



Royal College of  
Obstetricians &  
Gynaecologists

# Management of Genital Herpes in Pregnancy

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## **What's new in the 2014 *Management of Genital Herpes in Pregnancy* guideline?**

This guideline has been written as a consensus guideline between the British Association for Sexual Health and HIV (BASHH) and the Royal College of Obstetricians and Gynaecologists (RCOG) where previously there were two separate guidelines which in part gave conflicting advice.

Stronger recommendation to offer a vaginal delivery to women with recurrent genital herpes in pregnancy.

New section on genital herpes in preterm prelabour rupture of membranes.

New section on the management of HIV-positive women with genital herpes.

Flow chart for management of herpes in mother and neonate (Appendix 1).

# 1. Objective and scope

In 2007, the British Association for Sexual Health and HIV (BASHH) published its guidance on the management of genital herpes, including a section on management in pregnancy, and the Royal College of Obstetricians and Gynaecologists (RCOG) published their Green-top Guideline on the management of genital herpes in pregnancy.<sup>1,2</sup> In 2010, a European guideline on the management of genital herpes was published, which included a section on management in pregnancy.<sup>3</sup>

In order to achieve consensus, it was decided that a joint BASHH and RCOG guideline on the management of herpes in pregnancy should be written to update the previous guidance from the two organisations. For more detailed information on the general management of genital herpes infection in nonpregnant patients, this guideline should be considered in conjunction with the 2014 BASHH guideline on the management of genital herpes (currently undergoing consultation).

The scope of this guideline is the inpatient and outpatient management of genital herpes simplex virus infection in the antenatal, intrapartum and postnatal periods. For the prevention of genital herpes infection in uninfected mothers during pregnancy, please see the transmission prevention advice in the 2014 BASHH guideline on the management of genital herpes (currently undergoing consultation).

The population covered by this guideline includes pregnant women with a suspected or confirmed diagnosis of genital herpes simplex infection in primary or secondary care.

This guideline is aimed at healthcare professionals working in maternity units and departments offering level 3 care in the management of sexually transmitted infections within the UK. However, the principles of the recommendations should be adopted across all services, including community care.

## Stakeholder involvement

Clinicians from the Herpes Special Interest Group of BASHH and the RCOG Guidelines Committee have been involved in writing this guideline. The draft guideline was sent for consultation to the Herpes Viruses Association (HVA) for patient involvement. The guideline was posted on the BASHH and RCOG websites for 3 months for consultation, with a direct request to the Royal College of Paediatrics and Child Health (RCPCH) for external peer review.

## 2. 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: <http://www.bashh.org/guidelines>). A literature search was performed using PubMed/MEDLINE, EMBASE, Google, The Cochrane Library and relevant guidelines from January 1981 to January 2014.

A MEDLINE/PubMed and EMBASE search was carried out from January 1981 to January 2014 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'. 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 January 2014 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: 2010 European guideline for the management of genital herpes; 2007 BASHH guidance on the management of genital herpes; and the 2007 RCOG Green-top Guideline on the management of genital herpes in pregnancy.

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 on the basis of the best available evidence (Appendix 2). In areas where evidence is lacking, recommendations based on consensus opinion within the writing group have been made.

## 3. Background

Neonatal herpes is a very rare but serious viral infection with a high morbidity and mortality.<sup>4</sup> It is classified into three subgroups in the infant depending on the site of infection:

- disease localised to skin, eye and/or mouth
- local central nervous system (CNS) disease (encephalitis alone)
- disseminated infection with multiple organ involvement.

### Disease localised to skin, eye and/or mouth

Infants who present with symptoms localised to the skin, eye or mouth alone have the best prognosis and represent approximately 30% of neonatal herpes infections.<sup>5</sup> With appropriate antiviral treatment, neurological and/or ocular morbidity is less than 2%.<sup>6</sup>

### Local CNS disease and disseminated infection

70% of infants with neonatal herpes have disseminated and/or CNS infection and approximately 60% of infants with local CNS and/or disseminated disease will present without skin, eye and/or mouth infection.<sup>5</sup> Infants with local CNS disease often present late (generally between 10 days and 4 weeks of age). With antiviral treatment, mortality from local CNS disease is around 6% and neurological morbidity (which may be lifelong) is 70%. Disseminated disease carries the worst prognosis; with appropriate antiviral treatment, mortality is around 30% and 17% have long-term neurological sequelae. The poor outcomes of disseminated and local CNS disease have been attributed to delays between symptom onset and treatment.<sup>6</sup>

Neonatal infection occurs as the result of an infection at the time of birth; in contrast, congenital herpes is extremely rare and occurs by transfer of infection in utero.

### Incidence

Neonatal herpes is rare in the UK, in contrast to some other European countries and the USA. 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>7</sup> Subsequent surveillance from 2004 to 2006 showed an approximate doubling of incidence with 86 cases seen over the three-year surveillance period.<sup>5</sup> This increase may reflect the rise in the prevalence of sexually transmitted infections, demographic and social changes within the general population and improvements in diagnostic techniques.<sup>5</sup> Further published incidence data are awaited.

The incidence in the UK is around 50% of that reported from other European countries.<sup>8</sup> In the USA, the average reported incidence is 1 in 15 000, but there is considerable variation between populations and rates of up to 1 in 7500 have been reported in certain deprived inner-city populations.<sup>6,9</sup>

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## 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 the mother. Approximately 50% of neonatal herpes is due to HSV-1 and 50% due to HSV-2.<sup>5</sup> Most cases of neonatal herpes occur as a result of direct contact with infected maternal secretions, although in 25% of cases a possible source of postnatal infection was identified, usually a close relative of the mother.<sup>5,7</sup> Postnatal infection may occur as a result of exposure to oro-labial herpes infection.

