Diagnosis and treatment of genital herpes

The majority of people who develop genital herpes remain asymptomatic and a general lack of understanding of the disease leads to unnecessary morbidity, write Gerard Sheehan and Anthony Ryan

**GENITAL HERPES REMAINS WORTHY OF ATTENTION** despite representing only 3% of all notifications to the National Disease Surveillance Centre. Evidence from new type specific antibody tests shows that herpes simplex type 2 is common and that only about a third of those infected are clinically diagnosed.

There are clear differences between physicians’ and patients’ perceptions about the impact of genital herpes. Some doctors may view genital herpes as a trivial, easy to manage disease while failing to address the psychological impact. Many patients view genital herpes as an entity with a considerable stigma and embarrassment and tend to be unaware of the impact of asymptomatic shedding.

Some patients and doctors are unaware that oral sex is a common route of transmission. Evidence suggests that most transmission occurs from asymptomatic shedding of the virus. The general lack of understanding hinders efforts to control the spread of genital herpes and leads to unnecessary morbidity.

Topical therapy has little clinical benefit and is not recommended, while chronic suppressive therapy has clear clinical efficacy but is underutilised and expensive.

Atypical presentations of genital herpes are common and may lead to misdiagnosis. These include epithelial abnormalities, such as fissures, furuncles, excoriations and non-specific vulval erythema in women, and a linear fissure of the prepuce and red spots on glans penis in men. Extra-genital lesions can occur on the buttocks, groin and thighs, and are commoner in women than men.

In the future, more widespread availability of type specific antibody tests may aid diagnosis. Perinatal transmission is exceedingly rare but is the most serious complication of genital herpes. Genetic herpes has also been shown to magnify HIV transmission.

**Natural history**

Most cases are caused by herpes simplex virus type 2 (HSV-2) but many are due to herpes simplex virus type 1 (HSV-1), the usual cause of orolabial herpes. The mode of infection is via contact with infected secretions on oral or genital mucosal surfaces. With initial infection, HSV ascends peripheral sensory nerves and enters sensory root ganglia where latency is established and thus lifelong infection.

Initial infection with either virus type is termed primary infection and results in either symptomatic infection around the site or asymptomatic and unrecognised disease. Primary infection is often symptomatically severe and characterised by widespread external and internal genital vesiculation, ulceration and crusting followed by an array of systemic and local symptoms and the patient is often febrile.

Pain, itching, dysuria, vaginal or urethral discharge and tender inguinal adenopathy are the predominant local symptoms. The entire episode may take up to six weeks without treatment and is often more prolonged and severe in women.

Complications may include aseptic meningitis and urinary retention requiring catheterisation. Antivirals dramatically shorten and diminish symptoms in primary genital herpes compared to the more modest benefit derived from antiviral treatment of recurrences.

In contrast to the long duration of the primary attack, recurrences commonly last only a week and are rarely accompanied by fever. Prodromal symptoms occur in 90% of cases and range from a mild tingling sensation to shooting pains in the buttocks, legs and hips. These can occur anything from one hour to several days prior to an episode.

In 20% of episodes, lesions do not follow prodromal symptoms. Viral reactivation and clinical recurrences occur in almost all patients who present with a clinically apparent episode of genital herpes. Recurrence frequency in the genital area is much greater for HSV-2 than HSV-1 disease and decreases with time. Women tend to have more severe recurrences.

**Clinical diagnosis**

Lesions of genital herpes are usually painful when touched and this clinical sign helps differentiate from syphilis. Both primary and recurrent HSV are accompanied by tender lymphadenopathy while non-tender nodes are more commonly seen with syphilis.

Diagnosis can be made on clinical grounds if the patient presents with the classical symptoms of recurrent painful genital vesicles progressing to superficial ulceration.

Direct questioning about sexual practices such as homosexual contacts and contacts with commercial sex workers may help differentiate genital herpes from rarer causes of genital ulcers such as syphilis and chancroid.

Behcets syndrome should be considered as a differential in those who have recurrent painful genital and oral ulcers, often accompanied by urethritis, colitis, uveitis or stroke. The syndrome is rare in Ireland but common in Asia, especially Turkey.

Laboratory confirmation of herpes infection should be
sought in patients with atypical features, or where an alternative cause is possible.

**Laboratory diagnosis**

Viral culture provides definite diagnosis and can be achieved in general practice. Negative tests can arise if vesicular fluid is not swabbed or if the sample is sent when the lesion is healing. Patients may need to be reassessed on a number of occasions in order to make a definitive diagnosis.

Type specific antibody testing is currently not routinely available but may become available in the future. It may have a role in specific situations such as confirming diagnosis in an asymptomatic partner, which would mean that the issue of transmission risk would be irrelevant. In the case of a pregnant woman with a partner with a history of genital herpes, information from type specific antibodies may help prevent primary infection in the crucial third trimester. Non-specific antibody testing by complement fixation is of no clinical value due to the commonness of HSV-1 in the community at large.

**Subclinical shedding of virus**

Much of the evidence concerning asymptomatic shedding comes from an article in the New England Journal of Medicine. They have equivalent efficacy in reducing duration of symptoms by one to two days when used in an episodic fashion. However, for antiviral therapy, as this has been shown to have a significant benefit in shortening the duration of symptoms.

