

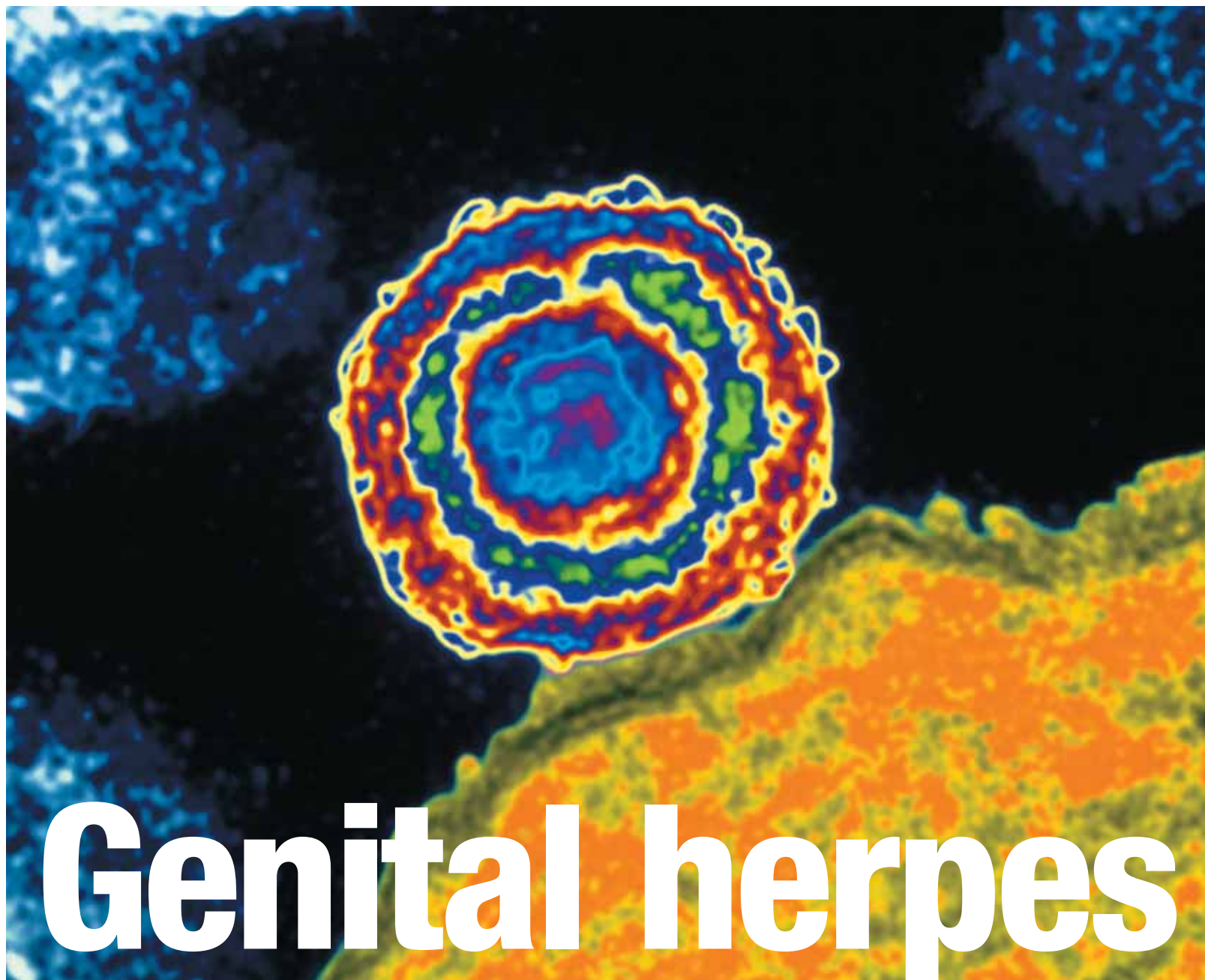
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Genital herpes

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The author



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Background

GENITAL herpes is a chronic lifelong infection. Its clinical course varies widely from person to person. Of the eight human herpes viruses, both herpes simplex 1 (HSV1) and herpes simplex 2 (HSV2) can establish latency in the neurons of the dorsal root ganglia and reactivate to cause genital herpes.

One of the most common sexually transmitted infections (STIs) worldwide, genital herpes infections are the most common cause of genital ulcer disease in Australia and among the most commonly managed STIs by Australian GPs.

Studies from overseas have indicated that genital herpes rates are rising, and the Australian experience reflects that of other developed countries. Between 1995 and 2004, the UK experienced a 16% increase in first presentations of genital herpes diagnosed. In the US, 40-60 million Americans are estimated to be living with genital herpes, with 1-2 million new infections annually.

In developing countries, HSV2 seroprevalence varies, depending on the country and the population studied, with epidemiological studies estimating prevalence rates of 20-80% in sub-Saharan Africa, 30-50% in Latin

America and 15-80% in South-East Asia.

In Australia, infection with either HSV1 or HSV2 is common; a nationwide seroprevalence study of more than 11,000 samples from Australian adults found seroprevalences of 76% for HSV1 and 12% for HSV2 (lower in men [8%] than women [16%]).

HSV2 rates vary among different populations; 61% of HIV-positive men attending a sexual health clinic in Melbourne were seropositive, while in Sydney 64.7% of heterosexual male sexual health clinic attendees were

seropositive. Similarly, rates of HSV2 seropositivity in women may vary from 14.5% in antenatal clinics to 58% in female prisoners.

While HSV2 has traditionally been associated with genital infection and HSV1 with orolabial infection, recent data have shown that the incidence of HSV1 in genital sites is increasing, particularly in younger patients. The decrease of orolabial exposure to HSV1 in childhood and subsequent increase in susceptible young adults at sexual debut, together with sexual behavioural changes, are theorised to be driving this shift.



