ANO-GENITAL HERPES

Introduction

Genital herpes is caused by infection with the herpes simplex viruses (HSV) of which there are two types (HSV-1 and HSV-2).

Definitions

- **Initial episode**: First episode with either HSV-1 or HSV-2. Dependent on whether the individual has had prior exposure to the other type, this is further subdivided into:
  - ***Primary infection***: first infection with either HSV-1 or HSV-2 in an individual with no pre-existing antibodies to either type.
  - ***Non-primary infection***: first infection with either HSV-1 or HSV-2 in an individual with pre- existing antibodies to the other type.
- **Recurrent episode**: recurrence of clinical symptoms due to reactivation of pre-existent HSV-1 or HSV-2 infection after a period of latency.

Natural History

- Disease episodes may be symptomatic or asymptomatic. It is likely that the majority of infections are acquired sub-clinically as at least 80% of persons seropositive for HSV type-specific antibodies are unaware that they have been infected.
- Prior infection with HSV-1 modifies the clinical manifestations of first infection by HSV-2.
- After childhood, symptomatic primary infection with HSV-1 is equally likely to be acquired in the genital area or oral areas.
- Primary genital herpes in the UK is equally likely to be caused by HSV-1 as by HSV-2 (HSV1 greater in men <35 yrs and women <50 yrs)
- Following primary infection, the virus becomes latent in local sensory ganglia, periodically reactivating to cause symptomatic lesions or asymptomatic, but infectious, viral shedding.

Signs and Symptoms

- Blisters or painful ulceration of external genitalia, may also involve the cervix and / or rectum
- Dysuria
- Vaginal or urethral discharge
- Systemic symptoms of fever and myalgia are more common in primary infection
- Lesions of recurrent episodes are often atypical, resembling fissures, erosions and superficial erythema rather than ulcers
- Tender inguinal lymphadenitis usually bilateral in initial episodes but may be unilateral
- HSV is significant cause of proctitis, especially HIV+ men.
- 70% of HSV proctitis in MSM had no visible signs of external anal ulceration

Potential Complications

- urinary retention (result of severe pain or autonomic neuropathy)
- autoinoculation to fingers and adjacent skin e.g. thighs

- aseptic meningitis
- mother to child transmission perinatally – please refer to "*Pregnancy and STIs*" protocol for all pregnant females with suspected or confirmed ano-genital herpes

Diagnosis

Virus Detection & Characterisation

Confirmation and typing of the infection is essential for diagnosis and counselling on prognosis, transmission and management. Laboratory diagnosis is based on direct detection by PCR of HSV from genital lesions; this yields the highest sensitivity of all tests and allows virus typing. The quality of sample is crucial; specimens should be collected using a swab taken ideally from a vesicle or, alternatively, directly from the base of an ulcer. Material from several lesions should be taken, to maximise diagnostic yield. Ensure that you use a VPSS vial (viral PCR sample solution) and that the virology request form is ticked for genital ulcers and includes appropriate information about lesions and risk-behaviour groups (eg genital ulcer and MSM). Consider dark field microscopy for detection of syphilis, especially if there are systemic symptoms or lymphadenopathy: discuss with a senior clinician if uncertain.

Clients should be informed that a syphilis PCR is taken automatically on the sample. Please request the combined 'HSV/syphilis' PCR for the appropriate anatomic site(s) on NaSH.

The results of genital ulcer PCR tests will be available via telephonetics (green card), with all three results (HSV1, HSV2, syphilis) being read back to the caller separately. Turn round time is usually a few days. If the result is positive, the patient will also be sent a text message (where permission exists) stating:

"This is the Sandyford. Your recent test confirms Herpes Virus type 1. You can call 0141 211 8634 for more info or follow this link

http://www.healthscotland.com/uploads/documents/3421-What%20do%20you%20know%20about%20Genital%20Herpes-06-16.pdf"

"This is the Sandyford. Your recent test confirms Herpes Virus type 2. You can call 0141 211 8634 or follow this link

http://www.healthscotland.com/uploads/documents/3421-What%20do%20you%20know%20about%20Genital%20Herpes-06-16.pdf"

If either of the HSV results are negative the telephonetics will also say '**If these results do not explain your symptoms, please call 0141 211 8130 for further advice'.**

Type Specific Serology

Type-specific serology is available in very limited situations via the Specialist Virology Centre, and is sent to the HPA lab in England. Send an EDTA sample to virology and they will forward to the HPA lab and complete HPA paperwork. Clinical information can be added to a blue microbiology form and sent with the sample.

Indications include pregnant women not known to have HSV who have a partner with known HSV, and patients with recurrent genital ulceration of unknown cause. Type-specific serology is particularly advised for women presenting with suspected first-episode herpes in last 6 weeks of pregnancy as confirmation that there are type-concordant antibodies present may avert the need for a caesarean section (see RCOG/BASHH guideline). Cases should be discussed with a senior GUM clinician.

Several type specific commercial assays (mainly for HSV-2) are now marketed, including one near-patient test. However, even highly sensitive and specific assays have poor predictive values in low prevalence populations (see below).