Antivirals

All patients with primary infection should be considered for antiviral therapy, as this has been shown to have a significant benefit in shortening the duration of symptoms. Those who present within five days of the onset of an episode or who have lesions still forming should certainly have a course of one of the three available antiviral therapies (see Tables). They have equivalent efficacy in reducing the severity and duration of an episode. The doses recommended are based on clinical studies and appear in *The Sanford Guide To Antimicrobial Therapy* (31st Ed). 

A generic aciclovir is not available in Ireland but is available in the UK. Shorter courses of five to seven days duration of valaciclovir or aciclovir may be efficacious, but clinical studies have not been reported.

**Supportive measures**

Keep lesions dry and clean by washing two to three times daily. Some experts suggest drying the genital area with a hairdryer and using loosely fitting cotton underwear. Saline baths and topical anaesthetic agents can be used as an adjunct as well as appropriate analgesia.

**Counselling/prevention**

Despite an incubation period ranging from two days to three weeks, infection can be present without recognizable signs in themselves or their partners. Recent development of symptomatic vesicles does not necessarily imply infidelity. Direct questioning about oral sex and a history of cold sores in the partner may defuse a lot of unnecessary anxiety. Current partners may already have the virus without any symptoms.

People who develop actual obvious symptoms are only the tip of an iceberg, as the majority of cases remain asymptomatic. Reassurance should be given that there is no link with cervical cancer or infertility and that the tendency for attacks reduces with time.

One of the most difficult areas is discussing the diagnosis with future partners. Parallels with oral herpes (using the analogy of a cold sore on the genitals) may aid understanding, but they are by no means 100% effective due to the possibility of extragenital sites of viral shedding.

**Management of primary infection**

**Antivirals**

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<thead>
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<th>Treatment</th>
<th>Duration</th>
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<tbody>
<tr>
<td>Aciclovir 400mg tid for 10 days</td>
<td>200mg five times daily for 10 days</td>
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<tr>
<td>Famciclovir 250mg tid for 10 days</td>
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<tr>
<td>Valaciclovir 100mg bid for 10 days</td>
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**Management of recurrent genital herpes**

<table>
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<tr>
<th>Treatment</th>
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<tr>
<td>Aciclovir 400mg tid for 5 days</td>
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<tr>
<td>Famciclovir 125mg bid for 5 days</td>
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<tr>
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**Table 1**

**Table 2**

**Management of recurrent genital herpes**

Patients should be encouraged to return for follow-up appointments after their initial attack in order to avail of episodic antiviral treatment. A diary of recurrences may be useful to gauge whether chronic suppressive therapy is indicated.

Episodic treatment of genital herpes has been shown to be effective if started early in an attack and even then benefit is modest at best. If treatment is to be given, it should be oral and early, if even modest benefit is to occur. This may require the patient to have a back-up script or tablets at home.

Oral aciclovir, famciclovir and valaciclovir (see Tables 1 and 2) have all been shown to be beneficial in reducing symptoms by one to two days when used in an episodic fashion. We do not advocate the use of topical antivirals as they...
have little clinical benefit.12 The following table shows a cost analysis with recommended doses based on clinical evidence.8,9

**Indication for chronic suppression**

Chronic suppressive therapy is safe and effective but costly and under-utilised. It has been traditional practice to wait at least 12 months to observe the frequency of recurrences before initiating chronic suppressive therapy.

Most trials of suppressive therapy have been done in patients with a recurrence rate equivalent to or greater than six per annum. It is likely, however, that patients with a lower level of recurrence will also reduce their rate of recurrence.

It is our practice to commence chronic suppression if recurrences are having a substantial impact in terms of physical symptoms or psychological strain. Experience with suppressive therapy is most extensive with aciclovir where safety and resistance data now extend to over 11 years of continuous surveillance.

An option is to discontinue therapy after one year and reassess recurrence frequency. However indefinite therapy can be contemplated based on patients’ wishes. Short courses of suppressive therapy may be helpful for some patients in special circumstances (eg, exams). Chronic suppressive therapy is dispensed free of charge from STD clinics.

Chronic suppressive therapy may reduce asymptomatic shedding of genital herpes. In one study, 400mg of aciclovir twice daily was shown to reduce viral shedding in women.7 Whether this translates into a public health benefit, due to reduced transmission and a reduction in symptomatic cases, has yet to be demonstrated.

**Genital herpes in pregnancy**

This is a rare disorder which can result in severe neurological impairment or death (there are about 10 cases per year in the UK). Some 85% of cases of neonatal herpes result from perinatal transmission of the virus during vaginal delivery.

This may be a result of symptomatic or asymptomatic shedding of the virus in the genital tract. The risks are greatest if primary infection occurs in the third trimester and these women should be considered for caesarean section.

Women with primary infection in the first or second trimester should be considered for aciclovir. Current practice is to proceed to vaginal delivery unless lesions are present during labour.5 Women with recurrences during pregnancy should be reassured that these are usually brief and vaginal delivery is appropriate if no lesions are present at labour.7

**Key points**

- Genital HSV is under-diagnosed and frequently misdiagnosed
- Up to 50% of genital herpes cases are attributable to HSV-1 via oral sex
- Recurrences are commoner with HSV-2 compared to HSV-1
- All primary herpes cases should be offered oral therapy
- Topical preparations should be avoided due to lack of efficacy
- Lesions may occur on thighs and buttocks
- Patients should be informed that they may have recurrences and that the virus can be shed in the absence of symptoms.
- The main concern with pregnant women is acquisition of primary herpes in the third trimester.
- Once recurrences are causing significant morbidity, chronic suppressive therapy should be considered
- Genital herpes magnifies the transmission of HIV.

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**References**

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