Complete Summary

GUIDELINE TITLE

2002 national guideline for the management of chancroid.

BIBLIOGRAPHIC SOURCE(S)

Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD). 2002 national guideline for the management of chancroid. London: Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD); 2002. Various p. [51 references]

COMPLETE SUMMARY CONTENT

SCOPE
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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY

SCOPE

DISEASE/CONDITION(S)

Chancroid

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Infectious Diseases
Obstetrics and Gynecology
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To present a national guideline on the management of chancroid

TARGET POPULATION

Men and women in the United Kingdom with chancroid

INTERVENTIONS AND PRACTICES CONSIDERED

Assessment/Diagnosis

1. Evaluation of clinical features
2. Demonstration of Haemophilus ducreyi
    - Culture of scrapings from the ulcer base or of pus aspirate from the bubo
    - Microscopy of Gram stained smear of scrapings from the ulcer base or of pus aspirate from the bubo
    - Detection of nucleic acid (DNA) by amplification techniques such as polymerase chain reaction
3. Criteria for making a "probable diagnosis"

Management/Treatment

1. Pharmacological interventions
    - Azithromycin
    - Ceftriaxone
    - Ciprofloxacin
    - Erythromycin
    - Fleroxacin
    - Spectinomycin
    - Oral single dose fluoroquinolones such as fleroxacin
    - Injectable single dose aminoside such as spectinomycin
2. Management of fluctuant buboes
    - Needle aspiration from adjacent healthy skin
    - Incision and drainage
3. Special treatment consideration for pregnant women, lactating mothers, and children
4. Follow-up
    - Examination in 3 to 7 days after initiation of therapy
    - Treatment failures: investigation of possible co-infections with Treponema pallidum or herpes simplex virus; or determination of possible resistance by isolation of Haemophilus ducreyi and susceptibility testing by the agar dilution technique or the simpler E-test
    - Needle aspiration (or drainage) of fluctuant lymphadenopathy
5. Partner examination and treatment (if sexual contact within 10 days of the onset of symptoms)

MAJOR OUTCOMES CONSIDERED

Clinical efficacy of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The previous guidelines from 1998 were largely based on several extensive reviews of the treatment of chancroid published in the late 1980´s, forming the basis of the 1993 and 1997 Centers for Disease Control and Prevention (CDC) recommendations, and on a Medline search spanning the years 1966-1998. The guideline has been updated by searching Medline from 1998-2000 using the search terms: "Chancroid and diagnosis"; "Chancroid and treatment"; "Haemophilus ducreyi diagnosis"; "Haemophilus ducreyi treatment"; and "Chancroid and randomized trial". The Cochrane Library was searched from 1957-2000 using the MeSH headings "chancroid" and "Haemophilus ducreyi". The search was supplemented by checking references of retrieved articles, reviewing abstracts of international conferences and AIDS and Meetings of the International Society for STD Research (ISSTDR) over the last decade.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence:

Ia

- Evidence obtained from meta-analysis of randomised controlled trials

Ib

- Evidence obtained from at least one randomised controlled trial

IIa

- Evidence obtained from at least one well designed controlled study without randomisation

IIb

- Evidence obtained from at least one other type of well designed quasi-experimental study

III

- Evidence obtained from well designed non-experimental descriptive studies such as comparative studies, correlation studies, and case control studies

IV

- Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The revision process commenced with authors being invited to modify and update their 1999 guidelines. These revised versions were posted on the website for a 3 month period and comments invited. The Clinical Effectiveness Group and the authors concerned considered all suggestions and agreed on any modifications to be made.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grading of Recommendations:

A (Evidence Levels Ia, Ib)

- Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.

B (Evidence Levels IIa, IIb, III)

- Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation.

C (Evidence Level IV)

- Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities.
- Indicates absence of directly applicable studies of good quality.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The initial versions of the guidelines were sent to the following for review:

- Clinical Effectiveness Group (CEG) members
- Chairs of UK Regional GU Medicine Audit Committees who had responded to an invitation to comment on them
- Chair of the Genitourinary Nurses Association (GUNA)
- President of the Society of Health Advisers in Sexually Transmitted Diseases (SHASTD)
- Clinical Effectiveness Committee of the Faculty of Family Planning and Reproductive Health Care (FFP)

Comments were relayed to the authors and attempts made to reach a consensus on points of contention with ultimate editorial control resting with the Clinical Effectiveness Group. Finally, all the guidelines were ratified by the councils of the two parent societies.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Levels of evidence (I-IV) and grades of recommendation (A-C) are defined at the end of the "Major Recommendations" field.