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Transmission

FACTORS associated with HSV2 seropositivity include a history of STIs, low socioeconomic status, low level of education and being female (possibly due to a larger mucosal surface area potentially at risk). Behavioural risks include large numbers of sexual partners and early first coitus.

Infection occurs most commonly from direct skin-to-skin contact via infected secretions from oral, genital and anal mucosa. Most patients are unaware that transmission may occur in the absence of penetrative sex, with close genital-genital or oro-genital contact.

The virus multiplies at the epithelial layer at the site of inoculation, ascends along the sensory nerve root and establishes latency in the dorsal root ganglia. With reactivation, the virus descends the same pathway, resulting in either an outbreak or asymptomatic viral shedding, when the virus is detectable on the skin or mucosa without any clinical signs or symptoms (figure 1).

Individuals are most infectious when lesions are present because of the high levels of virus associated with the lesions. Despite this, about 70% of infections are transmitted during periods of asymptomatic viral shedding. HSV is inactivated at room temperature and by drying, hence fomite spread is rare.

Shedding occurs more commonly in people with HSV2 compared with those with HSV1, but rates vary in recurrent symptomatic infection, within the first year after infection and in those co-infected with HIV. Transmission between serodiscordant partners is more common in the first 3-6 months of the relationship and then estimated at 10% a year.

Prior HSV1 orolabial infection (cold sores) appears to protect individuals from HSV1 genital infections and reduce the severity of HSV2 genital infection. Similarly, an asymptomatic HSV2 orolabial infection may protect individuals from a genital HSV2 infection; however, the epidemiology of HSV2 orolabial infection in the absence of genital infection is unknown.

Other strategies for decreasing genital HSV transmission have been examined (table 1). Avoiding contact when the partner is symptomatic and decreasing the frequency of sexual activity lowers transmission risk. Use of male condoms for 25% of sex acts or more is significantly protective for HSV2 transmission to partners of infected men.

Knowledge of partners' HSV status has a protective effect. Breaches in mucous membranes may facilitate transmission of HSV, so treatment of concomitant STIs may decrease transmission risk. The effect of antiviral medication on transmission has been studied, with suppressive valacyclovir treatment shown to decrease asymptomatic viral shedding and frequency of outbreaks, significantly decreasing transmission to uninfected sexual partners.

Figure 1: HSV2 multiplies at the epithelial layer at the site of inoculation, ascends along the sensory nerve root and establishes latency in the dorsal root ganglia. With reactivation, the virus descends the same pathway, resulting in either an outbreak or asymptomatic viral shedding.