## Transmission

Factors associated with transmission include the type of maternal infection (primary or recurrent), the presence of transplacental maternal neutralising antibodies, the duration of rupture of membranes before delivery, the use of fetal scalp electrodes and the mode of delivery.<sup>6,9</sup> The risks are greatest when a woman acquires 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>6,9</sup>

Rarely, congenital herpes may occur as a result 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>10–12</sup>

Disseminated herpes is more common in preterm infants and occurs almost exclusively as a result of primary infection in the mother.

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 the localised forms of neonatal herpes: both local CNS disease and skin, eye and mouth infection. Transplacentally acquired HSV antibodies do not prevent herpes virus spreading to the brain of the neonate.<sup>13</sup>

Data from the USA suggest that around 2% of women acquire genital HSV infection in pregnancy<sup>4</sup> and most of these maternal infections are asymptomatic or unrecognised.<sup>4,9</sup> However, acquisition in the UK in pregnancy may vary markedly given differing rates of neonatal herpes between the UK and USA. It may be difficult to distinguish clinically between recurrent and primary genital HSV infections, as many first episode HSV infections are not true primary infections.<sup>14</sup>

## Disseminated herpes infection in the mother

Disseminated herpes, which may present with encephalitis, hepatitis, disseminated skin lesions or a combination of these conditions, is rare in adults. However, it has been more commonly reported in pregnancy, particularly in the immunocompromised. The maternal mortality associated with this condition is high.<sup>15</sup> All immunocompromised women, such as those infected with the HIV virus, 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>16,17</sup> As co-infection with HSV and HIV results in an increased replication of both viruses,<sup>18</sup> there are concerns that genital reactivation of HSV may increase the risk of perinatal transmission of both HIV and HSV,<sup>16,17</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 the mother, please refer to the 2014 BASHH guideline on the management of genital herpes.

## 4. Management of pregnant women with first episode genital herpes

### First or second trimester acquisition (until 27<sup>+6</sup> weeks of gestation)

- There is no evidence of an increased risk of spontaneous miscarriage with primary genital herpes in the first trimester. Level of evidence III
- C** • Women with suspected genital herpes should be referred to a genitourinary medicine physician who will confirm or refute the diagnosis by viral polymerase chain reaction (PCR), advise on management of genital herpes and arrange a screen for other sexually transmitted infections.
- Treatment, however, should not be delayed. Management of the woman should be in line with her clinical condition and will usually involve the use of oral (or intravenous for disseminated HSV) aciclovir in standard doses (400 mg three times daily, usually for 5 days). The use of aciclovir is associated with a reduction in the duration and severity of symptoms and a decrease in the duration of viral shedding. Aciclovir is not licensed for use in pregnancy but is considered safe and has not been associated with an increased incidence of birth defects. Transient neonatal neutropenia<sup>19-22</sup> has been reported but no clinically significant adverse maternal or neonatal effects have been reported. Aciclovir is well tolerated in pregnancy. For treatment courses no dose adjustment is necessary.<sup>23,24</sup> There is no evidence of an increased risk of birth defects with aciclovir, famciclovir or valaciclovir if used in the first trimester.<sup>22</sup> Level of evidence IV
- C** Safety data for aciclovir may be extrapolated to valaciclovir in late pregnancy, as it is the valine ester, but as there is less experience with the use of valaciclovir or famciclovir, they are not recommended as a first-line treatment.<sup>22</sup> Level of evidence III
- The obstetrician should be informed
- Paracetamol and topical lidocaine 2% gel can be offered as symptomatic relief. There is no evidence that either is harmful in pregnancy in standard doses.
- Women with suspected genital herpes who are having midwifery-led care should be referred for review by an obstetrician, ideally after review by a genitourinary medicine physician.
- Providing that delivery does not ensue within the next 6 weeks, the pregnancy should be managed expectantly and vaginal delivery anticipated. There is no evidence that HSV acquired in pregnancy is associated with an increased incidence of congenital abnormalities.<sup>25</sup> Level of evidence III
- A** • Following first or second trimester acquisition, daily suppressive aciclovir 400 mg three times daily from 36 weeks of gestation reduces HSV lesions at term and hence the need for delivery by caesarean section.<sup>26-31</sup> It has also been shown to reduce asymptomatic viral shedding (similar results have been seen with valaciclovir, although valaciclovir is not recommended for use in pregnancy in view of lack of experience with its use).<sup>27,32,33</sup> Level of evidence Ib



