INTERNATIONAL JOURNAL OF STD & AIDS

International Journal of STD & AIDS
0(0) 1–6
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DOI: 10.1177/0956462416687913
journals.sagepub.com/home/std
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2017 European guideline for the management of chancroid

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Abstract

Chancroid is a sexually acquired infection caused by *Haemophilus ducreyi*. The infection is characterized by one or more genital ulcers, which are soft and painful, and regional lymphadenitis, which may develop into buboes. The infection may easily be misidentified due to its rare occurrence in Europe and difficulties in detecting the causative pathogen. *H. ducreyi* is difficult to culture. Nucleic acid amplification tests can demonstrate the bacterium in suspected cases. Antibiotics are usually effective in curing chancroid.

Keywords

Haemophilus ducreyi, chancroid, sexually transmitted infection

Date received: 27 October 2016; accepted: 6 December 2016

Guideline development

This guideline has been updated by reviewing the previous European chancroid guideline (2011),[1] CDC guidelines (2015),[2] BASHH guideline (2014),[3] and conducting a comprehensive literature search of publications from 2010 to August 2016.

New information in this guideline since 2011 edition:

- Chancroid is disappearing even from most countries where *Haemophilus ducreyi* was previously epidemic, with the exception of North India and Malawi.[4,5]
- Nevertheless, recent sporadic case reports from Western Europe have been described, often initially misdiagnosed as genital herpes.[6,7]
- In contrast to a sustained reduction in the proportion of genital ulcer disease (GUD) caused by *H. ducreyi*, the bacterium is increasingly found in tropical countries – especially, the South pacific region – as a common cause of non-genital cutaneous ulcers, mostly in children.[8]
- Management: There are no new data for the management of chancroid.

Epidemiology

Chancroid is a sexually transmitted infection (STI) caused by the small Gram-negative bacterium *H. ducreyi*. Recommendations for the diagnosis and management of chancroid have been given by a number of different institutions, including Centers for Diseases Control and Prevention,[2] British Association for Sexual Health and HIV,[3] and Public Health Agency of Canada.[9] In contrast to genital herpes, the number of cases of chancroid is decreasing overall with rare exceptions such as Malawi with 15% of GUD[5] and North India with 24% of GUD.[4] The study from Malawi was published in 2013, although using data from 2004 to 2006. A recent systematic review[8] analyzed 49 studies on chancroid; 35 were published during 1980–1999 and 14 during 2000–2014. The proportion of genital ulcers caused by *H. ducreyi* ranged in the earlier period from 0% in Thailand and China to 68.9% in South Africa.

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During the later time period, the proportion was low (<10%) except for Malawi. Overall, chancroid accounted for eight cases (3%) of genital ulcers in an STD clinic in Paris from 1995 to 2005.[10] The substantial decrease in prevalence has followed the introduction of syndromic management for treating GUD by the WHO, and major social changes after 2000.[8] Nevertheless, the global epidemiology of *H. ducreyi* is poorly documented due to difficulties in confirming a microbiological diagnosis. Currently in Europe, chancroid is restricted to rare sporadic cases.[6,7] As a number of people travel from high-risk areas to work in the sex industry in Europe, the possibility of contracting chancroid in European countries should also be considered. Recent studies have identified *H. ducreyi* as a previously unrecognized cause of non-genital skin ulcers in children in tropical areas.[11,12] *H. ducreyi* has been demonstrated in asymptomatic individuals.[13] Male circumcision is associated with reduced risk of contracting chancroid.[14]

Clinical features

The incubation period for chancroid is short. Three to seven days after sexual intercourse with an infected person, tender erythematous papules develop, most often on the prepuce and frenulum in men and on the vulva, cervix, and perianal area in women.[15] The genital papules quickly progress into pustules, which rupture after a few days and develop into superficial ulcers with ragged and undermined edges. The bases of the ulcers are granulomatous with purulent exudate. The ulcers are soft and painful and may persist for months if left untreated. Secondary superinfection may cause induration. Autoinoculation from primary lesions on opposing skin may result in so-called 'kissing ulcers'. Inguinal lymphadenitis, usually unilateral and painful, develops in approximately half of patients and may further progress into buboes. Fluctuant buboes may rupture spontaneously. According to CDC,[2] a probable diagnosis of chancroid, for both clinical and surveillance purposes, can be made if all of the following criteria are met:

1. the patient has one or more painful genital ulcers;
2. the clinical presentation, appearance of genital ulcers and, if present, regional lymphadenopathy are typical for chancroid;
3. the patient has no evidence of *Treponema pallidum* infection by darkfield examination or nucleic acid amplification test (NAAT) of ulcer exudate or by a serologic test for syphilis performed at least seven days after onset of ulcers; and
4. a NAAT for HSV or HSV culture performed on the ulcer exudate is negative (IV, C).

