

Guidelines for the Management of Genital Herpes in New Zealand

8th Edition – 2007

Produced by the Professional Advisory Board (PAB)
of the Viral Sexually Transmitted Infection Education Foundation

*Endorsed by the N.Z. Committee of the Royal Australian and
New Zealand College of Obstetrics and Gynaecology*

The Mission Statement of the NZHF

*To enhance the social context in which people with genital herpes live,
by facilitating support networks, promoting education programmes, and
the optimal management of genital herpes.*

The Objectives of the NZHF

*To provide support, current educational material and management options
in a caring, friendly, confidential environment for people with genital herpes.*

*To liaise with health professionals, providing a support network to assist in
the responsible management of genital herpes.*

*Ultimately, to improve the social context in which people with genital herpes
live their lives.*

For a list of the Professional Advisory Board (PAB) members,
refer to page 47.

About This Document

These guidelines have been produced by considering all the available literature and basing the recommendations on the available evidence, both local and international. The three levels of evidence used are:

GRADE A: Very strong evidence

Based on evidence from well designed, prospective, randomised, controlled clinical trials.

GRADE B: Fairly strong evidence

Based on evidence from case-control or cohort studies, or clinical trials lacking one or more of the above features.

GRADE C: Weak evidence or firmly held opinion

Based on evidence from published case reports, well written reviews or consensus.

Table of Contents

	Page
Key Points	3
Epidemiology	4
Transmission	5
Diagnostic Tests	7
Definitions of Clinical Episodes of Genital Herpes	10
Management of First Clinical Episode	10
Treatment Algorithms – Management of First Episode of Genital Herpes	14
– Management of Recurrent Episodes of Genital Herpes	15
Management of Recurrent Episodes of Genital Herpes	16
Management of Genital Herpes in Immunocompromised Individuals	21
Summary Statements Concerning the Treatment of Genital Herpes	21
Management of Genital Herpes in Pregnancy	22
Treatment Algorithms – Management of First Episode Genital Herpes in Pregnancy	24
– Management of Recurrent Genital Herpes in Pregnancy	25
Management of Pregnant Women with First Episode Genital Herpes	26
Management of Pregnant Women with Recurrent Genital Herpes	27
Use of Aciclovir in Pregnancy and Breastfeeding	28
Prematurity	28
Prevention of HSV in the Neonate	29
Neonatal HSV Infection	30
Transmission to the Fetus and Newborn	30
Disease Classification	31
Management of Neonatal HSV Infection	33
Management of Genital HSV Infection in Childhood	39
Key Issues in Counselling Management	40
Key Information to Give Patients in Counselling	42
References	44
Members of Professional Advisory Board	47
Index (Alphabetical)	48
International Resources	Inside Back Cover
Appendices	
Appendix I Clinical course of primary genital HSV infection	43
Appendix II Prevalence of HSV-2 antibodies in relation to the number of lifetime sexual partners	43

Key Points

Genital herpes is a common infection

- As many as 1 in 5 adults in New Zealand may have genital herpes due to HSV-2 and genital herpes due to HSV-1 is becoming more common.

Genital herpes is under-recognised and under-treated

- “Typical” signs of genital herpes are not very common; any recurring localised anogenital symptoms or lesions strongly suggest HSV-2 infection.
- Laboratory confirmation of the diagnosis is important but should not delay treatment. Typing is also important.
- Oral antiviral treatment of first clinical episodes should always be offered regardless of time of symptom onset.

Antiviral therapy of recurrent genital herpes may be suppressive or episodic

- Oral antiviral treatment is safe, effective and cheap.
Generic aciclovir 200mg x 25 tabs = \$2.50 ex manufacturer
Generic aciclovir 400mg x 56 tabs = \$8.40 ex manufacturer
- Many patients prefer suppressive antiviral therapy. It is particularly recommended for those with frequent and/or severe recurrences or associated psychosocial morbidity.
- For those choosing episodic antiviral therapy, it is more effective when patients start therapy themselves at the first signs of a recurrence. This needs anticipatory advice and prescribing.

Specialist advice should be sought about managing genital herpes in pregnancy

- Neonatal HSV infection is a rare but potentially fatal disease. Most neonatal HSV infections are acquired at birth, generally from mothers with an unrecognised genital herpes infection acquired during pregnancy.
- Specialist advice should be sought whenever a woman has a history of genital herpes during pregnancy, including active lesions at delivery, and especially in the high risk situation of a first episode of genital herpes within 6 weeks of delivery.

A diagnosis of genital herpes can have a profound effect.

Patients tell us they want –

- To be given accurate up-to-date information
- To be provided with the best treatment available
- To be involved in decisions about treatment and management
- To be referred for specialist care or advice when appropriate

The NZHF have a range of resources to assist patients and clinicians.

Phone: Herpes Helpline **0508 11 12 13**

Website: **www.herpes.org.nz**

Epidemiology

Genital herpes is an infection caused by the Herpes simplex virus (HSV) and, for practical purposes, encompasses lesions on the genitals and nearby areas (i.e. buttocks, anal area and thighs). There are 2 types of HSV: type 1 (HSV-1) and type 2 (HSV-2). Although the infections are essentially the same, type 2 is more commonly associated with genital lesions and type 1 is more often associated with oral lesions. However, HSV-1 can infect the genital area and HSV-2 can infect the oral cavity. Therefore, the clinical presentation (and management) of genital herpes may involve infections with either HSV-1 or HSV-2. Typing of the virus may not influence the clinical management of the disease process, but is of value in counselling. Clinically apparent reactivation of genital herpes occurs 5 to 8 times more frequently with HSV-2 than with HSV-1, and the ease of transmission and asymptomatic shedding also vary with virus type.^[1-3]

Epidemiological evidence of genital herpes infection and transmission is generally based on serological evidence of HSV-2. HSV-2 seroprevalence varies with:

- **Age:** with increasing age, increasing rates of adults are HSV-2 seropositive^[4], with the most rapid increase occurring in early adulthood. The Dunedin cohort study found an increasing HSV-2 seroprevalence of 3%, 11% and 18% at ages 21, 26 and 32 years respectively.^[5-7]
- **Sex:** women are more likely than men to be HSV-2 seropositive.^[4] In 2004-5, at age 32, women in the Dunedin cohort study had an HSV-2 seroprevalence of 22% whilst that in men was 15%.^[7] In 1999-2000, Australian women aged from 25 to over 75 years had an HSV-2 seroprevalence of 16%, twice that in men (8%).^[8]
- **Population:** HSV-2 prevalence varies between countries and seems to be higher in the USA than in Europe and Australia. It also varies depending on ethnicity, locale, etc, of the population being tested.^[4] In 1999-2000, HSV-2 seroprevalence in Australian adults aged from 25 to over 75 years was 12%.^[8] Not surprisingly, sexual health clinic patients tend to have higher rates; a New Zealand study found nearly 26% seropositivity for HSV-2 in 1991-92.^[9]

Although HSV-2 is the most common cause of genital infection, the proportion of genital HSV-1 has increased over recent years. In Australia, HSV-1 anogenital isolates increased from less than 10% in the early 1980s to around 35% in the early 2000s.^[10] In 2004, an Auckland Sexual Health Clinic study found most true primary episodes of genital herpes were HSV-1 whilst non-primary first episodes and recurrences were mostly HSV-2.^[11] Like HSV-2, HSV-1 seroprevalence increases with increasing age, tends to be more common in women and varies between countries.

In summary:

- As many as 1 in 5 adults may have genital herpes due to HSV-2 but most will have asymptomatic or unrecognised infection (figure 1).
- Genital herpes due to HSV-1 is becoming more common.

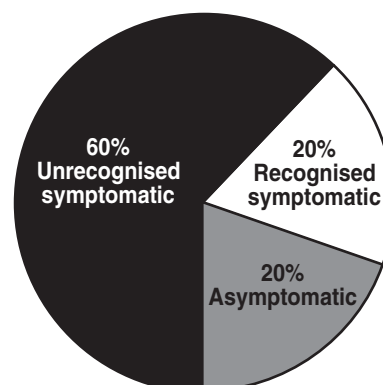


Figure 1: Prevalence, manifestations of genital herpes

Transmission

Genital herpes is transmitted through direct contact with an infected vesicle or ulcer or from a partner shedding virus asymptomatically, usually through sexual contact. Although not common, genital herpes can be spread by non-sexual contact (e.g. self-inoculation). The virus enters the body either through a break in the skin or through mucosal membranes. HSV-2 is usually transmitted during vaginal or anal sex. HSV-1 is usually 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.

However, approximately 75% of people who acquire genital herpes get it from someone who is unaware they are infected, who may have mild or asymptomatic infection.^[2]

It is important patients and their partners are not given the impression that there must be unfaithfulness within a stable relationship when herpes first manifests itself, as it is common for mild or asymptomatic infection to remain un-recognised. Further, if oral sex has occurred, or saliva used as a lubricant, the clinical episode may be due to HSV-1. Autoinoculation resulting in spread to different anatomical sites can occur (e.g. orolabial, whitlow), but it is not known how common this is.

Asymptomatic viral shedding

Nearly everyone, both men and women, with genital HSV-2 infection sheds virus at some time without symptoms. Asymptomatic viral shedding is detected on about 3% of days using viral culture and about 20% of days using PCR.^[12] This is why sexual transmission of HSV can occur during asymptomatic periods. Asymptomatic viral shedding is 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

For a given individual it is impossible to be certain when asymptomatic viral shedding occurs. It is important not to give the impression that people are infectious all the time.

Risk of transmission

Over a one-year period, 10% of people with genital herpes having sexual contact without the use of condoms may transmit the virus on to their partner even if they avoid sexual contact when symptomatic. This was shown by the following study:^[13]

144 couples were evaluated over a mean 334 days; they avoided sexual contact during visible genital herpes recurrences but did not use condoms.

Overall infection rate **nearly 10%**

Among 14 couples where transmission occurred, detailed information was available for 13 couples; 9 cases (70%) occurred when the infective partner was asymptomatic and 4 occurred during prodrome or within hours of the first lesion being observed.

From infected male to uninfected female **nearly 17%**
From infected female to uninfected male **nearly 4%**

So males transmit to females more readily than vice versa.

Acyclovir suppressive therapy reduces asymptomatic shedding by up to 95%.^[14] It has been shown that suppressive once daily valaciclovir resulted in reduced transmission to the discordant partner.^[15] 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. 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.^[16]

Barrier methods

Male and female latex condoms appear impermeable to HSV-2 but, in 'real-life', 100% condom usage is unlikely to give absolute protection; 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.^[17] Female condom use is less studied than male condom use. For male condoms, those reporting consistent condom use are significantly less likely to develop HSV-2 infection than those reporting less frequent condom use.^[18] **GRADE B**

Condom use in long-term monogamous relationships needs to be discussed and left to the individual couple's choice. Serological testing of partners can be of value for counselling couples in this situation. Where **both** partners have genital herpes, the value of using condoms is uncertain.

- Condom use needs to be assessed within the individual situation.
- Using condoms reduces, but does not eliminate, the risk of male to female and female to male transmission.
- Sexual contact should be avoided when lesions are present.

Transmission of herpes via oral sex

A UK study reports the seroprevalence for HSV-1 in 10-14 year olds has fallen over time.^[19] This may be one factor contributing to the increasing incidence of genital HSV-1 infection noted in many countries as people who do not acquire oral HSV-1 infection in childhood are at risk of genital HSV-1 infection as adults. This is most likely through receiving oral sex from someone who has oral HSV-1 infection, 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^[20] but will still shed HSV-1 virus.^[21] Oral HSV-2 isolation is uncommon. However, oral isolation of HSV-2 has been noted in HIV infection and in men who have sex with men, usually during a first episode of genital HSV-2 or during genital recurrence of HSV-2.^[22]

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.^[16] If HSV-2 genital infection is acquired first, then a new HSV-1 genital infection does not affect the frequency of recurrences.

Diagnostic Tests

Clinical diagnosis of genital herpes is insensitive and inaccurate, with a 20% false positive rate^[16] **Suspected genital herpes must be confirmed by appropriate laboratory tests.** Recurrent lesions, which may be atypical, likewise should be tested for HSV. **However, it is important not to delay appropriate therapy while awaiting confirmation.**

Detection of herpes *simplex* virus in the lesion establishes the diagnosis unambiguously. Viral detection may involve culture, HSV DNA or direct detection of antigen. Vesicles offer the best source of virus. However, as with all laboratory tests, results depend on multiple factors including the adequacy of the specimen. A negative result therefore may not exclude infection. If direct HSV tests are repeatedly negative and the symptoms are recurring, the patient should be advised to have type-specific herpes serology. **GRADE B**

Culture

Virus isolation in cell culture is sensitive and specific and in general is the test of choice. Herpes simplex virus grows readily in tissue culture although successful virus isolation is highly dependent on the stage of the clinical lesions, with an isolation rate of over 90% from vesicular or pustular lesions, 70% from ulcerative lesions but only 27% at the crusting stage.^[23] Prompt transport of the specimen to the laboratory is necessary. Positive results are usually reported within 2-5 days but occasionally may take longer so negative cultures are maintained for a further 5 days before reporting.

PCR

An experienced laboratory should undertake PCR. It is a rapid, highly sensitive and specific technique that avoids problems that may affect culture results such as inadequate quantity of specimen, bacterial contamination, and inadvertent inactivation of virus by sub-optimal handling and sample transport delays. Stringent quality control is necessary because of potential contamination by "carryover" DNA from other biological samples.^[24]

Direct immunofluorescence

Direct immunofluorescence testing for the viral antigen, present in the cells lining the base of the blister or the ulcerated lesion, is probably the least sensitive method for detecting genital HSV infection. Rapid diagnosis is possible but it requires operator expertise in obtaining an adequate specimen and a negative result should be interpreted with caution. **It is no longer recommended as a routine test.**

Serology

Serological tests detect antibodies to HSV in blood and indicate **past** infection. Type specific tests, based on glycoprotein G (gG) assays, detect antibodies to the type specific proteins gG-1 and gG-2 and so detect established infection with HSV-1 and HSV-2. Type specific tests are used in population surveys but their diagnostic reliability in individual patients is still debated. Seroconversion following initial infection is usually 2 to 6 weeks but may be as long as 6 months. Some do not seroconvert and, as with many other serological tests, reversal from seropositive to seronegative status may occur if there is minimal antigenic stimulation. **False negative and false positive results are common in low prevalence populations.** It is a useful test in some clinical situations but routine screening of asymptomatic individuals is currently not recommended. **GRADE B**

Situations where measurement of type-specific antibody might be helpful include:

- Recurrent or atypical genital symptoms with negative HSV cultures and/or PCR
- Confirming a clinical history of genital herpes in those without virological confirmation
- Management of herpes in pregnancy (*see page 22*)
- Where one partner in a relationship has symptomatic genital herpes; this may be important for a pregnant woman with a symptomatic male partner as primary genital herpes occurring days or even weeks before delivery confers a high risk of herpes infection of the baby. It may be appropriate to counsel abstinence in the last weeks of pregnancy for serologically discordant couples.

For patients with active lesions, direct viral detection by either culture or PCR, but not serology, is the recommended diagnostic method.

The person ordering serology should be able to supply appropriate pre- and post-test counselling. A positive HSV-2 serology result may cause significant psychological morbidity (*see page 12 & 13*).

