

Epidemiology of *Haemophilus ducreyi* Infections

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Release date: December 17, 2015; Expiration date: December 17, 2016

Learning Objectives

Upon completion of this activity, participants will be able to:

- Distinguish the clinical presentation of genital ulcer disease with *Haemophilus ducreyi*
- Assess the means used to diagnose *H. ducreyi* infection
- Identify global areas disproportionately affected by *H. ducreyi*-related genital ulcer disease
- Assess worldwide trends in the epidemiology of infection with *H. ducreyi*

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Thomas J. Gryczan, MS, Technical Writer/Editor, *Emerging Infectious Diseases*. Disclosure: Thomas J. Gryczan, MS, has disclosed no relevant financial relationships.

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The global epidemiology of *Haemophilus ducreyi* infections is poorly documented because of difficulties in confirming

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DOI: <http://dx.doi.org/10.3201/eid2201.150425>

microbiological diagnoses. We evaluated published data on the proportion of genital and nongenital skin ulcers caused by *H. ducreyi* before and after introduction of syndromic management for genital ulcer disease (GUD). Before 2000, the proportion of GUD caused by *H. ducreyi* ranged from 0.0% to 69.0% (35 studies in 25 countries). After 2000, the proportion ranged from 0.0% to 15.0% (14 studies in 13 countries). In contrast, *H. ducreyi* has been recently identified as a causative agent of skin ulcers in children in the tropical regions; proportions ranged from 9.0% to 60.0% (6 studies in 4 countries). We conclude that, although there has been a sustained reduction in the proportion of GUD caused by *H. ducreyi*, this bacterium is increasingly recognized as a major cause of nongenital cutaneous ulcers.

Haemophilus ducreyi, a fastidious gram-negative bacterium, is the causative agent of chancroid, a genital ulcer disease (GUD). The organism is usually spread during sexual intercourse through microabrasions, and the disease usually manifests as multiple painful superficial ulcers associated with inguinal lymphadenitis (1). As a result of the painful nature of the lesions, patients usually seek immediate treatment, and asymptomatic carriage is therefore uncommon (2). In addition to causing GUD, *H. ducreyi* has been found in several recent studies to be a major cause of chronic skin ulceration in children from developing countries (3–6).

The global epidemiology of chancroid is poorly documented, and it is not included in World Health Organization estimates of the global incidence of curable sexually transmitted infections (STIs). There are some key challenges in interpreting data on the epidemiology of *H. ducreyi* as a causative agent of GUD. First, genital herpes cases are easily misdiagnosed as chancroid on clinical examination. Thus, reports based only on clinical diagnosis can be erroneous. Second, laboratory culture is technically difficult, and the highly sensitive and specific nucleic acid amplification tests, such as PCR, are rarely available outside national reference laboratories or specialized STI research settings, which makes it difficult to confirm clinical diagnoses.

Determination of the true global incidence of chancroid is made more difficult by widespread adoption of syndromic management for bacterial GUD (i.e., treatment with antimicrobial drugs effective against syphilis and chancroid) without microbiological confirmation in many countries. Therefore, countries often report only the total number of GUD cases. In addition, identification of GUD etiology is rarely conducted in resource-poor countries to validate syndromic management for which chancroid could also be common.

Earlier studies of tropical skin ulcers did not generally test for *H. ducreyi*, with the exception of a small number of case reports (7–11). There are major limitations in describing the prevalence of causative agents in tropical skin lesions that typically occur in children in rural areas where there is no access to laboratory facilities. Pathogens such as *Fusobacterium fusiforme*, *Staphylococcus aureus*, and *Streptococcus pyogenes* have been reported from Gram staining of exudative material collected from tropical ulcers (12). However, cultures or PCR testing for definitive identification of fastidious pathogens involved has not been traditionally conducted. The purpose of this study was to improve our understanding of the epidemiology of *H. ducreyi* infection through a systematic review of published data on the proportion of genital and skin ulcers caused by this bacterium.

Methods

Search Strategy and Selection Criteria

A systematic review was conducted to identify all relevant studies that examined the etiology of GUD and nongenital skin ulcers involving *H. ducreyi*. We searched the National Library of Medicine through PubMed for “*H. ducreyi*,” “chancroid,” “genital ulcer,” OR “skin ulceration” AND “proportion” OR “prevalence.” The search was limited to studies published during January 1, 1980–December 31, 2014. In addition, we searched references of identified articles and other databases for other articles, and we reviewed abstracts, titles, and selected studies potentially containing information on chancroid epidemiology. We contacted researchers who were working with *H. ducreyi* to identify unpublished literature for inclusion. No language restrictions were set for searches.

The decision tree for inclusion or exclusion of articles is shown in Figure 1. We included studies if the proportion of etiologic agents in genital ulcers and nongenital skin ulcers, including *H. ducreyi*, was confirmed by laboratory techniques. Clinical diagnosis of chancroid is often based on the appearance of the ulcer, which is characteristically painful, purulent, and deep with ragged, undermined edges (Figure 2). However, because the appearance of these ulcers is similar to ulcers caused by other bacteria, clinical diagnosis can be nonspecific or insensitive and often requires laboratory confirmation (1). In addition, microscopy identification of typical morphologic features and serologic detection lack sensitivity and specificity (13,14). Thus, we only considered the following diagnostic methods as providing acceptable evidence of *H. ducreyi* infection: 1) isolation and identification by culture; or 2) PCR/real-time PCR.

Data Extraction and Synthesis

For all qualifying studies, extracted data included study country, year of study, diagnostic test used for confirmation, total number of *H. ducreyi*-positive cases, and sample size. Descriptive analyses of extracted data were conducted, and the number of *H. ducreyi*-confirmed cases was divided by the total number of cases to calculate the proportion of cases caused by *H. ducreyi*. Studies qualifying for data extraction were grouped into 2 categories: studies conducted before 2000 and studies after 2000. This date separates studies before and after widespread implementation of syndromic management of GUD. Study sites were also plotted by geographic region. No quantitative meta-analysis was undertaken.

