

# Joint British Association for Sexual Health and HIV and Royal College of Obstetricians and Gynaecologists national UK guideline for the management of herpes simplex virus (HSV) in pregnancy and the neonate (2024 update)

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## Abstract

This updated national UK guideline offers recommendations on the management of genital herpes simplex virus (HSV) in mothers and pregnant people during pregnancy and within 4 weeks following birth. It includes recommendations for first episode and recurrent HSV, HSV in preterm pre-labour rupture of membranes and in co-infection with HSV and HIV. Recommendations around management of the neonate are made, on prevention of postnatal transmission, management of breastfeeding, and the management of clinically discordant couples. This guideline is aimed at healthcare professionals working in sexual health clinics, maternity units, and those working on postnatal wards and neonatal units in the UK. However, the principles of the recommendations should be adopted across all services, including community care.

## Keywords

Europe, pregnancy, antiviral, women, HSV (herpes simplex virus), viral disease

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## What's new in the 2024 management of genital herpes in pregnancy guideline

The guidelines have been substantially revised and updates in brief include:

- Use of ulcer panel PCR testing for herpetic lesions in pregnancy.
- Antiviral suppressive therapy to start earlier at 32 weeks of pregnancy for all mothers and pregnant people requiring this, and at 22 weeks if there is a high risk of preterm delivery.

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- Use of valaciclovir as an alternative to aciclovir for treatment and/or suppression of genital herpes in the pregnant woman or person.
- A new section on the use of serology in the third trimester, and virology involvement in writing this guideline.
- Expansion of the neonatal management section, including risk stratification to guide investigations and treatment.
- Increased focus on the importance of the multi-disciplinary team (MDT) to include genitourinary medicine (GUM) physicians, obstetricians and neonatologists with formal documentation of a birth and postnatal care plan.
- Expansion of the prevention of postnatal transmission section, including a new section on breastfeeding.
- A new section on the management of clinically or serodiscordant couples.

## Objective and scope

The first joint British Association for Sexual Health and HIV (BASHH) and Royal College of Obstetricians and Gynaecologists (RCOG) guideline on the management of genital herpes in pregnancy was published in 2014; this updated guideline supersedes that of 2014.

For more detailed information on the general management of genital herpes infection in people who are not pregnant, please refer to the 2024 BASHH guideline on the management of genital herpes.<sup>1</sup>

The scope of this guideline is the inpatient and outpatient management of genital herpes simplex virus infection in the antenatal, intrapartum and postnatal periods in mothers and pregnant people, and neonates. This updated guideline also includes the prevention of genital herpes infection in uninfected women and people during pregnancy. The population covered by this guideline includes all the routine antenatal and perinatal care that mothers and pregnant people and their babies should receive, including those mothers and pregnant people with a suspected or confirmed diagnosis of genital herpes simplex infection and those at risk of acquisition in primary or secondary care.

This guideline is aimed at healthcare professionals working in sexual health clinics, maternity units, and those working on postnatal wards and neonatal units in the UK. However, the principles of the recommendations should be adopted across all services, including community care.

## Stakeholder involvement

This guideline has been developed by a writing group including clinicians working in the fields of genitourinary medicine, obstetrics, neonatology and virology, and patient and public representatives. Specific expertise was provided by members of the BASHH Herpes Simplex Advisory Panel, the RCOG and the Royal College of Paediatrics and Child Health (RCPCH). The guideline was posted on the

BASHH and RCOG websites for a 2-month consultation period, with direct requests for external peer review made to key bodies including the RCPCH. The guideline has been reviewed by the BASHH Public Panel and piloted in a representative clinic.

The guideline writing process was overseen by the BASHH Clinical Effectiveness Group. This is the most recent update of the BASHH/RCOG national guideline first written in 2014.

## Search strategy

This document was produced in accordance with the guidance set out in the BASHH Clinical Effectiveness Group's (CEG's) document 'Framework for guideline development and assessment' (available from: <https://www.bashh.org/guidelines>).

A literature search was performed using PubMed/MEDLINE, EMBASE, Google, The Cochrane Library and relevant guidelines from 2014 to 2023. A MEDLINE/PubMed and EMBASE search was carried out from 2014 to 2023 using the following search terms/Medical Subject Headings (MeSH): 'HSV/herpes', 'genital ulcers', 'HSV/herpes pregnancy', 'neonatal HSV/herpes', 'HSV/herpes drugs', 'pregnancy complications: infectious', 'Herpes genitalis' and 'Herpes simplex diagnosis', 'HSV/herpes breastfeeding'. The search was limited to humans and the English language. For some specific recommendations, an additional MEDLINE/PubMed search was performed when necessary.

A Google search was performed in 2023 with the search term 'HSV guideline(s)' and all relevant documents of the first 150 search results were reviewed. A search of The Cochrane Library included the Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects and Cochrane Central Register of Controlled Trials. The following guidelines were reviewed in detail: 2017 European guideline for the management of genital herpes<sup>2</sup>; 2024 BASHH guidance on the management of genital herpes.<sup>1</sup> The members of the guideline development group selected studies relevant to the scope of the guideline. Article titles and abstracts were reviewed and if relevant the full-text article obtained. Priority was given to randomised controlled trial and systematic review evidence and, where possible, recommendations were made and graded based on the best available evidence ([Appendix 1](#)). In areas where evidence is lacking, recommendations based on consensus opinion within the writing group have been made.

## Background

Neonatal herpes is a very rare but serious viral infection with a high morbidity and mortality.<sup>3</sup> It is classified into three subgroups in the infant depending on the site of infection: disease localised to only skin, eye and/or mouth

(SEM), local central nervous system (CNS) disease (encephalitis alone or with SEM lesions) or disseminated disease with multiple organ involvement.

Neonatal infection occurs as the result of an infection at the time of birth (85%), in the immediate postnatal period (10%) or, very rarely, in utero (5%) - termed congenital herpes.<sup>4</sup>

Although neonatal HSV infection is very rare, the suspicion of possible neonatal HSV infection in infants with compatible symptoms or risk factors for perinatal or postnatal exposure is much more common. Thus the demand for diagnostic investigation of possible neonatal HSV infection is significant.

### *Disease localised to skin, eye and/or mouth (SEM)*

Infants who present with symptoms localised to the skin, eye or mouth alone have the best prognosis. They represent approximately 32% of neonatal herpes cases, with median presentation at 8 days of life.<sup>5</sup> They typically present with vesicular lesions or ulcers on the skin, eye or mouth and have no CNS or visceral organ involvement.<sup>6</sup>

With appropriate antiviral treatment to prevent progression, mortality is 0% and neurological and/or ocular morbidity is around 6% and more likely in those with at least 3 lesions or HSV-2.<sup>7</sup> However such infants are at risk of recurrent SEM disease during childhood, which may disrupt childcare and schooling, and may be misdiagnosed, for example, as recurrent varicella.

### *Central nervous system disease/meningoencephalitis*

In the UK, 35% have CNS disease with a median presentation of 14 days.<sup>5</sup> They may present with a variety of signs including lethargy, poor feeding, or seizures and may not have skin, eye and/or mouth lesions.<sup>6</sup> Median admission CRP may not be raised and was 3.9 mg/L in recent UK wide surveillance.<sup>5</sup>

Prior to antiviral therapy, 50% of infants with CNS disease died within 1 year.<sup>8</sup> With antiviral treatment, mortality from CNS disease is around 15% and more likely in those who are semi-comatose or comatose, in premature infants, and in those with delayed time to treatment.<sup>7</sup> Neurological morbidity (including developmental delay, epilepsy, blindness and cognitive disabilities) is common at 64%, and more frequent in those with seizures, HSV-2 infection, and those with delayed time to antiviral treatment.<sup>6,7</sup>

### *Disseminated infection*

In the UK, 33% of infants with neonatal herpes have disseminated disease with a median presentation of 6 days.<sup>5</sup> Multiple organs are involved and may include the liver, lungs and brain, and skin, eye and/or mouth symptoms may

be absent. Features of dissemination are typically non-specific with only 18% presenting with fever and 79% presenting with 'sepsis'.<sup>5,6</sup> Median admission CRP may not be significantly raised and was 20 mg/L in recent UK wide surveillance.<sup>5</sup>

