Abstract  Genital ulcers are important cofactors of HIV transmission in the countries most severely affected by HIV/AIDS. Chancroid is a common cause of genital ulcer in all 18 countries where adult HIV prevalence surpasses 8% and is rare in countries with low-level HIV epidemics.  

Haemophilus ducreyi, the causative organism of chancroid, is biologically vulnerable and occupies a precarious epidemiological niche. Both simple, topical hygiene and male circumcision greatly reduce risk of infection and several classes of antibiotics — some of which can be administered in single-dose treatment regimens — provide rapid cure. H. ducreyi depends on sexual networks with high rates of partner change for its survival, thriving in environments characterized by male mobility and intensive commercial sex activity. Elimination of H. ducreyi infection from vulnerable groups results in disappearance of chancroid from the larger community.

Once endemic in Europe and North America, chancroid began a steady decline early in the twentieth century, well before the discovery of antibiotics. Social changes — resulting in changing patterns of commercial sex — probably disrupted the conditions needed to sustain chancroid as an endemic disease. Sporadic outbreaks are now easily controlled when effective curative and preventive services are made available to sex workers and their clients. More recently, chancroid prevalence has declined markedly in countries such as the Philippines, Senegal, and Thailand, a development that may contribute to stabilization of the HIV epidemics in these countries. Eradication of chancroid is a feasible public health objective. Protecting sex workers and their clients from exposure to sexually transmitted diseases (STDs) and improving curative services for STDs are among the proven strategies that could be employed.

Keywords  Chancroid/history/epidemiology/prevention and control; HIV infections/transmission; Prostitution (source: MeSH).

Mots clés  Chancre mou/histoire/épidémiologie/prévention et contrôle; HIV, Infection/transmission; Prostitution (source: INSERM).

Palabras clave  Chancroide/historia/epidemiología/prevención y control; Infecciones por VIH/transmisión; Prostitución (fuente: BIREME).


Voir page 823 le résumé en français. En la página 824 figura un resumen en español.

Introduction

Chancroid has evaded scrutiny as an important sexually transmitted disease (STD), even though an estimated 7 million cases of chancroid occur yearly (1). Chancroid is the soft chancre of Haemophilus ducreyi and is common in many of the world’s poorest regions with the weakest public health infrastructure, such as areas of Africa, Asia, and the Caribbean. Where chancroid is endemic, genital ulcers are common, sometimes surpassing discharges as the most common STD syndrome (2–4). These regions also have some of the highest rates of human immunodeficiency virus (HIV) infection in the world and chancroid is common in all 18 countries where adult HIV prevalence surpasses 8%. This confluence of high rates of chancroid, genital ulcers, and HIV points to a cofactor that may account for a large proportion of new HIV infections acquired heterosexually in the most severely affected countries of the world.

Chancroid was endemic in most parts of the world well into the 20th century. Several decades before the discovery of sulfa drugs and penicillin, however, chancroid began a steady decline in Europe and North America, and disappeared as a major STD even before it could be recognized as such. Similar declines have been seen in other countries, including China, the Philippines, Senegal, and Thailand. A review of this epidemiological transition could suggest ways of eliminating chancroid from other regions.

This paper considers the feasibility and potential benefits of chancroid eradication. Evidence
from the literature on the biological and epidemiological aspects of *H. ducreyi* infection and the role of chancroid in facilitating HIV transmission is summarized. The historical evidence for the global decline in chancroid is presented, together with a discussion of the social and public health conditions that appear to maintain chancroid in a tenuous biological niche.

**Biological and epidemiological features of chancroid**

**Etiological agent**
Chancroid is caused by the Gram-negative bacillus *H. ducreyi* and results in superficial ulcerations, often with suppurant regional lymphadenopathy. Its biology and pathogenesis have been well described (5, 6); in its classic form, it is differentiated from syphilis by the soft, irregular borders of the ulcerations (soft chancres) that are painful. Most infections are clinically apparent, although there is some controversy over the extent and importance of asymptomatic disease in women (7, 8). However, clinical differentiation from other types of genital ulcers is not reliable (9, 10) and *H. ducreyi* is also hard to culture (11), factors which pose a problem for control strategies based on etiological identification. For these reasons, current international standards recommend syndromic cotreatment of chancroid and syphilis for effective case management of patients with genital ulcers (12, 13).