Diagnosis

The main methods of diagnosis revolve around the identification of Haemophilus ducreyi (Van Dyck & Piot, 1994; Ronald & Albritton, 1999; Lewis, 2000) by:

(i) Culture of scrapings from the ulcer base or of pus aspirate from the bubo; culture media include Mueller-Hinton agar or gonococcal agar base enriched with 1% to 2% bovine haemoglobin, 5% fetal calf serum, 1% isovitalex and 3 mg/L vancomycin; modification of these techniques by substitution of 0.2% activated charcoal instead of fetal calf serum has proven equally effective and is much cheaper (Lockett et al., 1991); the use of more than one medium increases sensitivity (Dangor et al., 1992). Since Haemophilus ducreyi is a fastidious organism, patients' specimens should be plated out directly at the clinic or sent rapidly (within 4 hours) to the laboratory; calcium alginate or plastic swabs should be used for sample collection; unfortunately, special, not widely available, transport medium needs to be used.

or

(ii) Microscopy of a Gram stained smear (or other stains) of scrapings from the ulcer base or of pus aspirate from the bubo: demonstration of characteristic gram-negative coccobacilli, with occasional chaining.

or

(iii) Detection of nucleic acid (DNA) by amplification techniques such as polymerase chain reaction techniques, using nested techniques. (Trees & Morse, 1995; West et al., 1995; Webb et al., 1996)

Expert opinion has estimated that, in endemic areas, a positive Haemophilus ducreyi culture is achievable in 60% to 80% of patients considered to have chancroid on clinical grounds. Microscopy is only 50% sensitive compared with culture, and prone to multiple errors given the polymicrobial flora of many ulcers. Polymerase chain reaction is the most sensitive technique, and has been demonstrated to be 95% sensitive compared to culture; conversely culture may be only 75% sensitive relative to polymerase chain reaction. Yet polymerase chain reaction may be negative in a number of culture-proven chancroid cases, owing to the presence of Taq polymerase inhibitors in the DNA preparations extracted from genital ulcer specimens. (Lewis, 2000) A multiple polymerase chain reaction assay has also been developed for the simultaneous amplification of DNA targets from Haemophilus ducreyi, Treponema pallidum and herpes simplex virus types 1 and 2. (Orle et al., 1996) Unfortunately, it is not commercially available, except for research purposes.

Other Diagnostic Methods

Other diagnostic tests have included various antigen-detection techniques involving immunofluorescence or radio-isotopic probes. Serologic diagnosis of chancroid has been useful in a number of epidemiological studies, using enzyme-linked immunoassays (EIAs) using either lysed whole cell, lipo-oligosaccharide (LOS) or outer membrane proteins (OMPs) as antigen sources. (Museyi et al., 1988; Alfa et al., 1993) However, for the individual patient, the method lacks sensitivity, specificity (cross-reaction with other Haemophilus species) and cannot distinguish between remote and recent infection.

To circumvene the many problems of positive diagnosis of chancroid, the U.S. Centers for Disease Control (CDC) proposes that a "probable diagnosis", for both

clinical and surveillance purposes, be made if the patient has one or more painful genital ulcers, and (a) no evidence of Treponema pallidum infection by dark field examination of ulcer exudate or by a serologic test for syphilis performed at least 7 days after onset of ulcers, and (b) the clinical presentation, appearance of the genital ulcers and regional lymphadenopathy, if present, is typical for chancroid and a test for herpes simplex virus is negative.

Management

General Advice

1. Patients should be advised to avoid unprotected sexual intercourse until they and their partners(s) have completed treatment and follow-up.
2. Patients should be given a detailed explanation of their condition with particular emphasis on the long-term implications for the health of themselves and their partners(s). This should be reinforced by giving them clear and accurate written information.