Prior to antiviral therapy, 85% of infants with disseminated infection died within 1 year.<sup>8</sup> Disseminated disease carries the worst prognosis – with appropriate antiviral treatment, mortality is still around 66% and more likely in those who are semi-comatose or comatose, have HSV pneumonitis, disseminated intravascular coagulopathy, are premature, or with delayed antiviral treatment.<sup>5,7</sup> 41% of infants have long term morbidity and this is more likely in those with seizures, HSV-2 infection, or delayed antiviral treatment.<sup>7</sup>

Recent UK surveillance data has demonstrated an overall mortality of 24% (all presentations of neonatal HSV). 33% of preterm infants died in comparison with 19% of term infants. Mortality was more frequent in those with HSV-2 than those with HSV-1 infection (68% versus 29%), although previous studies have suggested that mortality may be higher in those with HSV-1 infection.<sup>5,7</sup>

### *Incidence*

Neonatal herpes is very rare in the UK, but surveillance data suggests that the incidence may be rising. Active surveillance by the British Paediatric Surveillance Unit (BPSU) between 1986 and 1991 found 76 cases over the five-and-a-half-year surveillance period with an incidence of 1.65/100 000 live births annually (95% CI 1.3–2.0).<sup>9</sup> Subsequent surveillance from 2004 to 2006 showed an approximate doubling of incidence with 86 cases seen over the three-year surveillance period, incidence 3.58/100,000.<sup>10</sup> A single centre study in Nottingham in 2006–2013 found an incidence of 17.5/100 000 live births, suggesting an increase in neonatal herpes of almost 5 times the UK wide incidence previously published.<sup>11</sup> Further surveillance by the BPSU between 2019 and 2022 reported 118 confirmed cases with 4 still pending and estimated incidence as 6.9/100,000 live births.<sup>5</sup>

The incidence in the UK is around 50% of that reported from other European countries and the USA.<sup>12,13</sup> In the USA, the average reported incidence is 10/100,000 or 1 in 10,000, but there is considerable variation between populations and rates of up to 1 in 7,500 have been reported in certain deprived inner-city populations, and 1 in 3,000 in Florida.<sup>14–16</sup> Data from the USA and Europe (as in the UK) suggest that incidence of neonatal herpes may be increasing over time.<sup>13,17,18</sup>

Recent data on seroprevalence of antibodies to HSV-1 and/or HSV-2 in mothers and pregnant people in the UK are lacking. However, studies in the USA and Europe suggest that antibodies to HSV-1 and -2 may be declining over time, rendering an increased number of mothers and pregnant

people vulnerable to primary herpes acquisition during pregnancy.<sup>14,19,20</sup> Over the last decade the incidence of primary genital herpes in women in the UK has remained fairly static, but reporting has been significantly affected by the impact of COVID-19 on sexual health clinics.<sup>21</sup>

### Aetiology

Neonatal herpes may be caused by herpes simplex virus type 1 (HSV-1) or herpes simplex virus type 2 (HSV-2) as either viral type can cause genital herpes in mothers and pregnant people, and HSV-1 may also be acquired due to post-natal contact. In recent UK surveillance, approximately 52% of neonatal herpes is due to HSV-1 and 48% due to HSV-2.<sup>5</sup>

Most cases of neonatal herpes occur as a result of either direct contact with infected vaginal secretions at birth (75–85%) or postnatal acquisition (10–25%) which may occur as a result of exposure to oro-labial herpes infection, usually from a close relative, friend of the parents or possibly a health care worker.<sup>4,9,10,22</sup> Trans-placental spread in viraemic mothers may very rarely cause in utero congenital herpes (5%).<sup>4</sup>

### Transmission

Genital herpes infection is classified as follows<sup>1</sup>:

- *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.

An initial episode may not be recognized as such as only approximately one third of patients present with symptoms following acquisition.<sup>23,24</sup> Therefore, what appears to be an initial episode may be a recurrent episode.

- *Recurrent episode*: recurrence of clinical symptoms due to reactivation of pre-existent HSV-1 or HSV-2 infection after a period of latency.

Factors associated with transmission of neonatal herpes include the type (primary/non-primary or recurrent) and timing of maternal infection, the absence of transplacentally-acquired maternal neutralising antibodies, the duration of rupture of membranes before delivery, the mode of delivery, and the use of assistance (vacuum, forceps or fetal scalp electrodes).<sup>25,26</sup> The risk of transmission is greatest when mothers and pregnant people acquire a new

infection (primary genital herpes) in the third trimester, particularly within 6 weeks of delivery, as viral shedding may persist and the baby is likely to be born before the development of protective maternal antibodies.<sup>25,26</sup>

Rarely, congenital herpes may occur because of transplacental intrauterine infection. Case reports suggest that the skin, eyes and CNS may be affected and there may be fetal growth restriction or fetal death.<sup>4,27–29</sup>

Although recurrent genital herpes is associated with a very low risk of neonatal herpes, recurrent herpes at the time of delivery, which is commonly asymptomatic or unrecognised, may cause neonatal herpes. HSV-2 type-specific antibody correlates with protection from severe neonatal HSV-2 in infants exposed to HSV-2 at birth.<sup>30</sup>

Data from the USA suggest that around 2% of women acquire genital HSV infection in pregnancy and most of these maternal infections are asymptomatic or unrecognised.<sup>3,26</sup> However, acquisition in the UK in pregnancy may vary markedly given differing rates of neonatal herpes between the UK and USA. It is difficult to distinguish clinically between recurrent and primary genital HSV infections, as many first noted episodes of HSV are not true primary infections.<sup>24</sup>

*Transmission associated with prematurity*. In the UK, 7.4% of live births are preterm (<37 weeks).<sup>31</sup> Preterm infants are at higher risk of neonatal herpes as, if delivered before 32–34 weeks gestation, they may not have received sufficient maternal antibodies to be protective, even where the parent is HSV seropositive. Recent UK surveillance data shows that 32% of babies with neonatal herpes are born <37 weeks (compared to the 7.4% national average): 6% < 28 weeks, 4% 28–31 + 6 weeks, 23% 32–36 + 6 weeks, 64% were term and 3% unknown gestation.<sup>5</sup> Outcomes were worse in premature infants with 33% of those born <37 weeks gestation dying in comparison with 19% of term (>37 weeks) infants, with increasing mortality associated with reducing gestation.<sup>5</sup> Disseminated herpes is more common in preterm infants and occurs mainly as a result of primary infection in mothers and pregnant people.<sup>5</sup> Furthermore, disseminated herpes has the highest mortality, again mortality increases with reducing gestation.<sup>5</sup>

Several studies have demonstrated that commencing prophylactic aciclovir or valaciclovir at 36 weeks in mothers and pregnant people with a history of genital herpes reduces maternal genital tract viral load and lesions at delivery.<sup>32–39</sup> It is therefore proposed that maternal antiviral suppressive therapy may reduce neonatal herpes, but this has not been studied sufficiently to definitively demonstrate that this is the case.<sup>40,41</sup> Recent UK surveillance BPSU demonstrates that 33% of all babies with neonatal HSV are born at or before 36 weeks and therefore would not benefit from suppressive aciclovir started at 36 weeks.<sup>5</sup> One randomised controlled trial in Uganda of 200 pregnant women known to be HSV-2 seropositive (excluding those with active lesions

at randomisation) demonstrated a significant reduction in preterm delivery in those commenced on aciclovir prophylaxis at 28 weeks compared to those commencing at 36 weeks.<sup>42</sup> Birth cohort data have demonstrated no significant increase in major birth defects in infants exposed to aciclovir or valaciclovir in the first trimester.<sup>43,44</sup>

Regarding risk benefit analysis of the timing of commencing antiviral prophylaxis in mothers and pregnant people known to have genital herpes in the UK population, where 23% of babies with neonatal herpes are born between 32 and 36 + 6 weeks gestation with only a further 4% born 28 to 31 + 6 weeks gestation, it is consensus opinion of the writing group that antiviral prophylaxis should be routinely offered from 32 weeks. This is a change from the previous guidance to start antiviral prophylaxis at 36 weeks. For those at significantly increased risk of preterm delivery, consensus opinion is to start antiviral prophylaxis from 22 weeks.