**Treatment**
Chancroid can be treated with macrolides, quinolones, and some third-generation cephalosporins (14–16). Single doses of certain antibiotics, such as ciprofloxacin and azithromycin, are highly effective (14, 17) although longer treatments may be more effective in uncircumcised males and patients with HIV infection (4, 18, 19). Antibiotics may also provide some protection from reinfection: one study estimated that the prophylactic effect of a single dose of azithromycin against new *H. ducreyi* infection lasted as long as two months after treatment (20).

**Protection against infection**
Topical hygiene is also effective in reducing *H. ducreyi* transmission. During the First World War, simple washing with soap and water within a few hours of sexual exposure was effective in reducing risk of chancroid (21, 22). Male circumcision is highly protective against both *H. ducreyi* (6) and HIV infection (23–26), and the interaction of chancroid and HIV infection accounts for at least part of the HIV-protective effect of circumcision.

**Spread of the disease**
Chancroid is closely associated with prostitution (27–30). Data from chancroid-endemic regions have documented that most cases of chancroid occur in people who had direct exposure with a commercial sex worker or whose partner had direct exposure, and outbreaks typically show high male to female ratios (7, 27). This pattern is a sign of the relative vulnerability of *H. ducreyi* compared to other common bacterial pathogens that cause STDs: *H. ducreyi* has a short duration of infectivity and requires frequent contacts to spread within a population. *H. ducreyi* can survive (i.e. maintain a reproductive rate greater than one) only in subgroups of the population with a sufficient turnover of sex partners. Based on reproductive rate calculations, minimal rates of partner change are estimated to be 15–20 sex partners per year (6, 31). Chancroid is thus not a sustainable infection in sexual networks with low rates of partner change. In theory, control measures that eliminate infection from subgroups with the highest rates of partner change would eradicate chancroid from the larger community. Importantly for disease control, *H. ducreyi* has no non-human reservoir.

**Cofactors in HIV transmission**
Genital ulcer disease is a recognized risk factor for HIV infection. Strong associations between HIV seropositivity and genital ulcer disease (23, 32) have been reported and the odds and risk ratios are higher than for non-ulcerative STDs (33). Cross-sectional and prospective population studies do not accurately measure the increased risk of HIV infection, however, and underestimate the importance of genital ulcer disease as a cofactor in HIV transmission. Data from Kenya and Thailand, for example, suggest that genital ulcers may increase the risk of HIV infection as much as 50–300 times per unprotected act of vaginal intercourse (34–36) and facilitate a large proportion of new HIV infections in countries where genital ulcers are common.

In many countries with high HIV-infection rates chancroid is the most common cause of genital ulcer disease, and there are strong associations between chancroid and HIV seropositivity (37–39). The incidence and prevalence of chancroid varies greatly by country and region, however, for reasons that are poorly understood (1). Indeed, the global epidemiology of chancroid is so poorly documented that it is not included in WHO estimates of the global incidence of curable STDs (40). However, there is a close geographical association between chancroid and HIV infection (Table 1). In countries of eastern and southern Africa, where chancroid is endemic, the HIV-infection rates are the highest in the world (41, 58). In Asia, the four countries with generalized HIV epidemics all had endemic levels of chancroid when their HIV epidemics started (Thailand subsequently reduced chancroid to non-endemic levels). In contrast, chancroid is rare in countries with low HIV-infection rates.
The disappearance of chancroid from Europe and North America

Prevalence
Although distinctions between venereal diseases were blurred during the 1800s, available evidence suggests that chancroid was commonplace in Europe and North America during the 19th and early 20th centuries. Conditions favourable to transmission certainly existed (59); 19th-century economic expansion fuelled migration and unprecedented numbers of men were drawn to urban areas, which stimulated demand for commercial sex. As late as 1913, a British commission estimated that 10% of the urban population had syphilis and an even greater proportion had gonorrhoea (60). Such conditions and STD rates are comparable to those in many developing countries today.

