

# Genital ulceration

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## Abstract

Genital ulceration can represent one of the more complex presentations encountered within genitourinary medicine. There are a wide range of causes, which can make accurate diagnosis a challenge. These include common and rare sexually transmitted infections (STIs), dermatological conditions and trauma. This chapter aims to provide an overview of genital ulceration secondary to STIs. The most common causes of genital ulceration secondary to STI diagnoses in the developed world are genital herpes, primary syphilis and lymphogranuloma venereum. Rarer STI presentations of donovanosis and chancroid typically present in travellers returning from endemic areas. We highlight the typical course and pattern of symptoms for each diagnosis alongside relevant diagnostic tests and current recommended treatment regimens. When not caused by an STI, genital ulceration can occur following local trauma or as a manifestation of an underlying dermatological condition.

**Keywords** Chancroid; donovanosis; genital herpes; genital ulceration; herpes simplex type 1; herpes simplex type 2; lymphogranuloma venereum; MRCP; primary syphilis; tropical STIs

## Genital ulceration

Genital ulceration can represent one of the more complex presentations encountered within genitourinary medicine. A wide range of aetiologies are identified in the pathogenesis of the presentation, which can make accurate diagnosis a challenge. These include common and rare sexually transmitted infections (STIs), dermatological conditions and trauma. This chapter aims to provide an overview of genital ulceration secondary to STIs.

In assessing any patient presenting with genital ulceration, a clinician should ensure that a comprehensive sexual history is taken, including an up-to-date travel history. This should be coupled with a thorough examination of both genital and extragenital skin.

The course and pattern of symptoms aid in diagnosis. Categorizing symptoms into painful or painless ulceration and whether there is involvement at multiple or single sites can help to narrow the possible causes. The most common causes of genital ulceration secondary to STI diagnoses in the developed world are genital herpes, primary syphilis and lymphogranuloma venereum (LGV). Rarer presentations of donovanosis and

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## Key points

- The differential diagnosis of genital ulceration is wide; causes include sexually transmitted infections, dermatological conditions and trauma.
- The most common cause of ulceration is genital herpes simplex infection. Syphilis and lymphogranuloma venereum are other important infective causes.
- When individuals are diagnosed with herpes simplex virus it is essential that they are counselled regarding natural history, transmission and complications.
- An accurate travel history is essential for any individual presenting with genital ulceration to consider investigation for rarer tropical sexually transmitted infections (STIs), donovanosis and chancroid. A relapsing course, the involvement of multiple mucosal and extragenital sites makes a non-STI cause more likely.

chancroid typically present in travellers returning from endemic areas.

It is recognized that the presence of genital ulcer disease increases the risk of both acquisition and transmission of human immunodeficiency virus (HIV). Therefore both initial exclusion and appropriately timed follow-up to exclude HIV should be performed in individuals identified as at risk.

## Genital herpes

Genital herpes simplex virus (HSV) is the most common cause of genital ulceration, with local, systemic and psychosexual complications. It is caused by HSV type 1 (HSV-1) or type 2 (HSV-2).

Historically, most HSV-1 infections manifested as oropharyngeal infection in childhood, with a typical presentation of recurrent cold sores. Over time, oropharyngeal infection has become less common, resulting in increased susceptibility to HSV-1 at sexual debut. In the UK, HSV-1 is now the principal cause of first-episode genital infection in most young men and women. Although initial infections with HSV-1 and HSV-2 disease are indistinguishable, HSV-2 disease is likely to recur most frequently.

## Natural history

The herpesviruses cause latent and recurrent infections in humans and animals.<sup>1,2</sup> They comprise three subfamilies ( $\alpha$ ,  $\beta$ ,  $\gamma$ ). HSV is a human  $\alpha$ -herpesvirus.

Following initial infection, replication of HSV at the portal of entry results in infection of sensory nerve endings.<sup>2</sup> The virus enters into the distal axonal processes of the sensory neurone and travels to the dorsal root ganglion, where it remains in a latent state.<sup>2</sup> The virus periodically reactivates, travelling down the axon and into the basal skin layers.<sup>2</sup> On virus reactivation, some patients develop symptoms, whereas others remain asymptomatic. In cells outside the sensory nervous system,  $\alpha$ -herpesvirus infection does not achieve latency, because viral replication leads eventually to cell death through lysis.<sup>2</sup>

Transmission occurs through genital-to-genital and orogenital contact.<sup>1–3</sup> It is most likely when there are visible lesions, but most transmissions occur in the absence of local symptoms in the source partner. Infectivity is increased in the prodrome and immediately after lesion healing. Viral shedding has been shown to occur on an average of 2% of days in the absence of symptoms or visible lesions.<sup>2</sup> Several factors affect transmission:

- Infection is more easily passed from male to female than from female to male individuals.<sup>2</sup>
- The impact of previous infection with the other viral type on a partner's susceptibility has not been clearly established. However, subsequent infections tend to be milder. The risk of infection remains high, and the overall average annual risk of disease acquisition is about 10% per year of exposure, regardless of previous HSV infection.<sup>2</sup>
- It is generally believed that there is little risk of reinfection when the partner has already been infected with the same viral type. Laboratory studies show that immunity to subsequent reinfection is present at the site of initial infection but can be overcome.<sup>2</sup>