Results

We identified 277 records in which we found 46 articles describing 49 studies on GUD that met our inclusion

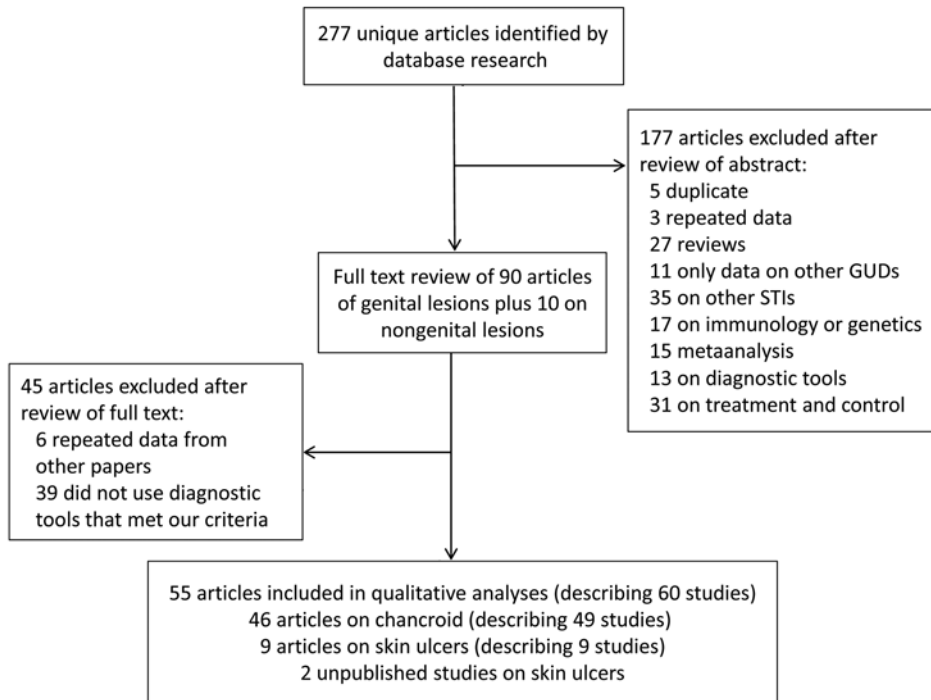


Figure 1. Procedure for selecting eligible references on the epidemiology of *Haemophilus ducreyi* as a causative agent of genital ulcers. GUDs, genital ulcer disease; STI, sexually transmitted infections.

criteria (Tables 1, 2; online Technical Appendix, <http://wwwnc.cdc.gov/EID/article/22/1/15-0425-Techapp1.pdf>). All identified studies were based on cohorts of patients attending STI clinics, including 3 studies that enrolled only commercial sex workers. The age group for all cases was adults >18 years of age, except for 3 studies in

Zambia, South Africa, and China, which included patients >16 years of age, and 1 study in Madagascar, which included patients >14 years of age. A total of 9 published studies and 2 unpublished reports that described nongenital skin ulcers caused by *H. ducreyi* were also included in our systematic review.

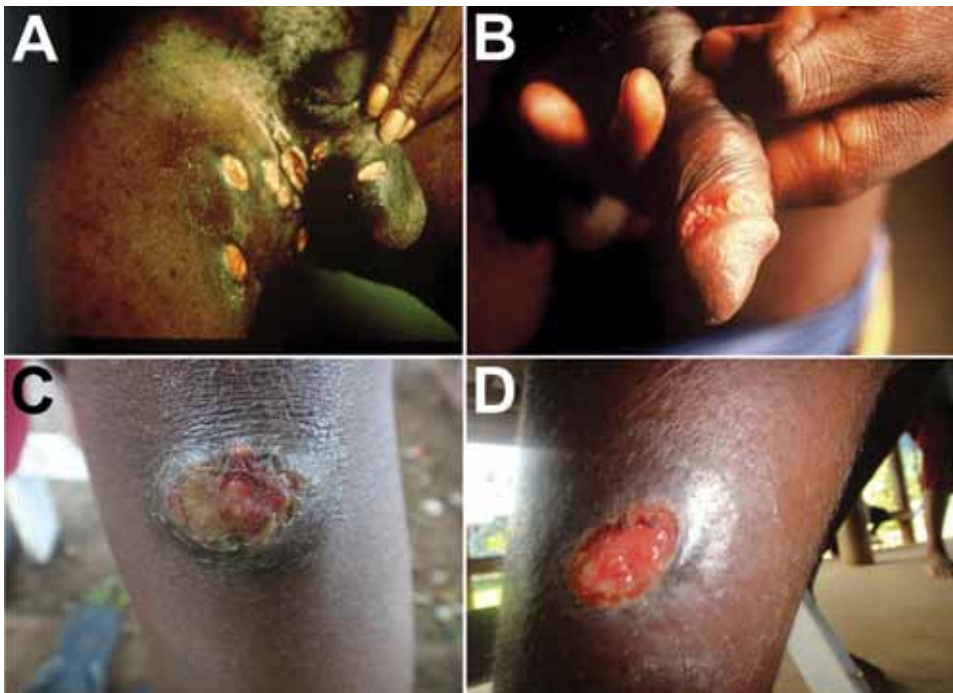


Figure 2. Ulcers caused by infection with *Haemophilus ducreyi*. A, B) Genital ulcers in adult patients from Ghana (provided by David Mabey). C, D) Skin ulcers in children from Papua New Guinea (provided by Oriol Mitjà).

