

# EPIDEMIOLOGY AND TRANSMISSION

## Epidemiology

### KEY POINTS

- As many as one in five adults have genital herpes due to HSV-2, most will have asymptomatic or unrecognised disease.
- Genital herpes due to HSV-1 (through oral to genital transmission) has also become common; HSV-1 is a frequent cause of primary genital herpes.
- The natural history of genital HSV-1 infection is towards significantly fewer clinically apparent recurrences and less subclinical shedding than HSV-2.

Genital herpes is an infection caused by the herpes simplex virus (HSV) and, for practical purposes, encompasses lesions on the genital area and nearby areas (i.e. buttocks, anal area and thighs). Genital herpes may be due to HSV-1 (the usual cause of orolabial herpes) or HSV-2 (more commonly associated with genital lesions). It is a very common infection that is often under-recognised, as a person may be asymptomatic or have only very minor symptoms.

### HSV-2

HSV-2 prevalence varies between countries, being higher in the USA than in Europe, Australia and New Zealand. It also varies depending on the demographics of the population being tested.<sup>2</sup> Consistent findings between countries are that HSV-2 seroprevalence increases with:

**Age:** The incidence of new infections is highest amongst young adults, but as infection is lifelong, overall prevalence increases with increasing age.<sup>2</sup> Participants in the Dunedin Multidisciplinary Health and Development cohort study provided serum for HSV-2 antibody status at the ages of 21, 26, 32 and 38. By the age of 38, 26.8% of women had been positive for HSV-2 compared to 17.3% for men, confirming a higher biological susceptibility to infection for women. The infection rate for women was highest at age 21–26 compared to 26–32 for men and then declined in both genders with age, consistent with decreasing infectivity of long-term prevalent infections.<sup>3</sup>

### HSV-1

HSV-1 seroprevalence studies cannot distinguish between oral and genital infection sites which makes it much more difficult to estimate the prevalence of genital HSV-1 infection. Clinical case data has limitations as well. That said, HSV-1 accounts for 35% of confirmed anogenital infections in Australia<sup>4</sup> and similarly a Waikato-wide study found 30–40% of anogenital isolates are due to HSV-1 each year.<sup>5</sup> In that study, HSV-1 accounted for 53% of positive isolates from under-25 year olds, 30% in the 25–35 year olds, and 26% from over-35 year olds. Likewise, an Auckland Sexual Health Clinic study in 2004 found most true primary (see Glossary of Terms **page 3**) episodes of genital herpes were HSV-1, whilst non-primary first episodes (see Glossary of Terms **page 3**) and recurrences were mostly HSV-2.<sup>6</sup>

Like HSV-2, HSV-1 seroprevalence increases with increasing age and tends to be more common in women.<sup>7</sup>

**Note:** Routine typing of isolates enhances a clinician's ability to give prognostic information and optimal clinical care. It is no longer accurate to assume that genital herpes is due to HSV-2 infection, as a substantial proportion of people will have HSV-1.<sup>8</sup> The natural history of genital HSV-1 infection is towards significantly fewer clinically apparent recurrences and much less subclinical shedding.<sup>9,10</sup> Also, prior HSV-1 infection does not alter the risk of acquisition of HSV-2, although it does lessen the symptoms; it is important for those diagnosed with HSV-1 genital herpes to understand that they remain at risk of HSV-2 infection.

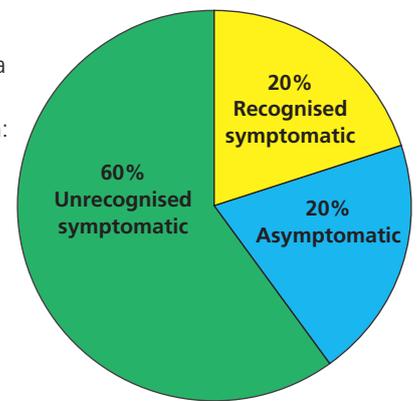


Figure 1: Prevalence, manifestations of genital herpes

# Transmission

## KEY POINTS

- Transmission occurs during skin-to-skin contact when virus is being shed.
- HSV-1 is commonly transmitted through oral to genital contact.
- HSV-2 is transmitted through genital to genital contact.
- Shedding of virus occurs during outbreaks and also when individuals are asymptomatic.