### *Disseminated herpes infection and post-partum presentation in mothers and pregnant people*

In adults, disseminated herpes simplex infection is rare and may present with encephalitis, hepatitis, disseminated skin lesions, viral sepsis or a combination of these conditions. However, it has been more commonly reported in pregnancy, particularly in the immunocompromised. The mortality of the pregnant woman or person associated with this condition is high.<sup>45</sup>

The adult may present unwell with HSV in pregnancy or in the days after delivery, with local or disseminated disease. Their infants may have been exposed to HSV viraemia via the placenta and/or early asymptomatic lesions via the birth canal and are also at risk of severe HSV disease and death. In babies for whom their previously pregnant mother or parent presents with primary HSV up to 4 weeks following birth, HSV testing and treatment of the infant must be initiated urgently.

All immunocompromised people (which may include those living with HIV with suppressed CD4 counts), are at increased risk of more severe and frequent symptomatic recurrent episodes of genital herpes during pregnancy and of asymptomatic shedding of HSV at term.<sup>46,47</sup> As coinfection with HSV and HIV results in an increased replication of both viruses,<sup>48</sup> there are concerns that genital reactivation of HSV may increase the risk of perinatal transmission of both HIV and HSV,<sup>46,47</sup> although this has not been realised in practice in the UK.

For more detailed information on the diagnosis and management of HSV infection in adults, please refer to the 2024 BASHH guideline on the management of genital herpes.<sup>1</sup> Detailed management of disseminated herpes simplex infections in adults is beyond the scope of this guideline, but in brief:

- Consider disseminated HSV in all unwell pregnant or perinatal women and people with a sepsis-like illness or with deranged or worsening liver function tests.
- Send samples of blood, skin lesions, CSF, and relevant bodily fluids for urgent HSV PCR as well as blood for HSV IgG (liaise directly with virology to ensure rapid testing).
- Commence high dose IV aciclovir (at a dose of 10 mg/kg three times a day based on ideal body weight) urgently prior to receiving results, at doses in accordance with the BNF, taking into account renal function and other relevant co-morbidities.<sup>49</sup>
- Liaise early with virology/microbiology/infectious diseases, and HDU/ITU teams if deteriorating.
- Urgently inform the neonatal team to review, the infant should be managed as a highest risk neonatal case (see section 'Management of the neonate').

### **Management of first episode genital herpes in mothers and pregnant people during pregnancy and within the 4 weeks following birth**

#### *Management points for acquisition at any gestation (to be read in conjunction with the following relevant section for stage of gestation)*

- At the first antenatal (booking) appointment (and later if appropriate), all mothers and pregnant people should have a discussion and be given information on infections that can impact on the baby in pregnancy or during birth (including herpes simplex virus).<sup>50</sup> This should take place regardless of whether they are known to have herpes simplex virus already, or not [1D].

Data on the impact of herpes simplex infection during pregnancy upon adverse pregnancy outcomes are varied. A meta-analysis found that herpes simplex virus infection during pregnancy increased the risk of spontaneous miscarriage, premature birth and stillbirth.<sup>51,52</sup> However, a study specifically reviewing first trimester acquisition found no evidence of an increased risk of spontaneous miscarriage with primary genital herpes.<sup>53</sup> Some studies have demonstrated increased perinatal morbidity (preterm labour and low birthweight), together with stillbirth,<sup>3,54</sup> however this was not shown in other studies.<sup>52,55</sup> No additional monitoring of such pregnancies is recommended.

There is no evidence of an increased risk of birth defects from maternal HSV infection,<sup>56–58</sup> apart from rare cases of congenital herpes simplex infection where case reports suggest that the skin, eyes and CNS may be affected and there may be fetal growth restriction or fetal death.<sup>27–29</sup>

- A careful history from mothers and pregnant people should be taken to identify any previous possible herpetic symptoms or diagnoses as per NICE guidance<sup>50</sup> [1D].
- Mothers and pregnant people with suspected genital herpes should be referred to a genitourinary medicine (GUM) physician who will confirm or refute the diagnosis, advise on management of genital herpes, and arrange a screen for other sexually transmitted infections [1D].
- Polymerase chain reaction (PCR) testing from ulcers should routinely include type specific HSV, varicella zoster virus (VZV) and *Treponema pallidum* for syphilis. Where available, enterovirus PCR should be considered, and (depending on risk factors) MPOX and LGV PCR may be considered in addition to testing for other tropical ulcerative diseases<sup>59–63</sup> [1D].
- Full screening for other sexually transmitted infections should also be undertaken including chlamydia, gonorrhoea, syphilis, HIV and (depending on risk factors) hepatitis B and C as per BASHH guidelines<sup>64</sup> [1D].
- Treatment should not be delayed whilst awaiting test results. Management of mothers and pregnant people should be in line with their clinical condition and will usually involve the use of oral (or intravenous for disseminated HSV at 10 mg/kg three times a day based on ideal body weight) aciclovir in standard doses (400 mg three times daily, usually for 5 days) or oral valaciclovir (500 mg twice daily, usually for 5 days) as per the BASHH guidelines.<sup>1</sup> Immunosuppressed mothers and pregnant people will require higher doses for a longer duration as per the BASHH guidelines.<sup>1</sup> Famciclovir should not be used in pregnancy due to lack of safety data<sup>44</sup> [1B].

The use of antivirals is associated with a reduction in the duration and severity of symptoms and a decrease in the duration of viral shedding.<sup>32–39</sup> A study from the USA found that having untreated genital HSV in the first or second trimester was associated with an increased risk of preterm delivery, but this association was not seen in women and people who were treated with antiviral medication.<sup>65</sup> Aciclovir and valaciclovir are not licensed for use in pregnancy but are considered safe and have not been associated with an increased incidence of birth defects.<sup>43,44</sup> Transient neonatal neutropenia<sup>44,66–68</sup> has been reported but no clinically significant adverse maternal or neonatal effects have been reported. Aciclovir and valaciclovir are well tolerated in pregnancy. For treatment courses no dose adjustment is necessary.<sup>69,70</sup>

- Other management of the symptomatic first episode should be in line with BASHH guidelines and may include the use of supportive therapies including paracetamol and topical lidocaine 2% gel or 5% ointment.<sup>1</sup> There is no evidence that either is harmful in pregnancy in standard doses [1D].
- Mothers and pregnant people with suspected genital herpes who are having midwifery-led care should be

referred for review by an obstetrician and have review by a genitourinary medicine (GUM) physician. The neonatologist should also be informed, and a delivery and postnatal management plan documented involving genitourinary medicine, obstetrics and neonatal collaboration [1D].

- Following acquisition, suppressive antivirals should be recommended. These reduce asymptomatic HSV shedding and lesions at term, and may also reduce premature delivery, but have not been studied sufficiently to definitively demonstrate prevention of neonatal HSV disease.<sup>32–42</sup> Aciclovir and valaciclovir have not been associated with an increase in major birth defects when given in pregnancy<sup>43,44</sup> and should be given at the following doses:
  - For all mothers and pregnant people: aciclovir 400 mg three times daily or valaciclovir 500 mg two times daily from 32 weeks of gestation.<sup>69</sup> In third trimester acquisition, it may be more convenient simply to continue the treatment dose antivirals until delivery, even if suppression is starting prior to 32 weeks [1C].
  - For all mothers and pregnant people assessed as being at high risk of premature delivery: aciclovir 400 mg two times daily or valaciclovir 500 mg once daily from 22 weeks of gestation, followed by aciclovir 400 mg three times daily or valaciclovir 500 mg two times daily from 32 weeks of gestation [1C].
  - Should mothers and pregnant people experience frequent recurrences of genital herpes despite being adherent to a suppressive antiviral regimen, dose adjustment may be considered after discussion with a genitourinary medicine (GUM) physician. In these cases, the possibility of HSV resistance to aciclovir (although rare) should be considered and discussed with a virologist.<sup>1</sup> Drug resistance testing may be obtained via the UK HSA laboratory at Collingdale and may be particularly considered for those who are immunosuppressed (including those with haemopoietic stem cell transplant, solid organ transplant or advanced HIV).
- Parents should be advised to seek urgent medical help if they have concerns regarding their baby in the first 6 weeks of life, and if they develop symptoms of:
  - Skin, eye and mucous membrane lesions.
  - Lethargy/irritability.
  - Poor feeding.
  - Fever [1D].
- Parents must be told to inform the doctor that they had genital herpes in pregnancy and that their symptomatic baby needs testing and treating for herpes infections unless another diagnosis is made [1D].
- Birthing mothers and parents who present with first episode genital herpes and/or disseminated HSV up to the 4 weeks following birth are likely to have been shedding at delivery. The adult may have been unwell without

classical herpetic lesions. This places the baby at high risk of neonatal HSV, they should be managed as a highest risk neonatal case (see section ‘Management of the neonate’) [1D].