Key information to discuss with a patient who asks for a blood test:

- **Explain** whether the test is for HSV-1 and HSV-2 antibodies or just HSV-2 antibodies.
- **If** the blood test being done only tests for HSV-2 antibodies a negative test does not rule out the possibility of the person having genital herpes caused by type 1.
- **Because** false negatives and false positives occur, the results have to be weighed together with the clinical presentation and patient's history.
- **Window period** for antibodies developing following infection is usually 2 to 6 weeks but may be up to 6 months.
- **Implications** for the presence of only HSV-1 antibodies need to be explained. HSV-1 is a common infection, usually acquired in childhood, and may be shed from the oropharynx by asymptomatic individuals. Infection with HSV-1 does not necessarily imply sexual exposure but genital infection with HSV-1 is increasingly common.

	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. Does not specify site of infection but genital infection is more likely with HSV-2.
HSV-1 positive	No HSV-2 antibodies detected*; consider at risk of infection to HSV-2. HSV-1 antibodies imply prior infection but does not specify site of infection. Genital HSV-1 infection is increasingly common.	HSV-1 and HSV-2 antibodies imply prior infection with both. Does not specify site of infection for HSV-1 but genital infection is more likely with HSV-2.

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

Sample collection

The following tests have 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 and, for culture in particular, on correct specimen handling and prompt transportation to the laboratory. It is important to be aware of locally available tests so that an appropriate sample is taken. **Viral typing should be requested routinely.**

Culture

1. Select appropriate swab (NZ dedicated viral transport swabs – ‘Virocult’® – are available. These are usually ‘green-topped’ and packaged with a sleeve containing a small amount of viral transport medium).
2. Swab the lesion firmly. The aim is to collect any vesicular fluid that may be present, and to collect virus-infected cells from the base of the lesion.
3. Insert swab in sleeve.
4. Place on e.g. melting ice or slika pad, and send chilled to the virus laboratory. The swab should ideally arrive the same day since some of this virus will decay with transport time.

PCR

1. Check with local laboratory if PCR is routinely available. If not, may need to specify “for herpes simplex DNA” and offer clinical explanation as to why this is the preferred test over culture e.g. CSF sample.
2. Swab as for viral culture
3. Transport time to the laboratory is less important than with culture.

Direct immunofluorescence

Scraping the lesion may cause discomfort; the procedure should be explained to the patient.

1. Clean the lesion of excess debris, e.g. mucus exudate.
2. Scrape the base of the vesicle, e.g. with flat side of scalpel blade, to obtain cells from base of lesion.
3. Spread cells on minimum of 3 distinct areas on slide (it may be necessary to repeat scraping of lesion base several times to obtain sufficient cells).
4. Air-dry and send to laboratory.

Definitions of Clinical Episodes of Genital Herpes

Primary infection: recently acquired infection with HSV-1 or HSV-2 with an absence of antibodies to either type on serological testing.

Non-primary infection: recently acquired infection with a virus type in the presence of antibodies to the other virus type; e.g. HSV-2 in a person with previous antibodies to HSV-1 but absence of antibodies to HSV-2 on serological testing.

First episode: the first clinical episode of genital HSV-1 or HSV-2. This may represent a primary HSV infection or a new non-primary infection or a recurrence of a previously asymptomatic infection. It is not possible to reliably distinguish between these on clinical grounds alone.

Recurrence: Previously acquired HSV-1 or HSV-2 infection with antibodies to the same type on serological testing.

Management of First Clinical Episode of Genital Herpes

The first clinical episode or manifestation of genital herpes may, but does not always, reflect recent infection. However, as first episode genital herpes is generally more severe and/or more prolonged, **treatment should always be offered regardless of time of symptom onset. Do not confuse the treatment of first episode genital herpes with the "72 hour" Herpes zoster rule.** Aciclovir prescriptions do not require specialist authorisation and the medication is available through any pharmacy. Patients are often very unwell and **therapy should be initiated regardless of how long the lesions have been present and before virological confirmation.** This is based on evidence that the virus is shed from the infected area for a median of 11 days, with systemic and local symptoms lasting 2 to 3 weeks if untreated (see Appendix I). Oral antiviral therapy substantially reduces the duration and intensity of symptoms.^[25,26] **GRADE A**

Management for patients presenting with a first episode of genital herpes should encompass the following:

1. History
2. Examination
3. Virus swab for culture or PCR for diagnosis
Consider screening for other STIs if appropriate, although this may be deferred to a follow-up visit, as it is often too painful.
4. Treatment involving:
 - Oral antiviral therapy
 - Symptomatic treatment
 - Education concerning transmission, epidemiology, etc; provide written material
 - Acknowledgement of the psychosocial impact of the infection
 - Referral to support systems – toll free Herpes Helpline **0508 11 12 13**
5. Appropriate follow-up arrangements.

It is not necessary or desirable to attempt to cover all these issues at the initial clinical assessment. However, recognition of the psychosocial impact of the diagnosis, and the provision of adequate information and/or referral to the Helpline, is important.

It may be helpful to discuss how results will be given e.g. in person, over the phone. If giving results over the phone, check the person is alone, or in an appropriate situation to receive the call.

History and examination

Symptoms may appear 2 to 20 days following infection with the virus. However, initial symptoms of genital herpes may not be recognised or may first occur months to years later. Symptom severity differs markedly between individuals with most severe cases having lesions lasting up to 3 weeks.

The prodrome (if experienced) is signalled by flu-like symptoms of fever, headache and general myalgia, accompanied by local tingling, irritation and/or pruritus or pain in the genital region. Rapidly, pruritic erythematous plaques appear followed by a cluster of small vesicles that contain clear to cloudy fluid. These vesicles rupture within 1 to 2 days to form painful, sloughy, shallow ulcers with irregular margins, which may become confluent. Small ulcerated areas may be surrounded by oedema and be extremely tender. The ulcers then dry to form crusts and later heal, leaving a transient red macule with minimal scarring (if any). Less commonly, lesions can pass through the blister phase quickly and blisters may not be noticed. Lesions may also appear extra-genitally, commonly on thighs and buttocks and rarely on hands, lips, face and breasts. Inguinal nodes are invariably enlarged and tender.

Pain on urination is typical, particularly in women. Acute urinary retention occasionally complicates vulvovaginal or anal HSV and should not be overlooked. Aseptic meningitis may accompany HSV infections.

Examination should include inspection of the genital region; speculum examination should be considered but may need to be delayed if discomfort is anticipated.

Diagnosis

Laboratory confirmation of the diagnosis is important but should not delay the initiation of treatment. A negative result does not necessarily exclude a diagnosis of HSV (see page 7).

Pharmacological treatment

If there is a possibility of pregnancy, please refer to page 22.

Refer immunocompromised patients, or those with herpetic proctitis, to an appropriate specialist e.g. infectious diseases, sexual health.

1. Oral antiviral treatment

The only available oral antiviral in New Zealand is aciclovir. Valaciclovir and famciclovir are no longer subsidised or marketed here.

Recommended treatment regimens for first episode genital herpes include:

- Oral aciclovir 200mg 5 times daily for 5 days (and a further 5 days is sometimes required)
- Oral aciclovir 400mg 3 times daily for 5 days (and a further 5 days is sometimes required)

Treatment should always be offered unless the lesions are clearly resolving. After commencing oral antiviral treatment the virus usually ceases replication within 72 hours. Lesions are not expected to completely heal over during the course of drug treatment and a further 5 day course of therapy is not required in most cases. The use of antivirals during the first episode does not alter the subsequent natural history of HSV recurrences.^[27]

2. Topical Antivirals

Topical acyclovir creams are less effective than oral acyclovir and are not recommended (*see page 20*). **GRADE B**

Symptomatic treatment

In addition to oral antivirals, other measures to control symptoms should be suggested. Bathing in salt water (e.g. half a cup of ordinary household salt in the bath or 2 teaspoons per litre of warm water for topical application) may help relieve pain and promote healing. Adequate pain relief should be provided. Paracetamol 4 hourly is usually adequate but stronger pain relief may be necessary. Drinking fluids hourly appears to reduce the incidence of urine retention and produces dilute urine that is less painful to void. Female patients can be advised to sit in a bath or bowl of warm water to pass urine. Catheterisation should be avoided; where necessary, a suprapubic catheter should be used. Advice about drying lesions with the lowest setting of a hair dryer may be helpful. Topical anaesthetic jelly such as lignocaine (xylocaine) gel applied 5 minutes before micturition helps relieve the pain. **GRADE C**

Education

It is important to ensure that patients receive accurate up-to-date information about genital herpes. NZHF resources are available to assist patients and clinicians with education and counselling. A range of printed materials can be ordered – please refer to resources listed on inside front cover – primary care practitioners should have access to these resources or be able to advise their patients on how to obtain them. Primary care practitioners should also be aware of the Herpes Helpline **0508 11 12 13**, a telephone service that is free to all New Zealanders.

Informing the patient of the diagnosis can be a delicate matter. A diagnosis of genital herpes can have a profound effect on patients.^[28] They may become upset and distressed; guilt, depression, lowered self-esteem and fear of rejection are common reactions.^[29] For some, extra-genital (including facial) herpes lesions may also have a considerable psychological impact. Although initial counselling can be provided at the first visit, it may be preferable at times to wait until the initial outbreak settles to discuss chronic aspects of the infection. Written materials, such as the NZHF Facts Book and the Partner's Book, should be offered to patients at the first visit with discussion and further questions encouraged at the follow-up and subsequent visits.

Counselling

Possible social and psychological issues should be acknowledged and addressed both at the first appointment and at follow-up. Topics that are helpful to discuss include how a diagnosis of genital herpes can be managed by a patient and their partner(s). The opportunity for the partner to have their questions answered should be offered as well. The NZHF toll free Helpline **0508 11 12 13** offers expert help in this area. The practitioner may choose to refer patients on to professional counselling, if this is available. Practice nurses or nurses who have training in this area may also be a good source of counselling support. Confidentiality and sensitivity are paramount. Patients need to agree to a third party becoming involved.

There are three main aspects or levels of counselling:

- Basic health counselling (which involves information concerning the disease process).
- Psychological impact of the infection on the patient and their relationships (particularly important in the long term).
- Support offered in the community (e.g. Helpline, support groups).

See Key Information to Give Patients in Counselling on page 42. GRADE C

Follow-up

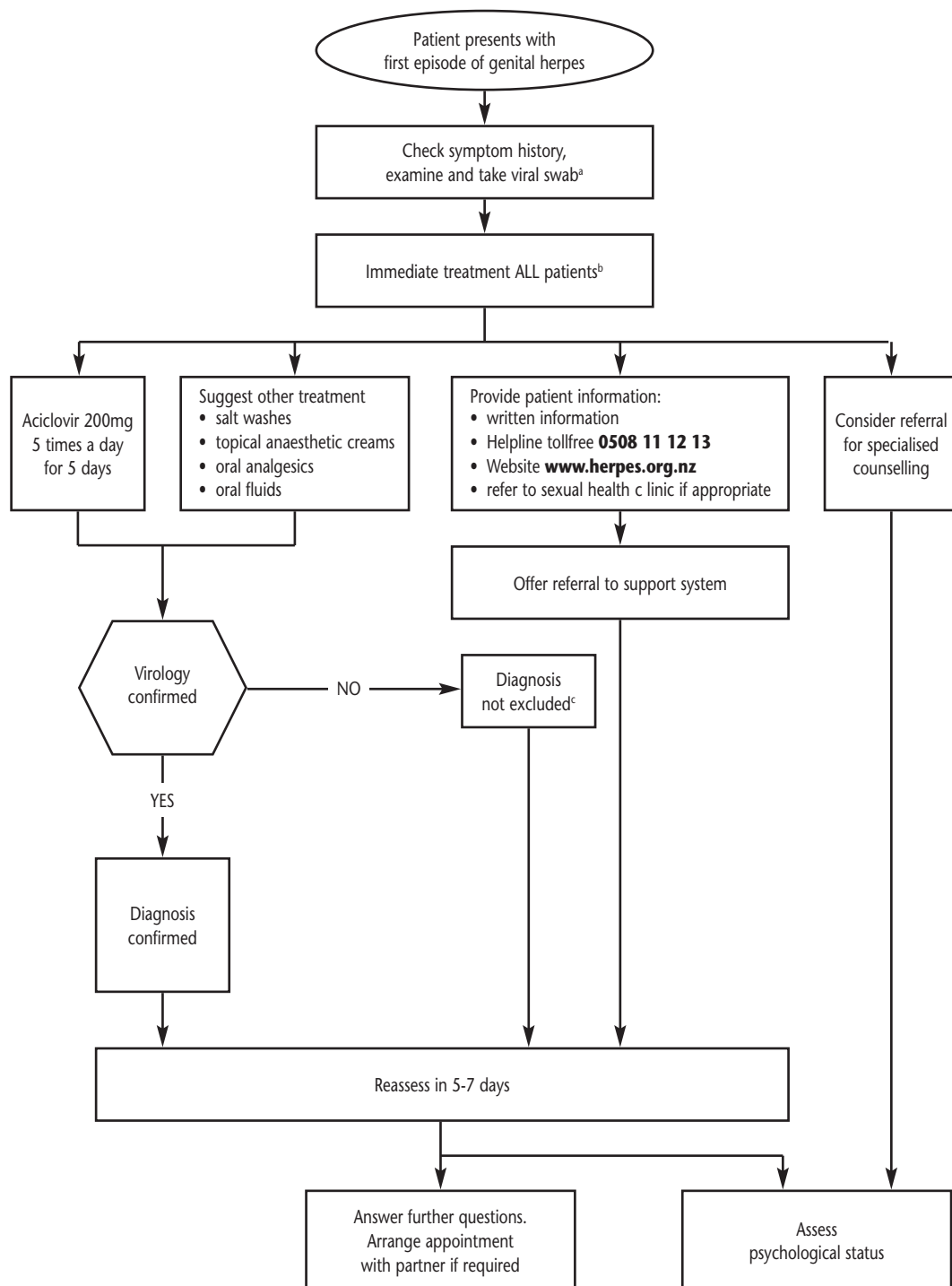
Follow-up is important for those with first episode herpes. At the initial visit, a follow-up appointment should be offered for 5 to 7 days later so as to evaluate symptoms, their psychological status, complete a full STI screen, if appropriate, discuss results, answer any questions they may have and, if necessary, prescribe a further 5 day course of treatment. It should be noted, however, that it might take longer than 5 days for the skin lesions to heal completely. A further 5 day course of therapy is not required in most cases. However, this option is available for severely affected patients.

For most patients, one visit is insufficient to properly manage the impact of genital herpes. Counselling and advice often form the major part of a follow-up appointment and time should be allowed for this. Practice nurses with counselling skills are a valuable resource for follow-up visits. Useful resources include the Herpes toll free Helpline **0508 11 12 13**, the herpes website **www.herpes.org.nz**, or local sexual health clinic for both management advice and/or referral. Discussing the role of support groups is often helpful; the patient should understand the reassurance that can be gained by discussions with people who have a similar problem.

The practitioner should be alert to the possibility of further psychological problems manifesting after a diagnosis of genital herpes.