Most infections are acquired from someone who is unaware they are infected, who may have mild or asymptomatic infection.

Herpes simplex virus enters the body, either through a break in the skin or through mucous membranes, during direct contact with infected secretions or mucosal surfaces. For genital infections, this is usually during sexual contact, with HSV-2 commonly transmitted during vaginal or anal sex and HSV-1 commonly passed on through oral-genital sex.

Transmission is most likely to occur:

- During sexual contact.
- When the skin is broken.
- When there are lesions (e.g. vesicles or ulcers) present.
- From men to women.

Therefore, sexual contact should be avoided when active lesions are present.

Transmission may occur when a partner is shedding virus asymptotically. Most people who acquire genital herpes get it from someone who is unaware they are infected, who may have mild or asymptomatic infection.<sup>10</sup>

It is important to remember that not all first episodes of HSV-1 or HSV-2 represent a new or recently acquired infection. It may be a first clinically recognised episode of a previously unrecognised or asymptomatic infection acquired weeks, months or years previously.

The virus is readily inactivated at room temperature and by drying; hence, non-contact forms of spread, for example via fomites (inanimate objects) are considered unlikely. Autoinoculation resulting in spread to different anatomical sites can occur (e.g. orolabial, whitlow), although this is believed to be uncommon. **GRADE C**

## Asymptomatic viral shedding

Nearly everyone, both men and women, with genital HSV-2 infection sheds virus from time-to-time without symptoms, which is why sexual transmission can occur during asymptomatic periods. These intermittent episodes of asymptomatic viral shedding are more frequent:

- With genital HSV-2 than genital HSV-1 infection.
- During the first 12 months after acquiring HSV-2.
- In those with more frequent symptomatic episodes.
- Within a week before or after a symptomatic episode.
- In those with HIV infection.

The viral load threshold for transmission from an episode of asymptomatic shedding has not been established. For a given individual it is impossible to be certain when asymptomatic viral shedding occurs, but it is important not to give the impression that people are infectious all the time.

# Reducing Risk of Transmission

## KEY POINTS

- Consistent condom use reduces, but does not eliminate, the risk of transmission.
- Sexual contact should be avoided when oral or genital lesions are present.
- Suppressive oral antiviral treatment will significantly reduce, but not eliminate, the risk of transmission.
- Prior HSV-1 means HSV-2 infection is less likely to be symptomatic.

## Barrier methods

Male and female condoms do not give absolute protection for a variety of reasons: condoms do not cover all affected areas, condom breakage or slippage may occur, close genital contact or contact with infectious secretions may occur during foreplay, etc.<sup>11</sup> Nonetheless, consistent condom use offers moderate protection against HSV-2 infection in both men and women.<sup>12</sup> **GRADE B** Data on male condoms preventing transmission to men or on the efficacy of female condoms is lacking. Condom use should be discussed with the couple and tailored to the individual circumstances.

## Oral-genital contact

People who do not acquire HSV-1 during childhood are at risk of HSV-1 at any site, including genital infection, during adulthood. Transmission may occur whilst receiving oral sex from someone who has oral HSV-1, even if the source partner is asymptomatic. It is estimated that up to a third of persons who are HSV-1 antibody positive do not have a clinical diagnosis of oral herpes,<sup>13</sup> but will still shed HSV-1 virus.<sup>14</sup> It is generally accepted that prior orolabial HSV-1 infection protects an individual against genital HSV-1. Possible exceptions may be those infected simultaneously at more than one site or those with very recent HSV-1 infection who have not yet seroconverted. Oral HSV-2 in isolation is uncommon.

Oral-genital contact should be avoided when oral lesions are present. **GRADE C**

## Antivirals

Aciclovir, famciclovir and valaciclovir all suppress symptomatic and asymptomatic shedding, by up to 80–95%.<sup>15</sup> Also, it has been shown that suppressive once-daily valaciclovir results in reduced transmission to the discordant partner.<sup>16</sup> For partners, there was a 48% reduction in acquisition of HSV infection and a 75% reduction in clinical symptomatic genital herpes. Other antivirals may be similarly effective, but this has not been proven in clinical trials.