### ***Additional considerations for first or second trimester acquisition (until 27+6 weeks of gestation), including second trimester acquisition with delivery within 6 weeks of acquisition***

- Where the pregnant woman or person is not known to have both HSV-1 and HSV-2, HSV serology should be performed, and the result used to inform the management of pregnancy and the birth plan (a birth plan is available in [appendix 3](#) but local birth plans informed by the BASHH guidelines may be used instead). Further information on HSV serology is found in the section ‘Serology in third trimester acquisition’ [1D].
- For mothers and pregnant people with first and second trimester acquisition of genital herpes who are not known to have both HSV-1 and HSV-2, a discussion should be had around considering avoiding sex in the third trimester, including sex with condoms and oral sex [IV, C]. This is to remove uncertainty about whether any lesions presenting in the third trimester are recurrences of their known HSV type or are an acquisition episode of the other type. Undertaking serology may avoid this discussion [2D].
- Providing that delivery does not ensue within the next 6 weeks the pregnancy should be managed expectantly, and vaginal delivery anticipated [IV, C]. However, if delivery ensues within 6 weeks of acquisition, Caesarean section should be the recommended mode of delivery as shedding may continue for up to 6 weeks, although it can last for longer than this. The risk of neonatal transmission of HSV is very high at 41% for those who have acquired primary herpes simplex in the third trimester and are shedding at the time of delivery<sup>3,71–73</sup> [1B] and it is anticipated that these same (or higher) risks exist for those acquiring primary herpes simplex in the second trimester who deliver within 6 weeks of acquisition.

### ***Additional considerations for third trimester acquisition (from 28 weeks of gestation) and up to the 4 weeks following birth***

- HSV serology should be performed. Further information on HSV serology in the third trimester is found in the following section ‘Serology in third trimester acquisition’ [1D].
- Caesarean section should be the recommended mode of delivery for all people developing first primary/non-primary episode genital herpes in the third trimester,

particularly those developing symptoms within 6 weeks of expected delivery as shedding may continue for up to 6 weeks, although it can last for longer than this. The risk of neonatal transmission of HSV is very high at 41% for those who have acquired primary herpes simplex in the third trimester and are shedding at the time of delivery<sup>3,71–73</sup> [1B].

**Serology in third trimester acquisition.** It can be difficult to distinguish clinically between initial and recurrent genital HSV infections, as in up to 15% of cases where mothers and pregnant people present with a first episode of clinical HSV infection, it will actually be a recurrent infection.<sup>24</sup> Serology may support identifying this, and therefore impact on pregnancy and birth management plans. The presence of antibodies of the same type as the HSV isolated from genital swabs would confirm this episode to be a recurrence rather than a primary infection and elective caesarean section would not be indicated to prevent neonatal transmission. HSV-1 serology does not differentiate between oro-labial and genital infection, but it is reasonable to assume that HSV-2 serology is consistent with genital infection.<sup>74</sup>

- Further information on HSV serology is found in the BASHH herpes guidelines and these should be read in conjunction with this section<sup>1</sup> [1D].
- Until results are received, an initial plan of delivery should assume that all first episode lesions are primary/non-primary initial genital herpes. This plan can then be modified if HSV antibody test results subsequently confirm a recurrent, rather than primary/non-primary, infection [1D].
- As interpretation of serology is complex, results should be discussed with a virologist or a genitourinary medicine physician [1D].
- For people presenting with first episode genital herpes in the third trimester, type-specific HSV antibody testing (immunoglobulin G (IgG) assays differentiating HSV-1 from HSV-2 infections) should be performed. Although a negative type-common antibody test result (which do not differentiate between HSV-1 and -2) may be helpful, type specific testing should not be delayed while waiting for a negative type-common result as this may delay management decisions [1B].
- Initial HSV-1 and HSV-2 infections can be identified by detecting seroconversion to IgG in paired serum samples. HSV serological testing on the antenatal booking bloods in addition to serology at the time of presentation is therefore helpful to confirm HSV antibody status when HSV-1 or -2 DNA is detected by PCR [1D].
- However, false positives and negatives may occur as people may fail to seroconvert, may serorevert, or may

have reduced test sensitivity due to a number of factors<sup>1,75–82</sup> [1B].

- As time to serology results may be prolonged in clinics without local HSV serology testing, clinicians should establish links with their laboratory service to ensure that timely results are available [1D].

### Management of mothers and pregnant people with a diagnosis of genital herpes prior to pregnancy, including those with recurrent herpes during pregnancy

- At the first antenatal (booking) appointment (and later if appropriate), all mothers and pregnant people should have a discussion and be given information on infections that can impact on the baby in pregnancy or during birth (including herpes simplex virus).<sup>50</sup> This should take place regardless of whether they are known to have herpes simplex virus already, or not [1D].
- Mothers and pregnant people with a diagnosis of genital herpes prior to pregnancy should be informed that the risk of neonatal herpes is low, even if lesions are present at the time of delivery (0%–3% for vaginal delivery),<sup>72</sup> and that there is no increase in the incidence of congenital abnormalities in the presence of recurrent genital herpes infection<sup>83</sup> [1C].
- Mothers and pregnant people with a previous genital herpes diagnosis should be referred to a genitourinary medicine physician who will advise on management of genital herpes and arrange a screen for other sexually transmitted infections if required [1D].
- Mothers and pregnant people with a previous genital herpes diagnosis who are having midwifery-led care should be referred for review by an obstetrician and have review by a genitourinary medicine physician. The neonatologist should also be informed, and a delivery and postnatal management plan documented involving genitourinary medicine, obstetrics and neonatal collaboration [1D].
- Suppressives antivirals for all mothers and pregnant people with known genital herpes should be recommended regardless of whether HSV recurrences occur during pregnancy [1D]. These reduce asymptomatic HSV shedding and lesions at term, and may also reduce premature delivery, however maternal antiviral suppressive therapy has not been studied sufficiently to definitively demonstrate that it prevents neonatal HSV disease.<sup>32–42</sup> Aciclovir and valaciclovir have not been associated with an increase in major birth defects when given in pregnancy<sup>43,44</sup> and should be given at the following doses:
  - For all mothers and pregnant people: aciclovir 400 mg three times daily or valaciclovir 500 mg two times daily from 32 weeks of gestation.<sup>69</sup>

- For all mothers and pregnant people assessed as being at high risk of premature delivery: aciclovir 400 mg two times daily or valaciclovir 500 mg once daily from 22 weeks of gestation, followed by aciclovir 400 mg three times daily or valaciclovir 500 mg two times daily from 32 weeks of gestation<sup>84</sup> [1C].
- Should mothers and pregnant people experience frequent recurrences of genital herpes despite being adherent to a suppressive antiviral regimen, dose adjustment may be considered after discussion with a genitourinary medicine (GUM) physician. In these cases, the possibility of HSV resistance to aciclovir (although rare) should be considered and discussed with a virologist.<sup>1</sup> Drug resistance testing may be obtained via the UK HSA laboratory at Collingdale and may be particularly considered for those who are immunosuppressed (including those with haemopoietic stem cell transplant, solid organ transplant or advanced HIV).
- For mothers and pregnant people with known genital herpes who are not known to have both HSV-1 and HSV-2, a discussion should be had around considering avoiding sex in the third trimester, including sex with condoms and oral sex [2D]. This is to remove uncertainty about whether any lesions presenting in the third trimester are recurrences of their known HSV type or are an acquisition episode of the other type. Undertaking serology in this situation may help clarify the situation and avoid the need for this discussion [2D].
- Vaginal delivery should be anticipated in the absence of other obstetric indications for caesarean section [1D].
- Parents should be advised to seek urgent medical help if they have concerns regarding their baby in the first 6 weeks of life, and if they develop symptoms of:
  - Skin, eye and mucous membrane lesions.
  - Lethargy/irritability.
  - Poor feeding.
  - Fever [1D].
- Parents must be told to inform the doctor that they had genital herpes in pregnancy and the baby needs testing and treating for herpes infections unless another diagnosis is made [1D].