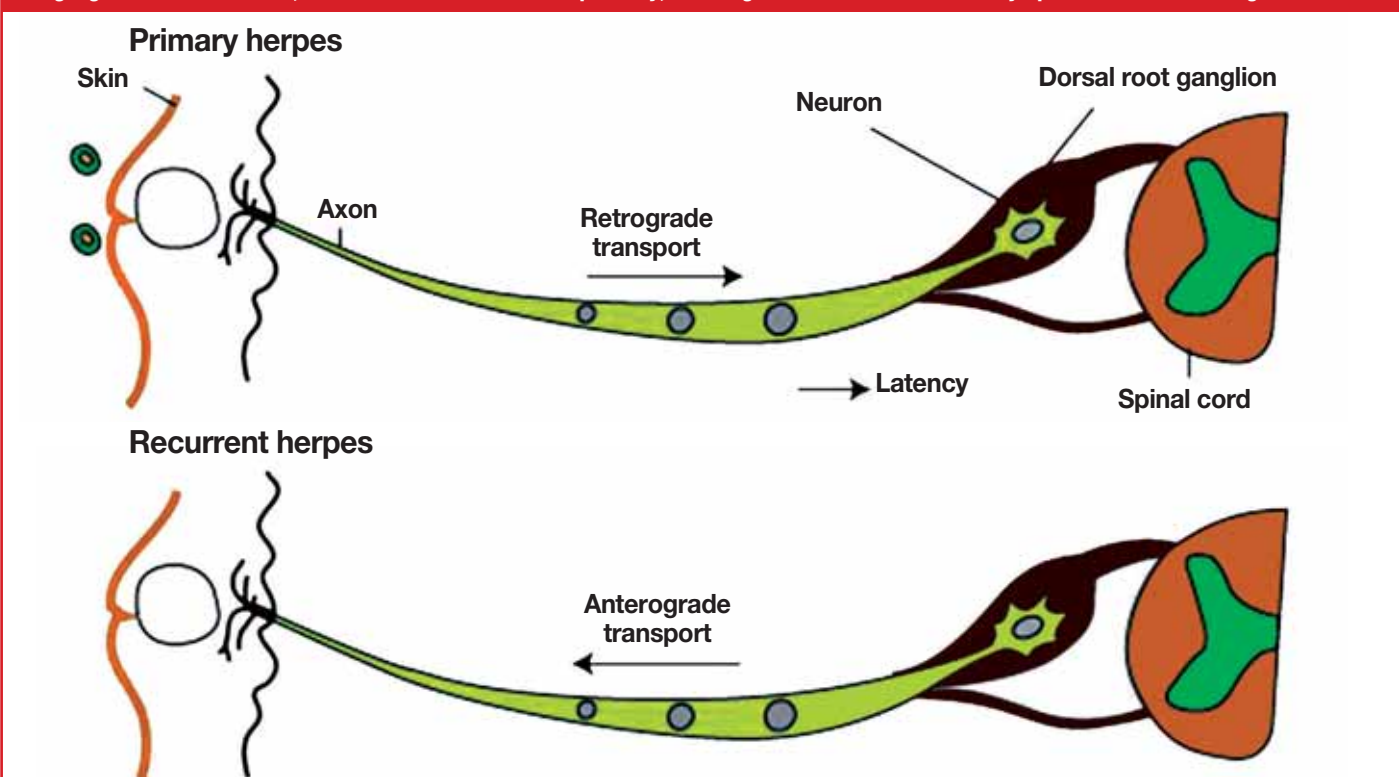


Table 1: Evidence-based medicine clinical recommendations

Intervention	Comment	Evidence
Preventing transmission: sexual partners		
Male condoms	Prevent transmission from infected men to sexual partners Prevent transmission from infected women to men	B D
Female condoms	No systematic reviews or RCTs	D
Antiviral treatment	Suppressive valacyclovir decreases clinical and subclinical viral shedding and reduces risk of transmission to uninfected sexual partner, compared with placebo	B
Preventing transmission: mother to neonate		
Caesarean section in women with lesions at delivery	C-section associated with significant maternal morbidity and mortality. Greatest risk to the neonate is new maternal infection in late pregnancy; risk is low in established maternal infection. Case studies show HSV2 neonatal transmission can occur despite C-section	D
Antiviral medication in late pregnancy (≥36/40 weeks) with history of genital herpes	Use may reduce rate of C-section. Studies not powered sufficiently, therefore limited information on adverse effects	D
Serological screening in late pregnancy	No systematic reviews or RCTs	D
Treatment in first episode		
Oral antiviral treatment with aciclovir	Decrease lesion duration, symptoms and viral shedding compared with placebo	A
Oral antiviral treatment with other agents	No difference in clinical outcomes compared with aciclovir	D
Reducing impact of recurrences		
Episodic therapy	All antiviral agents. Benefit was greatest if treatment was initiated within six hours of symptom onset	A
Suppressive therapy	All antiviral agents. All well tolerated	A

RCT = randomised controlled trial.

A. Beneficial. Effectiveness demonstrated in systematic reviews, RCTs or similar, and associated harm is minimal.

B. Likely to be beneficial. Effectiveness is less well established than 'A'.

C. Balance of benefit and harm. Where benefit should be weighed against harmful effect. Considered on an individual basis, based upon need and priority.

D. Unknown effectiveness. Insufficient or inadequate data.

E. Unlikely to be beneficial. Lack of effectiveness less well established than 'F'.

F. Likely to be ineffective or harmful. Ineffectiveness or associated harm has been clearly demonstrated.

Clinical spectrum — symptoms and signs

GENITAL HSV1 and HSV2 infections are clinically indistinguishable. Regardless of the HSV type, infection is mostly asymptomatic (20%) or unrecognised (60%). Only 20% of patients will experience 'classic' symptoms — erythema, clusters of clear fluid-filled vesicles and then ulceration (figure 2), which may be preceded by a prodrome characterised by up to 24 hours of tingling, burning or pain.

In recurrent herpes, viral titres peak in the first 24 hours, eliciting a vigorous immune response that curtails infection, resulting in resolution of lesions, which crust, re-epithelialise and

Only 20% of patients will experience 'classic' symptoms.

heal without scarring.

Symptoms associated with unrecognised infection include erythema, itch, burning and fissuring, and may often be confused with other genital conditions such as vulvovaginal candidiasis and candidal balanitis (figure 3, page 30). Differential diagnoses for genital herpes are listed in table 2 (page 30).

Most seroconversions are asymptomatic. When primary infection (no pre-existing antibodies to HSV1 or HSV2) does occur, it tends to be more severe and prolonged than either non-primary first-episode genital herpes (first infection in a patient with antibodies to

the other HSV type) or recurrent genital herpes (pre-existing antibodies) (see table 3, page 30).

Despite HSV1 and HSV2 presenting similarly, the behaviour of both may vary over time. Genital HSV1 is likely to be more severe during the initial episode and commonly be associated with a primary infection. The relatively less severe presentations associated with HSV2 may be due to higher rates of HSV1 infection in the community, thus tempering signs and symptoms of HSV2. Compared with HSV2 genital infection, asymptomatic shedding of

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Figure 2: Classical genital herpes vesicles and surrounding erythema.



from previous page

HSV1 is infrequent and recurrences are few, with most patients being recurrence free after 12 months.

For patients with recurring symptoms, clinical reactivations are more frequent within the first six months of infection and in the immunocompromised host. Lesions may be preceded by a prodrome; however, prodromal symptoms do not always result in lesions and vice versa. Most recurrences are spontaneous. However, they have been associated with factors such as stress, menstruation, fatigue, trauma, concurrent infection and sexual intercourse.

Recurrences at non-genital sites such as the buttocks and thighs occur as a result of viral reactivation within the distribution of the affected dermatome or from

Table 2: Differential diagnoses of genital herpes

Common
Candidiasis/thrush
Folliculitis
Trauma
Iatrogenic
Dermatitis
Scabies
Fixed drug reactions
Uncommon
Syphilis
Circinate balanitis (Reiter's syndrome)
Behçet's syndrome
Recurrent aphthous ulcers
Inflammatory bowel disease

autoinoculation at the time of a primary infection, before the development of protective antibodies (figure 4).