The incubation period of HSV infection is 5–14 days and the average untreated episode lasts 22–28 days.<sup>1–3</sup> Fewer than 50% of those infected with HSV develop signs or symptoms during initial acquisition.<sup>1–3</sup>

The frequency and severity of recurrent episodes vary widely between patients and also vary in an individual over time.<sup>3</sup> Genital recurrences are the most common in individuals infected with HSV-2, particularly in the months immediately after the initial infection. On average, patients experience 0.34 recurrences per month, which is approximately four recurrences per year with HSV-2.<sup>3</sup> Recurrence is four times less frequent with HSV-1.<sup>3</sup> A significant proportion of patients suffer 12 or more episodes per year.<sup>3</sup> Recurrence rates typically decline over time, but this is variable.<sup>3</sup>

Transmission in pregnancy should be avoided where possible.<sup>3</sup> Transmission in the third trimester of pregnancy carries a significant risk of transmitting HSV to the neonate if vaginal delivery is attempted.<sup>3</sup> Mother-to-baby transmissions are rare, but because of the serious consequences of neonatal disease, expert advice should be sought in relation to all third-trimester acquisitions to reduce risk at delivery (which in these cases needs to be by caesarean section).<sup>2,3</sup> The risk of recurrent infections at term is small, and many guidelines now emphasize the relative safety of a conservative approach to delivery – even in the presence of a suspected genital HSV recurrence.<sup>2,3</sup>

Strong epidemiological data implicate HSV infection in either partner as facilitating both the transmission and acquisition of HIV.<sup>1–3</sup> The background prevalence of HIV worldwide varies proportionately with HSV-2 prevalence. It is estimated that HSV accounts for 30% of HIV, and that the presence of genital HSV doubles the risk of HIV acquisition.<sup>2</sup>

### Epidemiology

The prevalence of HSV infection worldwide is highly variable. Reports from Public Health England indicate that the incidence of genital herpes infection in the UK have been relatively stable in men and women since 2013, following a period of increasing incidence from 2007 to 2012.<sup>2</sup> Rates of HSV-2 in both Germany

and the USA are, however, declining. Because of the variability of symptoms, a significant proportion of those affected remain without a diagnosis, as only a minority present for clinical evaluation. Studies have shown that <30% of HSV-2-seropositive individuals are aware of their genital herpes, and 20% have no symptoms.<sup>1–3</sup>

### Clinical features

**Primary genital infection:** the 'first episode' of HSV infection is defined as the first presentation with symptoms and signs of infection. This could be at initial acquisition of HSV or some time after initial exposure.<sup>1–3</sup>

Initial erythematous papules form, followed by a characteristic eruption of herpetic vesicles.<sup>1–3</sup> At the time of clinical presentation, the vesicles have usually ruptured, and the resulting ulceration is the dominant feature.<sup>2,3</sup> (Figure 1) Herpetic ulcers are intensely painful; the typical appearance is a superficial ulcer with an erythematous outline and a greyish base.<sup>2,3</sup> Lesions tend to be bilateral and painful, with associated tender inguinal lymphadenitis.<sup>1–3</sup> Symptoms of primary genital herpes are usually severe; they are typically more severe in women and homosexual men, in whom larger areas of epithelium are often involved.<sup>2</sup> The most common systemic symptoms are headache, malaise and photophobia, which are reported in up to 10% of patients.<sup>2</sup>

Local complications, particularly candidal fungal infections and streptococcal bacterial superinfection, are common, typically presenting in the second week of lesion progression.<sup>2</sup> Severe external dysuria can lead to urinary retention in the absence of neurological involvement.<sup>2</sup> Extensive ulceration can occasionally result in labial and vaginal adhesions. Uncircumcised men can develop phimosis and paraphimosis. Up to 10% of patients develop lesions in distant sites, particularly the pharynx. Up to one-third of individuals with severe primary HSV have symptoms suggesting meningeal irritation, although few require hospitalization.<sup>2</sup> Autoinoculation to fingers and adjacent skin can occur in primary infection. Autoinoculation to damaged or inflamed skin is observed in both primary and recurrent disease.<sup>2</sup>

Rarer complications include autonomic nervous system dysfunction, which can present with difficulties with urination, constipation and altered sensation in the perineal, sacral and lower back areas. Transverse myelitis is another rare complication; in this, the symptoms of autonomic dysfunction are coupled with absent deep tendon reflexes and reduced strength in the legs.<sup>2</sup>

**Recurrent episode:** recurrent episodes occur when latent virus is reactivated, and are usually milder and of shorter duration (up to 8–12 days).<sup>1–3</sup> Women are affected more severely than men. Lesions appear in localized sites and are usually unilateral. Lymphadenopathy occurs in only 25% of people and is usually confined to the side affected by the lesions.<sup>1,2</sup> Dysuria is uncommon in recurrent episodes.

Many patients link the development of recurrence to specific triggers such as local trauma, menstruation or ultraviolet radiation.<sup>1,2</sup> About 50% of patients develop symptoms in the prodromal phase of the illness. These vary from mild tingling sensations in the areas affected by the eruption, to severe, shooting pains in the thigh, buttocks or groin.<sup>1,2</sup> Other prodromal

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