However, as neither specificity nor sensitivity of microscopy, serology, or antigen detection tests are comparable to nucleic acid detection, the latter is preferable to identify alternative diagnoses. Such diagnostic tests are available in many European countries. Extra-anogenital skin ulcers due to *H. ducreyi* (or cutaneous chancroid) has have reported in children and adults[16,17] and may represent a particular diagnostic challenge, as clinical suspicion may be low and the infection is not sexually transmitted. DNA from *H. ducreyi* has even been demonstrated in oesophageal lesions[18] although the significance of this finding is uncertain. No adverse effects of chancroid on pregnancy outcome or on the foetus have been reported.

Diagnosis

Microscopy

H. ducreyi appears as small Gram-negative rods. Microscopy may be done on ulcer swabs. Due to low sensitivity and specificity, microscopy is, however, not recommended for diagnosis.

Culture. *H. ducreyi* is a very fastidious bacterium, and selective, enriched culture media are required for its isolation. Several different media have been used to isolate *H. ducreyi* from clinical specimens.[19,20] As strains differ in their ability to grow on different media, a combination of at least two different media may be used for optimal recovery rates. Samples should be taken with a cotton-tipped swab from the base at the undermined edge of a lesion after cleansing by flushing with sterile saline. *H. ducreyi* will only survive a few hours on the swab, and bedside inoculation of culture plates followed by immediate incubation can be done to reduce loss of viable bacteria during transportation. However, bedside plating is often not possible, and the swab should then be send to the laboratory in an appropriate transport medium, e.g. Amies or Stuart's medium.[21] Minimizing transport time and keeping the specimen at 4°C during transit will increase the chance of positive culture of *H. ducreyi*. Inoculated culture plates should be incubated at 33°C in a humid atmosphere containing 5% CO_2 for more than three days. Culture of material from buboes obtained by puncture and aspiration is less sensitive than culture from ulcers. Culture of *H. ducreyi* ensures a definite diagnosis of chancroid, but it does not rule out other concomitant infections. Culture is particularly important when further characterization of the bacterium such as antimicrobial susceptibility pattern is needed, e.g. in cases of therapeutic failure.

A definitive diagnosis of chancroid requires the identification of *H. ducreyi* on culture media; however, the

advent of more sensitive DNA amplification techniques has demonstrated that the sensitivity of culture of *H. ducreyi* reaches only 75% at best (III, B).[22–24]

NAAT. Nucleic acid amplification techniques (NAATs) are excellent for demonstrating *H. ducreyi* in clinical sample material. Individual strain specific growth requirements do not influence the outcome of NAATs and NAATs show higher detection rates than culture. As these methods do not depend on live bacteria, samples may be analyzed in laboratories placed remotely from the patient, which is relevant in Europe where only a few laboratories provide NAATs for *H. ducreyi*. Specimens should be obtained as described for culture; no specific transport medium is required unless special procedures related to individual NAATs indicate otherwise. Specimens taken for culture may also be used for NAATs. The exudate from the ulcer should be collected by vigorous rubbing of the base of the lesion with a sterile cotton-tipped swab.

Various different in-house PCR methods have been described, some of which have the advantage of simultaneously testing for other relevant pathogens, in particular *T. pallidum* and herpes simplex virus (III, B).[25–30]

Serology. Detection of antibodies against *H. ducreyi* is not helpful for the diagnosis of acute chancroid, as has been demonstrated by experimental inoculation of the bacterium into volunteers.[31]

Management

Information, explanation, and advice should be given to the patient.

Patients should be informed that chancroid is a bacterial infection that is sexually transmitted but curable with antibiotics and that it is a cofactor for HIV transmission, as are genital herpes and syphilis (IV, C).

Symptoms should resolve within one to two weeks of commencing antibiotic therapy (III, B).

Patients should abstain from any sexual contact until they and their partner(s) have completed therapy (IV, C).