Table 1. Characteristics of 35 studies of genital ulcers caused by *Haemophilus ducreyi*, 1980–1999*

Area, reference†	Country	Year of study	Diagnostic method	No. patients with GUD	No. cases <i>H. ducreyi</i> infection	% (95% CI)
Africa						
Paz-Bailey et al. (16)	Botswana	1993	Culture	108	27	25.0 (17.7–33.9)
Steen (17)	Côte d'Ivoire	1996	PCR	NA	NA	47
Mabey et al. (18)	Gambia	1987	Culture	104	54	51.9 (42.4–61.2)
Hawkes et al. (19)	Gambia	1995	M-PCR	18	8	44.4 (24.5–66.2)
Nsanze et al. (20)	Kenya	1980	Culture	97	60	61.8 (51.9–70.9)
Kaul et al. (21)	Kenya	1997	Culture	189	54	28.5 (22.6–35.3)
Morse et al. (22)	Lesotho	1994	M-PCR	105	55	53.3 (43.8–62.6)
Harms et al. (23)	Madagascar	1992	Culture	12	61	19.6 (11.6–31.3)
Behets et al. (24)	Madagascar	1997	M-PCR	196	64	32.6 (26.4–39.5)
Behets et al. (25)	Malawi	1995	M-PCR	778	204	26.2 (23.2–29.4)
Hoyo et al. (26)	Malawi	1999	M-PCR	137	41	29.0 (22.8–38.0)
Bogaerts et al. (27)	Rwanda	1992	Culture	395	115	29.1 (24.8–33.7)
Totten et al. (28)	Senegal	1992	PCR	39	22	56.4 (40.9–70.7)
Crewe-Brown et al. (29)	South Africa	1981	Culture	100	45	45 (35.5–54.7)
Dangor et al. (30)	South Africa	1989	Culture	240	164	68.3 (62.2–73.8)
Chen et al. (31)	South Africa	1994	M-PCR	538	171	31.7 (27.9–35.8)
Lai et al. (32)	South Africa	1994	M-PCR	160	232	68.9 (62.7–74.5)
	South Africa	1998	M-PCR	94	186	50.5 (43.4–57.6)
Meheus et al. (33)	Swaziland	1979	Culture	155	68	43.8 (36.3–51.7)
Ahmed et al. (34)	Tanzania	1999	PCR	102	12	11.7 (6.8–19.4)
Le Bacq et al. (35)	Zimbabwe	1991	Culture	90	22	24.4 (16.7–34.2)
Asia						
Wang et al. (36)	China	1999	M-PCR	96	0	0.0 (0.0–3.8)
Risbud et al. (37)	India	1994	M-PCR	302	84	27.8 (23.0–33.1)
Rajan et al. (38)	Singapore	1983	Culture	670	56	8.3 (6.4–10.7)
Beyrer et al. (15)	Thailand	1996	M-PCR	38	0	0.0 (0.0–9.1)
North America						
Dillon et al. (39)	United States	1990	Culture	82	27	32.9 (23.7–43.6)
Mertz et al. (40)	United States	1995	M-PCR	143	56	39.1 (231.5–47.3)
Mertz et al. (41)	United States	1996	M-PCR	516	16	3.1 (1.9–4.9)
South America						
Sanchez et al. (42)	Peru	1995	M-PCR	61	3	4.9 (1.6–13.4)
Caribbean						
Sanchez et al. (42)	Dominican Republic	1996	M-PCR	81	21	25.9 (17.6–36.4)
Behets et al. (43)	Jamaica	1996	M-PCR	304	72	23.6 (19.2–28.7)
Bauwens et al. (44)	Bahamas	1992	PCR	47	7	14.8 (7.4–27.6)
Middle East						
Madani et al. (45)	Saudi Arabia	1999	Culture	3,679	78	2.1 (1.7–2.5)
Europe						
Kyriakis et al. (46)	Greece	1996	Culture	695	32	4.6 (3.2–6.4)
Bruisten et al. (47)	The Netherlands	1996	M-PCR	368	3	0.8 (0.2–2.3)

*GUD, genital ulcer disease; NA, not available; M-PCR, multiplex PCR.

†References 41–47 provided in the online Technical Appendix (<http://wwwnc.cdc.gov/EID/article/22/1/15-0425-Techapp1.pdf>).

Laboratory confirmation of chancroid by PCR or culture was reported in 33 (67%) and 16 (32%) of the 49 studies, respectively. Of 16 studies that used culture, 7 (43%) used Mueller-Hinton agar with a nutritional supplement (e.g., IsoVitalax; Becton Dickinson, Franklin Lakes, NJ, USA), 1% used hemoglobin, and 5 (31%) used chocolate agar-based media; the remaining studies used other culture media. Five (31%) of 16 studies incubated agar plates at low temperatures (33°C–35°C), and 2 (12%) incubated plates at 36°C. Remaining articles did not specify incubation temperature.

Different PCR primer targets were used to amplify DNA sequences, including the 16S rRNA gene, the *gro-EL* gene, and the hemolysin gene. In addition to herpes s

implex virus (HSV) PCR, 23 studies used a multiplex PCR that could simultaneously detect the 3 major causes of GUD (*H. ducreyi*, *Treponema pallidum*, and HSV types 1 and 2) (15). Studies encompassed 33 countries: 17 in Africa, 4 in Southeast Asia, 3 in Europe, 2 in the Middle East, 3 in South America, and 2 in the Caribbean, 1 in the United States, and 1 in Australia.

Incidence of Chancroid

Of 49 studies on chancroid analyzed, 35 were published during 1980–1999 (Table 1) and 14 during 2000–2014 (Table 2). In general, data showed a clear decrease in the proportion of chancroid during 1980–2014 in all areas analyzed (Figure 3).

Table 2. Characteristics of 14 studies of genital ulcers caused by *Haemophilus ducreyi*, 2001–2014*

Area, reference†	Country	Year of study	Diagnostic method	No. patients with GUD	No. cases <i>H. ducreyi</i> infection	% (95% CI)
Africa						
Paz-Bailey et al. (16)	Botswana	2002	PCR	137	1	0.7 (0.1–4.0)
Mehta et al. (48)	Kenya	2007	M-PCR	59	0	0.0 (0.0–6.1)
Phiri et al. (49)	Malawi	2006	M-PCR	398	60	15.0 (11.8–18.9)
Zimba et al. (50)	Mozambique	2005	PCR	79	3	3.8 (1.3–10.9)
Tobias et al. (51)	Namibia	2007	PCR	199	0	0.0 (0.0–1.8)
O'Farrell et al. (52)	South Africa	2004	M-PCR	162	2	1.2 (0.3–4.6)
Lewis et al. (53)	South Africa	2006	M-PCR	613	10	1.6 (0.9–2.9)
Nilsen et al. (54)	Tanzania	2001	PCR	232	12	5.1 (2.9–8.8)
Suntoke et al. (55)	Uganda	2006	M-PCR	100	2	2.0 (0.5–7.0)
Makasa et al. (56)	Zambia	2010	PCR	200	0	0 (0.0–1.8)
South America						
Gomes Naveca et al. (57)	Brazil	2009	PCR	434	0	0 (0.0–0.8)
Middle East						
Maan et al. (58)	Pakistan	2009	Culture	521	20	3.8 (2.5–5.8)
Europe						
Hope-Rapp et al. (59)	France	2005	Culture	278	8	2.8 (1.4–5.5)
Oceania						
Mackay et al. (60)	Australia	2002	M-PCR	64	0	0.0 (0.0–5.6)

*GUD, genital ulcer disease; M-PCR, multiplex PCR.