Table 3: Clinical features associated with primary infection or first episode vs recurrent genital herpes

Symptom or sign	Primary infection/ first episode	Recurrent infection
Pain	Moderate to severe	Mild
Lesions	Multiple	Single/few
Localised signs	Oedema and erythema common	Uncommon
Anatomical site	Extensive/bilateral	Localised/unilateral
Cervical involvement	Common; may present with watery haemosanguineous vaginal discharge	Rare
Systemic symptoms	Common, may include: ■ Fever ■ Malaise ■ Lethargy ■ Headache	Rare
Duration of lesions	Up to three weeks	5-10 days
Viral titres	High	Low
Complications	Uncommon, may include: ■ Urinary retention ■ Sacral radiculopathy ■ Secondary bacterial infection ■ Proctitis	Rare
Prodrome	Uncommon	Common

Figure 3: Genital herpes in the subcoronal region, with concurrent candidal balanitis.



Figure 4: Genital herpes recurrence located on the buttock.



Most recurrences are spontaneous. However, they have been associated with factors such as stress, menstruation, fatigue, trauma, concurrent infection and sexual intercourse.

Investigations and diagnosis

AS most patients have atypical symptoms, clinical diagnosis is unreliable and consequently genital herpes infections are largely underdiagnosed. In symptomatic infection, direct detection tests are preferred, as they are both site and symptom specific.

Patients with consistently negative swab tests or who are asymptomatic at the time of presentation may be offered type-specific serology to determine previous exposure, although site of infection cannot be confirmed.

With all patients a comprehensive sexual history, including history of cold sores, will add valuable information and aid the clinician in interpreting results and providing appropriate counselling.

Direct detection with HSV PCR has surpassed culture as the gold-standard test, offering prompt diagnosis and higher sensitivity, particularly for atypical and resolving lesions. When lesions are present, samples should be obtained by swabbing the ulcer base. This may involve breaking vesicles or gently removing forming crusts.

Despite a specificity of almost 100%, culture sensitivity is greatly dependent on specimen quality, transport and timing of specimen collection, as sensitivity declines quickly as lesions heal and viral load drops.

Other methods such as HSV immunofluorescence have quick turn-around time but low sensitivity (80%), as they rely on experienced laboratory staff and the presence of significant viral load. False-negative results may occur with all methods, and a negative test should not exclude genital herpes.

Serology

Increased public awareness, readily available resources such as the Internet and high patient acceptability have led to more patients requesting HSV serological testing. Western blot remains the gold standard because of its high sensitivity and specificity for HSV1 and HSV2, but is expensive and not widely available.

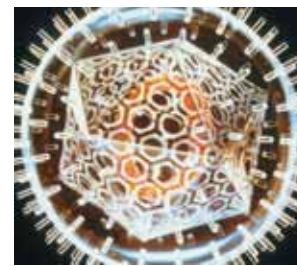
Other commercial serological tests are available, but only type-specific tests (which differentiate between HSV1 and HSV2) based on glycoprotein G have acceptable accuracy and are of diagnostic use. False-positive HSV2 results may occur because of cross-reactivity with HSV1 antibodies, and clinicians should be aware that the positive predictive value (a positive result being a true positive) will fall in low-prevalence populations. Seroconversion usually

Table 4: Most important concerns of patients with genital herpes at diagnosis*

Question	n	% of respondents
Does this mean the end of my love/sex life?	838	53
Is there a cure?	593	37
How easily can I give this to someone else?	577	36
How did I get this?	496	31
I can't tell anyone about this!	415	26
Is there treatment?	303	19
How can I reduce the number of outbreaks I have?	296	19
Will I still be able to have children?	266	17
Will I (or my partner) always have to use condoms?	251	16
How much physical discomfort/pain will the next outbreaks cause?	250	16
How long will I have it for?	158	10
What (other) symptoms will I experience?	113	7
How much will treatment cost?	58	4

23% (n=483) did not respond to this question. Of those who responded (n=1592), 96% (n=1521) chose three answers, 4% (n=57) gave two answers and <1% (n=14) gave only one answer.

*From a survey of 2075 patients from 78 countries.



Molecular model of the structure of HSV2.

occurs within 2-4 weeks of infection but may take 3-6 months. Using serology to distinguish between a new and recurrent infection may prove difficult after an HSV IgG response has been established, as recurrences may be associated with a transient HSV IgM response. Subsequent seroreversion, or false negatives, have also been known to occur in tests such as ELISA, which are based on titre readings.

Serological testing should be accompanied by counselling. Patients should be made aware of the test limitations and the possibility of false-positive and false-negative results. In the worried well, in whom treatment is inappropriate, a positive result may be of little value, as it will not determine the site of infection and may cause significant psychological distress.

Serological testing has several applications:

- In symptomatic patients with consistently negative swab results.
- Risk may be determined for asymptomatic patients whose partners have genital herpes.
- In pregnant women, serological testing may determine the risk to the mother and neonate.

Discussing the diagnosis

The nature of delivery of a new diagnosis can affect how well the patient adjusts. Patients may react differently — from shock and anger to resigned acceptance — and normalisation is essential.

Regardless of whether patients experience symptoms, social stigma and sexual labelling associated with STIs still exist. For a new diagnosis the clinician has two main responsibilities — to provide therapeutic management and to provide patient support and counselling.

Individuals require differing levels of education. Information on the natural history and management of genital herpes may offer hope to some. Harm minimisation may also be addressed, raising awareness of high-risk behaviours and strategies for decreasing transmission.

While basic information and education is essential, consultations need to be tailored to individuals' needs, addressing any particular concern that may be raised.

A global study of patients' 'main concerns' showed that >50% of people were worried that genital herpes would mean the end of their love/sex life, with >35% of people wanting to know if there was a cure and how easily herpes was transmitted (table 4).

Patients should be offered follow-up appointments or referred for counselling if required. Take-home resources or web site addresses may also be useful (see Online resources, page 32).

Management

MOST patients with established genital herpes infection do not require treatment, as recurrences are few, short and associated with minimal symptoms. For most, counselling, education and information are sufficient tools to manage mild outbreaks.