Further Investigations

Screening for other possible causes of genital ulcerative disease should be arranged, particularly the diagnosis of Treponema pallidum and genital herpes, but also sometimes the diagnosis of lymphogranuloma venereum (LGV) (see the related guideline titled 2002 National Guideline for the Management of Lymphogranuloma Venereum or donovanosis (see the related guideline titled 2002 National Guideline for the Management of Donovanosis [Granuloma Inguinale]). In addition screening for serological syphilis and possibly for HIV should be offered. Biopsy of lymph nodes may be required to exclude neoplasia.

Treatment

Successful treatment of chancroid should cure infection, resolve clinical symptoms, and prevent transmission to sexual partners.

The main treatment options are presented in Table 1 (summarised below) and most are similar to the 1997 U.S. Centers for Disease Control and Prevention guidelines (Guidelines for treatment of sexually transmitted diseases. MMWR Morbid Mortal Wkly Rep 1997:1-116). Evidence of their clinical efficacy has been obtained in randomised controlled trials for most (Level of Evidence Ib), however grading of recommendation will also take account of ease of administration, side effects and compliance.

Recommended Regimens

- Azithromycin 1 g orally in a single dose (Level of Evidence Ib, Grade of Recommendation A)

  or

- Ceftriaxone 250 mg intramuscularly in a single dose (Level of Evidence Ib, Grade of Recommendation B)

or

- Ciprofloxacin 500 mg orally in a single dose (Level of Evidence Ib, Grade of Recommendation B)

or

- Ciprofloxacin 500 mg orally two times a day for 3 days (Level of Evidence Ib, Grade of Recommendation B/A)

or

- Erythromycin base 500 mg orally four times a day for 7 days (Level of Evidence Ib, Grade of Recommendation B/A)

Table 1. Drugs Shown to be Effective in the Treatment of Chancroid

Drug	Dose	Route	Grading of Recommendation	Level of Evidence
Azithromycin*	1 g STAT	Oral	A	Ib
Ceftriaxone*	250 mg STAT	Intramuscular	B	Ib
Ciprofloxacin*	500 mg twice daily for 3 days * or	Oral	B/A	Ib
	500 mg STAT	Oral	B	Ib
Erythromycin*	500 mg four times	Oral	B/A	Ib

	daily for 7 days * or			
	500 mg three times daily for 7 days or	Oral	A	Ib
	250 mg three times daily for 5 days	Oral	C	III
Fleroxacin	400 mg STAT or	Oral	B	Ib
	400 mg once daily for 5 days #	Oral	C	III
Spectinomycin	2 g STAT	Intramuscular	B	IIa

*Recommended by U.S. Centers for Disease Control and Prevention (Centers for Disease Control and Prevention (CDC), 1997).

#Proposed for HIV-positive patients

Azithromycin and ceftriaxone offer the advantage of single dose therapy. They have excellent in vitro activity against Haemophilus ducreyi with no reported resistance to date. (Ronald & Albritton, 1999) Erythromycin given at high doses for 7 days is the World Health Organization (WHO)-recommended first line treatment for chancroid. (World Health Organization, 1994) Although efficacious (with cure rates of 93% noted in Kenya [Tyndall et al., 1994] and India [D'Souza et al., 1998]), poor compliance and gastrointestinal intolerance make alternative therapy desirable (Level of Evidence Ib, Grade of Recommendation B). Lower dosage and simpler regimens of erythromycin have been evaluated in two separate trials in Kenya. Cure rates of 91% were achieved in a randomised double blind trial of erythromycin 500 mg three times daily for 7 days (versus a single dose of ciprofloxacin) (Malonza et al., 1999) (Level of Evidence Ib, Grade of Recommendation B). The efficacy of an even shorter regimen (250 mg three times daily for 5 days) was reportedly high in a small trial conducted by the same team, but this was not a randomized comparative trial (Kimani et al., 1995) (Level of Evidence III, Grade of Recommendation C). Worldwide, several isolates with intermediate resistance to either ciprofloxacin or erythromycin have been reported, thus single dose ciprofloxacin and the shorter (5-day) regimen of erythromycin may not be effective, as has been reported by teams in Rwanda and Malawi. (Bogaerts et al., 1995; Behets et al., 1995) However, the recent double-blind randomised-controlled trial conducted in Nairobi showed comparable cure rates for single dose ciprofloxacin (92%) and the standard 7-day course of erythromycin (91%) (Malonza et al., 1999). The single dose nature and relatively lower cost of the ciprofloxacin regimen makes it an attractive option for many low-income countries. Widespread resistance to trimethoprim-sulfamethoxazole (TMP-SMX) renders this cheap and once effective alternative almost useless, even using high dosages, outside specific settings where susceptibility has still recently been documented (Knapp et al., 1993; Van Dyck et al., 1994).