### Third trimester acquisition (from 28 weeks of gestation)

<b>B</b>	<ul style="list-style-type: none"><li>• There is some evidence of increased perinatal morbidity (preterm labour and low birthweight), together with stillbirth,<sup>4,34</sup> however the data are conflicting<sup>4</sup> so no additional monitoring of such pregnancies is recommended. There is insufficient evidence to suggest an association between HSV and stillbirth as a cause of fetal death<sup>35</sup> with some studies demonstrating no association.<sup>36</sup></li></ul>	Level of evidence III
<b>C</b>	<ul style="list-style-type: none"><li>• Treatment should not be delayed. Management of the woman should be in line with her clinical condition and will usually involve the use of oral (or intravenous for disseminated HSV) aciclovir in standard doses (400 mg three times daily, usually for 5 days). In the third trimester, treatment will usually continue with daily suppressive aciclovir 400 mg three times daily until delivery.</li></ul>	
<b>B</b>	<ul style="list-style-type: none"><li>• Caesarean section should be the recommended mode of delivery for all women developing first episode genital herpes in the third trimester, particularly those developing symptoms within 6 weeks of expected delivery, as the risk of neonatal transmission of HSV is very high at 41%.<sup>4,37–39</sup></li></ul>	Level of evidence IIb
<b>C</b>	<ul style="list-style-type: none"><li>• It can be difficult to distinguish clinically between primary and recurrent genital HSV infections, as in up to 15% of cases where a woman presents with a first episode of clinical HSV infection, it will actually be a recurrent infection.<sup>14</sup> For women presenting with first episode genital herpes in the third trimester, particularly within 6 weeks of expected delivery, type-specific HSV antibody testing (immunoglobulin G [IgG] antibodies to HSV-1 and HSV-2) is advisable. For these women, characterising the infection will influence the advice given regarding mode of delivery and risk of neonatal herpes infection. 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. However, it should be noted that it may take 2–3 weeks for the results of this test to become available. It is therefore recommended that an initial plan of delivery should be based on the assumption that all first episode lesions are primary genital herpes. This plan can then be modified if HSV antibody test results subsequently confirm a recurrent, rather than primary, infection. As interpretation of serology can be complicated, results should be discussed with a virologist or genitourinary medicine physician.</li></ul>	Level of evidence IV

## 5. Management of pregnant women with recurrent genital herpes

- B** • Women with recurrent genital herpes 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).
- C** • Although there is no evidence that aciclovir is unsafe in early pregnancy, the majority of recurrent episodes of genital herpes are short-lasting and resolve within 7–10 days without antiviral treatment. Supportive treatment measures using saline bathing and analgesia with standard doses of paracetamol alone will usually suffice.
- Vaginal delivery should be anticipated in the absence of other obstetric indications for caesarean section.
- C** • Daily suppressive aciclovir 400 mg three times daily should be considered from 36 weeks of gestation.  
There is insufficient evidence to determine whether this reduces the incidence of neonatal herpes; however, it reduces viral shedding and recurrences at delivery so may reduce the need for caesarean section. Limited information exists regarding the neonatal safety of prophylaxis. The risks, benefits and alternatives to daily suppressive therapy should be discussed with women who have a history and prophylaxis initiated for women who desire intervention.<sup>33</sup>
- C** • This increase from the standard suppressive dose of 400 mg twice daily is recommended in view of the greater volume of distribution of the drug during pregnancy.<sup>26,40</sup>
- B** • Sequential PCR culture during late gestation to predict viral shedding at term,<sup>17</sup> or at delivery to identify women who are asymptotically shedding HSV, is not indicated.
- There is no increased risk of preterm labour, preterm prelabour rupture of membranes or fetal growth restriction associated with women seropositive for HSV. The incidence of congenital abnormalities is not increased in the presence of recurrent genital herpes infection.<sup>41</sup>

Level of evidence  
III

Level of evidence  
Ia

Level of evidence  
IIa

## 6. Management of women with primary or recurrent genital lesions at the onset of labour

### General management

- C** • Management of a woman with genital herpes at the onset of labour will be based on clinical assessment as there will not be time for confirmatory laboratory testing. The clinician must take a history in order to ascertain whether this is a primary or recurrent episode. A viral swab from the lesion(s) should nonetheless be taken, since the result may influence management of the neonate.
- The neonatologist should be informed.

### Primary episode

- B** • Caesarean section should be recommended to all women presenting with primary episode genital herpes lesions at the time of delivery, or within 6 weeks of the expected date of delivery, in order to reduce exposure of the fetus to HSV which may be present in maternal genital secretions.<sup>9</sup>
- C** • There is some evidence to suggest that the benefit of caesarean section reduces if the membranes have been ruptured for greater than 4 hours.<sup>42</sup> However, there may be some benefit in performing a caesarean section even after this time interval.
- Intravenous aciclovir given intrapartum to the mother (5 mg/kg every 8 hours) and subsequently to the neonate (intravenous aciclovir 20 mg/kg every 8 hours) may be considered for those mothers opting for vaginal delivery.<sup>13,25</sup> It is unknown whether intrapartum aciclovir reduces the risk of neonatal HSV infection.
- 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>4,37-39</sup>
- The risk of perinatal transmission depends on the timing of maternal acquisition of HSV, with the highest risk in infants born to women who have not completed HSV seroconversion during pregnancy (most commonly in the third trimester, within 6 weeks of delivery).
- C** • Although vaginal delivery should be avoided if possible, in women who deliver vaginally in the presence of primary genital herpes lesions, invasive procedures (application of fetal scalp electrodes, fetal blood sampling, artificial rupture of membranes and/or instrumental deliveries) should be avoided.<sup>4,43-45</sup>