For others, antiviral medication may be indicated in early infection only, or at times recognised by the patient when recurrences are most likely or when outbreaks are particularly unwanted (table 1, page 29).

All patients presenting with first-episode genital herpes should receive oral antiviral treatment. Primary infection may be associated with significant morbidity and on occasion can be clinically indistinguishable from recurrent or first-episode non-primary infection. In the absence of positive tests, treatment should not be delayed for any patient with a high suspicion of genital herpes.

Although some patients may disagree, studies have found that topical treatments for genital herpes have little to no effect. For symptomatic patients, oral antiviral treatment is the standard of care. Three medications are available on the Australian market (table 5). All three nucleoside analogues are effective in treatment for primary, first-episode and recurrent outbreaks.

Treatment timing can be episodic (intermittent use from prodrome or lesion outset), aiming to improve symptoms and speed recovery, or continuous suppressive therapy to reduce recurrences. Maximal benefit with episodic therapy occurs with early treatment initiation to coincide with the highest viral replication and titre peak. Effective treatment is associated with reduced number of symptomatic lesions, associated pain and viral load.

Although episodic treatment is usually prescribed for five days, studies have shown that shorter courses of 1-3 days may be effective. Shorter treatment courses may be associated with convenience, better compliance and lower



Table 5. Antiviral medication for genital herpes*

	Primary infection or first-episode herpes	Recurrent infection	Suppressive treatment
Aciclovir	400mg tds 5-10 days	400mg tds for five days	200mg bd for six months or 400mg bd for six months**
Famciclovir	125mg bd 5-10 days [†]	1g oral, bd for one day or 125mg oral, bd for five days or 500mg oral, bd for seven days [†]	250mg bd for six months or 500mg oral, bd for six months [‡]
Valaciclovir	500mg bd for 5-10 days	500mg bd for three days	500mg daily for six months [¶] or 1g oral, daily for six months [§] or 500mg oral, bd for six months [‡]

*Source: *Antibiotic Guidelines*. July 2007.

**Consider in pregnancy; [†]Famciclovir is not available on the PBS for this indication;

[‡]Immunocompromised patients; [¶]Fewer than 10 recurrences a year; [§]More than 10 recurrences a year.

cost. In one study the efficacy of three-day treatment with oral valaciclovir 500mg bd was equivalent to that of standard five-day dosing, with the primary endpoint time to lesion healing.

Studies investigating two days of 800mg tds aciclovir demonstrated a significant decrease in healing time compared with placebo. Similarly, a single day of 1000mg bd famciclovir also demonstrated a significant decrease in healing time compared with placebo, although this was associated with higher rates of side effects. Both these strategies have yet to be trialled against standard therapy.

Suppressive treatment reduces recurrence frequency and rate of asymptomatic shedding and should be considered on an individual

basis. Although costly and requiring daily or twice-daily dosing, suppressive therapy may render patients largely symptom free, benefiting those with frequent severe recurrences or those having difficulty adjusting to their diagnosis.

Authority prescriptions for suppressive therapy previously required patients to have experienced more than six outbreaks a year. Now a diagnosis of 'moderate to severe recurrent genital herpes' together with microbiological confirmation is adequate. Patients should be reassessed after six months of suppressive treatment, with ongoing management as appropriate.

All three antiviral agents have a good safety profile and are well tolerated. There is more than 20 years' experience with aciclovir, the first

antiviral for genital herpes, licensed in 1983. Similarly its prodrug, valaciclovir, and famciclovir are rarely associated with side effects, which may include nausea, vomiting, headaches and diarrhoea. Resistance is rare, reported in <0.5% of immunocompetent patients and 5% in the immunocompromised patient.

Pregnancy

Neonatal herpes results from neonatal exposure to either HSV1 or HSV2, and is associated with significant morbidity and a mortality rate of up to 60%. Incidence in Australia is estimated at 3.2 per 100,000 live births, with the greatest risk occurring via direct exposure to virus at delivery, in maternal primary infection in the third trimester.

In new infection, when maternal antibody has yet to develop and provide protection to the neonate via transplacental transfer, infection results from direct exposure during delivery. Neonatal transmission is estimated at about 30-50% for mothers who seroconvert six weeks before delivery, compared with a risk of <3% if mothers seroconvert before 30-34 weeks' gestation.

In women with recurrent infection, the risk is estimated at <1% in all (<1-3% with active lesions at delivery; 0.02-3% with shedding at delivery). Transmission rarely occurs antepartum from virus ascending from maternal genital infection or in the event of maternal disseminated infection. In the postpartum period, transmission results uncommonly from direct exposure to adults or children with oral lesions or who are actively shedding.

Women with longstanding infection may deliver vaginally; however, some obstetricians may consider caesarean section if active lesions are present at the time of onset of labour. Oral therapy to prevent neonatal transmission should be considered in late diagnoses, when neonatal risk may be higher, or in some women with frequent severe recur-

rences. Serial antepartum genital screening does not predict infants' exposure risk and is not recommended.

Women with recurrent infection or who seroconvert before 30-34 weeks' gestation should be treated as clinically indicated. The possibility of caesarean section should be addressed in the event of clinical lesions at delivery. All three available antiviral agents are category B in pregnancy and there is extensive worldwide clinical experience with aciclovir, with few ill effects identified.

Specialist referral is appropriate for pregnant women with new presentations of genital herpes and in severe recurrent infections. Management for herpes in pregnancy should be discussed with the obstetrician and/or midwife or specialist sexual health service. Prompt and effective treatment is essential for infants at risk.