Testing for syphilis and herpes simplex virus should always be done in patients suspected to suffer from chancroid, both because the three diseases may clinically be difficult to distinguish from each other and because co-infections occur (IV, C). As mentioned above, tests based on nucleic acid detection are preferable if available.

Therapy

Since the 1970s, beta-lactamase producing strains of *H. ducreyi* emerged and treatment failures were common. Subsequently, further plasmid-mediated resistance to tetracycline, sulfonamides, chloramphenicol, and aminoglycosides also has been reported.[32] Little is known about chromosomally-mediated resistance in *H. ducreyi*, but decreased susceptibilities to various antibiotics in absence of identifiable resistance plasmids suggests evolution of such mechanisms. Based on in vitro susceptibility the most active drugs against *H. ducreyi* are azithromycin, ceftriaxone, ciprofloxacin, and erythromycin. Worldwide, several isolates with intermediate resistance to either ciprofloxacin or erythromycin have been reported.

Successful treatment for chancroid cures the infection and resolves the clinical symptoms. In advanced cases, scarring can occur, despite successful therapy. The World Health Organization has proposed syndromic approaches for treatment of genital ulcers, to be used in settings where appropriate laboratory diagnosis is not available.[33] The antibiotics treatment should be based on local epidemiology and antibiotic susceptibility patterns.

Several antibiotic regimens have been recommended for confirmed cases of chancroid:

- First line –
  - Ceftriaxone as a single intramuscular injection of 250 mg (Ib, A) or
  - Azithromycin, as a single 1 g oral dose, (Ib, A)
  - The response is generally good although failures, especially in HIV-positive individuals, have been reported.
- Second line –
  - Ciprofloxacin 500 mg orally twice a day for three days (Ib, B), or
  - Erythromycin orally 500 mg four times a day for seven days (Ib, B)

Azithromycin and ceftriaxone offer the advantage of single-dose therapy. Children can be treated with ceftriaxone. Ciprofloxacin is contraindicated for pregnant and lactating women as well as for children and adolescents less than 18 years where erythromycin or ceftriaxone regimens should be used. The multiple day regimens are recommended for HIV-positive patients rather than the single dose treatments.[34]

An unblinded, prospective study designed to determine the efficacy of single-dose azithromycin for the treatment of chancroid was done in 133 patients who were randomized to receive 250 mg of ceftriaxone i.m. or 1 g of azithromycin orally, both given as a single dose.[35] Azithromycin and ceftriaxone were equally effective in healing ulcers for which cultures were negative, and azithromycin was as effective as ceftriaxone 23 days post-treatment (Ib, A). Although no antimicrobial susceptibility data for *H. ducreyi* have been published

for two decades, it is still assumed that the infection will respond adequately to treatment with the recommended regimens.[36]

Adjunctive therapy

Patients with fluctuant buboes will experience symptomatic relief if these are emptied. Needle aspiration is effective but may need to be repeated. Incision and drainage is an alternative[37] but some authorities believe that it may lead to sinus formation. Antibiotic cover is recommended if this is done (IV, C).

Partner notification

Sexual partners of patients who have chancroid should be examined and treated, regardless of whether symptoms of the disease are present, if they had sexual contact with the patient in the 10 days preceding the patient's onset of symptoms (IV, C).[3] Partners should also be offered testing for other STIs, including HIV.

Follow-up

All patients diagnosed with chancroid should be followed up after treatment:

- to ensure resolution of symptoms and signs of infection; successful treatment should improve symptoms within three to seven days. A test of cure is not necessary.
- to evaluate healing that might be slower for some HIV-infected patients and uncircumcised men.
- to document treatment failure, considering antibiotic resistance, re-infection, other causes of ano-genital ulcers, or an underlying immunodeficiency.
- to check that adequate partner notification has been completed.
- to address any patient concerns.
- to arrange suitable testing for syphilis and HIV.

Prevention/health promotion

Patients diagnosed with chancroid should be counseled regarding prevention of other STIs:

- Offer regular sexual health screening.
- Patients should be retested for syphilis and HIV three months after the diagnosis of chancroid, if the initial test results were negative.
- Condom use should be demonstrated and promoted.

Auditable outcome measures (target 95% for all)

- All cases of suspected chancroid should be subjected to laboratory investigations.
- Sexual contacts within 10 days preceding the patient's onset of symptoms should be traced, tested, and treated.
- HIV and syphilis serological testing should be offered, as well as screening for concomitant STIs.
- Suspected or confirmed cases of chancroid should be reported and relevant surveillance data collected according to local and national guidelines.