Alternative regimens:

- Oral single dose fluoroquinolones such as fleroxacin 400 mg (Plourde et al., 1992; Tyndall et al., 1993b) or norfloxacin 800 mg (Schmid, 1989) (Level of Evidence Ib, Grade of Recommendation B)
- Injectable single dose aminoside such as spectinomycin 2 g intramuscularly (Fransen et al., 1987; Guzman, Guzman, & Bernal, 1992) (Level of Evidence IIa, Grade of Recommendation B)

Allergy

Patients allergic to quinolones or cephalosporins should be treated with the erythromycin regimen.

Treatment for pregnant or lactating mothers and children

The safety of azithromycin for pregnant and lactating women has not been established. Ciprofloxacin is contraindicated for pregnant and lactating women, children, and adolescents less than 18 years of age. The erythromycin or ceftriaxone regimens should be applied. No adverse effects of chancroid on pregnancy outcome or on the fetus have been reported.

Special Considerations

Human Immunodeficiency Virus (HIV) Infection

Patients co-infected with HIV should be closely monitored. There have been concerns that healing may be slower among HIV infected people (Behets et al., 1995; Kimani et al., 1995) and treatment failures have been frequently recorded in Kenya using azithromycin (Tyndall et al., 1994), ceftriaxone (Tyndall et al., 1993a), or single dose fleroxacin (Tyndall et al., 1993b), or in Malawi with low dose erythromycin or ciprofloxacin (Behets et al., 1995). A higher treatment failure rate among HIV infected patients has, however, not been observed by the same Kenyan team in a more recent study using low dose erythromycin or single dose ciprofloxacin (Malonza et al., 1999). In Rwanda, researchers found that HIV and the degree of immunosuppression as measured by CD4 counts had no effect on bacteriological and clinical outcomes and that treatment failures were entirely attributable to resistance of Haemophilus ducreyi to trimethoprim-sulfamethoxazole (TMP-SMX) (Bogaerts et al., 1995). Dosage and duration of the fleroxacin regimen also needed to be increased to treat HIV infected patients in Nairobi (Plourde et al., 1992). The U.S. Centers for Disease Control and Prevention recommends that "since data on therapeutic efficacy with the recommended ceftriaxone and azithromycin regimens among patients infected with HIV are limited, those regimens should be used among persons known to be infected with HIV only if follow-up can be assured." (CDC, 1997) Some experts suggest using the full dose erythromycin 7-day regimen for treating HIV infected persons.

Management of Fluctuant Buboes

The classic strategy has been to needle-aspirate fluctuant buboes from adjacent healthy skin. The procedure is simpler and safer than incision, which is prone to complications (sinus formations). A randomised study conducted during an outbreak of chancroid in the United States (Ernest, Marvez-Valls, & Martin, 1995) has shown that careful incision and drainage is an effective and safe method for treating fluctuant buboes and avoids frequent needle re-aspirations. This procedure should always be performed under effective antibiotic cover.

Follow-up

Patients should be re-examined 3-7 days after initiation of therapy. If treatment is successful, ulcers improve symptomatically within 3 days and substantial re-epithelialisation occurs within 7 days after onset of therapy. The time required for complete healing is related to the size of the ulcer (and perhaps HIV); large ulcers may require more than 2 weeks.

Treatment failures should warrant: (i) investigation of possible co-infections with Treponema pallidum or herpes simplex virus; or (ii) determination of possible resistance by isolation of Haemophilus ducreyi and susceptibility testing by the agar dilution technique or the equally effective but simpler E-test (Lewis, 1997).

Clinical resolution of fluctuant lymphadenopathy is slower than that of ulcers and may require frequent needle aspiration (or drainage).