Bassereau and Ricord distinguished the soft from the indurated (syphilitic) chancre in 1852 and Ducrey identified the causative organism of chancroid in 1889 (6, 61).

<table>
<thead>
<tr>
<th>Country</th>
<th>Adult HIV prevalence rate as a %</th>
<th>Chancroid prevalence rate as a %</th>
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*Source of HIV prevalence data: ref. 41. Dates of HIV data do not correspond with dates of cited chancroid studies.

b GUD = genital ulcer disease.

STD = sexually transmitted disease.

c C = culture.

d P = polymerase chain reaction.

e CD = clinical diagnosis.

f S = serology.

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The disappearance of chancroid from Europe and North America

Prevalence
Although distinctions between venereal diseases were blurred during the 1800s, available evidence suggests that chancroid was commonplace in Europe and North America during the 19th and early 20th centuries. Conditions favourable to transmission certainly existed (59); 19th-century economic expansion fuelled migration and unprecedented numbers of men were drawn to urban areas, which stimulated demand for commercial sex. As late as 1913, a British commission estimated that 10% of the urban population had syphilis and an even greater proportion had gonorrhoea (60). Such conditions and STD rates are comparable to those in many developing countries today.

Bassereau and Ricord distinguished the soft from the indurated (syphilitic) chancre in 1852 and Ducrey identified the causative organism of chancroid in 1889 (6, 61). In 19th-century debates over how to reliably differentiate syphilitic sores likely to “affect the constitution” from the “simple sore” of shorter duration that did not, the latter was said to occur “four times as frequently as the true syphilitic...
sore” (62). Puche in 1858 noted that over 80% of 10,000 ulcers in a series of French patients were classified as being of the soft type (61). Sullivan, writing in 1939, noted that “the disease occurs endemically in Italy and Northern Africa where indigent prostitutes more or less consistently harbor the bacillus ... and the number of chancroidal infections exceeds that of syphilitic infections” (5).

Another picture of the social conditions that favoured transmission of STDs in general, and of chancroid specifically, can be constructed from descriptions of 19th-century urban America and its thriving tenderloin areas with overt street- and brothel-based prostitution (63). According to Gilfoyle, “many women chose or felt compelled at some point to engage in prostitution in numbers unmatched in New York’s history, either before or since” (64). Walt Whitman noted in the late 1850s “that 19 out of 20 of the mass of American young men, who live in or visit the great cities, are more or less familiar with houses of prostitution and are customers to them” (64). Available statistics certainly reveal a high incidence of STDs at that time (65) and venereal rates among prostitutes were estimated to be 75–90% (21).

A disease on the decline

Despite the evidence that chancroid was prevalent in the 19th and early 20th centuries, there were signs that the disease was declining. In England, for example, Hall reported that chancroid was prevalent until the early 20th century (60). Sullivan, in 1939, noted: “very likely it is less common now than it was in the last century” (5). Data from military sources support this idea (66, 67): in the United States Army in 1908, chancroid was more prevalent than syphilis, but declined more rapidly than syphilis between 1908 and 1930 (Fig. 1). Hall also pointed out that sulfonamides, introduced in 1937, were “also effective against chancroid, the incidence of which was already declining remarkably for reasons which are obscure” (60).

Following the introduction of sulfa drugs and penicillin, chancroid became a rarity in Europe, with occasional outbreaks linked to imported cases (68). In 1995, fewer than four ulcers per 1000 people seen at genitourinary clinics in Great Britain were classified as chancroid, lymphogranuloma venereum, or donovanosis (2). Reliable statistics for North America became available following the Second World War, when antibiotic treatment drove a new approach to STD control. Reported rates of chancroid in the United States civilian population decreased by more than 80-fold between 1947 and 1997 (Fig. 2) and chancroid had essentially disappeared as an endemic disease by the late 1950s. Subsequent outbreaks, including a sustained increase in the late 1980s, were usually linked to imported cases and limited to commercial sex networks, and were rapidly controlled through focused case finding and presumptive treatment of genital ulcers (70–73).