Appendices

Composition of editorial board: www.iusti.org/regions/Europe/pdf/2013/Editorial_Board.pdf

List of contributing organizations: www.iusti.org/regions/Europe/euroguidelines.htm

Tables of levels of evidence and grading of recommendations: www.iusti.org/regions/Europe/pdf/2013/Levels_of_Evidence.pdf

Acknowledgements

Thanks to Jonathan Ross and Raj Patel for valuable comments.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Kemp M, Christensen JJ, Lautenschlager S, et al. European guideline for the management of chancroid. *Int J STD AIDS* 2011; 22: 241–244.
2. Centers for Disease Control and Prevention. Sexually transmitted treatment guidelines. *MMWR Recomm Rep* 2015; 64: 26–27.
3. O'Farrell N and Lazaro N. UK National Guideline for the management of Chancroid. *Int J STD AIDS* 2014; 25: 975–983.
4. Hassan I, Anwar P, Rather S, et al. Pattern of sexually transmitted infections in a Muslim majority region of North India. *Indian J Sex Transm Dis* 2015; 36: 30–34.
5. Phiri S, Zadrozny S, Weiss HA, et al. Etiology of genital ulcer disease and association with HIV infection in Malawi. *Sex Transm Dis* 2013; 40: 923–928.

6. Fouéré S, Lassau F, Rousseau C, et al. First case of chancroid in 14 years at the largest STI clinic in Paris, France. *Int J STD AIDS* 2016; 27: 805–807.
7. Barnes P and Chauhan M. Chancroid – desperate patient makes own diagnosis. *Int J STD AIDS* 2014; 25: 768–770.
8. Gonzalez-Beiras C, Marks M, Chen CY, et al. Epidemiology of *Haemophilus ducreyi* infections. *Emerg Infect Dis* 2016; 22: 1–8.
9. Public Health Agency of Canada. Canadian guidelines on sexually transmitted infections. *Chancroid*, http://www.health.gov.nl.ca/health/publications/diseasecontrol/s5_sexually_transmitted_and_bloodborne_pathogens.pdf, 2016 (accessed 27 November 2016).
10. Hope-Rapp E, Anyfantakis V, Fouere S, et al. Etiology of genital ulcer disease. A prospective study of 278 cases seen in an STD clinic in Paris. *Sex Transm Dis* 2010; 37: 153–158.
11. Mitja O, Lukehart SA, Pokowas G, et al. *Haemophilus ducreyi* as a cause of skin ulcers in children from a yaws-endemic area of Papua New Guinea: a prospective cohort study. *Lancet Glob Health* 2014; 2: e235–e241.
12. Marks M, Chi KH, Vahi V, et al. *Haemophilus ducreyi* associated with skin ulcers among children, Solomon Islands. *Emerg Infect Dis* 2014; 20: 1705–1707.
13. Hawkes S, West B, Wilson S, et al. Asymptomatic carriage of *Haemophilus ducreyi* confirmed by the polymerase chain reaction. *Genitourin Med* 1995; 71: 224–227.
14. Weiss HA, Thomas SL, Munabi SK, et al. Male circumcision and risk of syphilis, chancroid, and genital herpes: a systematic review and meta-analysis. *Sex Transm Infect* 2006; 82: 101–109.
15. Lautenschlager S. Chancroid. In: Goldsmith LA, Katz SI, Gilchrest BA, et al. (eds) *Dermatology in general medicine*. Vol. 2, New York: McGraw Hill, 2012, pp.2501–2505.
16. Ussher JE, Wilson E, Campanella S, et al. *Haemophilus ducreyi* causing chronic skin ulceration in children visiting Samoa. *Clin Infect Dis* 2007; 44: e85–e87.
17. McBride WJ, Hannah RC, Le Cornec GM, et al. Cutaneous chancroid in a visitor from Vanuatu. *Australas J Dermatol* 2008; 49: 98–99.
18. Borges MC, Colares JK, Lima DM, et al. *Haemophilus ducreyi* detection by polymerase chain reaction in oesophageal lesions of HIV patients. *Int J STD AIDS* 2009; 20: 238–240.
19. Jones CC and Rosen T. Cultural diagnosis of chancroid. *Arch Dermatol* 1991; 127: 1823–1827.
20. Pillay A, Hoosen AA, Loykissoonlal D, et al. Comparison of culture media for the laboratory diagnosis of chancroid. *J Med Microbiol* 1998; 47: 1023–1026.
