

2018 UK national guideline for the management of donovanosis

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Abstract

The objective of this guideline is to provide guidance for the diagnosis and management of donovanosis, a now rare sexually transmitted infection. This guidance is primarily for professionals working in UK Sexual Health services (although others may find it useful) and refers to the management of individuals presenting with possible symptoms of donovanosis who are over the age of 16. An updated literature review since the last Clinical Effectiveness Group (CEG) guideline produced for this condition in 2011 has shown few new developments. Most reports in the literature relate to cases of unusual presentations of the condition.

Keywords

Antibiotic, donovanosis

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What's new in the 2018 update?

- Literature search updated to March 2018
- Continued decrease in cases globally
- Most recent articles are case reports
- The Grade system for reporting strength of evidence adopted

Methods

Search strategy

A Medline search using the terms donovanosis and granuloma inguinale between 1950 and March 2018 was undertaken. Due to the rarity of the condition in the UK, piloting of the guideline was not considered possible and we were not able to locate a patient to provide input or identify patient representatives to review the guideline.

Limitations include the lack of recent drug studies and the continued decrease in reported cases.

Aetiology

There is still debate about the correct nomenclature of the causative organism. The cause was originally identified as *Calymmatobacterium granulomatis*. However, based on evidence of phylogenetic similarity with

Klebsiella species, a proposal was put forward that the organism be reclassified as *Klebsiella granulomatis comb nov.*¹ However, similarities of only 95% to *Klebsiella* were identified in another study.²

Transmission

Whether donovanosis is always sexually transmitted has been questioned. However, the majority of cases are in the 20–40-year age group, the most sexually active. Amongst sexual partners of index cases, wide variations in the rates of infection have been reported ranging from 1–2% in Papua New Guinea³ and the USA⁴ to 50% of marital partners in India.^{5,6}

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Epidemiology

Donovanosis is now a rare infection and appears to be dying out. The main foci in recent times have been in Papua New Guinea, southern Africa, parts of India and Brazil. An eradication programme in Australia has led to its virtual elimination there.⁷

As a cause of genital ulceration that bleeds readily, the risk of associated HIV infection is increased and HIV testing should be recommended for all cases.⁸

Clinical features

The first sign of infection is usually a firm papule or subcutaneous nodule that later ulcerates. Four types of donovanosis are described classically⁹:

1. Ulcerogranulomatous is the most common variant; non-tender, fleshy, exuberant, single or multiple, beefy red ulcers that bleed readily when touched.
2. Hypertrophic or verrucous type, an ulcer or growth with a raised irregular edge, sometimes with a walnut appearance.
3. Necrotic, usually a deep foul-smelling ulcer causing tissue destruction.
4. Sclerotic, with extensive fibrous and scar tissue.

The genitals are affected in 90% of cases and the inguinal area in 10%. Extragenital cases occur in 6% of cases: sites include the lip, gums, cheek, palate and pharynx. Atypical cases are reported in children, usually affecting the facial region.¹⁰

Lymphadenitis is uncommon. Dissemination is rare; secondary spread to liver and bone may occur and is usually associated with pregnancy and cervical lesions.

The usual sites of infection are in men, the prepuce, coronal sulcus, frenum and glans penis and in women, the labia minora and fourchette. Lesions tend to grow more rapidly during pregnancy.

Squamous cell carcinoma of the penis may both mimic and complicate donovanosis, and a biopsy should be done if antibiotics fail to effect resolution of ulcers.¹¹

Laboratory diagnosis

Direct microscopy

This is the quickest and most reliable method. A rapid Giemsa can be used to stain tissue smears that should be prepared by rolling a swab firmly across the ulcer and rolling this swab evenly across a glass slide to deposit ulcer material.¹² Characteristically, there are large mononuclear cells with intracytoplasmic cysts filled with deeply-stained Gram-negative Donovan

bodies. These bodies are pleomorphic and sized $1-2 \times 0.5-0.7 \mu\text{m}$. Depending on the stain used, bipolar densities and a capsule may be visible.

Histologic examination for Donovan bodies is best done using Giemsa or Silver stains. The characteristic picture shows chronic inflammation with infiltration of plasma cells and polymorphonuclear leucocytes. Polymerase chain reaction (PCR) methods include a colorimetric detection method^{13,14} and a genital ulcer multiple PCR test using an in-house nucleic acid amplification technique with *C. granulomatis* primers.¹⁵ However, there are no commercial PCR tests for donovanosis currently available. Culture has only been accomplished in two laboratories in recent times and is not available routinely.^{16,17} Serology has been used in the past but is not reliable or routinely available.

Management

Samples for analysis should ideally be taken before treatment is given, but antibiotics should not be delayed whilst waiting for results. Patients should be reassured that donovanosis is a treatable condition that will be cured if the correct antibiotic course is completed. A fact sheet for patients has been produced by the New South Wales Communicable Diseases section, Australia – <http://www.health.nsw.gov.au/Infectious/factsheets/Pages/Donovanosis.aspx>. Routine screening for other sexually transmitted infections is required.

Recommended regimens (all regimens are for three weeks or until lesions have completely healed)

1. Azithromycin 1 g weekly or 500 mg daily orally: 1B.¹⁸

Alternative regimens

1. Co-trimoxazole 160/800 mg bd orally: 1B¹⁹
2. Doxycycline 100 mg bd orally: 1C (evidence is not available from clinical trials, but older tetracyclines have been observed to be effective)²⁰
3. Erythromycin 500 mg four times daily orally. Recommended in pregnancy: 1C²¹
4. Gentamicin 1 mg/kg every 8 h parenterally can also be used as an adjunct if lesions are slow to respond 1C³

Treatment in pregnancy

1. Erythromycin 500 mg qds orally is recommended in pregnancy: 1C. Azithromycin could also be used: 1 g weekly: 1D

Treatment of children

1. Azithromycin 20 mg/kg orally once daily: 1C
Prophylactic antibiotics should be considered in neonates born to mothers with genital lesions; the recommended regimen is azithromycin 20 mg/kg once daily for three days 1C.²²

Partner management

In the absence of any reliable screening test and the long incubation period, all sexual contacts of cases in the last six months should be checked for possible lesions by clinical examination.

Follow-up

Patients should be followed up until lesions have healed completely.

Auditable outcome measures

All cases should be subjected to clinicopathological review by an experienced microscopist.

Editorial independence

The guideline was commissioned, edited and endorsed by the British Association of Sexual Health and HIV (BASHH) Clinical Effectiveness Group (CEG) without external funding being sought or obtained.

All members of the guideline writing committee completed the BASHH conflict of interest declaration at the time the final draft was submitted to the CEG.

Declaration of conflicting interests

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