Sexual Partner(s) Management

Persons who have had sexual contact with a patient who has chancroid within the 10 days before onset of the patient's symptoms should be examined, and treated even in the absence of symptoms, as asymptomatic carriage of Haemophilus ducreyi has been proved to occur (Plummer, 1989; Hawkes et al., 1995).

Definitions:

The following rating scheme was used for major management recommendations.

Levels of Evidence:

Ia

- Evidence obtained from meta-analysis of randomised controlled trials

Ib

- Evidence obtained from at least one randomised controlled trial

IIa

- Evidence obtained from at least one well designed controlled study without randomisation

IIb

- Evidence obtained from at least one other type of well designed quasi-experimental study

III

- Evidence obtained from well designed non-experimental descriptive studies such as comparative studies, correlation studies, and case control studies

IV

- Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

Grading of Recommendations:

A (Evidence Levels Ia, Ib)

- Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.

B (Evidence Levels IIa, IIb, III)

- Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation.

C (Evidence Level IV)

- Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities.
- Indicates absence of directly applicable studies of good quality.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is graded and identified for select recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

If treatment is successful, ulcers improve symptomatically within 3 days and substantial re-epithelialisation occurs within 7 days after onset of therapy. The time required for complete healing is related to the size of the ulcer (and perhaps human immunodeficiency virus [HIV]); large ulcers may require more than 2 weeks. Appropriate treatment may also control transmission of chancroids to others.

POTENTIAL HARMS

Not stated

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The Clinical Effectiveness Group reminds the reader that guidelines in themselves are of no use unless they are implemented systematically. The following auditable outcome measures are provided:

- All cases of suspected chancroid should be subject to laboratory investigations. Target 100%.

- Sexual partners should be traced and treated. Serological syphilis and HIV testing should be offered to all patients.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD). 2002 national guideline for the management of chancroid. London: Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD); 2002. Various p. [51 references]

ADAPTATION

The recommendations are largely based on the 1997 version of the U.S. Centers for Disease Control and Prevention (CDC) "Guidelines for Treatment of Sexually Transmitted Diseases" (MMWR Morbid Mortal Wkly Rep 1997:1-116).

DATE RELEASED

1999 Aug (revised 2002)

GUIDELINE DEVELOPER(S)

British Association of Sexual Health and HIV - Medical Specialty Society

SOURCE(S) OF FUNDING

Not stated

GUIDELINE COMMITTEE

Clinical Effectiveness Group (CEG)

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Author: Philippe Mayaud and Duncan McCormick

Clinical Effectiveness Group (CEG) Members: Keith Radcliffe (Chairman); Imtyaz Ahmed-Jushuf; Jan Welch; Mark FitzGerald; Janet Wilson

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Conflict of interest: None

GUIDELINE STATUS

This is the current release of the guideline. This guideline updates a previously released version.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available in HTML format from the Association for Genitourinary Medicine (AGUM) Web site. Also available in Portable Document Format (PDF) from the Medical Society for the Study of Venereal Diseases (MSSVD) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following background documents are available:

- UK national guidelines on sexually transmitted infections and closely related conditions. Introduction. Sex Transm Infect 1999 Aug;75(Suppl 1):S2-3. Electronic copies: Available in Portable Document Format (PDF) from the Medical Society for the Study of Venereal Diseases (MSSVD) Web site.
- Revised UK national guidelines on sexually transmitted infections and closely related conditions 2002. Sex Transm Infect 2002;78:81-2

Print copies: For further information, please contact the journal publisher, BMJ Publishing Group.

The following related guidelines are available:

- 2002 national guideline for the management of donovanosis [granuloma inguinale]. London: Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD); 2002. Various p. See the National Guideline Clearinghouse (NGC) summary.
- 2002 national guideline for the management of lymphogranuloma venereum. London: Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD); 2002. Various p. See the NGC summary.

Electronic copies: Available in HTML format from the Association for Genitourinary Medicine (AGUM) Web site. Also available in Portable Document Format (PDF) from the Medical Society for the Study of Venereal Diseases (MSSVD) Web site.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on December 8, 2000. The information was verified by the guideline developer on January 12, 2001. This summary was updated on June 24, 2002.

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