21. Dangor Y, Radebe F and Ballard RC. Transport media for *Haemophilus ducreyi*. *Sex Transm Dis* 1993; 20: 5–9.
22. Behets FM, Brathwaite AR, Hylton-Kong T, et al. Genital ulcers: etiology, clinical diagnosis, and associated human immunodeficiency virus infection in Kingston, Jamaica. *Clin Infect Dis* 1999; 28: 1086–1090.
23. Morse SA, Trees DL, Htun Y, et al. Comparison of clinical diagnosis and standard laboratory and molecular methods for the diagnosis of genital ulcer disease in Lesotho: association with human immunodeficiency virus infection. *J Infect Dis* 1997; 175: 583–589.
24. Lewis DA. Chancroid: clinical manifestations, diagnosis, and management. *Sex Transm Infect* 2003; 79: 68–71.
25. Beyrer C, Jitwatcharanan K, Natpratan C, et al. Molecular methods for the diagnosis of genital ulcer disease in a sexually transmitted disease clinic population in northern Thailand: predominance of herpes simplex virus infection. *J Infect Dis* 1998; 178: 243–246.
26. Mackay IM, Harnett G, Jeoffreys N, et al. Detection and discrimination of herpes simplex viruses, *Haemophilus ducreyi*, *Treponema pallidum*, and *Calymmatobacterium* (*Klebsiella*) *granulomatis* from genital ulcers. *Clin Infect Dis* 2006; 42: 1431–1438.
27. Orle KA, Gates CA, Martin DH, et al. Simultaneous PCR detection of *Haemophilus ducreyi*, *Treponema pallidum*, and herpes simplex virus types 1 and 2 from genital ulcers. *J Clin Microbiol* 1996; 34: 49–54.
28. Risbud A, Chan-Tack K, Gadkari D, et al. The etiology of genital ulcer disease by multiplex polymerase chain reaction and relationship to HIV infection among patients attending sexually transmitted disease clinics in Pune, India. *Sex Transm Dis* 1999; 26: 55–62.
29. Suntoke TR, Hardick A, Tobian AA, et al. Evaluation of multiplex real-time PCR for detection of *Haemophilus ducreyi*, *Treponema pallidum*, herpes simplex virus type 1 and 2 in the diagnosis of genital ulcer disease in the Rakai District, Uganda. *Sex Transm Infect* 2009; 85: 97–101.
30. Glatz M, Juricevic N, Altwegg M, et al. A multicenter prospective trial to asses a new real-time polymerase chain reaction for detection of *Treponema pallidum*, herpes simplex-1/2 and *Haemophilus ducreyi* in genital, anal and oropharyngeal ulcers. *Clin Microbiol Infect* 2014; 20: O1020–O1027.
31. Al-Tawfiq JA, Palmer KL, Chen CY, et al. Experimental infection of human volunteers with *Haemophilus ducreyi* does not confer protection against subsequent challenge. *J Infect Dis* 1999; 179: 1283–1287.
32. Dangor Y, Ballard RC, Miller SD, et al. Antimicrobial susceptibility of *Haemophilus ducreyi*. *Antimicrob Agents Chemother* 1990; 34: 1303–1307.
33. World Health Organisation. Sexually transmitted and other reproductive tract infections. Integrating STI/RTI care for reproductive health. A guide to essential practice, pp. 109–113, http://apps.who.int/iris/bitstream/10665/43116/1/9241592656.pdf (2005, accessed 27 November 2016).
34. Belda JW, Di Chiacchio NG, Di CN, et al. A comparative study of single-dose treatment of chancroid using thiamphenicol versus Azithromycin. *Braz J Infect Dis* 2009; 13: 218–220.

35. Martin DH, Sargent SJ, Wendel GD Jr, et al. Comparison of azithromycin and ceftriaxone for the treatment of chancroid. *Clin Infect Dis* 1995; 21: 409–414.
36. Lewis DA. Epidemiology, clinical features, diagnosis and treatment of *Haemophilus ducreyi* – a disappearing pathogen? *Expert Rev Anti Infect Ther* 2014; 12: 687–696.
37. Ernst AA, Marvez-Valls E and Martin DH. Incision and drainage versus aspiration of fluctuant buboes in the emergency department during an epidemic of chancroid. *Sex Transm Dis* 1995; 22: 217–220.