Level of evidence  
III

Level of evidence  
IV

Level of evidence  
III

### Recurrent genital herpes

<b>B</b>	<ul style="list-style-type: none"><li>• Women 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>1,38</sup></li><li>• Evidence from the Netherlands shows that a conservative approach, allowing vaginal delivery in the presence of an anogenital lesion, has not been associated with a rise in the number of neonatal HSV cases.<sup>46</sup></li></ul>	Level of evidence III
<b>C</b>	<ul style="list-style-type: none"><li>• Vaginal delivery should be offered to women with recurrent genital herpes lesions at the onset of labour. A caesarean section delivery can be considered but the risk to the mother and future pregnancies should be set against the small risk of neonatal transmission of HSV with recurrent disease (0–3% for vaginal delivery). The final choice of vaginal delivery versus caesarean section should be made by the mother, who should base her decision on the very low risk of transmission set against any other obstetric risk factors and the risks associated with caesarean section.</li><li>• It has been reported that invasive procedures (fetal blood sampling, application of fetal scalp electrodes, artificial rupture of membranes and/or instrumental deliveries) increase the risk of neonatal HSV infection.<sup>47</sup> However, given the small background risk (0–3%) of transmission in this group, the increased risk associated with invasive procedures is unlikely to be clinically significant so they may be used if required.</li><li>• Women should be managed in accordance with standard National Institute for Health and Care Excellence (NICE) intrapartum guidelines.<sup>45</sup></li></ul>	Level of evidence IV
<b>C</b>	<ul style="list-style-type: none"><li>• There is no evidence to guide the management of women with spontaneous rupture of membranes at term, but many clinicians will advise expediting delivery in an attempt to minimise the duration of potential exposure of the fetus to HSV.</li></ul>	Level of evidence III
<b>C</b>		Level of evidence IV

## 7. Genital herpes in preterm prelabour rupture of membranes (before 37<sup>+0</sup> weeks of gestation)

### Primary genital herpes in preterm prelabour rupture of membranes (PPROM)

- 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 physicians and will depend on the gestation that PPRM occurred. If the decision is made for immediate delivery then the anticipated benefits of caesarean section will remain. If there is initial conservative management, the mother should be recommended to receive intravenous aciclovir 5 mg/kg every 8 hours. Prophylactic corticosteroids should be considered to reduce the implications of preterm delivery upon the infant.<sup>48</sup> 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>49-51</sup>

Level of evidence  
IV

### Recurrent genital herpes in PPRM

- When PPRM is encountered in the presence of recurrent genital herpes lesions, the risk of neonatal transmission is very small and may be outweighed by the morbidity and mortality associated with premature delivery.
- C** • In the case of PPRM before 34 weeks there is evidence to suggest that expectant management is appropriate, including oral aciclovir 400 mg three times daily for the mother.<sup>49</sup> After this gestation, it is recommended that management is undertaken in accordance with relevant RCOG guidelines on PPRM<sup>52</sup> and antenatal corticosteroid administration<sup>53</sup> to reduce neonatal morbidity and mortality and is not materially influenced by the presence of recurrent genital herpes lesions.<sup>49,54</sup>

Level of evidence  
IV

## 8. Management of HIV-positive women with HSV infection

### Primary HSV infection

- HIV-positive women with primary genital HSV infection in the last trimester of pregnancy should be managed according to the recommendations for all women with primary genital HSV infection.

### Recurrent HSV infection

- There is some evidence that HIV antibody positive women with genital HSV ulceration in pregnancy are more likely to transmit HIV infection independent of other factors.<sup>17,55</sup> However, this is not a consistent finding across all studies.<sup>56</sup>
- C** • Women who are HIV antibody positive and have a history of genital herpes should be offered daily suppressive aciclovir 400 mg three times daily from 32 weeks of gestation to reduce the risk of transmission of HIV infection, especially in women where a vaginal delivery is planned. Starting therapy at this earlier gestation than usual should be considered in view of the increased possibility of preterm labour in HIV-positive women.
- The mode of delivery should be in line with the BHIVA HIV in pregnancy guideline recommendations according to obstetric factors and HIV parameters such as HIV viral load.<sup>42,57</sup>
- There is currently no evidence to recommend daily suppressive treatment of HSV for HIV antibody positive women who are HSV-1 or -2 seropositive but have no history of genital herpes.<sup>56</sup>

Level of evidence  
III

Level of evidence  
IV

## 9. Management of the neonate

### General management

- C** • In all cases the neonatal team should be informed.

### Management of babies born by caesarean section in mothers with primary HSV infection in the third trimester

- C** These babies are at low risk of vertically transmitted HSV infection so conservative management is recommended.
  - Liaise with the neonatal team.
  - Swabs from the neonate are not indicated.
  - No active treatment is required for the baby.
  - Normal postnatal care of the baby is advised with a neonatal examination at 24 hours of age, after which the baby can be discharged from the hospital if well and feeding is established.
- C** • Parents should be educated regarding good hand hygiene and due care to reduce risk of postnatal infection.
- C** • Parents should be advised to seek medical help if they have concerns regarding their baby. In particular, they should be advised to look for:
  - skin, eye and mucous membrane lesions, lethargy/irritability, poor feeding.

### Management of babies born by spontaneous vaginal delivery in mothers with a primary HSV infection within the previous 6 weeks

These babies are at high risk of vertically transmitted HSV infection.

- Liaise with the neonatal team.

If the baby is well:

- Swabs of the skin, conjunctiva, oropharynx and rectum should be sent for herpes simplex PCR.
- A lumbar puncture is not necessary.
- Empirical treatment with intravenous aciclovir (20 mg/kg every 8 hours) should be initiated until evidence of active infection is ruled out.
- Strict infection control procedures should be put in place for both mother and baby.

- C** • Breastfeeding is recommended unless the mother has herpetic lesions around the nipples.
- Parents should be warned to report any early signs of infection such as poor feeding, lethargy, fever or any suspicious lesions.

If the baby is unwell or presents with skin lesions:

- Swabs of the skin, lesions, conjunctiva, oropharynx and rectum should be sent for herpes simplex PCR.
- A lumbar puncture should be performed even if CNS features are not present.

- Intravenous aciclovir (20 mg/kg every 8 hours) should be initiated until evidence of active infection is ruled out.