### Managing recurrences in pregnancy

- Polymerase chain reaction (PCR) testing from ulcers should routinely include type specific HSV, varicella zoster virus (VZV) and *Treponema pallidum* for syphilis. Where applicable, enterovirus PCR should be considered, and (depending on risk factors) MPOX and LGV PCR may be considered in addition to testing for other tropical ulcerative diseases.<sup>59–63</sup> In the third trimester, the laboratory should be informed to enable rapid return of results. A clinically typical recurrence may be an acquisition episode of another HSV type, or indeed a different sexually transmitted infection [1D].



- Where the pregnant woman or person is not known to have both HSV-1 and HSV-2, HSV serology should be performed, and the result used to inform the management of pregnancy and the birth plan (a birth plan is available in [appendix 3](#) but local birth plans informed by the BASHH guidelines may be used instead). Further information on HSV serology is found in the section ‘Serology in third trimester acquisition’ [1D].
- Most recurrent episodes of genital herpes are short-lasting and resolve within 7–10 days without antiviral treatment. Supportive treatment measures using saline bathing, topical lidocaine 2% gel or 5% ointment, and analgesia with where standard doses of paracetamol alone will usually suffice [1D].
- Where antiviral episodic treatment is required to manage symptoms, the risks, benefits and alternatives should be discussed with mothers and pregnant people. Use of antivirals should be in line with their clinical condition and will usually involve the use of oral aciclovir in standard doses for episodic treatment (400 mg three times daily, usually for 5 days) or oral valaciclovir (500 mg twice daily, usually for 5 days) as per the BASHH guidelines.<sup>1</sup> Immunosuppressed mothers and pregnant people will require higher doses for a longer duration as per the BASHH guidelines.<sup>1</sup> Famciclovir should not be used in pregnancy due to lack of safety data<sup>44</sup> [1B].
- Where antiviral suppression is required for symptom management prior to 32 weeks, the risks, benefits and alternatives should be discussed with mothers and pregnant people. Suppression should be given as aciclovir 400 mg two times daily or valaciclovir 500 mg once daily, followed by aciclovir 400 mg three times daily or valaciclovir 500 mg two times daily from 32 weeks of gestation [1D].
- Other management aspects are discussed above in the ‘Management of mothers and pregnant people with a diagnosis of genital herpes prior to pregnancy, including those with recurrent herpes during pregnancy’ section [1D].
- Urgent referral should be made to a genitourinary medicine (GUM) physician, consultant obstetrician and neonatologist and an urgent delivery and postnatal management plan documented [1D].
- Polymerase chain reaction (PCR) testing from ulcers should routinely include type specific HSV, varicella zoster virus (VZV) and *Treponema pallidum* for syphilis. Where applicable, enterovirus PCR should be considered, and (depending on risk factors) MPOX and LGV PCR may be considered in addition to testing for other tropical ulcerative diseases.<sup>59–63</sup> The laboratory should be informed to enable rapid return of results. Although results are unlikely to be available in time to impact on delivery decisions, they may influence management of the neonate [1D].
- HSV serology should be performed. Further information on HSV serology in the third trimester is found in the following section ‘Serology in third trimester acquisition’ [1D].
- Parents should be advised to seek urgent medical help if they have concerns regarding their baby in the first 6 weeks of life, and if they develop symptoms of:
  - Skin, eye and mucous membrane lesions.
  - Lethargy/irritability.
  - Poor feeding.
  - Fever [1D].
- Parents must be told to inform the doctor that they had genital herpes in pregnancy and the baby needs testing and treating for herpes infections unless another diagnosis is made [1D].

### *First episode genital herpes at onset of labour (to be read in conjunction with the general management section above)*

Where primary episode genital herpes lesions are present at the time of delivery and the baby is delivered vaginally, the risk of neonatal herpes is estimated to be 41%.<sup>3,71–73</sup> For non-primary episode (mother or pregnant person already has one type of herpes and has newly acquired the second type) genital herpes lesions at birth, the risk is estimated 25%.<sup>85</sup> The risk of perinatal transmission depends on the timing of maternal acquisition of HSV, with the highest risk in infants born to people who have not completed HSV seroconversion during pregnancy (most commonly in the third trimester, within 6 weeks of delivery), and possibly those with low antibody avidity.<sup>86</sup>

## **Management of mothers and pregnant people with primary or recurrent genital lesions at the onset of labour or within the 4 weeks following birth**

### *General management*

Management of mothers and pregnant people with genital herpes at the onset of labour will be based on clinical assessment as there will not be time for confirmatory laboratory testing.

- A careful history from mothers and pregnant people should be taken to identify any previous possible herpetic symptoms or diagnoses as per NICE guidance<sup>50</sup> [1D].
- Caesarean section should be recommended to all mothers and pregnant people presenting with primary/non-primary episode genital herpes lesions at the time of delivery, to reduce exposure of the fetus to HSV which may be present in maternal genital secretions [1C].
- There is some evidence to suggest that the benefit of Caesarean section reduces if the membranes have been

ruptured for greater than 4 h.<sup>87</sup> However, there may be some benefit in performing a Caesarean section even after this time interval, and Caesarean section should be expedited in mothers and pregnant people whose membranes have ruptured to ensure that delivery occurs within 4 h where possible [1C].

- For those who decline a Caesarean section and proceed with vaginal delivery:
  - Intravenous aciclovir should be given intrapartum to mothers and pregnant people (5 mg/kg every 8 h) and subsequently to the neonate (intravenous aciclovir 20 mg/kg every 8 h).<sup>58,88</sup> It is unknown whether this reduces the risk of neonatal HSV infection.
- For those who proceed with a Caesarean section, especially where the membranes have already ruptured:
  - Intravenous aciclovir should be considered intrapartum to mothers and pregnant people (5 mg/kg every 8 h) and subsequently to the neonate (intravenous aciclovir 20 mg/kg every 8 h).<sup>58,88</sup> It is unknown whether this reduces the risk of neonatal HSV infection.
- Mothers and previously pregnant people who present with first episode genital herpes and/or disseminated HSV up to the 4 weeks following birth are likely to have been shedding at delivery. The adult may have been unwell without classical herpetic lesions. This places the baby at high risk of neonatal HSV, they should be managed as a highest risk neonatal case (see section 'Management of the neonate') [1D].

*Recurrent genital herpes at onset of labour when primary/non-primary infection was acquired before the 3<sup>rd</sup> trimester or more than 6 weeks prior to delivery (to be read in conjunction with the general management section above)*

- Mothers and pregnant people presenting with recurrent genital herpes lesions at the onset of labour should be advised that the risk to the baby of neonatal herpes is low (0%–3% for vaginal delivery)<sup>72</sup> [1C].
- Vaginal delivery should be offered to mothers and pregnant people where there is confidence that genital herpes lesions noted at the onset of labour are associated with recurrent rather than primary/non-primary infection. Evidence from the Netherlands shows that a conservative approach, facilitating vaginal delivery in the presence of an anogenital lesion, has not been associated with a rise in the number of neonatal HSV cases<sup>72</sup> [1B].
- Where suppressive antivirals for the pregnant woman or person with known genital herpes has been started earlier in pregnancy, these reduce asymptomatic HSV shedding and lesions at term, and may also reduce premature delivery. However maternal antiviral suppressive therapy has not been studied sufficiently to definitively demonstrate that it prevents neonatal HSV disease.<sup>32–42</sup>

- Where mothers and pregnant people with only one known HSV type have remained sexually active in the third trimester, a risk assessment should be undertaken to determine whether this could be a primary episode of the other HSV type [1D].
- A Caesarean section delivery for the purpose of reducing the risk of herpes transmission should not be recommended in view of the very low risk. The final choice of vaginal delivery versus caesarean section should be made by the pregnant woman or person, who should be advised to base their decision on the very low risk of transmission set against any other obstetric risk factors and the risks associated with caesarean section in accordance with National Institute for Health and Care Excellence (NICE) intrapartum guidelines<sup>89</sup> and considering guidance from their obstetric team [1D].
- There is no evidence to guide the management of mothers and pregnant people with spontaneous rupture of membranes at term, but many clinicians will advise expediting delivery to minimise the duration of potential exposure of the fetus to HSV [1D].