HIV

Depending on the level of immunosuppression, genital herpes may be clinically more aggressive in patients with HIV infection, presenting with prolonged, painful, atypical lesions, more frequent recurrences and higher rates of HSV shedding.

Research has shown a synergistic relationship between HIV and HSV2. As with other ulcerative conditions, genital herpes causes breaches in the skin and mucous membranes, which facilitates both the acquisition and transmission of HIV. HSV2 infection can double the risk of HIV acquisition during sexual activity.

Conversely, coinfection with HSV is associated with increased HIV infectiousness, particularly during herpes recurrences, when there is increased HIV shedding from lesions and genital mucosa. Research suggests that HSV2 infection increases HIV replication.

Some specialists recommend serological HSV testing in all HIV-positive patients, with a view to possible suppressive treatment, although this is not current standard of care.

Areas of research

DEVELOPMENT of HSV vaccines has led to cautious optimism in the medical and public health arena. The most promising prophylactic vaccine to date, currently in phase 3 trials worldwide, is the HSV2 glycoprotein D subunit vaccine.

In randomised clinical trials this vaccine was >70% effective in preventing serologically detected genital herpes and about 40% effective in preventing clinical infection, but

only in women who were negative for both HSV1 and HSV2. Research into therapeutic vaccines has been less successful, with no randomised clinical trials to date demonstrating promising results.

Microbicide studies have yielded disappointing results and there are none available that inhibit HSV, although many do inactivate the virus. In fact, facilitation of HSV infection may occur when micro-



Linear skin fissuring associated with candidiasis.

bicides cause trauma to epithelium, as in the case of nonoxynol-9.

There is ongoing research investigating currently available agents. Imiquimod 5%, an immune response modifier used for genital warts and skin neoplasm, has shown mixed results when used for genital herpes, mostly limited by associated side effects. Although of no benefit in the immunocompetent patient, case studies have

shown it may offer an alternative treatment in immunocompromised patients with aciclovir resistance.

Interestingly, studies of an investigational topical immune response modifier, resiquimod 0.01%, suggest that reactivation and lesion clearance time may be influenced.

Other topical methods have been evaluated, such as the topical application of honey. Although

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some minimal benefits were achieved, sample size was small and the inconvenience of honeyed genitals was not reported. The use of topical povidone-iodine (Betadine) was reported as useful in a recurrent episode.

The future

Genital herpes is an extremely common condition affecting millions worldwide, usually with few serious sequelae. Reassurance, normalisation and education remain foundations for patient care, with oral treatment

when appropriate.

The diagnosis of genital herpes has been dogged by stigma and shame. As public awareness and knowledge improves, treatment courses shorten and become increasingly simple, and patients are educated to manage their infections effectively, herpes may eventually be regarded as a simple chronic condition.

Indeed, with a vaccine on the horizon and new strategies to decrease both transmission and symptomatic illness, genital herpes may no longer continue to bear the scarlet letter it still does today.

Practice points

- It is estimated that 60% of patients with genital herpes have atypical symptoms, including erythema, itch, burning and fissuring.
- Although highest risk of transmission occurs with active lesions, up to 70% of transmission occurs with asymptomatic viral shedding.
- Direct detection tests, eg, genital swab for herpes PCR, are preferred, as they are both site and symptom specific.
- Patients should be made aware of the limits associated with type-specific serology (false results, positive predictive value).
- Treatment should be prompt and not delayed by pending results.
- When managed effectively, genital herpes need not impact on relationships and lifestyle.

Author's case studies

Jonno

JONNO, 26, presented for an STI screen. He gave a history of penile rash that lasted about a week and was currently resolving. He described it as initially itchy and red, although not sore. He had noticed some small blisters.

Jonno thought that he had 'jock itch' from wearing wet swimming trunks all day and had self-treated with his girlfriend's thrush cream. On further history, he had experienced a similar occurrence five months previously and had thought little of it. He had not had cold sores in the past and was otherwise well.

Examination was unremarkable. Tests for chlamydia were done and Jonno was advised to return if the 'rash' recurred.

Jonno returned to the clinic five weeks later very concerned about genital herpes. He had seen ads on TV and started trawling the Internet for information. He was convinced he had herpes and wanted confirmation. As he was asymptomatic, Jonno was given information and asked to return as soon as the rash represented.

He returned a few days later with penile blisters, erythema and localised genital discomfort. Examination findings were consistent with classic genital herpes, and a viral culture was taken. Jonno was treated immediately with antiviral medication and given further information and education regarding transmission, natural history and sensitivity of the viral culture. He declined counselling at this time.

Several weeks later, a negative swab result was returned and Jonno was asked to re-attend for testing if the blisters recurred. He re-attended four weeks later with similar symptoms and on this occasion a viral PCR swab test was taken. When he returned for his results it was discovered that the lab had performed a viral culture test instead.

It was now more than eight months since Jonno reported first experiencing genital symptoms, and more than three months since he



He gave a history of penile rash that lasted about a week and was currently resolving.

first attended the clinic. Given the recurrent nature of his symptoms and the distress he had experienced awaiting sequential testing, group-specific serology with a Western blot was ordered.

The result was negative for both HSV1 and HSV2. Jonno was advised to return for repeat HSV serology in three months' time (six months after first attending) and to attend for swabs if the symptoms recurred. The six-month test was again negative for both HSV1 and HSV2. He had actually seen his GP one month after the first blood test and the result was the same.

Jonno next attended the service several months later, with genital blisters identical to those of his previous presentations and an HSV PCR was performed. This result was HSV2 positive.