Positive predictive values for HSV-2 antibody assays		
	Prevalence	PPV*
STI clinic	25%	86%
General population antenatal clinics	5%	50%

** For an assay with 95% sensitivity and specificity*

Management

First Episode Genital Herpes

All clients with suspected first episode HSV should be reviewed by a practitioner competent to give all relevant information

Antivirals

Patients presenting within 5 days of the start of the episode, or while new lesions are still forming, should be given oral antiviral drugs. There is no evidence of benefit for greater than 5 days but it can be considered if new vesicles are forming. Aciclovir is the preferred treatment choice at Sandyford as there is no evidence of additional benefit from other antivirals.

Immunocompetent: Aciclovir 400 mg three times daily for FIVE days

Immunosuppressed (incl advanced HIV): Aciclovir 400mg five times daily for TEN days or **Valaciclovir** 1g bd for TEN days

Sexual Health Screen

Chlamydia/gonorrhoea NAAT and Syphilis/HIV serology should be done at first presentation; full examination with eg speculum or proctoscope if needed may need to be deferred depending on local symptoms.

Supportive measures

If clients with first diagnosis HSV require more information or support, refer to the sexual health advisers on that day or at a follow up appointment when HSV type available.

Saline bathing and the use of appropriate analgesia is recommended. Topical anaesthetic agents (e.g. 5% lidocaine ointment) should be used with caution, because of the potential for sensitisation and delayed healing, but may help with severe dysuria.

Management of complications

Hospital admission may be required for:

- severe pain or constitutional symptoms
- meningism (aseptic spinal meningitis and encephalitis rare complications)
- urinary retention (secondary to pain and sacral radiculopathy)

GP correspondence

Clarify and document if GP can be contacted and informed of HSV diagnosis and management plan. A template letter can be sent by SHA office when they are texting/phoning the positive result. If diagnosis confirmed a letter can be sent to the GP advising to put treatment course on repeat prescription for any future outbreaks.

Immunosuppressed and HIV positive Individuals

There are no recent data regarding optimum management of people living with HIV (PLWHIV) who are well established on effective antiretroviral therapy. It is therefore suggested, particularly if a patient is profoundly immunosuppressed, to seek advice from a senior GUM physician regarding management.

Recurrent Genital Herpes

Recurrences of genital herpes are generally self-limiting and usually cause minor symptoms. Management strategies include supportive therapy only, episodic antiviral treatments and suppressive antiviral therapy. The most appropriate strategy for managing an individual patient will vary over time, dependent on the patient's psychological coping strategies, recurrence frequency, symptom severity and relationship status. Frequent recurrent episodes can be managed with *supportive therapy* only, *episodic therapy* or *suppressive therapy*. If patient re-attends service offer full sexual health screen if new contacts especially if they have not been tested for HIV previously.

– see Table below.

	Management Options for Recurrent Genital Herpes		
	Supportive only	**Episodic Treatment**	**Suppressive Treatment***
Frequency of episodes	Infrequent/rare	Infrequent - frequent	Consider the clinical context and impact on patient quality of life; Recurrence rate >6/yr
Duration of each episode	Minimal	**>4 days**	Clinical context
Severity of each episode	Minimal	Moderate/severe	Moderate/severe
Other factors	-	Patient opts not to take suppressive Rx; Recurrences respond rapidly	Distressed, relationship difficulties, underlying medical issues, immunosuppression; Special event i.e. holiday or exams
Regimen	-	**Aciclovir 800 mg three times daily for 2 days**	**Aciclovir 400 mg BD**

Supportive only

Saline bathing, Yellow soft paraffin ("Vaseline"), analgesia advice

Episodic antiviral treatment

Oral antiviral therapy shortens recurrent episodes in patients who have recurrences lasting more than 4 days and will abort approximately 10% of lesional recurrences when started early (within 24 hours of symptoms developing). This is best managed as a self-start medication. Patients are best arranging a supply via GP repeat prescription.

The regimen recommended is:-

Aciclovir 800 mg three times daily for 2 days*

*No evidence to support this regime in PLWHIV discuss patients with immunosuppressive illnesses with a senior GUM physician

Suppressive therapy

*Patients with confirmed genital herpes and a recurrence rate of more than six episodes of genital herpes in 12 months will benefit from daily suppressive treatment. Patients do not have to have experienced 6 painful recurrences to be eligible – someone with a recurrence every month for 3 months meets this recurrence rate and should be offered suppressive therapy. There may also be psychosocial indications for initiating suppressive therapy.

All patients with genital herpes should be made aware of the option of suppressive therapy. **Patients do not need to see a consultant to start suppressive therapy if the above criteria are met**. GUM consultant clinic referral should only be offered to patients where *problematic* recurrence of HSV is an issue (or in pregnancy or women trying to conceive)

Experience with suppressive therapy is most extensive with aciclovir. Safety and resistance data on patients taking long term therapy now extend to over 20 years of continuous surveillance. There is NO need for any routine monitoring or baseline tests except in known severe renal disease

There is no evidence of clinical superiority of valaciclovir or famciclovir over aciclovir; on economic grounds, aciclovir is therefore the drug of choice at Sandyford.