**Genital herpes in preterm prelabour rupture of membranes (before 37 + 0 weeks of gestation)**

*Primary/non-primary genital herpes in preterm prelabour rupture of membranes (PPROM)*

- The premature neonate is at high risk of neonatal HSV, they should be managed as a highest risk neonatal case (see section 'Management of the neonate') [1D].
- There is limited evidence to inform best obstetric practice when PPRM is complicated by primary HSV infection. Management should be guided by multidisciplinary team discussion involving the obstetricians, neonatologists and genitourinary medicine (GUM) physicians and will depend on the gestation that PPRM occurred. A delivery and postnatal management plan should be documented [1D].
- If the decision is made for immediate delivery, then the anticipated benefits of Caesarean section will remain in reducing the risk of neonatal herpes. If there is initial conservative management, mothers and pregnant people should be recommended to receive intravenous aciclovir 5 mg/kg every 8 h until delivery [1D].
- Prophylactic corticosteroids should be considered to reduce the implications of preterm delivery upon the infant as per NICE guidelines<sup>90</sup> [1B]. Prophylactic corticosteroids have been demonstrated to decrease mortality, respiratory problems, cerebral bleeding and developmental delay. There are no data on any impact of corticosteroids on HSV acquisition.
- If delivery is indicated within 6 weeks of the primary infection, delivery by Caesarean section may still offer

some benefit despite the prolonged rupture of membranes<sup>91–93</sup> [1D].

### **Recurrent genital herpes in PPRM**

- The premature neonate is at high risk of neonatal HSV, they should be managed as a highest risk neonatal case (see section ‘Management of the neonate’) [1D].
- Management should be guided by multidisciplinary team discussion involving the obstetricians, neonatologists and genitourinary medicine (GUM) physicians and will depend on the gestation that PPRM occurred. A delivery and postnatal management plan should be documented [1D].
- When PPRM is encountered in the presence of recurrent genital herpes lesions, the risk of neonatal transmission depends on the gestation and whether transplacental transfer of maternal HSV antibody has occurred [1D].
- Antiviral suppression for mothers and pregnant people with oral aciclovir 400 mg three times daily or valaciclovir 500 mg twice daily should be started and continued until delivery [1C].
- In the case of PPRM before 34 weeks there is evidence to suggest that expectant management is appropriate.<sup>91</sup> After this gestation, it is recommended that management is undertaken in accordance with relevant Royal College of Obstetricians and Gynaecologists (RCOG) guidelines on PPRM.<sup>94</sup> Antenatal corticosteroid administration<sup>95</sup> should be considered to reduce neonatal morbidity and mortality. Outcomes are not materially influenced by the presence of recurrent genital herpes lesions<sup>91,96</sup> [1B].

### **Management of mothers and pregnant people living with HIV with HSV infection**

There is evidence that a correlation exists between an HSV-2 diagnosis and HIV vertical transmission. However, studies are difficult to interpret given that many did not adjust for antiretroviral therapy (ART) use, and an association is often not demonstrated in studies adjusting for effective ART.<sup>97,98</sup> Genital shedding of HSV-2 or HSV ulceration at term has not been consistently associated with vertical transmission of HIV, and again many studies do not adjust for ART use among other important factors.<sup>47,99–103</sup>

- Management of mothers and pregnant people living with HIV is now aligned with treatment for HIV negative women and people – refer to the relevant section of this guideline [1D].
- When considering mode of delivery, recommendations within this guideline, the British HIV Association HIV in pregnancy guideline, in addition to obstetric factors should be considered<sup>104</sup> [1D].

### **Management of the neonate**

These guidelines are produced for the management of babies born to mothers and pregnant people with known previous genital HSV infection or suspected HSV genital infection at delivery. Management of infants suspected to have neonatal HSV but without a suspected parental risk are outside the scope of this guideline.

- All cases of possible neonatal HSV, irrespective of route of acquisition should be discussed with the regional Paediatric Infectious Diseases Team [1D].

### **General management prior to delivery**

- At the first antenatal (booking) appointment (and later if appropriate), all mothers and pregnant people should have a discussion and be given information on infections that can impact on the baby in pregnancy or during birth (including herpes simplex virus).<sup>50</sup> This should take place regardless of whether they are known to have herpes simplex virus already, or not [1D].
- In all cases the neonatal team should be informed at an early stage and should contribute, with genitourinary medicine (GUM) physicians and obstetricians, to the counselling of mothers and pregnant people, and in documentation of a delivery and postnatal management plan. The management plan should include the timing of investigations and any treatment to be offered [1D].

### **General management post delivery**

- In all cases urgently inform the neonatal team [1D].
- Undertake investigations and management as per the following investigations and management sections [1D].
- Where investigations are required, liaise with the laboratory team to ensure rapid return of results and support with interpretation of complex results by virologists].

### **Symptoms of neonatal HSV**

A high index of suspicion for HSV infection and rapid instigation of therapy are essential to successful management. This guideline is provided to support the care of mothers and pregnant people with known herpes infection, but most neonatal herpes presents in neonates born to mothers and pregnant people not known to have herpes infection.

Neonatal herpes may present as disease localised to only skin, eye and/or mouth (SEM), local central nervous system (CNS) disease (encephalitis alone or with SEM lesions) or disseminated disease with multiple organ involvement. Further information on these presentations is found in the ‘Background’ section of these guidelines. Symptoms which may indicate neonatal HSV infection are non-specific but include a progressive illness. Non-diagnostic associated symptoms may include:

- Poor feeding.
- Lethargy.
- Skin vesicles (present in approximately one third).
- Fever (present in approximately a quarter).
- Seizures.
- Changes in consciousness ranging from lethargy to coma.
- Liver dysfunction (more common in disseminated HSV).<sup>5</sup>
- Coagulopathy.
- Pneumonitis.
- Unwell birth mother or parent without known cause or with disseminated HSV.
- Although rare, neonatal herpes presenting in infants whose birthing mothers or people have received antiviral suppressive therapy, may have an atypical clinical presentation and drug resistance.<sup>41</sup> Where drug resistance is suspected, discuss with a virologist and consider sending samples for drug resistance testing (available at the UK HAS laboratory at Collingdale).
- Any neonate under 4 weeks where blood cultures are being considered should be reviewed for possible viral sepsis including HSV and have a blood PCR sent (EDTA sample) [1D].
- All local sepsis and antibiotic guidelines should refer to when to test for HSV. Superficial swabs of skin lesions, conjunctiva, mouth and anus, as well as blood and (where appropriate) CSF should all be sent urgently for HSV PCR. The laboratory should be contacted to ensure urgent return of results [1D].
- As oral herpetic lesions (cold sores) may be a source of neonatal herpes, the following advice should be given to pregnant parents to limit possible exposure to HSV during the first 4–6 weeks of life [1D]:
  - Everyone should wash their hands prior to touching the baby.
  - The baby should not be kissed by people who are not very close family members or carers of the baby.
  - Those kissing the baby should kiss the top of the baby's head and avoid kissing near the baby's mouth, nose and eyes (to avoid mucous membranes).
  - People with current cold sores should never kiss the baby, and those with a history of cold sores should avoid kissing the baby.
  - People with active herpes lesions at any site should avoid touching the baby unless they are very close family members or carers of the baby, and in this case, they should practice good hand hygiene.
- Health care professionals with current active lesions, or recurrent cold sores or herpetic whitlows who work on neonatal wards, other wards with babies <6 weeks of age, on delivery suite, or with immunosuppressed patients should liaise with their Occupational Health department and a risk reduction plan agreed [1D]. Great care should be taken to avoid transmission including covering lesions, careful hand hygiene, and consideration of antiviral suppression.

### Immediate investigations and management

- All cases of possible neonatal HSV should be discussed urgently with the regional Paediatric Infectious Diseases Team [1D].
- Any positive HSV test from an infant must be managed as highest risk [1D] immediate investigations and management should be undertaken as per [Table 1](#).