Recommendations on counselling and follow-up are based on internationally accepted standards of practice. **GRADE C**

Management of First Episode of Genital Herpes

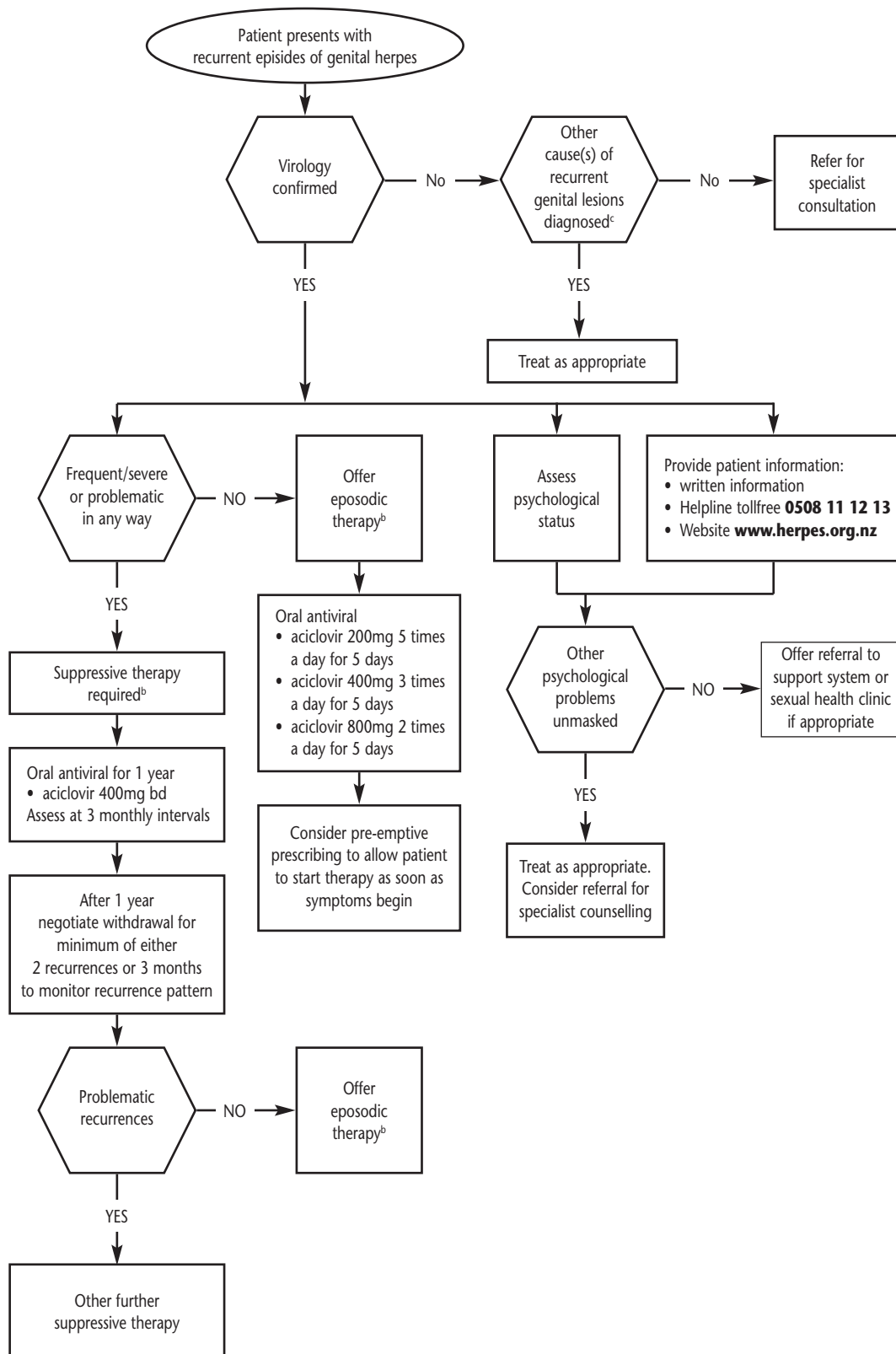


a In cases of immunocompromised patients or herpes proctitis, refer to specialist.

b Use in pregnancy requires specialist consultation.

c Recommend early presentation for viral swab if recurrence.

Management of Recurrent Episodes of Genital Herpes



Management of Recurrent Episodes of Genital Herpes

Management of recurrent herpes depends on whether there is virological confirmation of infection. In straightforward cases where the diagnosis is confirmed by laboratory testing, management by the primary care practitioner is preferable. However, in instances without virological confirmation or any other complicating factors, specialist consultation is recommended. **GRADE C**

Management of patients presenting with recurrent herpes should encompass the following:

1. History
2. Examination
3. Virus swab for culture or PCR for diagnosis; confirmation of diagnosis at least once is strongly recommended.

Consider exclusion of other STIs, if appropriate.

4. Treatment involving:
 - Consideration of oral antiviral therapy – either intermittent episodic therapy or suppressive therapy where appropriate
 - Symptomatic treatment
 - Education concerning transmission, epidemiology, etc; provide written material
 - Acknowledgement of the psychosocial impact of the infection
 - Referral to support systems – toll free Herpes Helpline **0508 11 12 13**
5. Appropriate follow-up arrangements.

Sufficient time should be allowed to address all these aspects. Shared management is important for the patient to feel a measure of control over the infection; the clinician should aim to be the facilitator of education and treatment options for the patient.

History, examination and diagnosis

Only 10–25% of persons who are HSV-2 seropositive report a diagnosis of genital herpes, which suggests that most have unrecognised symptomatic or completely asymptomatic infections.^[12] However, once told they are HSV-2 seropositive, more than 50% are able to identify clinically symptomatic recurrences that may have previously been thought to be due to other conditions.

In straight-forward cases, the clinical history is often the principle means of determining that the patient has a recurrent episode but other genital conditions, e.g. candida (thrush), may mimic and/or coexist with recurrent herpes, and careful examination of the genitalia should always form part of the diagnostic procedure. For example, recurrent ulceration may be due to aphthous ulcers, Stevens Johnson syndrome, fixed drug eruption, self-inflicted (sometimes unknowingly) trauma and autoimmune blistering disease (rare). Other infections may cause genital ulcers, not necessarily recurrent, e.g. other herpes viruses such as Herpes zoster virus, Epstein-Barr virus, primary syphilis and chancroid.

The atypical or non-ulcerative presentations of genital herpes can mimic most genital diseases, hence the need to consider more than one diagnosis at any given time. For example, lichen sclerosus results in increased skin fragility; because this condition is usually itchy, secondary scratching may cause superficial erosions and haemorrhagic bullae are not uncommon. Eczema and less commonly psoriasis complicated by scratching may cause superficial erosions. Herpes lesions may become secondarily infected with staphylococcus aureus and will give the appearance of a folliculitis, similar

to mild forms of hydradenitis suppurativa, primary folliculitis, or scabetic nodules. In most cases extra-genital lesions provide a useful clue to other pathology.

All these examples serve to underpin the importance of taking a detailed history and thorough physical examination of the whole skin, including oral mucosa. Atypical presentation is not unusual and HSV should be considered in any recurrent intermittent inflammatory genital lesions regardless of appearances. **Any recurring lesion of 1-2mm in size, occurring in the same genital area, is strongly suggestive of HSV-2 infection.**

All genital lesions not previously diagnosed should have a viral swab taken with an explanation to the patient why this has been done. **GRADE B**

It is desirable, but not always possible, to obtain virological confirmation. Typically, the viral load is reduced in recurrences compared with the first episode. There is a significant false-negative rate in the laboratory tests for HSV, although this is less for PCR. The best method of obtaining confirmation during a recurrence is to take a swab for culture or PCR within 24 hours of symptoms developing. **GRADE B**

An option is to instruct patients how to take a swab themselves and deliver direct to the laboratory. Other causes of recurrent genital lesions should be considered but in the event of continuing recurrent lesions and viral culture swabs remaining negative, PCR testing of lesions or type-specific herpes serology testing may aid diagnosis.

Education and counselling

It is important to ensure that patients receive accurate up-to-date information about genital herpes. NZHF resources are available to assist patients and clinicians with education and counselling. A range of printed materials can be ordered – please refer to resources listed on inside front cover – primary care practitioners should have access to these resources or be able to advise their patients on how to obtain them. Primary care practitioners should also be aware of the Herpes Helpline **0508 11 12 13**, a telephone service that is free to all New Zealanders. Written materials, such as the NZHF Facts Book and the Partner's Book, should be offered to patients with discussion and further questions encouraged at follow-up visits.

It is important to understand the impact that a diagnosis of genital herpes may have.^[29] Issues that should be raised with patients (and perhaps their partners) include:

- The effect of genital herpes on self esteem and self image
- How herpes will affect their current relationships
- How herpes will affect their ability to form new relationships
- The disclosure of their condition to partners or potential partners
- The lifelong nature of the condition and how this affects them
- Fears concerning transmission or the infectious nature of the infection
- Fears concerning future fertility
- Fears concerning cancer
- Fear of discovery
- Alterations in social activities and lifestyle
- Stress management
- Feelings of isolation
- The attitude of the general public towards this infection

For key information to give patients, see page 42.

People with genital herpes may manifest other psychological problems, for example, anxiety or depression or other psychological problems such as obsessive-compulsive disorders may be unmasked by a diagnosis of genital herpes. Specialist referral may be necessary for severe or complicated cases. In general, assisting the patient to take responsibility for, and control of, their infection and its treatment will help the patient overcome some of the psychological difficulties.

GRADE B

Recommendations on education and counselling and follow-up are based on internationally accepted standards of practice. **GRADE C**

Episodic antiviral therapy

The aim of episodic treatment is to reduce symptoms and duration of viral shedding during recurrences, rather than reduce the frequency of recurrences. Further, early therapy may abort episodes, that is, lesions may be prevented from progressing beyond the papular stage.^[30,31] In situations where patients have well recognised prodromes and/or have less frequent recurrences, some may find episodic treatment preferable to continuous suppressive therapy.

Effective episodic antiviral treatment of recurrent herpes requires initiation of therapy during the prodrome that precedes some outbreaks or within 1 day of lesion onset.^[30,31] Beyond this time frame, there is no clear benefit so it is important that a prescription is readily available. In consultation with the patient, sufficient quantities of medication may be prescribed with instructions to start treatment as soon as symptoms begin. Shorter courses of patient-initiated therapy, e.g. single-day famciclovir^[31] or two-days of acyclovir,^[32] have been shown to be as effective as a longer 5 day course. **GRADE A**

Recommended dosage regimen

If the patient is pregnant, specialist consultation is recommended (*see page 22*).

In cases of immunocompromised patients refer to appropriate specialist.

The only available oral antiviral in New Zealand is aciclovir; valaciclovir and famciclovir are no longer subsidised or marketed. Recommended aciclovir treatment regimen for intermittent episodes:

- Oral aciclovir 200mg 5 times daily for 5 days

Suppressive antiviral therapy

Suppressive therapy is an oral antiviral taken continuously over a given period of time that effectively reduces the frequency of recurrences.^[33,34] **GRADE A**

The main aims of suppressive therapy are:

- To empower the patient, giving them a measure of control over the infection.
- To allow the patient to have a break from experiencing recurrences of the infection.

Suppressive antiviral therapy is an effective strategy for improving the quality of life of patients with recurrent genital herpes.^[35,36]

Suppressive once daily valaciclovir resulted in reduced transmission to an uninfected partner;^[15] for partners in Corey's study, 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. Patients may wish to consider this as a useful adjunct to safe sex behaviour and the use of condoms for the prevention of genital herpes transmission.

Indications for suppressive therapy

Suppressive therapy should be considered in the following circumstances:

- Frequent and/or severe recurrences or associated psychosocial morbidity. Consider suppressive therapy in conjunction with other management. **GRADE B**
- For HSV-2 positive male partners of pregnant women (see page 29).

With long-term suppressive therapy it is strongly advisable to have virological confirmation of the diagnosis before commencing treatment. **Patients who do not have virological confirmation of recurrences or who have complications or severe problems relating to their herpes should see a specialist.**

Recommended dosage regimen

If the patient is pregnant, specialist consultation is required (*see page 22*).
In cases of immunocompromised patients refer to appropriate specialist.

The only available oral antiviral in New Zealand is aciclovir; valaciclovir and famciclovir are no longer subsidised or marketed. The recommended treatment regimen for suppressive therapy is:

- Oral aciclovir 400mg 2 times daily

The duration of therapy should be negotiated between the patient and the clinician; however, a treatment period of a year is recommended with periodic reassessment. 20-25% of patients will experience recurrent episodes whilst on suppressive therapy.^[34,37] Patients with ongoing genital symptoms while on suppressive therapy, even if these are suggestive of breakthrough recurrences, are advised to see a specialist. The usual recommended dose of aciclovir may need to be altered if breakthrough episodes are confirmed. Suppressive therapy does not alter the natural history of recurrences long term and it is common to have a recurrence soon after withdrawal of therapy. It is helpful to anticipate this and to provide sufficient medication to allow prompt self-initiated treatment of any early recurrences. **GRADE C**

Patients should be given a reasonable break from therapy to reassess their pattern of recurrence to determine whether it has reduced with time. It is suggested that either a minimum of 2 recurrences or approximately 3 months without suppressive therapy is necessary to establish the new pattern. At all times this process should be one of negotiation with the patient, as the pattern and severity of recurrent episodes is unpredictable.

Some patients may need to be on suppressive therapy for years. Aciclovir is well tolerated and safety and efficacy data are supportive of longer-term use.^[38] Neurotoxicity (lethargy, confusion, hallucinations and involuntary movements) has been reported in those with renal impairment.

Intermittent suppressive antiviral therapy

The use of intermittent suppressive therapy is also considered a point for negotiation with the patient. Practitioners should be aware that this type of therapy is an option, particularly for patients who are keen to avoid a recurrence during a specified period, e.g. a holiday, exams, honeymoon, etc. **GRADE C**

Topical antiviral therapy

Topical acyclovir creams may be helpful for mild recurrences in some patients^[39] but are less effective than oral acyclovir. Further, not all topical formulations are bioequivalent.^[40] Hence, use of topical treatment is not recommended. Topical antiviral creams are available over the counter but are no longer subsidised on the pharmaceutical schedule.

Newer topical agents such as immune modulators are currently in clinical trials.

Other therapies

Evidence for other therapies (oral L-lysine, aspirin, liquorice root cream, lemon balm, aloe vera cream, etc.) is limited and should be considered as such.^[27]

Management of Genital Herpes in Immunocompromised Individuals

Although rare in immunocompetent individuals, clinically refractory (large, severe and sometimes atypical) lesions due to genital HSV may occur in patients with severe immunodeficiency, including late stage HIV infection. Immunocompromised individuals need referral to specialist care.

Summary Statements Concerning the Treatment of Genital Herpes

- Oral aciclovir 200mg 5 times daily for 5 days is the recommended therapy for the first episode. A second course may be required in severe cases.
- Analgesia and topical anaesthetic jellies can be suggested if necessary
- Encourage intake of oral fluids.
- Patients should be advised to bathe herpetic lesions in salt water, and women be advised to urinate while seated in warm water to prevent pain.
- Effective episodic treatment of recurrent herpes requires prompt initiation of therapy during the prodrome or within 1 day of symptom onset. Sufficient quantities of medication may be prescribed with instructions to start treatment as soon as symptoms begin.
- Suppressive therapy should be considered for those with frequent and/or severe recurrences or associated psychosocial morbidity. Consider suppressive therapy in conjunction with other management.
- The recommended therapy for suppression of herpes recurrences is aciclovir 400mg twice daily. The recommended period of treatment is 12 months, with review at 3 month intervals. Repeat year-by-year, if necessary.
- Withdrawal of therapy should be for a sufficient length of time to establish whether the pattern of recurrence has changed, for example, a minimum of 2 recurrences or for 3 months.