†References 48–60 provided in the online Technical Appendix (<http://wwwnc.cdc.gov/EID/article/22/1/15-0425-Techapp1.pdf>).

During 1980–1999, the proportion of genital ulcers caused by *H. ducreyi* in these studies ranged from 0.0% in Thailand and China to 68.9% in South Africa (Table 1). Eleven (31.4%) studies reported high proportions (>40%) of cases of infection with *H. ducreyi*. All of these studies were conducted in countries in Africa (Côte d'Ivoire, Gambia, Kenya, Lesotho, Senegal, South Africa, and Swaziland). Slightly lower proportions (20%–40% of cases) were observed in 15 (42%) studies: 10 in countries in Africa, 2 in the United States during localized outbreaks, 1 in Jamaica, 1 in the Dominican Republic, and 1 in India.

Only a few countries reported low proportions (<10%) of genital ulcers infected with *H. ducreyi*, including Singapore (8.3%), Peru (5%), Greece (4.6%), the Netherlands (0.9%), United States (3.1%), and Saudi Arabia (2.1%). The study in Saudi Arabia was conducted during 1995–1999; a total of 27,490 patients were examined for STIs. Chancroid was diagnosed by culture and was reported as the least common STI during this survey. The only studies that reported no cases of chancroid were conducted in Thailand in 1996 and China in 1999; both studies used multiplex PCR for detection of GUD cases.

During 2000–2014, the proportion of *H. ducreyi* infections was low (<10%) in all studies analyzed, except for 1 study in Malawi (15%) (Table 2). Studies in 5 countries (Kenya, Namibia, Zambia, Brazil, and Australia) did not report any cases of infection with *H. ducreyi*. Other studies reporting proportions of infections <10% were conducted in Botswana, Mozambique, South Africa, Uganda, Pakistan, and France. No reports were found for studies in North America, Southeast Asia, or the Caribbean.

Nongenital Skin Infections with *H. ducreyi*

During 1988–2010, several case reports described 4 children and 4 adults with nonsexually transmitted infections with *H. ducreyi* that manifested as lower leg lesions but no genital lesions. The reported case-patients were travelers who had been to Fiji (7), Samoa (8), Vanuatu (9), or Papua

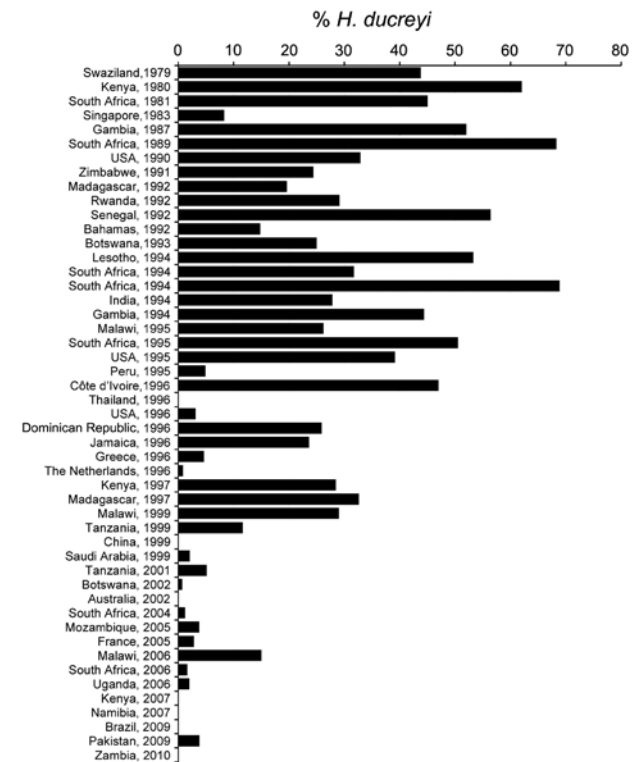


Figure 3. Trend of proportion of genital ulcers caused by infections with *Haemophilus ducreyi*, 1979–2010.

Table 3. Characteristics of 11 studies on skin ulcers caused by *Haemophilus ducreyi*, 1988–2014*

Reference	Country	Year of study	Diagnostic method	No. patients with skin ulcers	No cases <i>H. ducreyi</i> infection	% (95% CI)
Marckmann et al. (7)	Fiji Islands	1988	Culture	1 man	1	NA
Ussher et al. (8)	Samoa	2005	PCR	3 girls <10 y of age	3	NA
McBride et al. (9)	Vanuatu	2007	PCR	1 woman	1	NA
Peel et al. (10)	Vanuatu and Papua New Guinea	2010	PCR	2 men	2	NA
Humphrey et al. (11)	Sudan	2007	PCR	1 boy	1	NA
Mitjà et al. (3)	Papua New Guinea	2013	PCR	90	54	60.0 (49.6–69.5)
Mitjà et al. (6)	Papua New Guinea	2014	PCR	114	60	60.1 (54.3–65.5)
Marks et al. (4)	Solomon Islands	2013	PCR	41	13	31.7 (19.5–46.9)
Chen et al.†	Vanuatu	2013	PCR	176	68	38.6 (31.7–46.0)
Chen et al.†	Ghana	2013	PCR	179	49	27.3 (21.3–34.3)
Ghinai et al. (5)	Ghana	2014	PCR	90	8	8.8 (4.5–16.5)

*NA, not applicable.

†Pers. comm.