### Prevention of postnatal transmission and management of breastfeeding

Neonatal infection mostly occurs as the result of an infection at the time of birth, but in 10–25% of cases, a possible postnatal source is identified. Postnatal acquisition (10–25%) may occur as a result of exposure to oro-labial herpes infection (cold sore) or herpetic whitlow (lesion on the finger), usually from a close relative, friend of the parents or possibly a health care worker.<sup>4,9,10,22</sup>

Mothers and pregnant people diagnosed with HSV at least 3 months previously are likely to have HSV antibodies which may persist in the neonate up to around 6 months of age, providing a significant degree of protection.<sup>106</sup>

- Efforts to prevent postnatal transmission of HSV are important and advice should be given to the parents regarding this [1D].

### Management of breastfeeding

Breastfeeding contributes to the health of breastfeeding women and people, and their children in the short and longer term.

- Parents should be made aware of the benefits of breastfeeding, and advice given according to UK guidance<sup>107–110</sup> [1B].

### Use of antivirals in breastfeeding women and people

Aciclovir and valaciclovir are excreted in breast milk, but represent less than 1% of a therapeutic dose in the infant.<sup>111–113</sup> The presence of aciclovir or valaciclovir in breast milk has not been demonstrated to be harmful to infants.<sup>111</sup> Furthermore, aciclovir given orally to infants (at therapeutic doses) rarely causes serious side effects.<sup>114</sup> The manufacturer advises caution with use of aciclovir or valaciclovir when breastfeeding, but this is not based on evidence of harm.<sup>115</sup>

- When an antiviral is required by breastfeeding women and people, standard doses and durations of aciclovir or valaciclovir should be used as per the BASHH herpes guidelines<sup>1</sup> [1D].
- There are no human data on famciclovir in breastfeeding in humans,<sup>116</sup> and famciclovir should therefore not be used [1D].

**Table 1, Immediate investigations and management of the neonate by risk of neonatal herpes.**

Risk	Highest	High	Low	Lowest
Delivery method	All infants with symptoms consistent with HSV infection regardless of delivery method Babies with any positive HSV test even if this is suspected to be detection of maternal HSV Babies born by vaginal delivery in the presence of active initial herpes lesions Birthing mother or parent systemically unwell with possible HSV Birthing mother or parent presents post-partum with active primary herpes lesions within 4 weeks of delivery	Pregnant parent had an initial HSV infection within the previous 6 weeks and baby is asymptomatic and born by • Vaginal delivery OR • Caesarean section regardless of duration of rupture of membranes	Asymptomatic babies born by any delivery method in the presence of active recurrent herpes lesions Asymptomatic babies born at <37 weeks by any delivery method with no active lesions at delivery and a history of HSV infection more than 6 weeks previously	Asymptomatic babies born at >37 weeks by any delivery method with <sup>99</sup> with no active lesions in birthing woman or person at delivery AND a history of HSV infection more than 6 weeks previously
Clinical assessment	Urgently inform the neonatal team Urgent assessment soon after birth, bearing in mind that the presentation of neonatal HSV may be non-specific and that skin lesions may not be present Isolate infant from other babies and nurse using barrier methods to reduce the risk of postnatal transmission to other babies. Isolation should continue until neonatal herpes has been excluded or treatment completed in the event of neonatal HSV being confirmed Ophthalmology review	Urgently inform the neonatal team Urgent assessment soon after birth bearing in mind that the presentation of neonatal HSV may be non-specific and that skin lesions may not be present. If evidence of neonatal HSV is found, investigate as per symptomatic infants Isolate infant from other babies and nurse using barrier methods to reduce the risk of postnatal transmission to other babies. Isolation should continue until neonatal herpes has been excluded or treatment completed in the event of neonatal HSV being confirmed	Urgently inform the neonatal team Urgent assessment soon after birth bearing in mind that the presentation of neonatal HSV may be non-specific and that skin lesions may not be present. If evidence of neonatal HSV is found, investigate as per symptomatic infants	Inform the neonatal team No investigations required Normal postnatal with a neonatal examination at 24 h of age, after which the baby can be discharged from the hospital if well and feeding is established
Timing of investigations	Urgent (note maternal or birth parent HSV may still be detected on surface swabs, and therefore should be repeated if taken <24 h of life)	24 h post-delivery (note maternal or birth parent HSV may still be detected on surface swabs, and therefore should be repeated if taken <24 h of life)	24 h post-delivery (note maternal or birth parent HSV may still be detected on surface swabs taken <24 h of life)	
HSV PCR swab	Any visible lesions Throat swab Nose swab Conjunctival swabs Rectal swab	Throat swab Nose swab Conjunctival swabs Rectal swab	Throat swab Nose swab Conjunctival swabs Rectal swab	
Bloods	HSV PCR (1 mL EDTA required) (note may take >24 h for sufficient HSV replication to occur for a positive result to occur, and so a negative test does not exclude infection, may need to be repeated) <sup>105</sup> Full blood count Liver function tests Coagulation screen	HSV PCR (1 mL EDTA required) (note may take >24 h for sufficient HSV replication to occur for a positive result to occur, and so a negative test does not exclude infection, may need to be repeated) <sup>106</sup> Full blood count Liver function tests Coagulation screen	HSV PCR (1 mL EDTA required) (note may take >24 h for sufficient HSV replication to occur for a positive result to occur, and so a negative test does not exclude infection, may need to be repeated) <sup>106</sup>	

(continued)

Table 1, (continued)

Risk	Highest	High	Low	Lowest
Lumbar puncture for CSF	If clinically safe, undertake lumbar puncture for CSF and send for <ul style="list-style-type: none"> <li>• HSV PCR</li> <li>• Protein</li> <li>• Glucose</li> </ul>	If clinically safe, undertake lumbar puncture for CSF and send for <ul style="list-style-type: none"> <li>• HSV PCR</li> <li>• Protein</li> <li>• Glucose</li> </ul>		
Other tests	<ul style="list-style-type: none"> <li>• Cell count, microscopy and culture</li> </ul> As guided by the infant's clinical condition (for example chest X-ray) <p>In cases where drug resistance is a concern, discuss with a virologist and consider sending samples for drug resistance testing (available at the UK HAS laboratory at Collingdale)</p>	Cell count, microscopy and culture		
Management	Urgently start aciclovir 20 mg/kg IV without waiting for results. In cases where there is concern around possible aciclovir resistance or there is a shortage of IV aciclovir, IV foscarnet or cidofovir may be considered <p>Duration of treatment</p> <ul style="list-style-type: none"> <li>• All results are negative, and no other cause identified: 10 days</li> <li>• Skin, eye and mouth disease only: 14 days</li> <li>• CNS or disseminated disease, or no CNS obtainable but other positive HSV tests: 21 days.</li> </ul> Send blood and CSF (if previously positive) on day 17–20 (near as possible to day 21 depending on duration of laboratory result return times) for HSV PCR to ensure negative prior to stopping treatment on day 21. If CSF remains positive, continue IV aciclovir for a further week and repeat blood and CSF prior to stopping IV aciclovir. If a further positive test is obtained, provide a further week of IV aciclovir <p>A long line may be considered to avoid extravasation of IV aciclovir</p> Oral aciclovir prophylaxis at 300 mg/m <sup>3</sup> TDS for 6 months to start post IV therapy for all infants with CNS or disseminated disease and considered in infants with skin, eye and mouth disease to reduce risk of CNS recurrences <p>Practice good hand hygiene and take care to reduce risk of postnatal infection from maternal genital secretions or other sources including anyone with oral HSV-1</p> Seek urgent medical help if they have concerns regarding their baby in the next 6 weeks, in particular <ul style="list-style-type: none"> <li>• Skin, eye and mucous membrane lesions</li> <li>• Lethargy/irritability</li> <li>• Poor feeding</li> <li>• Fever</li> </ul>	Urgently start aciclovir 20 mg/kg IV without waiting for results. In cases where there is concern around possible aciclovir resistance or there is a shortage of IV aciclovir, IV foscarnet or cidofovir may be considered <p>Duration of treatment</p> <ul style="list-style-type: none"> <li>• All results are negative, and baby remains asymptomatic: 10 days</li> <li>• Positive skin swab from completely intact skin: 10 days</li> <li>• Positive skin swabs from areas of trauma without vesicles should be treated as per highest risk</li> <li>• If baby becomes symptomatic or if any test is positive manage as per highest risk</li> </ul> A long line may be considered to avoid extravasation of IV aciclovir	If any HSV test is positive, manage as per highest risk	
Advice to parents and carers				

### Breastfeeding with current or previous herpetic ulcers on the breast

Herpes DNA is detectable in breast milk,<sup>117</sup> but is not believed to be a source of infection for nursing infants. However, in the rare situation of breastfeeding women and people having current or previous herpetic lesions on the breast, transmission of HSV to the infant is possible by direct or indirect contact with lesions. The greatest risk of neonatal herpes is in the first 6 weeks of life.