Several factors probably contributed to the disappearance of chancroid as an endemic disease in developed western societies. The introduction of antibiotics clearly played an important role. It is likely, though, that the decline of chancroid began earlier with significant social changes and shifting patterns of prostitution. Commercial sex dynamics changed radically with reduced migration and improved economic options for women (21). The demise of the brothel and transformation of sex work to less overt forms with fewer partners probably reduced the size of the core group and limited opportunities for transmission. In Europe, 19th-century regulation of prostitution with periodic health examinations may also have contributed to lower rates of transmission by reducing contact between symptomatic sex workers and clients.

Epidemiological transition in developing countries

Today, the social and public health conditions in many developing countries are similar to those of western industrialized societies at the turn of the 20th century. Rapidly growing urban areas offer elusive alternatives to rural poverty and opportunities for women lag behind those for men. Urban migration is often disproportionately male, which drives demand for commercial sex services. Migrant labour and civil unrest further destabilize community and family life. Even though these conditions favour
STD transmission, chancroid has declined in some areas where it once was common.

**In Africa**

In southern and eastern parts of Africa, where rates of circumcision are low and HIV prevalence is high, chancroid is endemic. It is much less common in West Africa, however, where importation of chancroid from other regions may be important in maintaining transmission (38). In Kenya, where the importance of chancroid in HIV transmission was first described in the late 1980s (6, 74), interventions targeting sex workers and STD patients were implemented. Reported condom use by sex workers has since increased to over 80% in project areas and the incidence of genital ulcers has declined. Chancroid, once the most common ulcer etiology, now accounts for fewer than 10% of genital ulcers seen in clinics in Nairobi, Kenya (75).

In Senegal, HIV prevalence among pregnant women has been below 1% for more than a decade. A strong multisectoral response, an effective STD control programme and early legalization of prostitution have been credited for this low level (76). Special clinical services, for example, offer regular examination and treatment for registered sex workers. Not only has there been a significant decline in STD rates among sex workers and pregnant women between 1991 and 1996, but genital ulcers are also no longer common (77) and chancroid is reportedly rare (78).

In South Africa, migrant labour is employed on a large scale in mining and other industries, creating favourable conditions for transmitting *H. ducreyi*, HIV, and other STD pathogens. Recently, interventions providing curative and preventive services, including monthly presumptive antibiotic treatment to women at risk, have been implemented in several gold-mining communities. One community reported large reductions in curable STDs among the women using the services (79). At the start of the intervention, chancroid was the main cause of genital ulcers among the women attending, but after the third month of the intervention it was no longer seen, even among new clinic attendees (80). In miners living in the area, the prevalence of genital ulcers declined by 78% within nine months and ongoing surveillance shows a sustained reduction relative to the prevalence in other mining areas (81).

**In Asia**

Chancroid is rare in Asian countries with stable, low-level HIV epidemics. In the Philippines, for example, treatment for chancroid is not included in the national guidelines for treatment of genital ulcers, although chancroid once was common there (82). Genital ulcers are reportedly rare and HIV rates have remained at or below 1%, even among registered and freelance sex workers, who have much higher rates of other bacterial STDs (83). Low rates of chancroid and genital ulcers are also seen in other countries in the region with low-level HIV epidemics (84).

Among the four Asian countries with generalized HIV epidemics, chancroid is also prevalent, or was so when HIV was introduced in the 1980s. Thailand, however, succeeded in controlling the common curable STDs in the 1990s (85) and managed to significantly slow HIV transmission (86). Within five years of introducing the 100% condom policy in commercial sex establishments in 1989, the incidence of bacterial STDs fell by over 80% (57, 87). Chancroid led the decline with a 95% decrease (Fig. 3). While the condom policy targeting sex workers and their clients was probably the most important factor, it was not the only one. Both chancroid and gonorrhoea rates had started to decline several years earlier, probably in response to the widespread availability of quinolone antibiotics after 1986 (15). Also during this period, a focused effort to eliminate chancroid was carried out in 23 sex establishments in Bangkok. From 1990 to 1991, over 2000 lower-class female sex workers were offered presumptive treatment with ciprofloxacin (500 mg every 3 months). Chancroid among their male clients reportedly fell 46%, despite no change in condom use and limited coverage of sex establishments (88). Today, chancroid is rarely seen in Thailand, despite an active commercial sex industry and low rates of male circumcision.