### Management of babies born to mothers with recurrent HSV infection in pregnancy with or without active lesions at delivery

- B** In the case of recurrent genital herpes infections in the mother, maternal IgG will be protective in the baby and hence the infection risk is low. Conservative management of the neonate is advised.<sup>55</sup>
- Liaise with the neonatal team.
  - Surface swabs from the neonate are not indicated.
  - No active treatment is advised for the baby.
  - Normal postnatal care of the baby is advised with a neonatal examination at 24 hours of age, after which the baby can be discharged from the hospital if well and feeding is established.
  - Parents should be educated regarding good hand hygiene and due care to reduce risk of postnatal infection.
  - Parents should be advised to seek medical help if they have concerns regarding their baby. In particular, they should be advised to look for:
    - skin, eye and mucous membrane lesions, lethargy/irritability, poor feeding.

Level of evidence  
III

### In cases where there are concerns regarding the neonate (clinical evidence of sepsis, poor feeding)

- C** Liaise with the neonatal team. In addition to considering bacterial sepsis, HSV infection should be considered.
- Surface swabs and blood for HSV culture and PCR.
  - Intravenous aciclovir (20 mg/kg every 8 hours) should be given while awaiting cultures.
  - Further management by the neonatal team according to condition of the baby and test results.

See Appendix 1 for flow chart of management.



## 10. Prevention of postnatal transmission

- In 25% of cases a possible source of postnatal infection is responsible, usually a close relative of the mother.<sup>2</sup>
- Efforts to prevent postnatal transmission of HSV are therefore important and advice should be given to the mother regarding this.
- The mother and all those with herpetic lesions who may be in contact with the neonate, including staff, should practice careful hand hygiene.
- Those with oral herpetic lesions (cold sores) should not kiss the neonate.

C

Level of evidence IV

## 11. Performance measures

1. When a herpes antiviral drug is used against a previously undiagnosed genital herpes episode, a swab for herpes PCR should be sent – target 100%.
2. In order that a discussion on the mode of delivery is undertaken with an obstetrician, there must be documentation in the clinic notes that the obstetrician and/or GP have been advised of this need and that the patient has also been informed of this need – target 100%.
3. For women with suspected primary genital herpes in pregnancy diagnosed in level 1/2 services, primary care or obstetric services, referral to a genitourinary medicine physician should be made (unless in labour) – target 100%.
4. Where a first episode diagnosis of genital herpes is made in the third trimester, the woman's case should be discussed between the obstetrician and neonatologist with documentation of the agreed management – target 100%.
5. Pregnant women with genital herpes should be provided with written information on genital herpes in pregnancy (e.g. the RCOG patient information leaflet) – target 90%.

## 12. About this guideline

### Qualifying statement

The recommendations in this guideline may not be appropriate for use in all clinical situations. Decisions to follow these recommendations must be based on the professional judgement of the clinician and consideration of individual patient circumstances and available resources. All possible care has been undertaken to ensure the publication of the correct dosage of medication and route of administration. However, it remains the responsibility of the prescribing clinician to ensure the accuracy and appropriateness of the medication they prescribe.

### Editorial independence

This guideline was commissioned, edited and endorsed by the BASHH CEG and the RCOG without external funding being sought or obtained.

### Declarations of interest

All members of the guideline writing committee completed the BASHH conflict of interest declaration at the time that the guideline's final draft was submitted to the CEG.

Dr Rajul Patel has received honoraria for talks and fees for consultancy from Novatis, Becton Dickinson and Roche pharmaceutical and diagnostic companies.

### Resource implications

The resource implications of this guideline will have little impact on current recommendations for management of herpes in pregnancy. There may be a cost saving if women with recurrent genital herpes simplex virus infection elect to have a vaginal delivery when herpetic lesions are present at term rather than undergoing a caesarean section. The cost of suppressive aciclovir (400 mg three times daily) for 1 month is £6.45\*.

### Membership of the writing group

EF and EC drafted the initial document and redrafts, VAB and SH drafted the obstetric component and AP drafted the neonatal section. PO, NLB and RP commented on the drafts and redrafts of the document.

### Membership of the CEG

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Timescale for next review: 2018.

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\*Source of costing: British National Formulary September 2014 (different prices may be negotiated by NHS hospital trusts).<sup>58</sup>