- Herpetic lesions on the breast may be easily mistaken for impetigo or eczema. Possible lesions should therefore be tested promptly for HSV. Case reports suggest that herpetic lesions on the breasts are more likely to be due to HSV-1<sup>118–120</sup> [1D].
- In the presence of current herpetic ulcers on the breast, breastfeeding women and people should not breastfeed the infant from the affected breast and ensure that the infant does not touch the breast, until all lesions have healed [1D].
- Breast milk can be contaminated if it comes in contact with active herpetic lesions through touching the breast during hand expression or via the pump. Breastfeeding women and people should not feed the infant expressed breast milk from the affected breast until all lesions have healed. Expressed breast milk from the affected side should not be used. Breast pumps and bottles should be sterilised. Lesions on the affected breast should be completely covered to avoid transmission and good hand hygiene practices followed. Breastfeeding or expressing milk from the unaffected breast can continue [1D].
- Herpetic lesions should be reviewed by a clinician to ensure that they have healed and to confirm that the breastfeeding women and people can resume breastfeeding or expressing milk from the affected breast [1D].
- Some breastfeeding women and people may need additional support to maintain their milk production and may need to supplement with their expressed human milk (previously expressed milk or expressed milk from the unaffected breast) or formula while herpetic lesions on the breast are healing [1D].
- A first episode or recurrence of herpes on the breast should be treated with standard doses of aciclovir or valaciclovir as per the BASHH herpes guidelines<sup>1</sup> [1D].

There are no published data on asymptomatic shedding of HSV from the breast in those with a history of herpetic ulcers on the breast, but it may occur and may cause transmission. Asymptomatic shedding following a first episode of genital herpes is known to be significant, particularly in the first 3 months following herpes acquisition.<sup>121</sup>

Mothers and pregnant people diagnosed with HSV at least 3 months previously are likely to have HSV antibodies which may persist in the neonate up to around 6 months of age,

providing a significant degree of protection.<sup>106</sup> Guidelines from countries with high rates of neonatal herpes in comparison with the UK, do not address asymptomatic shedding and promote breastfeeding provided there are no active herpetic lesions on the breast.<sup>122</sup> Transmission due to asymptomatic shedding in this situation is therefore likely to be very low. There are no data on the use of aciclovir or valaciclovir suppression therapy in this situation, but antiviral suppression is likely to reduce shedding.

- After a first episode of herpes on the breast or where there are recurrent breast lesions, breastfeeding parents should continue with aciclovir or valaciclovir suppressive therapy at doses recommended in the BASHH herpes guidelines,<sup>1</sup> for at least 6 months, or until the infant reaches the age of 6 months, whichever is longer [1D].
- Where there is a history of previous breast ulcers, with no recurrences during breast feeding, breastfeeding parents may consider taking suppressive antivirals at doses as recommended in the BASHH herpes guidelines,<sup>1</sup> until the infant reaches the age of 6 weeks of life [1D].

### Management of clinically discordant couples

- At the first antenatal (booking) appointment (and later if appropriate), all mothers and pregnant people should have a discussion with the booking midwife and be given information on infections that can impact on the baby in pregnancy or during birth (including herpes simplex virus).<sup>50</sup> This should take place regardless of whether they are known to have herpes simplex virus already, or not [1D].
- Couples where the pregnant woman or person has no history of previous genital ulceration, and the sexual partner is known or suspected to have a previous diagnosis of genital HSV should be considered to be clinically discordant [1D].
- Serology may help identify couples who are sero-discordant although multiple caveats to its reliability apply (more information is in the following section ‘Use of serology in clinically discordant couples’) [1D].
- Advice on reducing transmission risk in non-pregnant clinically discordant couples is found in the BASHH herpes guidelines and should be reviewed with these guidelines<sup>1</sup> [1D].

There are a lack of data on reducing transmission to mothers and pregnant people. Data on risk reduction in non-pregnant women and people may not be able to be extrapolated to the pregnant population, as mothers and pregnant people may be at increased risk of HSV acquisition, and it is possible that interventions to reduce risk of acquisition may be less effective in this situation.

- Several strategies may be implemented to reduce risk of acquisition to mothers and pregnant people, who should be

advised to particularly avoid acquisition during the third trimester (as risk of neonatal herpes is increased), and in the 2 weeks prior to the third trimester (incubation period) [1D].

- Risk reduction options should be discussed with clinically discordant couples to ensure that couples can make an informed decision about which methods they wish to employ to attempt to reduce transmission risk [1D].
- Abstinence from sexual activity (including vaginal, anal and oral sex, and mutual masturbation) in the third trimester and the 2 weeks prior to this is likely to be the most effective way to reduce transmission risk, and this should be recommended to couples [1D].
- Where abstinence is unacceptable to couples, the following risk reduction strategies should be advised:
  - Selective abstinence during recurrences and prodromes.
  - Male condoms used consistently and correctly might reduce the risk of genital herpes transmission<sup>123–126</sup>
  - Antiviral suppression of the sexual partner with known HSV with aciclovir (400 mg twice daily) or valaciclovir (500 mg once daily) will suppress symptomatic and asymptomatic viral shedding and may reduce transmission risk,<sup>127–130</sup> and this should be offered to all couples [1D].
- Mothers and pregnant people without known orolabial herpes should be advised to abstain from receptive oral sex during the third trimester, and the two weeks prior to this (due to the incubation period for presenting with first episode genital herpes) to reduce the risk of genital HSV infection [IV, C]. Undertaking serology in this situation may help guide the discussion.

### Use of serology in clinically discordant couples

- Routine HSV-2 serologic screening of mothers and pregnant people is not recommended<sup>131</sup> [1D].
- In couples who are clinically discordant, undertake type-specific herpes serology in both the pregnant woman or person, and the partner known to have genital herpes [1D].
- When a pregnant woman or person is in a clinically discordant partnership and tests positive for HSV-2 on serology, manage as per recurrent disease. HSV-1 serology does not differentiate site of infection and so may indicate oro-labial infection or genital infection [1D].

Type-specific serologic tests may be useful for identifying mothers and pregnant people at risk for HSV infection acquisition due to having a clinically discordant sexual partner, to guide counselling to reduce acquisition risk. Serologic tests may also be useful for mothers and pregnant people with a history of genital ulceration with no confirmed diagnosis of genital herpes or another cause of the ulceration.

Interpretation of serology results is discussed in the BASHH Herpes guidelines and advice provided here should be reviewed with these guidelines.<sup>1</sup> It is important to

remember however that serology may be both falsely positive or negative, and positive predictive test value in people who have never had genital lesions may be low.<sup>131</sup> Serology can therefore only be used to guide advice around prevention of transmission rather than provide an absolute guarantee of herpes status. Expert virologist advice around interpretation of serological results may be helpful to guide advice.

### Performance measures

1. Mothers and pregnant people with genital ulcers should have an anogenital ulcer panel of PCR tests performed to include type specific HSV, and if appropriate varicella zoster virus (VZV) and *Treponema pallidum* for syphilis. Target 97%.
2. At the first antenatal (booking) appointment (and later if appropriate), all mothers and pregnant people should have a discussion and be given information on infections that can impact on the baby in pregnancy or during birth (including herpes simplex virus).<sup>50</sup> This should take place regardless of whether they are known to have herpes simplex virus already, or not, and should attempt to identify known or possible genital herpes in the patient and potential serodiscordance with their partners. Target 97%.
3. Pregnant women and people presenting with an initial episode of genital herpes should be commenced on acyclovir and referred promptly to a GUM service. If they are in active labour urgent GUM advice should be sought where this is available. Target 97%.
4. Mothers and pregnant people with genital herpes should be provided with written information on genital herpes in pregnancy. Target 90%.

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### Supplemental Material

Supplemental material for this article is available online.

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