Comment

This case highlights the difficulty with testing despite the strength of Western blot serology. This was very distressing for the patient, who felt he was unable to pursue relationships and psychologically deal with this condition without a definitive diagnosis. Also, despite the recurrent nature of the infection, Jonno was reluctant to consider suppressive treatment if it meant jeopardising a possible site-specific definitive diagnosis.

Sandy

Sandy, 38, attended the clinic for advice regarding

HSV and pregnancy. She was at 32 weeks' gestation in her fourth pregnancy and gave a previous history of intrauterine growth retardation and preterm delivery. She had a new sexual partner of 10 months who had longstanding genital herpes and was prescribed episodic therapy by his GP.

Sandy explained that they had not had sex for months. She gave no history of genital herpes. Both vulval PCR swab and vulval culture taken several months before this initial consultation (for minor vulval discomfort) were negative.

Her partner, Sam, was seen by another doctor in the clinic and the history given differed to Sandy's. Sam stated he had first experienced genital blisters and had been diagnosed on genital swab with HSV2 only two weeks before his visit. His last sex with Sandy had been several days earlier, without condoms. He did not disclose that his partner was pregnant.

Sandy had serology performed and was found to be HSV1 positive and HSV2 negative via Western blot. Sam was started on suppressive valaciclovir to reduce the risk of HSV2 transmission. The couple were advised that ideally they should avoid sexual contact until delivery, but to use condoms if they did have sex. They were counselled as to the risks of neonatal infection and Sam was advised to remain on sup-

pressive treatment.

Given the likelihood of transmission, recommendations were made that antenatal clinic staff ask about vulval symptoms and take a vulval PCR swab if lesions or symptoms were present. Plans were made for caesarean section if lesions occurred or a positive vulval HSV PCR developed before rupture of membranes, or if lesions were present at the time of labour.

Appointments were made for Sandy to return to the clinic at 34 weeks' gestation for repeat serology; however, she did not attend her appointment. Follow-up phone calls were made to the patient without any response. She was finally contacted at 37 weeks' gestation and informed staff that she did not want any interventions and would be birthing naturally, outside of the health service.

Once again she was informed of the risk of neonatal herpes and encouraged to return to the clinic and, at the minimum, to inform those involved in her delivery. Sandy was unresponsive to these suggestions and has been lost to follow-up.

Comment

This case raises many issues. First, the risk of transmission to both Sandy and infant. Given the recent nature of Sam's infection, transmission risk is theoretically higher than that of a longstanding infection. We did not know whether Sandy had already been exposed, as the window period for the Western blot may extend to six months, and indeed, as the previous case highlighted, may be falsely negative.

Given the differing histories from both Sandy and Sam, staff were careful not to breach patient confidentiality while still maintaining optimal care and management. Duty of care to the neonate was difficult to determine, as Sandy chose to disengage with all services, making it difficult to assess her risk of infection and the subsequent risk to her child.

Acknowledgement

Thank you to the Chapter of Sexual Health Medicine for use of the images.

References and further reading

Available on request from julian.mcallan@reedbusiness.com.au

Online and other resources

For information for patients and doctors:

- Sexual Health Infoline: 1800 451 624 Mon-Fri 9 am-5.30 pm (free and confidential information and referral service [toll free call in NSW]).

For a list of resources for patients and doctors:

- Australian Herpes Management Forum (AHMF): www.ahmf.com.au
- International Herpes Management Forum (IHMF): www.ihmf.org

GP's contribution



DR MARG TAIT
Picnic Point, NSW

Case study

SARA, 22, had experienced pain, photophobia, watering and reduced vision of her left eye for four days. Chloromycetin drops prescribed by another GP had shown no improvement after two days.

Examination revealed several small vesicles and ulcers on the lower eyelid. The conjunctiva was inflamed and fluorescein staining demonstrated a corneal dendritic ulcer. Her visual acuity was 6/9.

Sara reported no previous history of ocular or orolabial herpes infections. However, she did volunteer that for the past week she had perineal pain, dysuria and inflammation, which she had thought was caused by monilia but which had not responded to topical clotrimazole.

Examination showed bilateral perineal oedema, erythema, vesicles and ulceration consistent with genital herpes. Swabs for HSV PCR were taken from the base of both a genital ulcer and an



Sara agreed to be reviewed in a few weeks when she would start her cervical cancer vaccination.

ulcer adjacent to the eye.

Management of the ocular herpes included aciclovir ointment five times daily for 14 days and referral to an ophthalmologist for further assessment. The genital infection was managed with salt baths and analgesia.

Written and verbal information, including web site addresses, were given regarding the diagnosis. Three days

later Sara returned for results, accompanied by her boyfriend, Ben. He gave no history of genital herpes or unexplained genital symptoms; however, he did have a history of cold sores, the most recent outbreak occurring 2-3 weeks previously.

Sara's ocular symptoms had improved and the perineal lesions were marginally better. HSV1 was demonstrated from

the genital swab. The ocular swab was negative, with a comment that the fluorescein stain on the swab may interfere with PCR.

After discussion, Sara was still struggling with the possible judgments and stigma associated with genital herpes. It was agreed that she would be reviewed in a few weeks for further discussion and her routine Pap smear, as well as to start her cervical cancer vaccination.

Questions for the author

Would Sara have derived any benefit if she had been given an oral antiviral agent (non-PBS) at the time of her presentation to me?

Yes, oral treatment is indicated in any new suspected herpes infection. Given the possibility of a concurrent eye and genital infection, it is possible that this is a primary infection or non-primary first episode, with Sara not having any protective antibodies to the HSV type.

In this instance, oral treatment is indicated because of

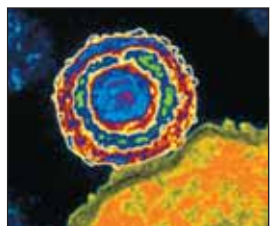
the possible increased severity and prolonged course associated with new infection. With genital lesions, Sara would have benefited from systemic oral therapy.