# References

1. Royal College of Obstetricians and Gynaecologists. *Management of Genital Herpes in Pregnancy*. Green-top Guideline No. 30. London: RCOG; 2007.
2. Clinical Effectiveness Group (British Association for Sexual Health and HIV). *2007 National Guideline for the Management of Genital Herpes*. Macclesfield: BASHH; 2007.
3. Patel R, Alderson S, Geretti A, Nilsen A, Foley E, Lautenschlager S, et al. *2010 European guideline for the management of genital herpes*. [place unknown]; International Union against Sexually Transmitted Infections; 2010.
4. Brown ZA, Selke S, Zeh J, Kopelman J, Maslow A, Ashley RL, et al. The acquisition of herpes simplex virus during pregnancy. *N Engl J Med* 1997;337:509–15.
5. British Paediatric Surveillance Unit. *BPSU 21st Annual Report 2006-2007*. London: British Paediatric Surveillance Unit/Royal College of Paediatrics and Child Health; 2007.
6. Brown Z. Preventing herpes simplex virus transmission to the neonate. *Herpes* 2004;11 Suppl 3:175A–186A.
7. Tookey P, Peckham CS. Neonatal herpes simplex virus infection in the British Isles. *Paediatr Perinat Epidemiol* 1996;10:432–42.
8. Hemelaar SJ, Poeran J, Steegers EA, van der Meijden WI. Neonatal herpes infections in The Netherlands in the period 2006-2011. *J Matern Fetal Neonatal Med* 2014 Jul 11 [Epub ahead of print].
9. Brown ZA, Wald A, Morrow RA, Selke S, Zeh J, Corey L. Effect of serologic status and cesarean delivery on transmission rates of herpes simplex virus from mother to infant. *JAMA* 2003;289:203–9.
10. Diguët A, Patrier S, Eurin D, Chouchene S, Marpeau L, Laquerrière A, et al. Prenatal diagnosis of an exceptional intrauterine herpes simplex type 1 infection. *Prenat Diagn* 2006;26:154–7.
11. Vasileiadis GT, Roukema HW, Romano W, Walton JC, Gagnon R. Intrauterine herpes simplex infection. *Am J Perinatol* 2003;20:55–8.
12. Lee A, Bar-Zeev N, Walker SP, Permezel M. In utero herpes simplex encephalitis. *Obstet Gynecol* 2003;102:1197–9.
13. Nahmias AJ. Neonatal HSV infection Part 1: continuing challenges. *Herpes* 2004;11:33–7.
14. Hensleigh PA, Andrews WW, Brown Z, Greenspoon J, Yasukawa L, Prober CG. Genital herpes during pregnancy: inability to distinguish primary and recurrent infections clinically. *Obstet Gynecol* 1997;89:891–5.
15. Young EJ, Chafizadeh E, Oliveira VL, Genta RM. Disseminated herpesvirus infection during pregnancy. *Clin Infect Dis* 1996;22:51–8.
16. Hitti J, Watts DH, Burchett SK, Schacker T, Selke S, Brown ZA, et al. Herpes simplex virus seropositivity and reactivation at delivery among pregnant women infected with human immunodeficiency virus-1. *Am J Obstet Gynecol* 1997;177:450–4.
17. Chen KT, Segú M, Lumey LH, Kuhn L, Carter RJ, Bulterys M, et al.; New York City Perinatal AIDS Collaborative Transmission Study (PACTS) Group. Genital herpes simplex virus infection and perinatal transmission of human immunodeficiency virus. *Obstet Gynecol* 2005;106:1341–8.
18. Heng MC, Heng SY, Allen SG. Co-infection and synergy of human immunodeficiency virus-1 and herpes simplex virus-1. *Lancet* 1994;i:255–8.
19. Andrews WW, Kimberlin DF, Whitley R, Cliver S, Ramsey PS, Deeter R. Valacyclovir therapy to reduce recurrent genital herpes in pregnant women. *Am J Obstet Gynecol* 2006;194:774–81.

20. Stone KM, Reiff-Eldridge R, White AD, Cordero JF, Brown Z, Alexander ER, et al. Pregnancy outcomes following systemic prenatal acyclovir exposure: Conclusions from the international acyclovir pregnancy registry, 1984-1999. *Birth Defects Res A Clin Mol Teratol* 2004;70:201–7.
21. Ratanajamit C, Vinther Skriver M, Jepsen P, Chongsuvivatwong V, Olsen J, Sørensen HT. Adverse pregnancy outcome in women exposed to acyclovir during pregnancy: a population-based observational study. *Scand J Infect Dis* 2003;35:255–9.
22. Pasternak B, Hviid A. Use of acyclovir, valacyclovir, and famciclovir in the first trimester of pregnancy and the risk of birth defects. *JAMA* 2010;304:859–66.
23. Frenkel LM, Brown ZA, Bryson YJ, Corey L, Unadkat JD, Hensleigh PA, et al. Pharmacokinetics of acyclovir in the term human pregnancy and neonate. *Am J Obstet Gynecol* 1991;164:569–76.
24. Kimberlin DF, Weller S, Whitley RJ, Andrews WW, Hauth JC, Lakeman F, et al. Pharmacokinetics of oral valacyclovir and acyclovir in late pregnancy. *Am J Obstet Gynecol* 1998;179:846–51.
25. Ács N, Bánhidly F, Puhó E, Czeizel AE. No association between maternal recurrent genital herpes in pregnancy and higher risk for congenital abnormalities. *Acta Obstet Gynecol Scand* 2008;87:292–9.
26. Sheffield JS, Hollier LM, Hill JB, Stuart GS, Wendel GD Jr. Acyclovir prophylaxis to prevent herpes simplex virus recurrence at delivery: a systematic review. *Obstet Gynecol* 2003;102:1396–403.
27. Watts DH, Brown ZA, Money D, Selke S, Huang ML, Sacks SL, et al. A double-blind, randomized, placebo-controlled trial of acyclovir in late pregnancy for the reduction of herpes simplex virus shedding and cesarean delivery. *Am J Obstet Gynecol* 2003;188:836–43.
28. Scott LL, Hollier LM, McIntire D, Sanchez PJ, Jackson GL, Wendel GD Jr. Acyclovir suppression to prevent recurrent genital herpes at delivery. *Infect Dis Obstet Gynecol* 2002;10:71–7.
29. Brocklehurst P, Kinghorn G, Carney O, Helsen K, Ross E, Ellis E, et al. A randomised placebo controlled trial of suppressive acyclovir in late pregnancy in women with recurrent genital herpes infection. *Br J Obstet Gynaecol* 1998;105:275–80.
30. Scott LL, Sanchez PJ, Jackson GL, Zeray F, Wendel GD Jr. Acyclovir suppression to prevent cesarean delivery after first-episode genital herpes. *Obstet Gynecol* 1996;87:69–73.
31. Braig S, Luton D, Sibony O, Edlinger C, Boissinot C, Blot P, et al. Acyclovir prophylaxis in late pregnancy prevents recurrent genital herpes and viral shedding. *Eur J Obstet Gynecol Reprod Biol* 2001;96:55–8.
32. Sheffield JS, Hill JB, Hollier LM, Laibl VR, Roberts SW, Sanchez PJ, et al. Valacyclovir prophylaxis to prevent recurrent herpes at delivery: a randomized clinical trial. *Obstet Gynecol* 2006;108:141–7.
33. Hollier LM, Wendel GD. Third trimester antiviral prophylaxis for preventing maternal genital herpes simplex virus (HSV) recurrences and neonatal infection. *Cochrane Database Syst Rev* 2008;(1):CD004946.
34. Brown ZA, Benedetti J, Selke S, Ashley R, Watts DH, Corey L. Asymptomatic maternal shedding of herpes simplex virus at the onset of labor: relationship to preterm labor. *Obstet Gynecol* 1996;87:483–8.
35. Syridou G, Spanakis N, Konstantinidou A, Piperaki ET, Kafetzis D, Patsouris E, et al. Detection of cytomegalovirus, parvovirus B19 and herpes simplex viruses in cases of intrauterine fetal death: association with pathological findings. *J Med Virol* 2008;80:1776–82.
36. Eskild A, Jeansson S, Stray-Pedersen B, Jenum PA. Herpes simplex virus type-2 infection in pregnancy: no risk of fetal death: results from a nested case-control study within 35,940 women. *BJOG* 2002;109:1030–5.