Costs

Current brands of aciclovir are fully subsidised and cost:

aciclovir	200mg x 25 tabs = \$2.50	ex manufacturer
aciclovir	400mg x 56 tabs = \$8.40	ex manufacturer

MANAGEMENT OF GENITAL HERPES IN PREGNANCY

Neonatal herpes is a rare but potentially serious infection, which may be associated with significant morbidity and mortality. About 90% of neonatal herpes infections are acquired during labour through direct contact with infected genital secretions. In 5% of cases the infection is acquired in utero (either ascending infection or transplacentally) and in 5% of cases the infection is acquired post partum.^[41]

Intrauterine infection before the 20th week of pregnancy may be associated with miscarriage.^[42] Primary infection in the second and third trimesters may be associated with preterm delivery. Rarely, primary infection may result in disseminated infection of the fetus with skin lesions, chorioretinitis or microcephaly or hydrocephalus at birth.^[43] The long-term outlook for these infants is very poor. A minority with late intrauterine HSV infection will present at delivery with skin or eye lesions. The prognosis for successful anti-viral therapy in these infants is far better than that for newborns with more long-standing intrauterine infection.^[44]

Several factors influence the risk of a newborn acquiring HSV infection, the most important of which is whether the mother has newly acquired vs. recurrent genital infection.^[45,46] The greatest risk of perinatal transmission is when a previously seronegative woman has a primary first episode of genital herpes near or at the time of delivery. Under such circumstances the risk of neonatal HSV infection is 57%, while vertical transmission rates of 25% are found in those with a non-primary first episode (infection with one virus type in the presence of antibodies to the other virus type) near or at the time of delivery.

Key Practice Points

- Neonatal HSV infection is a rare, but potentially fatal, disease of babies occurring within the first 4 to 6 weeks of life.
- Most neonatal HSV infections are acquired at birth, generally from mothers with an unrecognised genital herpes infection acquired during pregnancy.
- Women with genital herpes lesions during their pregnancy should be referred to a specialist obstetrician +/- sexual health physician.
- Women with symptomatic genital herpes in pregnancy should be offered aciclovir and symptomatic treatment.
- The risk of maternal fetal transmission (MFT) is highest with primary genital herpes infection during labour or within 6 weeks of delivery. Caesarean section is indicated.
- The risk of MFT is low with recurrent lesions, even during labour. Recurrent lesions at term are a relative (not absolute) indication for caesarean section.
- Suppressive aciclovir from 36 weeks gestation may reduce the chance of a recurrence at term and hence the need for caesarean section. This should be used selectively rather than routinely.
- Specialist paediatric advice on management should be sought whenever a woman has a history of genital herpes during pregnancy, including active lesions at delivery, and especially in the high risk situation of a first episode within 6 weeks of delivery (see neonatal section)
- Pregnant women should be asked about a history of genital herpes and given information on the potential risks of transmission in pregnancy; this includes the risk of genital HSV-1 from oro-genital contact
- Pregnant women whose partners have a history of genital herpes should be given advice about avoiding transmission.

In contrast, the transmission rates are lowest for women who acquire herpes before pregnancy, with the risk being about 0.05% for such women who have no signs or symptoms of an outbreak at delivery.^[45,47] If lesions are present at delivery, there is a small but still significant risk of transmission of 0.25-3% with maternal antibodies passing through the placenta offering protection.^[46]

Women with HIV and HSV-2 co-infection have a greater risk of transmitting HSV-2 as HSV-2 shedding is increased in HIV co-infected women.^[48]

Of infants with proven HSV infection, 80% have no documented history of herpes infection in either the mother or her partner.^[49]

Mode of delivery

There are no randomised, controlled trials to guide optimal delivery management for pregnant women with genital herpes.

In a large prospective cohort study of women who had herpes cultures taken in labour, HSV was isolated in 202 women and, overall, neonatal transmission occurred in 10 (5%)^[46]. Caesarean delivery significantly reduced the HSV transmission rate among women from whom HSV was isolated (1 [1.2%] of 85 Caesarean vs 9 [7.7%] of 117 vaginal). Risk factors for neonatal HSV infection included first-episode infection, HSV-1 vs HSV-2 isolation at the time of labour, the use of invasive monitoring, premature delivery and young maternal age. None of the 140 women with viral shedding due to HSV-2 reactivation infected their babies compared to 2/11 women with HSV-1 reactivation. Of 26 first episode cases, transmission occurred in 8. There was a high caesarean section rate in those noted to have genital lesions in labour.

However, caesarean section is not completely protective, as transmission of infection has occurred occasionally in the presence of intact membranes. Prolonged contact with infected secretions may further reduce the benefits of abdominal delivery.^[43]

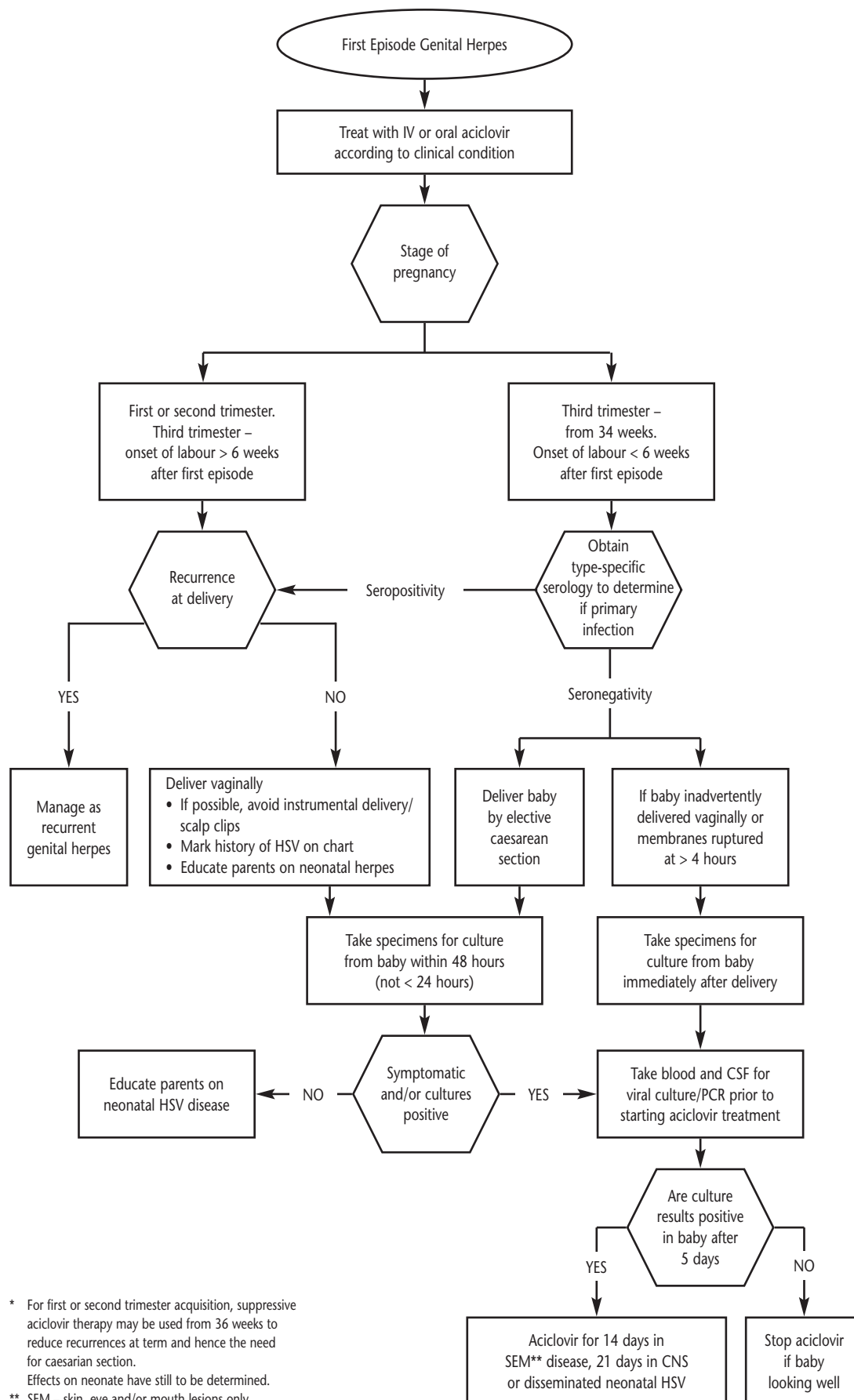
No definitive studies have been carried out on the relationship between the duration of rupture of membranes in the presence of clinical lesions and the transmission of HSV to the fetus. Previously, 4 hours has been suggested as a cut-off time beyond which caesarean section may be no longer beneficial. However, the ACOG guideline states that there is no evidence that there is a duration of premature rupture of membranes beyond which the fetus does not benefit from caesarean delivery.^[50]

Because the risk of maternal-fetal transmission is high when primary infection is acquired within 6 weeks of delivery, maternal and neonatal aciclovir therapy should be considered if there has been membrane rupture for more than 4 hours or where a vaginal delivery is unavoidable.^[51]

In the case of recurrent genital herpes, maternal antibodies are protective and it has been argued that the benefits of caesarean section are low in this group of women, even if lesions are present at the time of delivery. The USA policy has been to offer delivery by caesarean section if the woman has signs or symptoms of a recurrence at the onset of labour. In the Netherlands however, since 1987, it has been the policy not to offer women caesarean section in the presence of a recurrence at term and there has not been a resultant increase in the incidence of neonatal herpes (26 cases of neonatal herpes 1981-1986 compared to 19 cases 1987-1991).^[52] In other countries, guidelines recommend that women who have signs or symptoms of a recurrent infection in labour should be offered caesarean section but as a relative, rather than absolute, indication for abdominal delivery.^[53-55] It has also been shown that the presence of symptoms at delivery correlates relatively poorly with the detection of HSV from genital sites or lesions by culture or PCR.^[56]

continued on page 26

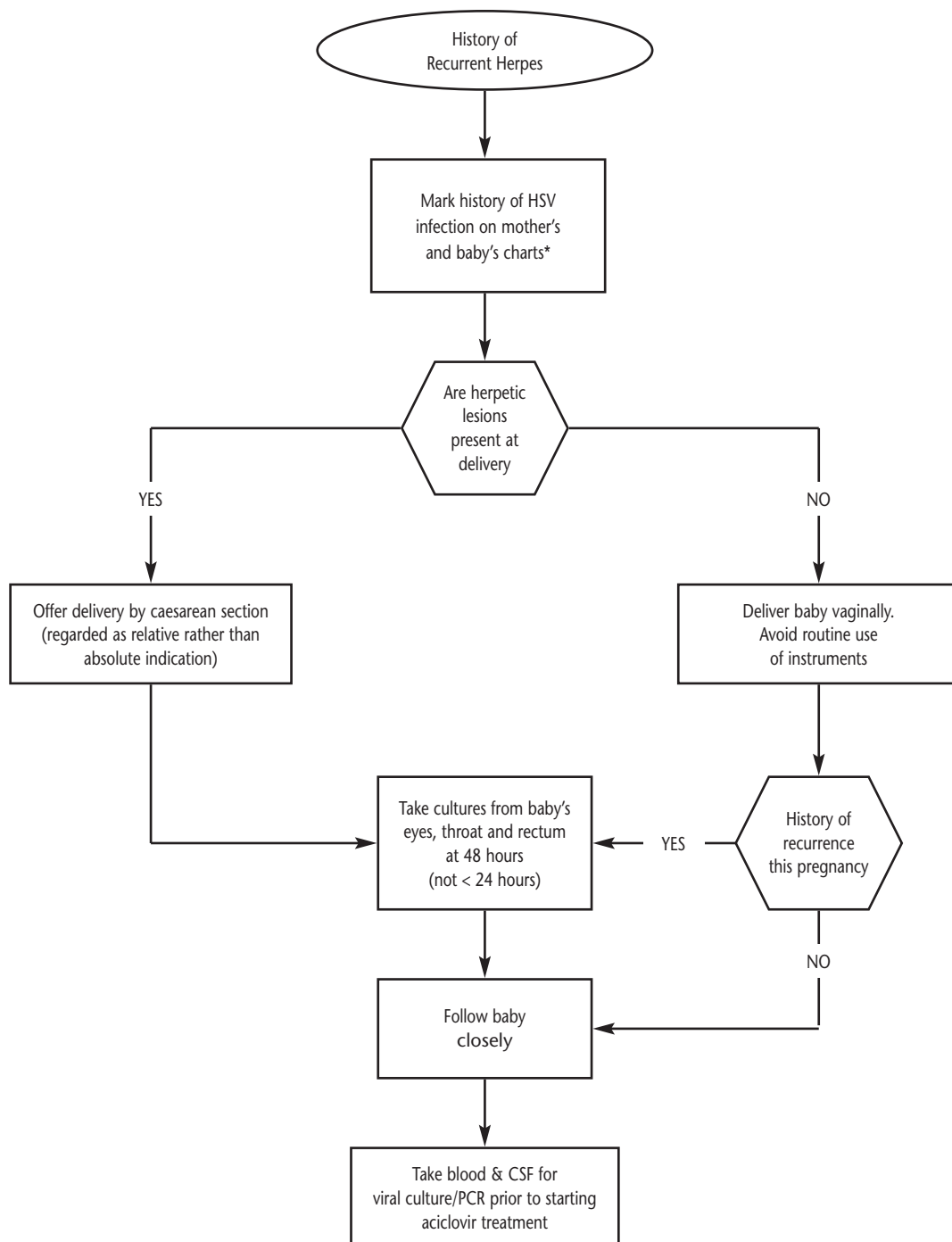
Management of First Episode Genital Herpes in Pregnancy (in consultation with a specialist)



* For first or second trimester acquisition, suppressive aciclovir therapy may be used from 36 weeks to reduce recurrences at term and hence the need for caesarian section. Effects on neonate have still to be determined.

** SEM – skin, eye and/or mouth lesions only.

Management of Recurrent Genital Herpes in Pregnancy (in consultation with a specialist)



* For women with recurrences during pregnancy, suppressive aciclovir therapy can be considered to reduce recurrence at term and hence the need for caesarean section. Effects on the neonate have still to be determined.

Use of prophylactic aciclovir

Small studies have shown that prophylactic use of aciclovir from 36 weeks decreases the number of clinical recurrences and reduces the need for caesarean section but treatment does not eliminate viral shedding completely.^[52,57-59] Two meta-analyses have confirmed that there is a reduction in clinical recurrences at delivery, a reduction in caesarean section for active herpes and a reduction in viral shedding.^[60,61] However, there are theoretical concerns that maternal aciclovir therapy may suppress the production of neutralising antibodies to the immunogen, glycoprotein D, thus having an effect on passive immunity to the fetus, and may suppress rather than treat newborn infections, thus leading to a delay in presentation of neonatal infection. **GRADE B**

In the absence of definitive data, it is recommended that prophylactic acyclovir from 36 weeks should be used selectively, rather than routinely offered, for women with a history of recurrent genital herpes until more information on the effects of aciclovir on the neonate is available.

Management of Pregnant Women with First Episode Genital Herpes

First and second trimester acquisition

Management of the woman should be in keeping with her clinical condition using aciclovir in standard doses as indicated (*see page 28*). **GRADE C**

Provided delivery does not ensue, the pregnancy should be managed expectantly and vaginal delivery anticipated. Continuous aciclovir in the last 4 weeks of pregnancy reduces the risk of both clinical recurrences at term and delivery by caesarean section. However, the effects on the neonate have not been fully evaluated.

For further management advice, 'management of recurrent genital herpes' on page 27.

Third trimester acquisition

Note: The first clinical episode may not be due to a primary infection, as previous infection may not have been recognised. Type specific culture or PCR and serological testing in conjunction with clinical evaluation will help identify primary HSV in pregnancy. All results should be discussed with an expert knowledgeable in interpreting these results and who is aware of the sensitivity and specificity of available testing methods. Consider treatment with aciclovir (*see page 28*).