The regimen recommended is:-

Aciclovir 400 mg twice daily for 6-12 months (initial supply for ONE month)

Prescription

Please give one month worth of aciclovir 400mg BD and send standard GP letter ("HSV Suppressive Therapy" on NaSH) with patients consent to request GP continue this on repeat prescription for up to one year.

We do NOT supply multiple months of therapy to patients, but can give them a one month starter pack while they arrange to see their GP. If patients feel unable to disclose the diagnosis to their GP then these concerns should be explored and a senior clinician involved as we cannot provide an ongoing supply from limited clinic stock

Advice to patient

If they experience flare up of symptoms whilst on suppressive therapy, they should increase the dose to 400mg TDS for 5 days and then step down again. If they have frequent recurrences on suppression, they should call sexual health department for a review appointment.

Dosage reductions are clinically inappropriate.

Twenty percent of patients will experience a reduction in recurrence frequency compared with pre-suppression symptomatic levels.

Please inform the patient that most people will have an episode on stopping suppressive treatment which should be managed symptomatically and to ensure they have medications for treatment on hand if needed. They should then monitor symptoms the recommended minimum period of assessment should include two recurrences If they have persistent symptoms they should call sexual health department for a review appointment.

Counselling & Support

In clinic counselling of patients with genital herpes should be as practical as possible and address the individual's particular personal situation; for instance, issues for someone in a long term relationship are likely to be different from those for someone seeking a partner. Diagnosis often causes considerable distress. Most people with recurrent genital HSV infection adjust over time, but antiviral treatment can reduce anxiety, assist adjustment and improve quality of life. Counselling should cover the following topics, and is most useful when the infecting viral type (HSV-1 or HSV-2) is known.

HSV diagnosis: 10 key points to discuss with patients

For symptomatic patients where tests are awaited:

1. Presumptive diagnosis based on clinical findings (until HSV PCR result known)
2. Limitations of HSV PCR including what to do if PCR is negative (return if symptoms recur)
3. How they will obtain HSV PCR results and direct them to written information (Sandyford website and BASHH PIL)

For patients with strong presumption of HSV or where this has been confirmed:

4. The natural history of HSV, including asymptomatic shedding
5. Recurrences; difference between type 1 and type 2
6. Treatment options; including short course (2 day) episodic therapy and availability of suppressive treatment if needed
7. Abstinence from sexual contact is recommended during lesion recurrences or prodromes
8. Transmission (related to the patients situation), including the risk as result of asymptomatic viral shedding, male condoms may reduce transmission and suppressive antiviral therapy reduces the rate of acquisition of symptomatic genital herpes in serodiscordant couples
9. Implications during pregnancy (to both male & female clients)
10. Disclosure is advisable in all relationships to promote trust and intimacy

It can be documented in clinical note that '10 key points of HSV diagnosis discussed'.

Direct patients to NHS inform website https://www.nhsinform.scot/illnesses-and-conditions/sexual-and-reproductive/genital-herpes

For patients who have significant distress they can be referred for counselling. Often one or two counselling sessions, with an invitation to return in case of difficulty, should be enough. Patients who have failed to adjust to the diagnosis within a year merit review for the consideration of more intensive counselling interventions.

Clients may consider seeking further information and advice via www.herpes.org.uk (0845 123 2305) or www.herpesalliance.org

Partner Notification

- There is no evidence on which to base recommendations for partner notification at a population level. There is no definitive evidence that either antiviral treatment or patient education/counselling alters transmission rates of HSV at a population level, however it seems logical to increase awareness of the diagnosis in partners when appropriate, with the aim of preventing onward transmission

When counselling patients, it is worth bearing the following in mind:

- Subclinical shedding plays a major role in the transmission of infection
- There is a subjudice case in England concerning the transmission of HSV.

Vaccination

There is currently no commercially available vaccination for HSV-1 or -2.

References

BASHH – 2014 UK National guideline for the Management of Ano-genital herpes http://www.bashh.org/documents/HSV_2014%20IJSTDA.pdf [accessed September 2020)

BASHH/RCOG Management of Genital Herpes in Pregnancy. Oct 2014 https://www.bashhguidelines.org/media/1060/management-genital-herpes.pdf [accessed September 2020].

BHIVA and BIA guidelines for the treatment of Opportunistic Infection in HIV-seropositive Individuals 2011 http://www.bhiva.org/OI-guidelines.aspx [accessed September 2020]

Appendix 1.
Letter to be sent to GP when starting suppressive HSV therapy - "*HSV Suppressive Therapy*" on NaSH:

This patient has been diagnosed with genital herpes simplex virus type _____. They have had frequent recurrences and are suitable for suppressive therapy as per national guidelines.

They have been given Aciclovir 400mg BD for 1 month, which they can increase to TDS for 5 days if symptoms occur on suppressive therapy.

Please would you kindly continue to prescribe this for up to one year, after which they will stop therapy and assess symptom recurrence. At this time, if they have persistent symptoms, we would be happy to review again in the sexual health service.

Many thanks for your help in this patient's management.

Yours sincerely

Sandyford Services