**Discussion**

*H. ducreyi* has demonstrated its extreme vulnerability in settings as diverse as Bangkok (Thailand), Nairobi (Kenya), New York (USA), and Paris (France). Without conscious effort or control programmes, chancroid has moved from endemcity to a sporadic epidemiological curiosity in many countries. Recent examples of elimination or control in endemic areas of Asia and Africa suggest that chancroid eradication may be a feasible objective.

Based on an examination of the decline in chancroid rates over the last century, interventions in three areas appear to undermine endemic chancroid. First, the organization and patterns of commercial sex appear to be primary determinants of chancroid transmission, and these are influenced by social factors such as migration and opportunities for women. Second, preventive measures, such as widespread condom use by commercial sex workers, can break the chancroid transmission cycle, even when conditions favour the spread of chancroid. Third, effective antibiotic treatment of the highest-risk populations can reduce chancroid transmission in the short term and lead to a rapid decline in chancroid prevalence.

Interventions in these three areas reduce the *H. ducreyi* reproductive rate ($R_0$), according to the equation $R_0 = βeD$, by lowering the rate of partner change ($c$), the transmission efficiency ($β$), and the duration of infectivity ($D$) in vulnerable sexual networks. By acting through separate mechanisms, the interventions are synergistic. In Thailand, for
example, despite emphasis on the 100% condom policy (87), all three factors (B, c, and D) probably played a role: STD transmission rates fell as fewer men sought commercial sex; the rates of partner change dropped; more commercial sex acts were protected by condoms; and effective STD treatment became widely available.

Feasibility of chancroid eradication

Biological and epidemiological factors determine whether infectious diseases are suitable for eradication, elimination, or enhanced control, and chancroid meets three important criteria required for eradication (89). First, it is identifiable, both syndromically and etiologically, which assists treatment and enables more accurate surveillance. Second, the infection is easily cured: there are several effective, single-dosed antimicrobial treatments, one of which provides extensive post-treatment prophylaxis. Third, *Haemophilus ducreyi* has no non-human reservoir and is not sustainable outside the most active human sexual networks. A highly focused effort to eliminate infection from those networks could therefore plausibly eradicate chancroid in endemic areas.

Experience of controlling chancroid outbreaks in non-endemic areas can provide insight into ways of eliminating chancroid infection and preventing its reoccurrence. Successful interventions include: targeted preventive and curative services for sex workers, since regular screening and presumptive treatment can rapidly reduce prevalence; effective syndromic management of genital ulcers, to sustain control; and peer interventions, to maintain high levels of preventive behaviour. Other interventions could also be investigated, such as post-exposure male hygiene or more affordable, accurate diagnostics. Research needs would be largely operational and should focus on adapting strategies to local conditions. As with other disease control efforts (86), interventions should ideally be implemented in a manner that strengthens existing services and forms links with other STD control objectives (such as syphilis elimination). For example, improved surveillance would benefit both chancroid and general STD control efforts. Syndromic surveillance of genital ulcers with periodic etiological confirmation would provide relevant indicators as well as facilitate the study of the role of genital ulcers in HIV transmission.

In summary, the continued existence of chancroid reflects a correctable imbalance. Conditions that appear to be necessary to sustain chancroid in a population include a commercial sex environment intensive enough to expose sufficient numbers of women to high numbers of sexual partners and the absence of basic preventive and curative control measures to blunt that exposure. In this sense, chancroid can be seen as a sentinel disease whose continued presence indicates that existing STD control efforts are wholly inadequate relative to sexual transmission dynamics. As STD control is a progressive and relative goal, controlling chancroid arguably represents an early step in the process. With the majority of new HIV infections occurring in remaining regions of high chancroid prevalence, it may be an opportune time to consider chancroid eradication as a priority for preventing HIV infection as well as for general STD control.

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Conflicts of interest: none declared.