Delivery should be by caesarean section, particularly in those women infected within 6 weeks of delivery because of high rates of asymptomatic shedding of HSV and insufficient time for a complete antibody response between infection and delivery. **GRADE B**

If vaginal delivery is unavoidable consider treatment of mother with aciclovir and request an urgent referral to a paediatrician experienced in HSV infection (see neonatal guidelines) **GRADE C**

Management of Pregnant Women with Recurrent Genital Herpes

Document the history in both mother's and infant's notes. Symptomatic recurrences during third trimester are usually brief and vaginal delivery is appropriate if no lesions are present at delivery.^[44] Prophylactic use of aciclovir from 36 weeks decreases the number of clinical recurrences and reduces the need for caesarean section but treatment does not eliminate viral shedding completely (*see page 26*) and should be used selectively rather than routinely. **GRADE B**

Sequential cultures in the third trimester to predict viral shedding at delivery are not indicated.^[62] Caesarean section should not be performed in women who do not have lesions at delivery.^[44] **GRADE B**

In women who have recurrent genital lesions at onset of labour:

- It is common practice to deliver by caesarean section because of the small risk of infection in the neonate.
- However, because the fetal risk is low, this must be set against the risks to the mother of caesarean section and this is therefore regarded as a relative rather than absolute indication for caesarean section.^[44] **GRADE C**
- Ideally, this scenario should be discussed with the woman early in pregnancy.
- Caesarean section does not itself provide total protection.^[63]
- If vaginal delivery occurs, scalp electrodes and instruments should not be used unless there is a clear obstetrical indication as skin trauma may increase the risk of transmission of HSV.
- Intrapartum aciclovir may be considered based on anecdotal evidence although there have been no trials to assess the value of such therapy.

Investigation and surveillance in the neonate

See "Management of Neonatal HSV Infection" on page 33.

Use of Aciclovir in Pregnancy and Breastfeeding

Data collected via the Aciclovir Pregnancy Register (1984-99) found the observed rates and types of birth defects for 1,234 pregnancies exposed to acyclovir did not differ significantly from those in the general population.^[64] Some studies on the use of valaciclovir (an aciclovir prodrug) from 36 weeks gestation have addressed toxicity issues and identified no safety concerns in mothers, fetuses or neonates.^[51,65] Monitoring in the neonates included assessment of white cell counts, renal and hepatic function. The studies were underpowered to confirm safety with certainty but the results, in conjunction with the lack of reported adverse events from other trials of prophylactic aciclovir and valaciclovir in late pregnancy, are reassuring.

While aciclovir is not licensed for use in pregnancy, there is substantial clinical evidence supporting its safety. Women who are inadvertently exposed to aciclovir in early pregnancy can be informed that the available information is reassuring and the use of aciclovir can be recommended where clinically indicated.

There are no established protocols for the use of aciclovir in pregnancy, but the following regimens are frequently used:

- **First episode:**

Aciclovir 200mg 5 times daily orally for 5 days.

- **First episode (severe infection) or in immunosuppressed:**

Aciclovir 5mg/kg IV (over 60 minutes) 8hourly until able to switch to oral therapy, based on symptoms.

- **Recurrent infection suppressive therapy:**

Aciclovir 400mg orally three or four times daily or 200mg 4 times daily (with more frequent dosing indicated because of increased clearance in pregnancy)

The American Academy of Pediatrics has approved use of aciclovir for treating first episode or recurrent genital herpes in breast-feeding mothers. Although concentrations are high in breast milk and the baby, toxicity is low.^[66] **GRADE B**

Prematurity

One study has shown expectant management of 29 women with preterm premature rupture of membranes at <31 weeks gestation, complicated by active recurrent genital herpes, was not associated with neonatal transmission. It was concluded that the risks of prematurity outweighed the risks of transmission of infection in the presence of a recurrent episode.^[67] The mean duration of membrane rupture was 13.2 days (range 1-35 days), 45% were delivered by caesarean section and 8% received antiviral therapy for control of symptoms. Little data is available on the management of preterm premature rupture of membranes in association with primary herpes simplex infection.

Prevention of HSV in the Neonate

All women should be asked at the first antenatal visit if they or their partner have had genital herpes. A study of 3192 pregnant women and their partners identified that 22% of women were at risk of HSV-1 or HSV-2.^[3] Of 582 women susceptible to HSV-1, 14 women or 2.5% (3.5% adjusted for length of gestation) acquired HSV-1; the only independent risk factor was a history of a partner with oral herpes. Of 125 women susceptible to HSV-2 infection, 17 or 14% (20% adjusted for length of gestation) acquired HSV-2 infection; the risk of becoming infected was 8 times greater in relationships of a year or less than for those in longer duration relationships. Most newly acquired infections were subclinical.

Although there is no clear evidence to support guidelines in the situation of the partner with a history of previous herpes infection, the following are recommended on theoretical grounds:

GRADE C

- Female partners of men with genital herpes should avoid sex when lesions are present.
- Conscientious use of condoms throughout pregnancy may prevent acquisition.
- Suppressive therapy should be considered in the male partner if the couple is discordant for antibodies to HSV-2.
- Pregnant women should be advised of the risk of acquisition of HSV-1 from oro-genital contact.
- Parents, staff and relatives/friends with active oral lesions should be advised about the risk of post-natal transmission.

Although routine serological screening in pregnancy has been recommended by some authors, universal screening is not likely to be cost effective because the number needed to treat to prevent a single case of neonatal herpes is high.^[68]

NEONATAL HSV INFECTION

Neonatal HSV infection rates vary from country to country with national surveys reporting a wide range in annual incidence. The number of cases per 100,000 live births in Western Europe (France 1.15, the United Kingdom 1.65, and the Netherlands 2.4)^[69-71] is lower than reported for Scandinavia (Sweden 6.5)^[72] and North America (the United States 4.0, and Canada 5.9).^[73,74] Marked differences in incidence can also exist within countries. For example, in the United States the incidence of neonatal HSV infection in Seattle is 31-48, in Atlanta 15-20 and in California less than 11 cases per 100,000 live births.^[46,75] While reliable New Zealand data are lacking, in Australia the incidence is estimated at 3.2 per 100,000 live births.^[76] These differences in rates may be explained, at least in part, by variations in HSV-1 and HSV-2 seroprevalence rates, which influence the risk of acquiring first episode genital infections during pregnancy.^[75,77] Other possible explanations include different sexual practices, maternal age, types of hospitals surveyed and neonatal and paediatric post-mortem rates. It is fortunate that neonatal HSV infection is a rare disease given the potential for exposure as, for example, 20-30% of the childbearing population in the United States is seropositive for HSV-2.^[78]

Key Practice Points for Lead Maternity Caregivers

- Neonatal HSV infection is a rare, but potentially fatal, disease of babies occurring within the first 4 to 6 weeks of life.
- Most neonatal HSV infections are acquired at birth, generally from mothers with an unrecognised genital herpes infection acquired during pregnancy.
- Any baby developing skin vesicles or atypical bullous, pustular skin lesions, particularly on the scalp or face (vaginal deliveries) or over the buttocks (breech presentation) must be referred immediately to a paediatrician.
- Specialist paediatric advice on management and anticipatory guidance should be sought whenever a woman has a history of genital herpes during pregnancy, including active lesions at delivery, and especially in the high risk situation of a first episode within 6 weeks of delivery.

Transmission to the Fetus and Newborn

HSV-1 and HSV-2 can be transmitted to the fetus or newborn infant at 1 of 3 times: intrauterine, perinatally and postnatally.^[79]

Intrauterine infection

Intrauterine infection causes approximately 5% of neonatal HSV infection. It results from either transplacental HSV transmission or an ascending HSV infection from the cervix.

Perinatal infection

The main risk of transmission to the neonate is at delivery where contact with HSV-infected secretions in the birth canal accounts for at least 85% of neonatal HSV infection.^[80] The site of entry is usually the eye, nasopharynx or an abrasion secondary to scalp electrodes or forceps. Roughly 60-80% of infants with neonatal HSV disease are born to women with unrecognised infection.^[49,80,81]

Several factors influence the risk of the newborn acquiring HSV infection, the most important of which is whether the mother has newly acquired or recurrent genital disease.^[45,46] The risk is greatest when a previously seronegative woman has a primary first episode of genital herpes near the time of delivery. Under such circumstances the risk of neonatal HSV infection is 57%, while vertical transmission rates of 25% are found in those with a non-primary first episode (infection with one virus type in the presence of antibodies to the other virus type). In contrast, the risk of neonatal transmission with recurrent HSV infection is just 2%.^[46] High maternal titres of type-specific neutralising antibody are associated with a substantially lower risk and severity of neonatal infection.^[46,81,82] Other risk factors include invasive obstetric procedures, such as fetal scalp electrodes, method of delivery, and prolonged rupture of membranes.^[46] Recent studies report an increasing proportion of genital and neonatal herpes infection from HSV-1 strains.^[74]

Postnatal infection

Postnatal infection accounts for approximately 10% of cases. Sources of postnatal HSV infection include maternal breast milk, skin and oral lesions, and HSV lesions on fathers, other family members and medical staff.

Disease Classification

Intrauterine HSV infection

This usually occurs after primary herpes infection in pregnancy. Transplacental transmission before the 20th week of pregnancy may cause spontaneous abortion in as many as 25% of cases. In contrast to neonatal herpes infection, the signs of intrauterine HSV infection are present at delivery and may include intrauterine growth retardation, hydranencephaly, chorioretinitis and skin scarring. The long-term outlook for these infants is very poor. A minority with intrauterine HSV infection will present at delivery with skin or eye lesions. There is frequently a history of prolonged rupture of membranes, often as long as 2 weeks. The prognosis for successful anti-viral therapy in these infants is far better than that for newborns with more long-standing intrauterine infection and complications such as hydranencephaly.^[44]

Neonatal HSV infection

The usual age for onset of symptoms in neonatal HSV infection is between 5 and 21 days of life, but there may be a delay in presentation if the significance of the symptoms is not initially recognised. Physicians caring for sick infants in the first 6 weeks of life should always be aware that neonatal HSV infection remains a possibility, even when no parental history of herpes infection is given.^[74]

Presenting symptoms of neonatal HSV infection include fever, lethargy, seizures and respiratory distress.

Vesicles may be present in only 40% at presentation and some infants will have no vesicles at any time during the course of their illness.^[49,83] Mortality is highest in those with an altered conscious state, seizures, disseminated intravascular coagulation, and if born preterm.^[44,63]

The following is a classification of neonatal HSV infection:^[44,63,79,84,85]

Type (% of total)	Mortality		Mean age at presentation	Normal outcome	
	Untreated	Treated		Untreated	Treated
SEM (45%)	< 1% (70% progress)	0%	10-11 days	62%	98%
CNS (30%)	50%	6%	16-19 days	33%	31%
DIS (25%)	90%	30%	9-11 days	50%	83%

SEM = Skin, Eyes and/or mouth, CNS = Central Nervous System, DIS = Disseminated

Disseminated disease

Disseminated disease develops in about one-quarter of neonates with HSV infection. It is more common in preterm infants and carries the worst prognosis. Symptoms generally develop in the first 14 days of life and the liver is the most commonly involved organ from primary viraemia. Multiple organs are seeded by a secondary viraemia, particularly the lung and adrenal glands. Focal embolisation of the brain may occur late in the illness. Clinical findings include a sepsis-like presentation with respiratory distress, haemodynamic instability, jaundice, hepatomegaly, elevated liver enzymes, bleeding with associated coagulopathy, and seizures with signs of meningitis or encephalitis. Vesicular skin lesions may not be present. Mortality in untreated patients is approximately 90% and many untreated survivors are severely impaired.

Central nervous system (CNS) disease

Almost one-third of neonates with HSV infection will have only encephalitis. It is believed that this represents axonal transmission of the virus to the brain. A history of recurrent genital herpes in the mother can act as a warning sign, since maternal transplacental antibodies may prevent disseminated disease, but not the virus spreading to the brain.^[86] Infants usually present between 10 days and 4 weeks of age with symptoms of fever or temperature instability, lethargy and irritability, followed by seizures, a bulging fontanelle and focal neurological signs. Cerebrospinal fluid (CSF) findings typically include 50-100 white blood cells x 10⁶ per litre, predominantly mononuclear cells, and elevated protein concentrations, both of which increase over the first few days. At presentation many are devoid of skin lesions. Untreated, the mortality rate approaches 50% with most survivors suffering severe neurological impairment.

Skin, eyes and/or mouth (SEM) infection

Nearly half of neonates with HSV infection will present with lesions confined to the skin, eyes or mucous membranes. This proportion has increased in recent decades and is attributed to recognising and treating SEM infection before it progresses to more severe manifestations of the disease.^[74,84] This is the most readily recognised form of the disease, with most babies having vesicular skin lesions at sites of trauma, such as over the presenting body part, fetal scalp electrode sites and eyelid margins. Lesions usually appear between 1 and 2 weeks of age, but are sometimes evident shortly after birth when prolonged rupture of membranes has been present. Typically vesicles overlie an erythematous base and contain clear or slightly cloudy fluid.

Although rarely fatal if lesions are confined to skin and mucosal sites, without antiviral treatment many neonates progress to either the disseminated or CNS forms of the disease. In addition, more than one-third of those with untreated localised SEM lesions develop signs of major neurological impairment such as microcephaly, spastic quadriplegia or sensory loss by 12 months of age. A study of infants with presumed SEM disease reported that 24% had HSV DNA detected in their CSF by PCR testing, suggesting that HSV can infect the CNS without overt neurological symptoms.^[87] It is also likely that a widespread rash represents underlying viraemia and greater risk of insidious reactivation later in infancy. There are data to suggest that 3 or more recurrences of cutaneous vesicles in the first 6 months of life are predictive of poor neurological outcome.^[88] Specifically the likelihood of developing normally is nearly 100% when there are fewer than 3 recurrences within the first 6 months of life compared with only 79% when 3 or more recurrences occur during this period. At the time of such episodes PCR techniques can detect HSV-DNA in the CSF, which may explain the emergence of new neurological deficits.^[89]

Differential diagnosis for neonatal HSV

Bacterial pathogens responsible for neonatal sepsis, sometimes with skin lesions that may be mistaken for disseminated or CNS HSV infection, include group B streptococcus, *Listeria monocytogenes* and gram-negative bacilli. Cutaneous infections resulting in vesicular lesions similar to neonatal HSV are bullous impetigo, varicella zoster, enteroviruses and disseminated CMV infection. Other infectious agents that might be considered are toxoplasmosis, rubella and syphilis. Finally, non-infectious cutaneous disorders that could be confused with neonatal HSV infection include erythema toxicum, neonatal pustular melanosis, acropustulosis and incontinentia pigmenti.

Management of Neonatal HSV Infection

The poor prognosis associated with untreated neonatal HSV infection means that every effort should be made to obtain a diagnosis as early as possible. This includes prompt communication with the mother's lead maternity caregiver. Most cases will present without identifiable risk factors and many with disseminated or CNS disease will initially lack skin lesions to assist in a timely diagnosis. Consequently, most physicians should consider neonatal HSV infection when confronted with an infant younger than 6 weeks of age who has vesicular or atypical bullous, pustular skin lesions or a progressive febrile illness without a bacterial cause. This may be associated with one or more of the following: seizures, liver dysfunction, thrombocytopenia, coagulopathy or pneumonitis unresponsive to antibiotics. Skin and oral lesions must be carefully looked for on a daily basis, particularly on the scalp and face (vaginal deliveries) or over the buttocks (breech presentation) as these may develop later in the course of disseminated and CNS disease. If HSV infection is seriously considered, therapy with aciclovir must be instituted immediately without waiting for laboratory confirmation of the diagnosis.