New Guinea (10) (Table 3). Outside the south Pacific region, a 5-year-old refugee from Sudan who had lower leg ulceration was also given a diagnosis of infection with *H. ducreyi* (11).

A cohort study conducted in Papua New Guinea in 2014 showed evidence that *H. ducreyi* is a major cause of chronic skin ulceration; *H. ducreyi* DNA was identified by PCR in 60.0% of skin lesions in children (3). Similar studies in other areas reported laboratory-confirmed skin ulcers in children caused by *H. ducreyi* in Papua New Guinea (6), Solomon Islands (4), Vanuatu (C.Y. Chen, pers. comm.), and Ghana (5) (Table 3).

Discussion

Our review confirmed 2 major findings. First, reduction in the proportion of genital ulcers caused by *H. ducreyi* has been sustained for the past decade and a half. Second, there is increasing evidence that *H. ducreyi* is a common and newly recognized causative agent of chronic skin ulceration in children from developing countries.

In the 1990s, the global prevalence of chancroid was estimated to be 7 million (17). Chancroid was one of the most prevalent GUDs, particularly in resource-poor countries in Africa, Asia, Latin America, and the Caribbean (1; reference 51 in online Technical Appendix). Recommendations to introduce syndromic management for treatment of GUD caused by bacteria were published by the World Health Organization in 1991 and fully implemented by 2000 (reference 61 in online Technical Appendix). Since that time, global incidence of GUDs, particularly chancroid, has decreased substantially, and genital herpes viruses (HSV-1 and HSV-2) have become the predominant cause of GUD (reference 53 in online Technical Appendix). Currently in Europe and the United States, chancroid is restricted to rare sporadic cases. Transmission of *H. ducreyi* remains ongoing in only a few countries that have limited access to health services (2,6).

Our data show marked decreases in the proportion of GUD caused by *H. ducreyi* in several countries. Spinola et al. reported similar conclusions obtained from 25 PCR-based studies (reference 62 in online Technical Appendix). For example, in Botswana (16), Kenya, (20), and South Africa (29), the proportion of GUD caused by *H. ducreyi* decreased from 25%–69% to negligible (0.0%–1.2%) levels (16; references 48,52 in online Technical Appendix). Studies in Zambia (reference 56 in online Technical Appendix), Namibia (reference 51 in online Technical Appendix), and China (36) did not report any cases of chancroid during 2000–2009. A study in Thailand reported elimination of chancroid by introduction of a condom use program in the 1990s (reference 63 in online Technical Appendix). Similar decreases have been reported from Cambodia and Sri Lanka, with rapid elimination of chancroid and congenital syphilis in most settings (reference 63 in online Technical Appendix). However, these findings should be interpreted with caution because, given the short duration of infectivity, even a low prevalence of *H. ducreyi* in a population with GUD implies that a reservoir of infected persons with a high rate of sex partners is present.

Recent research has identified *H. ducreyi* as a previously unrecognized cause of nongenital skin ulcers in tropical areas. In 2013–2015, six studies in Papua New Guinea (3,6), the Solomon Islands (4), Vanuatu (C.Y. Chen et al., pers. comm.), and Ghana (5; C.Y. Chen et al., pers. comm.) showed that a high proportion of laboratory-confirmed skin ulcers were caused by *H. ducreyi*. Nearly half of the 690 enrolled patients with ulcers in these 6 studies had *H. ducreyi* detectable by PCR, whereas other bacteria, such as *T. pallidum* subsp. *pertenue*, the causative agent of yaws, were detected in 25% of patients.

These cases of infection with *H. ducreyi* confirmed by molecular analysis suggest that clinicians should be more aware of this newly recognized bacterium in skin ulcers of persons in tropical areas. In the context of new efforts to eradicate yaws, mass treatment with azithromycin in

Papua New Guinea reduced the absolute prevalence of ulcers not caused by yaws, which were mainly caused by *H. ducreyi*, from 2.7% to 0.6% (prevalence ratio 0.23, 95% CI 0.18–0.29) at 12 months after treatment (6). However, persistence of *H. ducreyi* at low levels after mass treatment in Papua New Guinea (3) and Ghana (5) suggest that 1 round of mass treatment might not be successful in eradicating *H. ducreyi* skin ulcers.

Our review has several limitations. First, the increase in HSV-related GUD as a result of immunosuppression by HIV infection would result in a decrease in the proportion of chancroid among all GUD case-patients. Second, the lack of sequential studies performed in similar clinical settings at multiple time points precludes an optimal interpretation of the apparent decrease. Third, results might be affected by poor-quality data from many developing countries and might be inflated by publication bias. Fourth, PCR is more sensitive than culture. Therefore, increasing diagnostic yield might have partially masked the scale of the decrease in *H. ducreyi* as a cause of GUD.

In summary, we observed a quantitative and sustained reduction in cases of chancroid as a result of antimicrobial drug syndromic management and major social changes. In addition, data from several research groups indicate that *H. ducreyi* can cause nongenital skin lesions in persons residing in different regions. Further studies of this newly described pathogen skin disease association are required, and appropriate policies are needed that include the routine practice of managing tropical skin ulcers.

M.M. is supported by a Wellcome Trust Clinical Research Fellowship (WT102807).