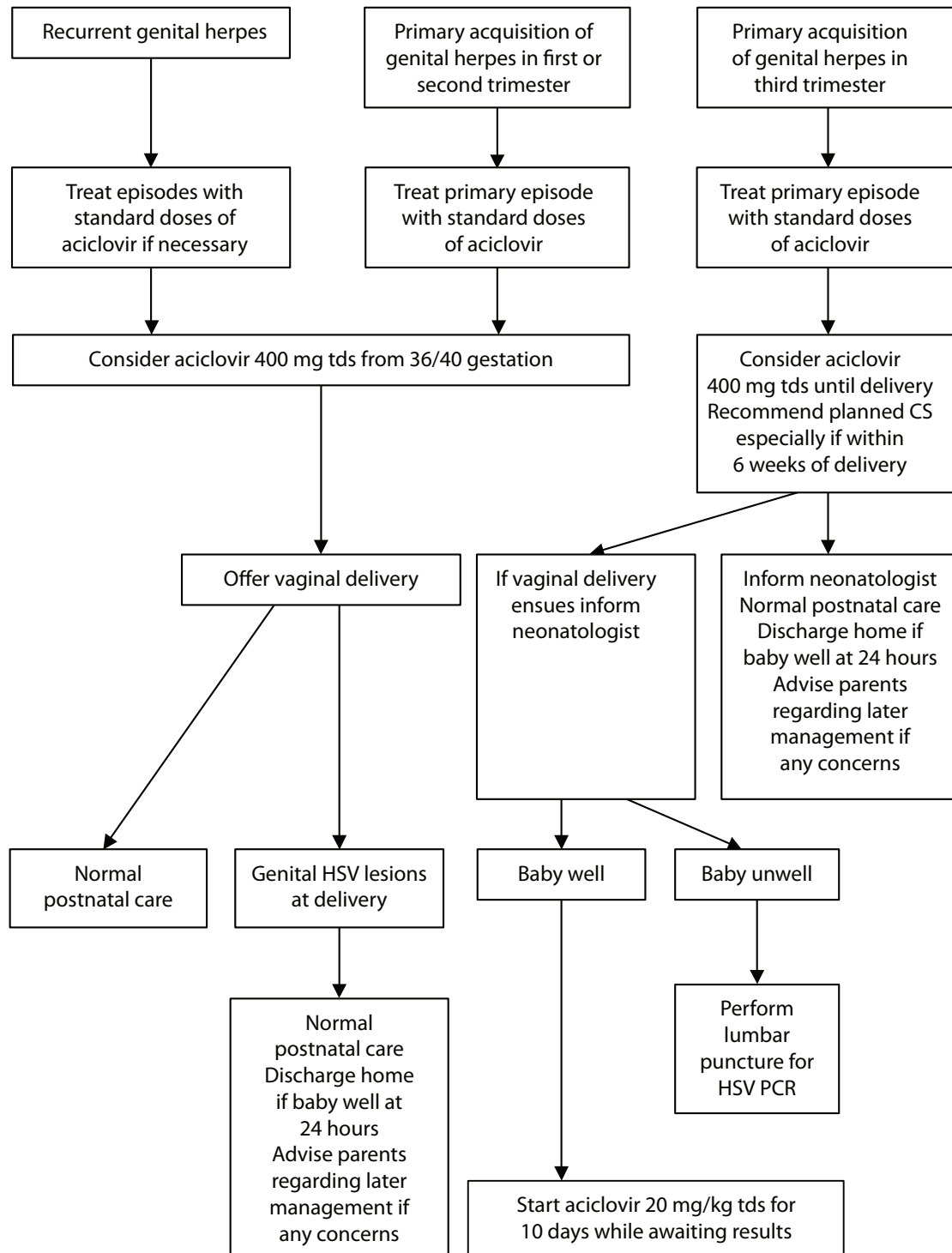
37. Brown ZA, Vontver LA, Benedetti J, Critchlow CW, Sells CJ, Berry S, et al. Effects on infants of a first episode of genital herpes during pregnancy. *N Engl J Med* 1987;317:1246–51.
38. Prober CG, Sullender WM, Yasukawa LL, Au DS, Yeager AS, Arvin AM. Low risk of herpes simplex virus infections in neonates exposed to the virus at the time of vaginal delivery to mothers with recurrent genital herpes simplex virus infections. *N Engl J Med* 1987;316:240–4.
39. Brown ZA, Benedetti J, Ashley R, Burchett S, Selke S, Berry S, et al. Neonatal herpes simplex virus infection in relation to asymptomatic maternal infection at the time of labor. *N Engl J Med* 1991;324:1247–52.
40. Gardella C, Brown ZA, Wald A, Morrow RA, Selke S, Krantz E, et al. Poor correlation between genital lesions and detection of herpes simplex virus in women in labor. *Obstet Gynecol* 2005;106:268–74.
41. Kim ID, Chang HS, Hwang KJ. Herpes simplex virus 2 infection rate and necessity of screening during pregnancy: a clinical and seroepidemiologic study. *Yonsei Med J* 2012;53:401–7.
42. Nahmias AJ, Josey WE, Naib ZM, Freeman MG, Fernandez RJ, Wheeler JH. Perinatal risk associated with maternal genital herpes simplex virus infection. *Am J Obstet Gynecol* 1971;110:825–37.
43. Kohelet D, Katz N, Sadan O, Somekh E. Herpes simplex virus infection after vacuum-assisted vaginally delivered infants of asymptomatic mothers. *J Perinatol* 2004;24:147–9.
44. Amann ST, Fagnant RJ, Chartrand SA, Monif GR. Herpes simplex infection associated with short-term use of a fetal scalp electrode. A case report. *J Reprod Med* 1992;37:372–4.
45. National Institute for Health and Clinical Excellence. *Intrapartum care: Care of healthy women and their babies during childbirth*. NICE clinical guideline 55. Manchester: NICE; 2007.
46. Singhal P, Naswa S, Marfatia YS. Pregnancy and sexually transmitted viral infections. *Indian J Sex Transm Dis* 2009;30:71–8.
47. Parvey LS, Ch'ien LT. Neonatal herpes simplex virus infection introduced by fetal-monitor scalp electrodes. *Pediatrics* 1980;65:1150–3.
48. Kimberlin DW, Baley J; Committee on Infectious Diseases; Committee on Fetus and Newborn. Guidance on management of asymptomatic neonates born to women with active genital herpes lesions. *Pediatrics* 2013;131:e635–46.
49. Major CA, Towers CV, Lewis DF, Garite TJ. Expectant management of preterm premature rupture of membranes complicated by active recurrent genital herpes. *Am J Obstet Gynecol* 2003;188:1551–4; discussion 1554–5.
50. Utlely K, Bromberger P, Wagner L, Schneider H. Management of primary herpes in pregnancy complicated by ruptured membranes and extreme prematurity: case report. *Obstet Gynecol* 1987;69(3 Pt 2):471–3.
51. Dietrich YM, Napolitano PG. Acyclovir treatment of primary herpes in pregnancy complicated by second trimester preterm premature rupture of membranes with term delivery: case report. *Am J Perinatol* 2002;19:235–8.
52. Pinninti SG, Kimberlin DW. Management of neonatal herpes simplex virus infection and exposure. *Arch Dis Child Fetal Neonatal Ed* 2014;99:F240–4.
53. Royal College of Obstetricians and Gynaecologists. *Antenatal Corticosteroids to Reduce Neonatal Morbidity and Mortality*. Green-top Guideline No. 7. London: RCOG; 2010.
54. Ehsanipoor RM, Major CA. Herpes simplex and HIV infections and preterm PROM. *Clin Obstet Gynecol* 2011;54:330–6.
55. Drake AL, John-Stewart GC, Wald A, Mbori-Ngacha DA, Bosire R, Wamalwa DC, et al. Herpes simplex virus type 2 and risk of intrapartum human immunodeficiency virus transmission. *Obstet Gynecol* 2007;109:403–9.