Anticipatory management of newborn infant with known risk for neonatal HSV

High risk

This category involves a subgroup of infants born to mothers with their first episode of genital herpes during pregnancy, that is, those women infected near or at term. A paediatrician experienced in identifying the signs of neonatal HSV infection should examine these newborn infants. **GRADE C**

Women with first episode genital HSV infection associated with either genital lesions or subclinical shedding at delivery have a 25-57% chance of transmitting HSV to their babies if they deliver by the vaginal route.^[45] Although not completely protective, elective caesarean section significantly reduces the risk of transmission and is recommended for pregnant women who have a known or presumed first episode of genital herpes within 6 weeks of delivery, even if receiving suppressive anti-viral therapy.^[45] **GRADE B**

Because of the high risk of infection, an asymptomatic infant inadvertently delivered vaginally from a woman with active first episode genital lesions should be managed as for suspected neonatal HSV infection. This means the immediate collection of specimens, including CSF, for culture and PCR testing (see below) and initiation of anticipatory aciclovir therapy. Also check the mother's total and type-specific HSV serological status to confirm that this is a first episode of genital herpes and not a recurrence. **GRADE C**

Similarly, when the woman has active first episode genital lesions and is febrile, or has ruptured membranes for more than 4 hours, or when fetal scalp electrodes or forceps have been used, irrespective of the mode of delivery, the infant should be managed as for suspected neonatal HSV infection. **GRADE C**

Anticipatory aciclovir therapy is continued for at least 5 days. It can be discontinued at this time if the neonate remains well, viral cultures and molecular diagnostic testing have not identified HSV, and the CSF studies including PCR results are normal. Treatment is continued for 14 days when HSV is identified but CSF results are normal and for 21 days, if there is an abnormal CSF finding.^[90] **GRADE B & C**

Low risk

Within this category are most infants born to mothers with their first episode of genital herpes during pregnancy and those with recurrent genital lesions at the time of delivery. A paediatrician experienced in identifying the signs of neonatal HSV infection should examine these newborn infants. **GRADE C**

Anticipatory guidance, including surveillance cultures, but no empiric aciclovir is reserved for well appearing infants without skin or mucosal lesions at birth and born to mothers within the following categories: **GRADE B & C**

1. First episode genital herpes more than 6 weeks before delivery
2. First episode genital herpes within 6 weeks of delivery where the mother has delivered by elective caesarean section
3. Active recurrent genital herpes at delivery
4. History of recurrent genital herpes during this pregnancy

The examining paediatrician should undertake the following:

Anticipatory guidance

1. Document risk of neonatal HSV infection on infant's chart
2. Notify the infant's lead maternity caregiver and general practitioner of risk
3. Advise mothers about hand washing and caution those with vesicular breast lesions not to breast-feed while vesicles are present. Particular care when handling the baby must be taken by those with recently acquired or reactivated oral or other skin lesions. In addition to hand washing, this includes covering skin sites and, for herpes labialis or stomatitis, wearing a surgical mask and not kissing the baby until the lesions have crusted and dried
4. Educate parents on risks of HSV and instruct them to report signs of fever, respiratory distress, jaundice, lethargy or irritability, poor feeding, skin, eye or oral mucosal lesions
5. If clinical symptoms, skin, eye or mucosal lesions appear, manage as for suspected neonatal HSV infection

Surveillance HSV cultures

1. Cultures should be taken at 48 hours of age (not at birth or within the first 24 hours of life because of possible contamination by maternal cervico-vaginal secretions).
2. Cultures should be obtained from eyes (conjunctiva), mouth, nasopharynx, urine and rectum.
3. Further clinical and laboratory evaluation, as for suspected neonatal HSV infection, followed immediately by aciclovir therapy is mandated, if cultures are positive.^[85] **GRADE A**

Management of Suspected Neonatal HSV Infection

Successful management relies upon a high index of suspicion of HSV infection and early institution of therapy. Only about 40% of affected neonates will initially have skin lesions and most lack a parental history of genital herpes.^[49,80,81,83] HSV infection should be considered in all infants with vesicular skin lesions or any unwell infants presenting in the first 6 weeks of life. Particular alerting symptoms are a progressive febrile illness without a confirmed bacterial cause, which is unresponsive to antibiotics and associated with one or more of the following: skin vesicles, hepatomegaly, liver dysfunction, pneumonitis, thrombocytopenia, coagulopathy or seizures. The index of suspicion is heightened by progressive abnormalities of liver function, particularly during the first week of life. When neonatal HSV infection is considered likely, undertake diagnostic tests and administer aciclovir immediately, before the results of definitive investigations are available.^[85] **GRADE A**

Diagnosis

As neonatal HSV infection may occur in the absence of skin lesions, other diagnostic methods are required. These confirm the diagnosis and determine the extent of disease.^[44] Acquisition of material for viral culture, from sites such as the eyes (conjunctiva), mouth, nasopharynx, urine and rectum, and from skin lesions (when present) is undertaken. **GRADE A**

Liver function tests, including serum transaminases, as well as viral culture and PCR of CSF determine the extent of disease.^[87,91] These tests are performed on all infants suspected of neonatal HSV infection. **GRADE A**

An ophthalmology consultation should be sought in suspected or confirmed cases of neonatal HSV infection to help identify and monitor ocular complications that may arise during the illness. **GRADE C**

PCR

An experienced laboratory should undertake PCR. It is a rapid, highly sensitive and specific technique that avoids problems, which may affect culture results such as inadequate quantity of specimen, bacterial contamination, and inadvertent inactivation of virus by sub-optimal handling and sample transport delays. Stringent quality control is necessary because of potential contamination by “carryover” DNA from other biological samples.^[24]

Suitable specimens for PCR include:

- CSF
- Peripheral WBC (EDTA or CPD sample – not heparin)
- Vesicle fluid

Culture

Viral culture should provide a result within 2-4 days and is highly sensitive for HSV in mucocutaneous lesions. However, in contrast to PCR, fewer than 20% of neonates with CNS disease have positive CSF cultures.

Suitable specimens for viral culture include:

- CSF
- Blood
- Vesicle fluid
- Throat swab
- Nasopharyngeal aspirate
- Eye (conjunctival) swab
- Stool or rectal swab
- Urine

Direct immunofluorescence

This is the least sensitive diagnostic technique and is no longer recommended. Clinical samples should be dedicated to the more sensitive techniques of PCR and/or culture. **GRADE B**

In addition, a sexual history from the parents is taken. The mother’s lead maternity caregiver is asked to obtain cultures or PCR of maternal genital secretions and to perform total and type-specific HSV serology. This is important, even when the presentation is weeks after the delivery. Infant acute and convalescent serum to determine seroconversion may aid long-term evaluation when clinical suspicion is high but cultures or PCR results are negative. However, in general, serology plays no role in the diagnosis of neonatal HSV disease.

Treatment

Intravenous aciclovir (20mg/kg every 8 hours) decreases the mortality and morbidity of neonatal HSV infections.^[85,87,90] Early therapy improves neurological outcome. The treatment duration is 14 days for SEM disease and 21 days for CNS and disseminated infections.^[90] The recommendation for the longer course of aciclovir also includes those infants with SEM disease but who have abnormal CSF parameters, including HSV DNA detected by PCR. **GRADE A & B**

Infants with persistent HSV DNA in the CSF following completion of antiviral therapy are more likely to die or suffer serious neurological impairment than infants whose post-therapy CSF specimens are PCR negative.^[90,92] All infants with HSV CNS involvement therefore should have a lumbar puncture at the end of aciclovir therapy to determine if the CSF is PCR negative for HSV. Those who remain PCR positive should continue receiving intravenous aciclovir until viral DNA in the CSF is no longer detected.^[63,87] **GRADE B**

As a rule neonatal HSV infections are presumed to be susceptible to aciclovir as the frequency of resistant strains is very low in this population. Use of agents such as foscarnet should only be considered if there is a slow response to therapy or if an initial improvement is followed by a subsequent deterioration.^[93] **GRADE C**

A role for routine suppressive aciclovir therapy for neonatal HSV infection to prevent cutaneous recurrences and neurological complications once therapeutic courses have been completed has not been established.^[89] **GRADE B**

General management points

A monocytic leukocytosis in the CSF is suspicious of CNS HSV infection.^[44] Treatment with aciclovir should be instituted before cultures or PCR results are available. After 5 days, aciclovir can be discontinued if the clinical course is no longer compatible with HSV CNS disease, all cultures (including PCR) are negative and a CT or MRI head scan is normal or does not suggest HSV encephalitis. Be aware however that a negative initial CSF culture or PCR result does not exclude CNS disease. It is well established that neonatal HSV CNS infection may occur despite the findings of normal CSF counts and biochemistry, and that a negative CSF HSV PCR result may occur, especially if the lumbar puncture was performed early in the course of the illness.^[87,94] Consequently, perform serial lumbar punctures when microbiological tests are negative, but clinical suspicion remains high. **GRADE B & C**

Empirical treatment with aciclovir of suspected disseminated HSV infection is recommended if after 48 hours the infant is critically ill despite antibiotic therapy, if bacterial cultures are negative, and if there are signs of progressive liver dysfunction with coagulopathy.^[95] **GRADE C**

In addition to the administration of aciclovir, other important aspects of the infant's management include:

- Respiratory support
- Control of circulation
- Management of seizures
- Maintenance of fluid and electrolyte balance
- Correction of coagulopathy
- Administration of antibiotics for concomitant bacterial infections

Infants with neonatal HSV disease should be managed by contact precautions throughout the course of their illness.^[96] **GRADE C**

Follow-up of neonatal HSV infection

Long-term follow-up in survivors is instituted to monitor for sequelae and should include assessment of hearing, vision and neurodevelopment. **GRADE C**

Management of cutaneous recurrences is difficult. Recurrences are more commonly associated with HSV-2 infections and a poorer prognosis.^[88,97] The benefit of routine suppressive therapy has not been established. Data from an uncompleted clinical trial indicate that oral aciclovir (300mg/m² 3 times daily) prevents HSV recurrences after SEM disease, but almost half the infants experienced neutropaenia while on treatment.^[89] While controversial,^[98] it is recommended that if there are 2 such episodes during the first 6 months of life suppressive oral aciclovir be considered and the white blood cell count monitored.^[99] It must be realised however that treatment failures resulting in serious disease have still been reported during aciclovir suppressive therapy.^[100] **GRADE B & C**

When a cutaneous recurrence is accompanied by fever and especially irritability, a CSF examination, including HSV DNA PCR, should be performed and if abnormal 3 weeks of intravenous aciclovir administered, followed by suppressive oral aciclovir until at least 6 months of age. **GRADE C**

Counselling

Neonatal HSV infection causes considerable stress within the family. The experience of many is that most couples eventually separate.^[101] This is because of concern over a critically ill infant, exacerbated by guilt over transmission of the virus and the demands of the long term care of an often severely impaired child. Because of the severe psychosocial sequelae of neonatal HSV, expert education and counselling is required. **GRADE C**

Breast-feeding and use of oral aciclovir

The American Academy of Pediatrics has approved use of aciclovir for treating first episode or recurrent genital herpes in breastfeeding mothers. Although concentrations are high in breast milk and the baby, toxicity is low.^[66] **GRADE B**

MANAGEMENT OF GENITAL HSV INFECTION IN CHILDHOOD

Genital herpes is less common in childhood than in adulthood but can occur. When assessing a child or young person with genital ulcers the diagnosis of herpes simplex should be considered but not presumed. Ulcers can occur as a manifestation of aphthosis in response to acute illness.^[102] The appearance of aphthous genital ulcers is also usually preceded by a history of fever, malaise and headache, but viral cultures are negative. Epstein-Barr virus and cytomegalovirus infections have also been reported to cause genital ulceration. Any genital ulcers should therefore be swabbed and cultured before decisions are made about management.

Pre-adolescent children

Genital herpes infection may present in preadolescent children. When it does it is important to explore carefully in the history the aetiology of the herpes infection. Possible sources of transmission include an orolabial lesion or a herpetic whitlow in another family member and autoinoculation. For example genital herpes in a child under 1 year of age may result from kissing “all over” by a pre-school aged sibling with orolabial herpes.

If an obvious source of the infection cannot be identified then sexual transmission should be considered. The diagnosis must be confirmed by culture or PCR with typing of the herpes virus. The presence of HSV-1 does not rule out sexual transmission but a non-sexual route of transmission should be carefully sought especially if there are no other pointers to suggest sexual abuse. Also the presence of HSV-2 in the genital area does not automatically imply sexual contact but does mean that sexual abuse, as a cause of the infection must be seriously considered. In a recent local review of 2,162 children who had an examination in the context of allegations of sexual abuse, 8 of the 1,909 children who underwent laboratory screening for sexually transmitted infections were positive for HSV and a sexual transmission was thought likely for 6 of these children.^[103]

Because of these very difficult issues in diagnosis all children with confirmed genital herpes infection should be referred to a Paediatrician for assessment and treatment. The Paediatrician may in turn seek advice from a DSAC (Doctors for Sexual Abuse Care) Doctor with special training in the area of recognition of child sexual abuse.

Adolescents

If genital herpes is present, a history suggesting aetiology should be carefully documented as for pre-adolescent children. During the interview it is important to ensure privacy. The adolescent should be asked whether they are sexually active and whether their involvement in sexual activity has been consensual. If non-consensual activity is reported and they are under the age of 17 then referral to the local Police and Children Youth and Family (CYF) Serious Abuse Team (SAT) should be seriously considered. It is preferable that this referral be made with the consent of the adolescent and his/her parents. If consent is not given and there are serious concerns about the safety of the young person then referral can be still be made under the protection of the Children and Young Persons' Act.

The above is based upon on internationally accepted standards of practice. **GRADE C**

KEY ISSUES IN COUNSELLING MANAGEMENT

Genital herpes is a common condition in people who are sexually active. However, conditioning and social values contribute to individuals having a range of emotional responses when given a diagnosis of genital herpes.^[104-107]

Emotional Feelings Related to the Diagnosis of Genital Herpes

- Grief
- Guilt
- Embarrassment
- Sense of isolation
- Loss of assertiveness
- Unworthiness
- Shock
- Dirtiness
- Anger
- Sense of injustice
- Confusion
- Fear
- Surprise
- Denial

Good therapeutic management acknowledges these emotional responses and addresses the patient's feelings and concerns. The patient who presents with genital herpes for the first time is very vulnerable. The clinician/counsellor should acknowledge how difficult it must have been for the patient to present for treatment.^[108]

Often the diagnosis is unexpected. The physician/counsellor should never be dismissive of the patient's disease; for some patients a diagnosis of genital herpes may be the most challenging health disruption they have ever experienced, given the stigma associated with sexually transmitted infections. The clinician/counsellor should show their empathy for the patient and allow the patient to talk. The counselling needs to take place at the patient's pace and not be rushed. If the patient is referred elsewhere for counselling, the diagnosing clinician should still address the acute issues at the first presentation.^[28,109]

Not all patients will want to take up the offer of counselling and support. Nevertheless, it is very important to offer it to all so that they can make this decision.

It is important that counselling and education about genital herpes take place in the appropriate setting. The following points should be considered:

- Comfortable setting
- Patient dressed
- Minimal interruptions
- Confidentiality assured
- Adequate time
- Attentive listening
- Avoidance of pejorative and prejudicial terms
- Empathic attitude
- Written information to take away and read
- Encouragement to return with list of questions.

The education process may include answering questions about the natural history of the disease including the likely triggers for reactivation. Few solid data exist, but patient experience suggests that stress appears to be associated with recurrences in some patients. Advice on how to manage stress and lead a healthy lifestyle (exercise, good diet etc) should be given with care. Too much advice on lifestyle may be stressful for the patient, heightening feelings of guilt and the belief that the disease is self-inflicted.