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References

- Lewis DA. Chancroid: clinical manifestations, diagnosis, and management. *Sex Transm Infect.* 2003;79:68–71. <http://dx.doi.org/10.1136/sti.79.1.68>
- Schmid G, Steen R, N'Dowa F. Control of bacterial sexually transmitted diseases in the developing world is possible. *Clin Infect Dis.* 2005;41:1313–5. <http://dx.doi.org/10.1086/496987>
- Mitjà O, Lukehart SH, Pokowas G, Moses P, Kapa A, Godornes C, 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:e235–41. [http://dx.doi.org/10.1016/S2214-109X\(14\)70019-1](http://dx.doi.org/10.1016/S2214-109X(14)70019-1)
- Marks M, Chi KH, Vahi V, Pillay A, Sokana O, Pavluck A, et al. *Haemophilus ducreyi* associated with skin ulcers among children, Solomon Islands. *Emerg Infect Dis.* 2014;20:1705–7. <http://dx.doi.org/10.3201/eid2010.140573>
- Ghinai R, El-Duah P, Chi KH, Pillay A, Solomon AW, Bailey RL, et al. A cross-sectional study of 'yaws' in districts of Ghana which have previously undertaken azithromycin mass drug administration for trachoma control. *PLoS Negl Trop Dis.* 2015;9:e0003496. <http://dx.doi.org/10.1371/journal.pntd.0003496>
- Mitjà O, Houinei W, Moses P, Kapa A, Paru R, Hays R, et al. Mass treatment with single-dose azithromycin for yaws. *N Engl J Med.* 2015;372:703–10. <http://dx.doi.org/10.1056/NEJMoa1408586>
- Marckmann P, Højbjerg T, von Eyben FE, Christensen I. Imported pedal chancroid: case report. *Genitourin Med.* 1989;65:126–7.
- Ussher JE, Wilson E, Campanella S, Taylor SL, Roberts S. *Haemophilus ducreyi* causing chronic skin ulceration in children visiting Samoa. *Clin Infect Dis.* 2007;44:e85–7. <http://dx.doi.org/10.1086/515404>
- McBride WJ, Hannah R, Le Cornec G, Bletchly C. Cutaneous chancroid in a visitor from Vanuatu. *Australas J Dermatol.* 2008;49:98–9. <http://dx.doi.org/10.1111/j.1440-0960.2008.00439.x>
- Peel TN, Bhatti D, De Boer J, Stratov I, Spelman D. Chronic cutaneous ulcers secondary to *Haemophilus ducreyi* infection. *Med J Aust.* 2010;192:348–50.
- Humphrey S, Romney M, Au S. *Haemophilus ducreyi* ulceration in a 5-year-old boy. Presented at: 65th Annual Conference of the American Academy of Dermatology; 2007 Feb 6–7; Washington, DC, USA.
- Montgomery J. The aerobic bacteriology of infected skin lesions in children of the Eastern Highlands Province. *P N G Med J.* 1985; 28:93–103.
- O'Farrell N, Hoosen AA, Coetzee KD, van den Ende J. Genital ulcer disease: accuracy of clinical diagnosis and strategies to improve control in Durban, South Africa. *Genitourin Med.* 1994;70:7–11.
- Chen CY, Mertz KJ, Spinola SM, Morse S. Comparison of enzyme immunoassays for antibodies to *Haemophilus ducreyi* in a community outbreak of chancroid in the United States. *J Infect Dis.* 1997;175:1390–5. <http://dx.doi.org/10.1086/516471>
- Beyrer C, Jitwatcharanan K, Natpratan C, Kaewwichit R, Nelson KE, Chen CY, 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;178:243–6. <http://dx.doi.org/10.1086/515603>
- Paz-Bailey G, Rahman M, Chen C, Ballard R, Moffatt HJ, Keyton T, et al. Changes in the etiology of sexually transmitted diseases in Botswana between 1993 and 2002: implications for the clinical management of genital ulcer disease. *Clin Infect Dis.* 2005;41:1304–12. <http://dx.doi.org/10.1086/496979>
- Steen R. Eradicating chancroid. *Bull World Health Organ.* 2001; 79:818–26.
- Mabey DC, Wall R, Bello CS. Aetiology of genital ulceration in the Gambia. *Genitourin Med.* 1987;63:312–5.
- Hawkes S, Wes B, Wilson S, Whittle H, Mabey D. Asymptomatic carriage of *Haemophilus ducreyi* confirmed by the polymerase chain reaction. *Genitourin Med.* 1995;71:224–7.
- Nsanze H, Fats MV, D'Costa LJ, Tukei P, Curran J, Ronald A, et al. Genital ulcers in Kenya. Clinical and laboratory study. *Br J Vener Dis.* 1981;57:378–81.
- Kaul R, Kimani J, Nagelkerke, NJ, Plummer FA, Bwayo JJ, Brunham RC, et al. Risk factors for genital ulcerations in Kenyan sex workers. The role of human immunodeficiency virus type 1 infection. *Sex Transm Dis.* 1997;24:387–92. <http://dx.doi.org/10.1097/00007435-199708000-00001>
- Morse SA, David LT, Htun Y, Radebe F, Orle KA, Dangor 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;175:583–9. <http://dx.doi.org/10.1093/infdis/175.3.583>
- Harms G, Matull R, Randrianasolo D, Andriamiadana J, Rasamindrakotroka A, Kirsch T, et al. Pattern of sexually transmitted