56. Chen KT, Tuomala RE, Chu C, Huang ML, Watts DH, Zorrilla CD, et al. No association between antepartum serologic and genital tract evidence of herpes simplex virus-2 coinfection and perinatal HIV-1 transmission. *Am J Obstet Gynecol* 2008;198:399.e1–5.
57. British HIV Association. *British HIV Association guidelines for the management of HIV infection in pregnant women 2012 (2014 interim review)*. London: BHIVA; 2014.
58. NICE Evidence Services. British National Formulary September 2014. Aciclovir (Acyclovir) [<http://www.evidence.nhs.uk/formulary/bnf/current/5-infections/53-antiviral-drugs/532-herpesvirus-infections/5321-herpes-simplex-and-varicellazoster-infection/aciclovir?q=ACICLOVIR>] Accessed 2014 Sep 16.



# Appendix I

## Algorithm for the management of herpes in pregnancy and care of neonate



**Abbreviations** – CS caesarean section; HSV herpes simplex virus; PCR polymerase chain reaction; tds three times daily

# Appendix II

## Levels of evidence and grading of recommendations

### Levels of evidence

- Ia Meta-analysis of randomised controlled trials
- Ib At least one randomised controlled trial
- IIa At least one well-designed controlled study without randomisation
- IIb At least one other type of well-designed quasi-experimental study
- III Well-designed non-experimental descriptive studies
- IV Expert committee reports or opinions of respected authorities

### Grading of recommendations

- A Evidence at level Ia or Ib
- B Evidence at level IIa, IIb or III
- C Evidence at level IV