Correct management of genital herpes is time-intensive. The likely impact of the disease on the patient and how well they are coping should be assessed. Psychological issues and concerns should start to be addressed at the first session. Many patients will be worried about the risk of having acquired HIV or other STIs or that they are seen to be promiscuous and may be worried about the doctor's opinion of them. In all cases (whether primary, non-primary or first symptomatic reactivation) the emotional consequences and perceived social stigma of the disease need to be addressed. The diagnosis of genital herpes will provoke a shock reaction in many patients and cause feelings such as guilt, anger, confusion and a sense of isolation.^[109-113] Patients with genital herpes are usually very concerned about the diagnosis of the disease, its potential impact on their lives and how their family and friends will view them. Common concerns of patients relate to the social stigma of the disease, transmitting the disease, fear of telling potential sexual partners who may then reject them and how it will affect their sex life and their social activities.^[106]

The above section on counselling is based on internationally accepted standards of practice.
GRADE C

Common Concerns of Patients with Genital Herpes

- Fear of discovery
- Intimate relationships and sex life affected
- Social activities and lifestyle altered
- Social stigma of STI
- Condition is 'incurable'
- Fear of transmission or contagion
- Fear of disclosure and subsequent rejection

Patients should be reassured that they are not alone in having genital herpes. The clinician or counsellor is encouraged to offer information about local herpes support groups and/or the NZ Herpes Foundation (toll free Helpline **0508 11 12 13**) or refer for specialist counselling to the local Sexual Health Clinic.

Key Information to Give Patients in Counselling

- Approximately 1 in 5 people have genital herpes but only 20% of them experience symptoms.
- Most people (80%) who become infected with genital herpes will not have any symptoms or have such mild symptoms that they will not be recognised or diagnosed as genital herpes.
- For most people who experience symptoms genital herpes is a sometimes-recurring “cold sore” on the genitals. It does not affect your overall health or longevity of life.
- A small percentage of people who get genital herpes may experience problematic recurrences. If this happens there is effective treatment available.
- People who experience a first episode of genital herpes will get better, lesions will heal and there will be no evidence of the initial lesions left.
- Most people who experience a first episode of HSV-2 will have recurrences but they are generally milder than the first episode. HSV-1 tends to cause fewer recurrences than HSV-2.
- Over 75% of people get herpes from a partner who has no history of ever having had herpes.
- Getting genital herpes in a long term monogamous relationship does not mean the other partner has been unfaithful. However, a full sexual health screen may be reassuring.
- Genital herpes is more common in women as it is easier to transmit from men to women, than from women to men.
- Oral to genital transmission is very common (more than 35% of genital herpes is caused by oral to genital transmission of HSV-1). This can happen when ‘cold sores’ are not causing symptoms.
- Genital herpes does not affect your fertility or stop you having children. Vaginal delivery is usual for most women with a history of genital herpes.
- Genital herpes does not stop you having sex.
- Anybody with genital herpes, whether they get symptoms or have never had symptoms, may shed the virus from time to time with no symptoms present.
- Only a small percentage of people with genital herpes get frequent recurrences.
- There is a very effective oral antiviral medication if genital herpes is problematic.
- There is no scientific evidence that genital herpes predisposes to or causes cancer of the cervix.
- The risk of transmission to a regular sexual partner over a one-year period (not using condoms but avoiding skin contact when symptoms are present) is 10%, i.e. there is a 90% chance of not passing it on over a one-year period.
- Even if the virus is passed on, the most likely outcome is that the person will never experience symptoms.
- Condoms reduce the risk of transmission. The use of condoms in a long-term relationship should be a matter of discussion between the individuals. It is advisable to avoid genital-to-genital contact, even with a condom, until any lesions are completely healed.

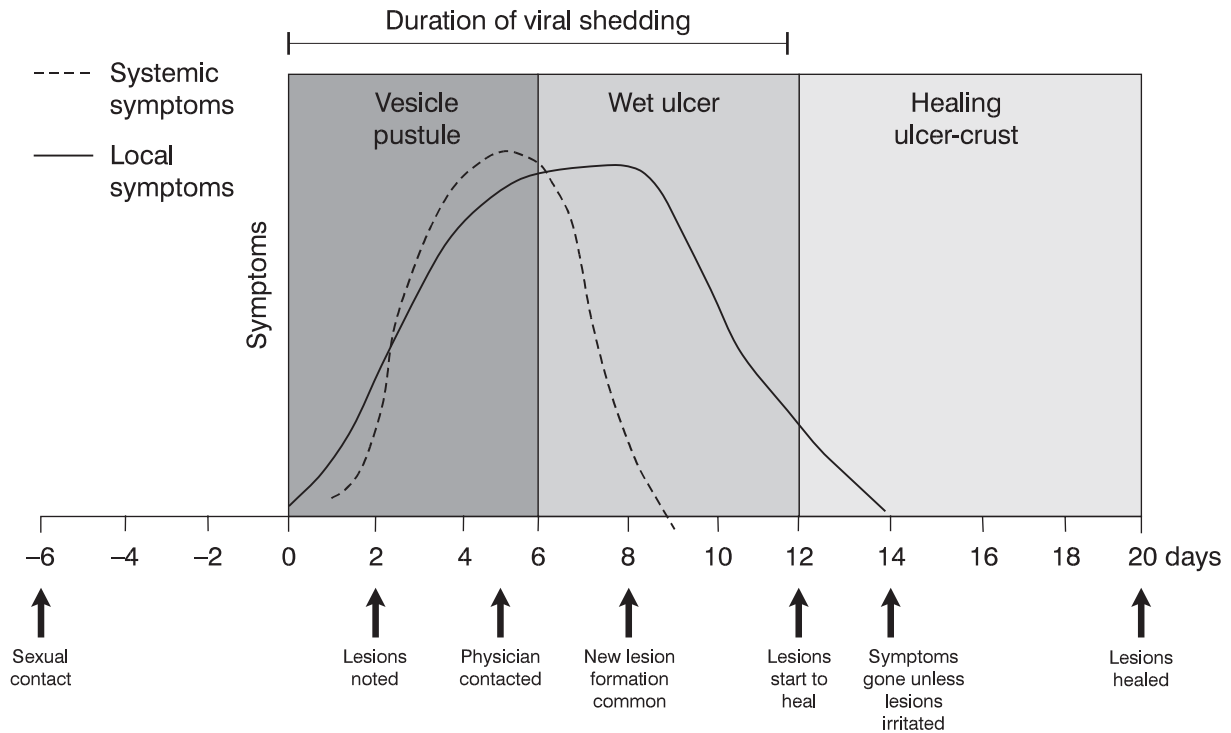
Ensure patients have access to the NZHF patient pamphlets and/or helpline – 0508 11 12 13 or www.herpes.org.nz.

Herpes in Pregnancy

- Neonatal herpes is serious but extremely rare; 1 in 10,000 live births.
- The commonest cause of neonatal herpes is a woman experiencing a first episode (often asymptomatic) in the last trimester. Early medical management will minimise the risk.
- Recurrent herpes in pregnancy has a much lower risk of transmission. Maternal antibodies contribute to protecting the baby and viral shedding in recurrences is low. It is important to notify the health professional(s) managing the pregnancy of the previous history.
- Vaginal delivery is usual for most women with a history of genital herpes.
- While neonatal herpes is rare it is important that parents are instructed on which symptoms to look out for if there is any possibility of transmission. Knowledge of the early symptoms of neonatal herpes will enable such infants to present early and will increase the likelihood of a good outcome for the infant.

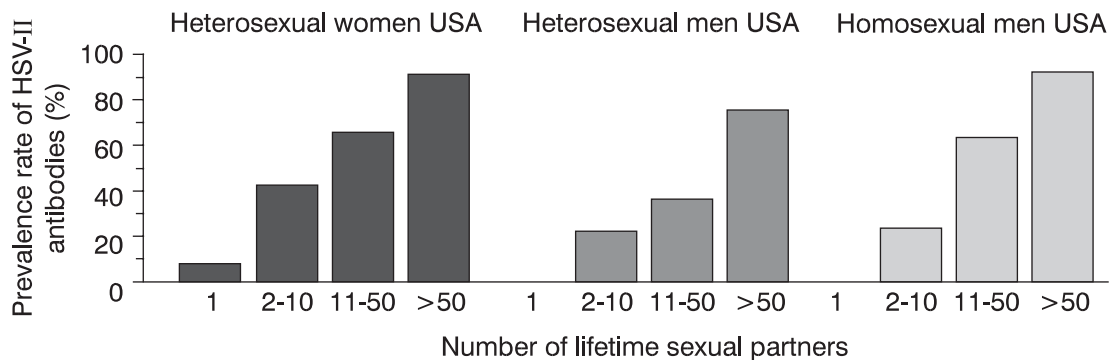
Appendix I

Clinical course of primary genital HSV infection. Reproduced with permission from the *Management Strategies on Herpes: The Medical Importance of Genital Herpes Simplex Virus Infection* booklet (ISBN0904052 51 6).



Appendix II

Prevalence of HSV-II antibodies in relation to the number of lifetime sexual partners. Reproduced with permission from the *Management Strategies on Herpes: The Medical Importance of Genital Herpes Simplex Virus Infection* booklet (ISBN0904052 51 6).



References

1. Corey L, McCutchan A, Ronald AR, et al., Evaluation of new anti-infective drugs for the treatment of genital infections due to herpes simplex virus. *Clin Infect Dis*, 1992. 15(Suppl.1): p.S99-S107.
2. Wald A, Herpes simplex virus type 2 transmission: risk factors and virus shedding. *Herpes*, 2004. 11 Suppl 3: p.130A-137A.
3. Gardella C, et al., Risk factors for herpes simplex virus transmission to pregnant women: a couples study. *Am J Obstet Gynecol*, 2005. 193(6): p.1891-9.
4. Pebody RG, et al., The seroepidemiology of herpes simplex virus type 1 and 2 in Europe. *Sex Transm Infect*, 2004. 80(3): p.185-191.
5. Eberhart-Phillips J, et al., Herpes simplex type 2 infection in a cohort aged 21 years. *Sex Transm Infect*, 1998. 74(3): p.216-218.
6. Eberhart-Phillips JE, et al., Rising incidence and prevalence of herpes simplex type 2 infection in a cohort of 26 year old New Zealanders. *Sex Transm Infect*, 2001. 77(5): p.353-357.
7. Dickson NP, et al., Risk of HSV-2 acquisition increases over early adulthood: evidence from a cohort study. *Sex Transm Infect*, 2006: p.sti.2006.020883.
8. Cunningham AL, et al., Prevalence of infection with herpes simplex virus types 1 and 2 in Australia: a nationwide population based survey. *Sex Transm Infect*, 2006. 82(2): p.164-168.
9. Perkins NL, et al., Seroprevalence of herpes simplex virus type 2 antibodies in New Zealand sexual health clinic patients. *N Z Med J*, 1996. 109(1032): p.402-5.
10. Haddow LJ, et al., Increase in rates of herpes simplex virus type 1 as a cause of anogenital herpes in western Sydney, Australia, between 1979 and 2003. *Sex Transm Infect*, 2006. 82(3): p.255-259.
11. Perkins N, personal communication. 2006.
12. Wald A, et al., Reactivation of genital herpes simplex virus type 2 infection in asymptomatic seropositive persons. *N Engl J Med*, 2000. 342(12): p.844-50.
13. Mertz GJ, et al., Risk factors for the sexual transmission of genital herpes. *Ann Intern Med*, 1992. 116(3): p.197-202.
14. Wald A, et al., Frequent genital herpes simplex virus 2 shedding in immunocompetent women. Effect of acyclovir treatment. *J Clin Invest*, 1997. 99(5): p.1092-7.
15. Corey L, et al., Once-daily valacyclovir to reduce the risk of transmission of genital herpes. *N Engl J Med*, 2004. 350(1): p.11-20.
16. Langenberg AGM, et al., A Prospective Study of New Infections with Herpes Simplex Virus Type 1 and Type 2. *N Engl J Med*, 1999. 341(19): p.1432-1438.
17. Langenberg A, Interrupting herpes simplex virus type 2 transmission: the role of condoms and microbicides. *Herpes*, 2004. 11 Suppl 3: p.147A-154A.
18. Wald A, et al., The relationship between condom use and herpes simplex virus acquisition. *Ann Intern Med*, 2005. 143(10): p.707-13.
19. Vyse AJ, et al., The burden of infection with HSV-1 and HSV-2 in England and Wales: implications for the changing epidemiology of genital herpes. *Sex Transm Infect*, 2000. 76(3): p.183-187.
20. Cowan FM, et al., Relationship between antibodies to herpes simplex virus (HSV) and symptoms of HSV infection. *J Infect Dis*, 1996. 174(3): p.470-5.
21. da Silva LM, et al., Herpes simplex virus type 1 shedding in the oral cavity of seropositive patients. *Oral Dis*, 2005. 11(1): p.13-6.
22. Wald A, et al., Oral shedding of herpes simplex virus type 2. *Sex Transm Infect*, 2004. 80(4): p.272-6.
23. Scoular A, Using the evidence base on genital herpes: optimising the use of diagnostic tests and information provision. *Sex Transm Infect*, 2002. 78(3): p.160-165.
24. Post JC, Ehrlich GD, The Impact of the Polymerase Chain Reaction in Clinical Medicine. *JAMA*, 2000. 283(12): p.1544-1546.
25. Bryson Y, et al., Treatment of first episodes of genital herpes simplex virus infection with oral acyclovir. A randomized double-blind controlled trial in normal subjects. *N Engl J Med*, 1983. 308(16): p.916-921.
26. Mertz GJ, et al., Double-blind placebo-controlled trial of oral acyclovir in first-episode genital herpes simplex virus infection. *JAMA*, 1984. 252(9): p.1147-1151.
27. Beauman J, Genital Herpes: A Review. *American Family Physician*, 2005. 72(8): p.1527-34.
28. Carney O, et al., A prospective study of the psychological impact on patients with a first episode of genital herpes. *Sex Transm Infect*, 1994. 70(1): p.40-45.
29. Green J, Psychosocial issues in genital herpes management. *Herpes*, 2004. 11(3): p.60-2.
30. Tyring SK, et al., A randomized, placebo-controlled comparison of oral valacyclovir and acyclovir in immunocompetent patients with recurrent genital herpes infections. The Valaciclovir International Study Group. *Arch Dermatol*, 1998. 134(2): p.185-91.
31. Aoki FY, et al., Single-day, patient-initiated famciclovir therapy for recurrent genital herpes: a randomized, double-blind, placebo-controlled trial. *Clin Infect Dis*, 2006. 42(1): p.8-13.
32. Wald A, et al., Two-day regimen of acyclovir for treatment of recurrent genital herpes simplex virus type 2 infection. *Clin Infect Dis*, 2002. 34(7): p.944-8.
33. Mertz GJ, et al., Long-term acyclovir suppression of frequently recurring genital herpes simplex virus infection. A multicenter double-blind trial. *JAMA*, 1988. 260(2): p.201-206.
34. Kaplowitz LG, et al., Prolonged continuous acyclovir treatment of normal adults with frequently recurring genital herpes simplex virus infection. The Acyclovir Study Group. *JAMA*, 1991. 265(6): p.747-751.
35. Patel R, et al., Impact of suppressive antiviral therapy on the health related quality of life of patients with recurrent genital herpes infection. *Sex Transm Infect*, 1999. 75(6): p.398-402.
36. Romanowski B, Marina RB, Roberts JN, Patients' preference of valacyclovir once-daily suppressive therapy versus twice-daily episodic therapy for recurrent genital herpes: a randomized study. *Sex Transm Dis*, 2003. 30(3): p.226-31.
37. Tyring SK, et al., Oral famciclovir for the suppression of recurrent genital herpes: the combined data from two randomized controlled trials. *J Cutan Med Surg*, 2003. 7(6): p.449-54.