- diseases in a Malagasy population. *Sex Transm Dis.* 1994;21:315–20. <http://dx.doi.org/10.1097/00007435-199411000-00004>
24. Behets FM, Andriamiadana J, Randrianasolo D, Randriamanga R, Rasamilalao D, Chen CY, et al. Chancroid, primary syphilis, genital herpes, and lymphogranuloma venereum in Antananarivo, Madagascar. *J Infect Dis.* 1999;180:1382–5. <http://dx.doi.org/10.1086/315005>
 25. Behets FM, Liomba G, Lule G, Dallabetta G, Hoffman IF, Hamilton HA, et al. Sexually transmitted diseases and human immunodeficiency virus control in Malawi: a field study of genital ulcer disease. *J Infect Dis.* 1995;171:451–5. <http://dx.doi.org/10.1093/infdis/171.2.451>
 26. Hoyo C, Hoffman I, Moser BK, Hobbs MM, Kazembe P, Krysiak RG, et al. Improving the accuracy of syndromic diagnosis of genital ulcer disease in Malawi. *Sex Transm Dis.* 2005;32:231–7. <http://dx.doi.org/10.1097/01.olq.0000149669.98128.ce>
 27. Bogaerts J, Vuylsteke B, Martinez Tello W, Mukantabana V, Akingeneye J, Laga M, et al. Simple algorithms for the management of genital ulcers: evaluation in a primary health care centre in Kigali, Rwanda. *Bull World Health Organ.* 1995;73:761–7.
 28. Totten PA, Kuypers JM, Chen CY, Alfa MJ, Parsons LM, Dutro SM, et al. Etiology of genital ulcer disease in Dakar, Senegal, and comparison of PCR and serologic assays for detection of *Haemophilus ducreyi*. *J Clin Microbiol.* 2000;38:268–73.
 29. Crewe-Brown HH, Krige FK, Davel GH, Barron C, Jasen Van Vuuren JA, Shipham SO, et al. Genital ulceration in males at Ga-Rankuwa Hospital, Pretoria. *S Afr Med J.* 1982;62:861–3.
 30. Dangor Y, Fehler G, Exposto F, Koornhof H. Causes and treatment of sexually acquired genital ulceration in southern Africa. *S Afr Med J.* 1989;76:339–41.
 31. Chen CY, Ballard RC, Beck-Sague CM, Dangor Y, Radebe F, Schmid S, et al. Human immunodeficiency virus infection and genital ulcer disease in South Africa. *Sex Transm Dis.* 2000;27:21–9. <http://dx.doi.org/10.1097/00007435-200001000-00005>
 32. Lai W, Chen CY, Morse SA, Htun Y, Fehler HG, Liu H, et al. Increasing relative prevalence of HSV-2 infection among men with genital ulcers from a mining community in South Africa. *Sex Transm Infect.* 2003;79:202–7. <http://dx.doi.org/10.1136/sti.79.3.202>
 33. Meheus A, Van Dyck E, Ursi JP, Ballard RC, Piot P. Etiology of genital ulcerations in Swaziland. *Sex Transm Dis.* 1983;10:33–5. <http://dx.doi.org/10.1097/00007435-198301000-00007>
 34. Ahmed HJ, Mbwana J, Gunnarsson E, Ahlman K, Guerino C, Svensson LA, et al. Etiology of genital ulcer disease and association with human immunodeficiency virus infection in two Tanzanian cities. *Sex Transm Dis.* 2003;30:114–19. <http://dx.doi.org/10.1097/00007435-200302000-00004>
 35. Le Bacq F, Mason PR, Gwanzura L, Robertson VL, Latif AS. HIV and other sexually transmitted diseases at a rural hospital in Zimbabwe. *Genitourin Med.* 1993;69:352–6.
 36. Wang Q, Yang P, Zhong M, Wang G. Validation of diagnostic algorithms for syndromic management of sexually transmitted diseases. *Chin Med J (Engl).* 2003;116:181–6.
 37. Risbud A, Chan-Tack K. 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. <http://dx.doi.org/10.1097/00007435-199901000-00009>
 38. Rajan VS, Sng E, Lim A. The isolation of *H. ducreyi* in Singapore. *Ann Acad Med Singapore.* 1983;12:57–60.
 39. Dillon SM, Cummings M, Rajagopalan S, McCormack WC. Prospective analysis of genital ulcer disease in Brooklyn, New York. *Clin Infect Dis.* 1997;24:945–50. <http://dx.doi.org/10.1093/clinids/24.5.945>
 40. Mertz KJ, Weiss JB, Webb RM, Levine WC, Lewis JS, Orle KA, et al. An investigation of genital ulcers in Jackson, Mississippi, with use of a multiplex polymerase chain reaction assay: high prevalence of chancroid and human immunodeficiency virus infection. *J Infect Dis.* 1998;178:1060–6. <http://dx.doi.org/10.1086/515664>
 41. Mertz KJ, Trees D, Levine W. Etiology of genital ulcers and prevalence of human immunodeficiency virus coinfection in 10 US cities. *J Infect Dis.* 1998;178:1795–8. <http://dx.doi.org/10.1086/314502>
 42. Sanchez J, Volquez C, Totten PA, Campos PE, Ryan C, Catlin M, et al. The etiology and management of genital ulcers in the Dominican Republic and Peru. *Sex Transm Dis.* 2002;29:559–67. <http://dx.doi.org/10.1097/00007435-200210000-00001>
 43. Behets FM, Brathwaite R, Hylton-Kong T. Genital ulcers: etiology, clinical diagnosis, and associated human immunodeficiency virus infection in Kingston, Jamaica. *Clin Infect Dis.* 1999;28:1086–90. <http://dx.doi.org/10.1086/514751>
 44. Bauwens JE, Orlander E, Gomez H. Epidemic Lymphogranuloma venereum during epidemics of crack cocaine use and HIV infection in the Bahamas. *Sex Transm Dis.* 2002;29:253–9. <http://dx.doi.org/10.1097/00007435-200205000-00001>
 45. Madani TA. Sexually transmitted infections in Saudi Arabia. *BMC Infect Dis.* 2006;6:3. <http://dx.doi.org/10.1186/1471-2334-6-3>
 46. Kyriakis KP, Hadjivassiliou M, Pappas VA, Fliemetakis A, Stavrianeas N, Katsambas A. Incidence determinants of gonorrhoea, chlamydial genital infection, syphilis and chancroid in attendees at a sexually transmitted disease clinic in Athens, Greece. *Int J Dermatol.* 2003;42:876–81. <http://dx.doi.org/10.1046/j.1365-4362.2003.01737.x>

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Neurocysticercosis—a Parasitic Brain Infection



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Epidemiology of *Haemophilus ducreyi* Infections