## Co-infection

In most studies, pre-existing HSV-1 infection does not decrease the risk of HSV-2 infection, but prior HSV-1 means HSV-2 infection is more likely to be asymptomatic. If HSV-2 genital infection is acquired first, then a new HSV-1 genital infection does not affect the frequency of recurrences.

## Diagnostic Tests

### KEY POINTS

- Suspected genital herpes should be confirmed by a nucleic acid amplification test (NAAT) e.g. PCR.
- PCR is the gold standard for diagnosis of active lesions.
- A negative result does not rule out HSV infection.
- Serology is not recommended (see [page 9](#)).

Clinical diagnosis alone is insensitive and inaccurate, with a 20% false positive rate.<sup>17</sup> **Suspected genital herpes must be confirmed by PCR.** Recurrent lesions, which have not been previously confirmed, likewise should be tested for HSV. However, it is important not to delay appropriate therapy while awaiting confirmation.

Detection of herpes simplex virus DNA by PCR in the lesion establishes the diagnosis. Vesicles offer the best source of virus. **However, results depend on multiple factors, including the adequacy of the specimen and the time delay between onset of symptoms and presentation, therefore a negative result may not exclude infection.**

## Sample collection

PCR has a low false positive rate. However, a negative test result does not necessarily exclude HSV infection since all methods are dependent on adequate collection of the specimen. Viral typing is routinely reported.

## Serology

**Serology is not recommended** for the following reasons:

- Serological tests detect antibodies to HSV in blood and indicate **past** infection.
- Serology is not accurate enough to be offered as a 'routine' test for HSV.
- Serology does not distinguish the anatomical site of infection (see Table 1 page 9).
- Seroconversion is highly variable. Following initial infection, some people seroconvert in 2–6 weeks, but may be longer (months). Also, some people do not seroconvert and reversal from seropositive to seronegative status may occur if there is minimal antigenic stimulation.

Situations where type-specific antibody might be helpful include:

- Herpes in pregnancy (see page 18). In a woman with no previous history of herpes, serology can be helpful to ascertain if it is a primary infection (with viremia, potentially, hence higher risk of transmission) or a recurrence (much lower risk).
- Discordant couples planning pregnancy (when the male partner has a history of herpes and the female doesn't). It can be helpful to ascertain if the female partner without a previous history of herpes has got antibodies or not, as it may be appropriate to counsel abstinence in the last weeks of pregnancy and/or for the male partner to take suppressive antiviral therapy.
- Recurrent or atypical genital symptoms with negative HSV results.

**For most partners of positive patients, education and not serology is recommended because of false positive/false negative serology results.**

**A positive HSV-2 serology result may cause significant psychological morbidity** (see page 13).

### KEY INFORMATION TO DISCUSS WITH A PATIENT WHO ASKS FOR A BLOOD TEST

- Explain that serology is not 'accurate' enough to be used as a 'herpes test' as there is reasonable risk of false negatives and false positives. It is not a helpful tool in assisting most patients.
- Some people take a long time to develop antibodies and some people don't develop antibodies at all.
- A blood test does not tell you the anatomical site of the infection.
- Discuss with a Sexual Health Specialist before ordering a test.

**Table 1: Interpreting Blood Test Results**

	HSV-2 Negative	HSV-2 Positive
HSV-1 Negative	No antibodies detected*; consider at risk of infection to both types.	No HSV-1 antibodies detected*; consider at risk of infection to HSV-1. HSV-2 antibodies imply prior infection. Probable genital HSV-2 infection because oral and other non-genital site infections are uncommon.
HSV-1 Positive	HSV-1 antibodies imply prior infection, but does not specify site of infection. No HSV-2 antibodies detected*; consider at risk of infection to HSV-2.	HSV-1 and HSV-2 antibodies imply prior infection with both. Probable genital HSV-2 infection, and oral HSV-1.

\* May be within window period, may not have seroconverted or may have seroreverted.