38. Tyring SK, Baker D, Snowden W, Valacyclovir for herpes simplex virus infection: long-term safety and sustained efficacy after 20 years' experience with acyclovir. *J Infect Dis*, 2002. 186 Suppl 1: p.S40-6.
39. Corey L, et al., A trial of topical acyclovir in genital herpes simplex virus infections. *N Engl J Med*, 1982. 306(22): p.1313-1319.
40. Trotter L, et al., Are all aciclovir cream formulations bioequivalent? *Int J Pharm*, 2005. 304(1-2): p.63-71.
41. Garland SM, Neonatal herpes simplex: Royal Women's Hospital 10-year experience with management guidelines for herpes in pregnancy. *Aust N Z J Obstet Gynaecol*, 1992. 32(4): p.331-4.
42. Young EJ, et al., Disseminated herpesvirus infection during pregnancy. *Clin Infect Dis*, 1996. 22(1): p.51-8.
43. Corey L, Wald A., Sexually Transmitted Diseases. 3rd ed, ed. K Holmes, Sparling, PF., Mardh, P, Lemon, SM., Stamm, W., Piot, P., Wasserheit, J. 1999: McGraw-Hill. 297-299.
44. Arvin A, Whitley, RJ., Gutierrez, KM., Herpes simplex infections., in *Infectious diseases of the fetus and newborn infant.*, KJWC Remington JS, Baker CJ, Editor. 2006, Elsevier Saunders: Philadelphia. p.845-866.
45. Brown ZA, et al., The Acquisition of Herpes Simplex Virus during Pregnancy. *N Engl J Med*, 1997. 337(8): p.509-516.
46. Brown ZA, et al., Effect of serologic status and cesarean delivery on transmission rates of herpes simplex virus from mother to infant. *Jama*, 2003. 289(2): p.203-9.
47. Randolph AG, Washington AE, Prober CG, Cesarean delivery for women presenting with genital herpes lesions. Efficacy, risks, and costs. *JAMA*, 1993. 270(1): p.77-82.
48. Ozouaki F, et al., Genital shedding of herpes simplex virus type 2 in childbearing-aged and pregnant women living in Gabon. *Int J STD AIDS*, 2006. 17(2): p.124-7.
49. Elder DE, Minutillo C, Pemberton PJ, Neonatal herpes simplex infection: keys to early diagnosis. *J Paediatr Child Health*, 1995. 31(4): p.307-11.
50. ACOG, ACOG practice bulletin. Management of herpes in pregnancy. Number 8 October 1999. Clinical management guidelines for obstetrician-gynecologists. *Int J Gynaecol Obstet*, 2000. 68(2): p.165-73.
51. Smith JR, Cowan FM, Munday P, The management of herpes simplex virus infection in pregnancy. *Br J Obstet Gynaecol*, 1998. 105(3): p.255-60.
52. Wald A, Genital herpes. *Clin Evid*, 2002(8): p.1608-19.
53. RCOG, Management of Genital Herpes in Pregnancy. 2002, Royal College of Obstetricians and Gynaecologists.
54. AHMF, Herpes Simplex in Pregnancy. 2004, Australian Herpes Management Forum.
55. BASHH, National Guideline for Management of Genital Herpes. 2001, Clinical Effectiveness Group, British Association of Sexual Health and HIV.
56. Gardella C, et al., Poor correlation between genital lesions and detection of herpes simplex virus in women in labor. *Obstet Gynecol*, 2005. 106(2): p.268-74.
57. Scott L, et al., Acyclovir suppression to prevent cesarean delivery after first-episode genital herpes. *Obstet Gynecol*, 1996. 87(1): p.69-73.
58. Brocklehurst P, et al., A randomised placebo controlled trial of suppressive acyclovir in late pregnancy in women with recurrent genital herpes infection. *Br J Obstet Gynaecol*, 1998. 105(3): p.275-80.
59. Watts DH, et al., A double-blind, randomized, placebo-controlled trial of acyclovir in late pregnancy for the reduction of herpes simplex virus shedding and cesarean delivery. *Am J Obstet Gynecol*, 2003. 188(3): p.836-43.
60. Sheffield JS, et al., Acyclovir Prophylaxis to Prevent Herpes Simplex Virus Recurrence at Delivery: A Systematic Review. *Obstet Gynecol*, 2003. 102(6): p.1396-1403.
61. Ramsey P, Andrews W, Antiviral suppression to prevent recurrence of herpes simplex virus (HSV) infections in pregnancy: a meta analysis. *Am J Obstet Gynecol*, 2003. 189(6): p.S98.
62. Arvin A, et al., Failure of antepartum maternal cultures to predict the infant's risk of exposure to herpes simplex virus at delivery. *N Engl J Med*, 1986. 315(13): p.796-800.
63. Kimberlin DW, et al., Natural history of neonatal herpes simplex virus infections in the acyclovir era. *Pediatrics*, 2001. 108(2): p.223-9.
64. Stone KM, et al., Pregnancy outcomes following systemic prenatal acyclovir exposure: Conclusions from the international acyclovir pregnancy registry, 1984-1999. *Birth Defects Res A Clin Mol Teratol*, 2004. 70(4): p.201-7.
65. Andrews WW, et al., Valacyclovir therapy to reduce recurrent genital herpes in pregnant women. *Am J Obstet Gynecol*, 2006. 194(3): p.774-81.
66. Sheffield JS, et al., Acyclovir concentrations in human breast milk after valaciclovir administration. *Am J Obstet Gynecol*, 2002. 186(1): p.100-2.
67. Major CA, et al., Expectant management of preterm premature rupture of membranes complicated by active recurrent genital herpes. *Am J Obstet Gynecol*, 2003. 188(6): p.1551-4; discussion 1554-5.
68. Cleary KL, et al., Type-specific screening for asymptomatic herpes infection in pregnancy: a decision analysis. *Bjog*, 2005. 112(6): p.731-6.
69. Braig S, Chanzy B, Management of genital herpes during pregnancy: the French experience. *Herpes*, 2004. 11(2): p.45-7.
70. Tookey P, Peckham CS, Neonatal herpes simplex virus infection in the British Isles. *Paediatr Perinat Epidemiol*, 1996. 10(4): p.432-42.
71. Gaytant MA, et al., [Incidence of herpes neonatorum in Netherlands]. *Ned Tijdschr Geneesk*, 2000. 144(38): p.1832-6.
72. Malm G, Berg U, Forsgren M, Neonatal herpes simplex: clinical findings and outcome in relation to type of maternal infection. *Acta Paediatr*, 1995. 84(3): p.256-60.
73. Stone KM, et al., National surveillance for neonatal herpes simplex virus infections. *Sex Transm Dis*, 1989. 16(3): p.152-6.
74. Kropp RY, et al., Neonatal herpes simplex virus infections in Canada: results of a 3-year national prospective study. *Pediatrics*, 2006. 117(6): p.1955-62.
75. Nahmias AJ, Neonatal HSV infection Part II: Obstetric considerations – a tale of hospitals in two cities (Seattle and Atlanta, USA). *Herpes*, 2004. 11(2): p.41-4.
76. Morris A, Ridley GF, Elliott EJ, Australian Paediatric Surveillance Unit: progress report. *J Paediatr Child Health*, 2002. 38(1): p.8-15.

77. Freedman E, Mindel A, Jones CA, Epidemiological, clinical and laboratory aids for the diagnosis of neonatal herpes – an Australian perspective. *Herpes*, 2004. 11(2): p.38-44.
78. Fleming DT, et al., Herpes Simplex Virus Type 2 in the United States, 1976 to 1994. *N Engl J Med*, 1997. 337(16): p.1105-1111.
79. Kimberlin DW, Herpes simplex virus infections in neonates and early childhood. *Semin Pediatr Infect Dis*, 2005. 16(4): p.271-81.
80. Whitley RJ, et al., The natural history of herpes simplex virus infection of mother and newborn. *Pediatrics*, 1980. 66(4): p.489-94.
81. Yeager AS, Arvin AM, Reasons for the absence of a history of recurrent genital infections in mothers of neonates infected with herpes simplex virus. *Pediatrics*, 1984. 73(2): p.188-93.
82. Yeager AS, et al., Relationship of antibody to outcome in neonatal herpes simplex virus infections. *Infect Immun*, 1980. 29(2): p.532-8.
83. Whitley RJ, Neonatal herpes simplex virus infections. *J Med Virol*, 1993. Suppl 1: p.13-21.
84. Whitley RJ, et al., Changing presentation of herpes simplex virus infection in neonates. *J Infect Dis*, 1988. 158(1): p.109-16.
85. Whitley R, et al., A controlled trial comparing vidarabine with acyclovir in neonatal herpes simplex virus infection. Infectious Diseases Collaborative Antiviral Study Group. *N Engl J Med*, 1991. 324(7): p.444-9.
86. Nahmias AJ, Neonatal HSV infection Part I: continuing challenges. *Herpes*, 2004. 11(2): p.33-7.
87. Kimberlin DW, et al., Application of the polymerase chain reaction to the diagnosis and management of neonatal herpes simplex virus disease. National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group. *J Infect Dis*, 1996. 174(6): p.1162-7.
88. Whitley R, et al., Predictors of morbidity and mortality in neonates with herpes simplex virus infections. The National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group. *N Engl J Med*, 1991. 324(7): p.450-4.
89. Kimberlin D, et al., Administration of oral acyclovir suppressive therapy after neonatal herpes simplex virus disease limited to the skin, eyes and mouth: results of a phase I/II trial. *Pediatr Infect Dis J*, 1996. 15(3): p.247-54.
90. Kimberlin DW, et al., Safety and efficacy of high-dose intravenous acyclovir in the management of neonatal herpes simplex virus infections. *Pediatrics*, 2001. 108(2): p.230-8.
91. Diamond C, et al., Viremia in neonatal herpes simplex virus infections. *Pediatr Infect Dis J*, 1999. 18(6): p.487-9.
92. Troendle-Atkins J, Demmler GJ, Buffone GJ, Rapid diagnosis of herpes simplex virus encephalitis by using the polymerase chain reaction. *J Pediatr*, 1993. 123(3): p.376-80.
93. Levin MJ, et al., Development of acyclovir-resistant herpes simplex virus early during the treatment of herpes neonatorum. *Pediatr Infect Dis J*, 2001. 20(11): p.1094-7.
94. De Tiege X, et al., Limits of early diagnosis of herpes simplex encephalitis in children: a retrospective study of 38 cases. *Clin Infect Dis*, 2003. 36(10): p.1335-9.
95. Scott LL, (Discussion; Prober, CG., Arvin, AM.), Perinatal herpes: current status and obstetric management strategies. *Pediatr Infect Dis J*, 1995. 14(10): p.827-32; discussion 832-5.
96. Sakaoka H, et al., Two outbreaks of herpes simplex virus type 1 nosocomial infection among newborns. *J Clin Microbiol*, 1986. 24(1): p.36-40.
97. Kimura H, et al., Relapse of neonatal herpes simplex virus infection. *Arch Dis Child Fetal Neonatal Ed*, 2003. 88(6): p.F483-6.
98. Gutierrez K, Arvin AM, Long term antiviral suppression after treatment for neonatal herpes infection. *Pediatr Infect Dis J*, 2003. 22(4): p.371-2.
99. Frenkel LM, Challenges in the diagnosis and management of neonatal herpes simplex virus encephalitis. *Pediatrics*, 2005. 115(3): p.795-7.
100. Fonseca-Aten M, et al., Herpes simplex virus encephalitis during suppressive therapy with acyclovir in a premature infant. *Pediatrics*, 2005. 115(3): p.804-9.
101. Kimberlin DW, Neonatal HSV infections: the global picture. *Herpes*, 2004. 11(2): p.31-2.
102. Huppert JS, et al., Vulvar ulcers in young females: a manifestation of aphthosis. *J Pediatr Adolesc Gynecol*, 2006. 19(3): p.195-204.
103. Kelly P, Koh J, Sexually transmitted infections in alleged sexual abuse of children and adolescents. *J Paediatr Child Health*, 2006. 42(7-8): p.434-40.
104. Fortenberry JD, et al., Relationships of Stigma and Shame to Gonorrhea and HIV Screening. *Am J Public Health*, 2002. 92(3): p.378-381.
105. Fortenberry JD, The effects of stigma on genital herpes care-seeking behaviours. *Herpes*, 2004. 11(1): p.8-11.
106. Green J, et al., Determinants of disclosure of genital herpes to partners. *Sex Transm Infect*, 2003. 79(1): p.42-44.
107. Patel R, Supporting the patient with genital HSV infection. *Herpes*, 2004. 11(3): p.87-92.
108. Sankar P, Jones NL, To tell or not to tell: primary care patients' disclosure deliberations. *Arch Intern Med*, 2005. 165(20): p.2378-83.
109. Nack A, Damaged goods: Women managing the stigma of STD's. *Deviant Behavior: An Interdisciplinary Journal*, 2000. 21(2): p.95-121.
110. Breitkopf CR, The theoretical basis of stigma as applied to genital herpes. *Herpes*, 2004. 11(1): p.4-7.
111. Inhorn M, Genital herpes: An ethnographic inquiry into being discreditable in American society. *Med Anthropology Quarterly*, 1986. 17: p.59-63.
112. Lee J, Craft E, Protecting oneself from a stigmatized disease... once one has it. *Deviant Behavior: An Interdisciplinary Journal*, 2002. 23(3): p.267-299.
113. Swanson JM, Dibble SL, Chenitz WC, Clinical features and psychosocial factors in young adults with genital herpes. *Image J Nurs Sch*, 1995. 27(1): p.16-22.

Members of the Professional Advisory Board (PAB) of the Viral Sexually Transmitted Infection Education Foundation 2006

Sexual Health Physicians

Dr Edward Couglan
Dr Jane Morgan (Chairperson)
Dr Janet Say

NZ Dermatological Society

Dr Darian Rowan

NZ College of Obstetricians and Gynaecologists

Dr Ron Jones
Dr Anne Robertson
Dr Richard Speed

Paediatric Society of New Zealand

Prof. Keith Grimwood

NZ College of General Practitioners

Dr Phil Jacobs

Virology

Dr Kitty Croxson

Family Planning

Dr Christine Roke

Counselling

Catherine Cook

Nursing

Claire Hurst
Georgina McPherson
Jessica Crawford

Patient Representative

Peter Fleming

Project Co-ordinator

Claire Hurst, PO Box 2437, Auckland
Tel: 09 360 1966 Fax: 09 360 2835 Email: info@herpes.org.nz

Index

Barrier Methods	6
Condom Use	6
Congenital Infection	22
Costs of Antivirals	21
Counselling First Episode	13
Recurrences	17
Key Issues	40
Common Concerns	41
Key Information	42
Culture	7
Diagnosis First Episode	7
Recurrences	7
Diagnostic Procedures	7
Education First Episode	12
Recurrences	17
Epidemiology	4
Episodic Therapy	18
Examination First Episode	11
Recurrences	16
Follow-up	13
History and Examination	
First Episode	11
Recurrences	16
Key Information to Give to Patients in Counselling	42
Laboratory Testing Methods	7
Management in Childhood	39
Management of First Episode	10
Algorithm	14
Management in Pregnancy	
First Episode	26
Algorithm	24
Special Cases – Male Partner HSV Positive	29
Recurrences	27
Algorithm	25
Use of Aciclovir in Pregnancy and Breastfeeding	28
Neonatal Herpes	30
Pharmacological Treatment	
First Episode	11
Recurrences	18
Pharmacological Treatment in Pregnancy	
First Episode	28
Recurrences	28
Serology Testing	8
Summary Statements	21
Suppressive Therapy	18
Transmission	5