Would you do serological tests on the boyfriend to confirm that his cold sores were caused by HSV1?

No. With Ben's history of cold sores and Sara's HSV1 result, we can assume that Ben is also HSV1 positive. HSV1 is the most common cause of cold sores. Although HSV2 can infect the orolabial area, it is much less likely to be symptomatic. A detailed sexual history from both partners may reveal any further risk of STIs.

What advice would you give Sara and Ben regarding the use of condoms?

Given that they are both HSV1 infected, condoms are not necessary for prevention of HSV1 transmission. However, they will provide protection against other STIs.



How to Treat Quiz

Genital herpes — 7 December 2007

INSTRUCTIONS

Complete this quiz to earn 2 CPD points and/or 1 PDP point by marking the correct answer(s) with an X on this form. Fill in your contact details and return to us by fax or free post.

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ONLINE

www.australiandoctor.com.au/cpd/ for immediate feedback

- Damien, 23, presents with painful vesicles and areas of ulceration on his penile shaft below the glans. Which TWO statements suggest a diagnosis of genital herpes?**
 - a) Tingling, burning or pain noticed before the lesions appeared
 - b) Similar previous episodes
 - c) Evidence of scarring from previous ulceration
 - d) Penile discharge
- To determine whether Damien has primary or recurrent herpes, which TWO statements suggest a primary infection?**
 - a) Associated systemic symptoms such as fever, lethargy and malaise
 - b) A prodrome of tingling, burning or pain before the appearance of the lesions
 - c) Lesions lasting up to one week
 - d) Multiple and significantly painful lesions
- Regarding investigation of Damien's lesions which TWO statements are true?**
 - a) Lesions and associated symptoms are distinctive, making clinical diagnosis very reliable, and investigations are not necessary
 - b) Herpes simplex virus (HSV) PCR is the test of choice
 - c) Viral culture is the test of choice
 - d) Damien may require testing for other STIs

- Which TWO treatments may be offered to Damien if this was his first episode of genital herpes?**
 - a) Valaciclovir 500mg twice daily for 5-10 days, before the test results are available
 - b) Ganciclovir 200mg twice daily for 5-10 days if test results for HSV are positive
 - c) Famciclovir 400mg three times daily for 5-10 days if test results for HSV are positive
 - d) Aciclovir 400mg three times daily for 5-10 days, before the test results are available
- Damien returns the next day, having performed an Internet search, and requests HSV serology. You should advise which TWO of the following?**
 - a) Positive HSV IgG results are found as soon as vesicles are present
 - b) HSV serology is recommended in these circumstances
 - c) HSV serology may not reliably distinguish between a new or recurrent infection
 - d) It may be useful if other investigation results are negative
- Damien has further episodes of these lesions and he finds them painful, humiliating and interfering with his life. HSV is confirmed on PCR. Regarding therapy, which TWO statements are true?**
 - a) Damien may benefit from episodic treatment with oral antiviral medication

- He may benefit from continuous suppressive oral antiviral medication**
 - Intermittent episodic topical aciclovir has been proven to be useful for management of mild-moderate recurrent genital herpes**
 - HSV confirmation is not an essential requirement for PBS prescribing of suppressive antiviral medication in these circumstances**
- Regarding HSV infection, which TWO statements are true?**
 - a) Genital herpes is always caused by HSV2
 - b) Transmission occurs only with penetrative sex
 - c) Viral shedding may occur without any visible lesions
 - d) Previous perioral cold sores may reduce the severity of genital herpes
 - Jenny is planning a pregnancy. Her partner, Tim, gets recurrent genital herpes. Jenny can recall no such infection herself. Which TWO pieces of advice do you offer?**
 - a) Transmission between partners occurs within the first six months of a sexual relationship. After this period, if Jenny has not had a primary infection, we can be confident she has had previous exposure
 - b) Suppressive valaciclovir for Tim will reduce the risk of transmission of HSV to Jenny

- Condoms do not offer any protection against HSV**
 - Serology may be useful to establish whether Jenny is at risk**
- Jenny develops a primary episode of genital herpes during the third trimester of her pregnancy. You advise which TWO of the following?**
 - a) The baby is at significant risk of infection ascending from the mother's genital tract
 - b) Neonatal herpes has a very high mortality rate
 - c) If lesions are present at the time of delivery, caesarean section will be recommended
 - d) Antiviral medication is not recommended in pregnancy due to known harmful effects, including convulsions in the neonate
 - Regarding HIV and HSV, which TWO statements are true?**
 - a) HSV2 infection increases the risk of acquiring HIV infection
 - b) Because of the severity of HSV infection in HIV patients, all HIV patients should be advised to be vaccinated against HSV
 - c) Genital herpes may present atypically in HIV-positive patients
 - d) Antiretroviral medications used for HIV have significant interactions with the antiviral medications used for HSV, limiting their use

CONTACT DETAILS

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The mark required to obtain points is 80%. Please note that some questions have more than one correct answer. Your CPD activity will be updated on your RACGP records every January, April, July and October.

NEXT WEEK Air travel exposes about two billion passengers a year, as well as air crew and pilots, to a range of unique physiological stresses and health risks, particularly when they have pre-existing medical conditions. The next How to Treat, the last for 2007, climbs above the clouds for a bird's eye view of flying and health. The author is **Associate Professor Tony Hochberg**, adjunct associate professor in aviation medicine and occupational medicine at Edith Cowan University school of postgraduate medicine, Perth; tutor, in occupational medicine at Curtin University, Perth; and medical director of Prime Health Group.

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