Technical Appendix

References

41. Mertz KJ, Trees D, Levine W. Etiology of genital ulcers and prevalence of human immunodeficiency virus coinfection in 10 US cities. *J Infect Dis.* 1998;178:1795–8 [PubMed](#). <http://dx.doi.org/10.1086/314502>
42. Sanchez J, Volquez C, Totten PA, Campos PE, Ryan C, Catlin M, et al. The etiology and management of genital ulcers in the Dominican Republic and Peru. *Sex Transm Dis.* 2002;29:559–67 [PubMed](#). <http://dx.doi.org/10.1097/00007435-200210000-00001>
43. Behets FM, Brathwaite R, Hylton-Kong T. Genital ulcers: etiology, clinical diagnosis, and associated human immunodeficiency virus infection in Kingston, Jamaica. *Clin Infect Dis.* 1999;28:1086–90 [PubMed](#). <http://dx.doi.org/10.1086/514751>
44. Bauwens JE, Orlander E, Gomez H. Epidemic Lymphogranuloma venereum during epidemics of crack cocaine use and HIV infection in the Bahamas. *Sex Transm Dis.* 2002;29:253–9 [PubMed](#). <http://dx.doi.org/10.1097/00007435-200205000-00001>
45. Madani TA. Sexually transmitted infections in Saudi Arabia. *BMC Infect Dis.* 2006;6:3 [PubMed](#). <http://dx.doi.org/10.1186/1471-2334-6-3>
46. Kyriakis KP, Hadjivassiliou M, Paparizos VA, Flemetakis A, Stavrianeas N, Katsambas A. Incidence determinants of gonorrhea, chlamydial genital infection, syphilis and chancroid in attendees at a sexually transmitted disease clinic in Athens, Greece. *Int J Dermatol.* 2003;42:876–81 [PubMed](#). <http://dx.doi.org/10.1046/j.1365-4362.2003.01737.x>
47. Bruisten SM, Cairo I, Fennema H, Pijl A, Buimer M, Peerbooms PG, et al. Diagnosing genital ulcer disease in a clinic for sexually transmitted diseases in Amsterdam, The Netherlands. *J Clin Microbiol.* 2001;39:601–5. [PubMed](#) <http://dx.doi.org/10.1128/JCM.39.2.601-605.2001>
48. Mehta SD, Green SJ, Maclean I, Hu H, Bailey RC, Gillevet PM, et al. Microbial diversity of genital ulcer disease in men enrolled in a randomized trial of male circumcision in Kisumu, Kenya. *PLoS ONE.* 2012;7:e38991. [PubMed](#) <http://dx.doi.org/10.1371/journal.pone.0038991>

49. Phiri S, Zadrozny S, Weiss HA, Martinson F, Nyirenda N, Chen CY, et al. Etiology of genital ulcer disease and association with HIV infection in Malawi. *Sex Transm Dis.* 2013;40:923–8. [PubMed](#)
<http://dx.doi.org/10.1097/OLQ.0000000000000051>
50. Zimba TF, Apalata T, Sturm WA, Moodley P. Aetiology of sexually transmitted infections in Maputo, Mozambique. *J Infect Dev Ctries.* 2011;5:41–7. [PubMed](#)
51. Tobias S, Shonhiwa S, Norbert F, Oke O, Ndjavera C, Chikukwa S, et al. Microbiological surveillance for sexually transmitted infections in Windhoek and Osahakati, Namibia. *Sex Transm Infect.* 2011;87:A103.
<http://dx.doi.org/10.1136/sextrans-2011-050108.10>
52. O'Farrell N, Morison L, Moodley P, Pillay K, Vanmali T, Quigley M, et al. Genital ulcers and concomitant complaints in men attending a sexually transmitted infections clinic: implications for sexually transmitted infections management. *Sex Transm Dis.* 2008;35:545–9. [PubMed](#)
<http://dx.doi.org/10.1097/OLQ.0b013e31816a4f2e>
53. Lewis DA, Müller E, Steele L, Sternberg M, Radebe F, Lyall M, et al. Prevalence and associations of genital ulcer and urethral pathogens in men presenting with genital ulcer syndrome to primary health care clinics in South Africa. *Sex Transm Dis.* 2012;39:880–5. [PubMed](#)
<http://dx.doi.org/10.1097/OLQ.0b013e318269cf90>
54. Nilsen A, Kasubi MJ, Mohn SC, Mwakagile D, Langeland N, Haarr L. Herpes simplex virus infection and genital ulcer disease among patients with sexually transmitted infections in Dar es Salaam, Tanzania. *Acta Derm Venereol.* 2007;87:355–9. [PubMed](#) <http://dx.doi.org/10.2340/00015555-0241>
55. Suntoke TR, Hardick A, Tobian AA, Mpoza B, Laeyendecker O, Serwadda D, 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. [PubMed](#) <http://dx.doi.org/10.1136/sti.2008.034207>
56. Makasa M, Buve A, Sandøy IF. Etiologic pattern of genital ulcers in Lusaka, Zambia: has chancroid been eliminated? *Sex Transm Dis.* 2012;39:787–91. [PubMed](#)
<http://dx.doi.org/10.1097/OLQ.0b013e31826ae97d>
57. Gomes Naveca F, Sabidó M, Amaral Pires de Almeida T, Araújo Veras E, Contreras Mejía Mdel C, Galban E, et al. Etiology of genital ulcer disease in a sexually transmitted infection reference center in Manaus, Brazilian Amazon. *PLoS ONE.* 2013;8:e63953. [PubMed](#) <http://dx.doi.org/10.1371/journal.pone.0063953>
58. Maan MA, Hussain F, Iqbal J, Akhtar S. Sexually transmitted infections in Pakistan. *Ann Saudi Med.* 2011;31:263–9. [PubMed](#) <http://dx.doi.org/10.4103/0256-4947.81541>

59. Hope-Rapp E, Anyfantakis V, Fouéré 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;37:153–8. [PubMed](#)
<http://dx.doi.org/10.1097/OLQ.0b013e3181bf5a98>
60. Mackay IM, Harnett G, Jeoffreys N, Bastian I, Sriprakash KS, Siebert D, et al. Detection and discrimination of herpes simplex viruses, *Haemophilus ducreyi*, *Treponema pallidum*, and *Calymmatobacterium (Klebsiella) granulomatis* from genital ulcers. *Clin Infect Dis.* 2006;42:1431–8. [PubMed](#)
<http://dx.doi.org/10.1086/503424>
61. World Health Organization. Guidelines for the management of sexually transmitted infections. Geneva: The Organization; 2001.
62. Spinola SM, Ballard RC. Chancroid. In: Morse SA, Holmes KK, Ballard RC, editors. Atlas of sexually transmitted diseases and AIDS. 4th ed. Philadelphia: W.B. Saunders; 2010. p. 141–56.
63. Steen R, Elvira W, Kamali A, Ndowa F. Control of sexually transmitted infections and prevention of HIV transmission: mending a fractured paradigm. *Bull World Health Organ.* 2009;87:858–65. [PubMed](#)
<http://dx.doi.org/10.2471/BLT.08.059212>