Résumé

Eradication du chancre mou

Les ulcérations génitales sont d’importants cofacteurs de la transmission du VIH dans les pays les plus gravement touchés par l’VIH/SIDA. Le chancre mou est une cause fréquente d’ulcération génitale dans les 18 pays où la prévalence du VIH chez l’adulte dépasse 8 % et est rare dans ceux où l’épidémie de VIH est de faible intensité. *Haemophilus ducreyi*, agent du chancre mou, est biologiquement vulnérable et occupe une niche épidémio-logique précaire. Une hygiène locale simple ainsi que la circoncision masculine réduisent largement le risque d’infection et plusieurs classes d’antibiotiques, dont certains peuvent être administrés en traitement unique, assurent une guérison rapide. La survie de *H. ducreyi* est favorisée par l’existence de réseaux sexuels avec changements fréquents de partenaires et ce germe se propage surtout dans les milieux caractérisés par une grande mobilité géographique des hommes et un recours intensif aux services des travailleurs sexuels. L’élimination de l’infection à *H. ducreyi* parmi les groupes vulnérables entraînera la disparition du chancre mou dans la communauté.
Aucrerais endémique en Europe et en Amérique du Nord, le chancre mou a connu un déclin régulier dès le début du XXe siècle, bien avant la découverte des antibiotiques. Les changements sociaux, qui se sont accompagnés d’une évolution des pratiques en matière de prostitution, ont probablement perturbé les conditions qui permettaient au chancre mou de se maintenir sur un mode endémique. Il est maintenant facile d’enquêter les flambées sporadiques lorsque les travailleurs sexuels et leurs clients ont accès à des services préventifs et curatifs efficaces. Récemment, la prévalence du chancre mou a considérablement baissé dans des pays comme les Philippines, le Sénégal et la Thaïlande, une tendance qui peut contribuer à stabiliser l’épidémie de VIH dans ces pays. L’éradication du chancre mou est un objectif de santé publique réalisable. Parmi les stratégies éprouvées, figurent la protection des travailleurs sexuels et de leurs clients contre l’exposition aux maladies sexuellement transmissibles (MST) et la fourniture de services préventifs et curatifs contre les MST.

Resumen

Erradicación del chancroide

Las úlceras genitales son un cofactor importante de la transmisión del VIH en los países más gravemente afectados por la epidemia de VIH/SIDA, y el chancroide es una causa común de úlceras genitales en los 18 países donde la prevalencia de la infección por el VIH en la población adulta sobrepasa el 8%, mientras que es infrecuente en los países de baja intensidad de la epidemia de VIH.

El microorganismo causante del chancroide, Haemophilus ducreyi, presenta unas características biológicas que lo hacen vulnerable y ocupa un nicho epidemiológico precario. Tanto la simple higiene tópica como la circuncisión masculina reducen considerablemente el riesgo de infección, y varios tipos de antibióticos, algunos de los cuales se pueden administrar en forma de una sola dosis, permiten lograr una rápida curación. H. ducreyi necesita redes sexuales promiscuas para su supervivencia, por lo que prospera en entornos caracterizados por la movilidad de los hombres y por un intenso comercio sexual. La eliminación de la infección por H. ducreyi entre los grupos vulnerables se traduce en la desaparición del chancroide en la comunidad general.

En su día endémico en Europa y América del Norte, el chancroide no ha cesado de retroceder desde principios del siglo XX, mucho antes del descubrimiento de los antibióticos. Determinadas mutaciones sociales, y los cambios experimentados consiguientemente por el comercio sexual, alteraron probablemente las condiciones que necesitaba el chancroide para persistir como enfermedad endémica. Los brotes esporádicos se pueden controlar actualmente con facilidad cuando los profesionales del sexo y sus clientes disponen de servicios curativos y preventivos eficaces. Más recientemente, la prevalencia del chancroide ha disminuido de forma marcada en países como Filipinas, el Senegal y Tailandia, lo que podría contribuir a que se stabilizara la epidemia de infección por el VIH en esos países. La erradicación del chancroide es un objetivo de salud pública viable. La protección de los profesionales del sexo y de sus clientes contra las enfermedades de transmisión sexual (ETS) y la mejora de los servicios de curación de las ETS son algunas de las estrategias de demostrada eficacia que pueden emplearse.

References


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