma inguinale by the author for an extended review of diagnosis and treatment of Donovanosis published in 1991 [1].

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