# CLINICAL GUIDELINE

# HSV in Pregnancy

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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**Important Note**:

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Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

# HSV in Pregnancy

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## Antenatal Booking appointment

- Discussion and information with midwife on all infections that can impact baby including HSV
- A careful history from should be taken to identify any previous possible herpetic symptoms or diagnoses as per NICE guidance

### Management of discordant couples

- Where the pregnant woman or person has no history of HSV and sexual partner is known to have had HSV they should be given advice on reducing transmission risk as per BASHH guidance such as avoiding acquisition especially in third trimester and in 2 weeks prior to 3rd trimester
- In couples who are clinically discordant, Obstetrics team undertake type-specific herpes serology in both the pregnant woman or person, and the partner known to have genital herpes. Results can be discussed with GUM team as needed

### Those with previous diagnosis of genital herpes

- Should be provided by the midwife with a patient information leaflet outlining HSV management in pregnancy and recommendation to start HSV suppression at 32 weeks (if high risk of premature birth start at 22 weeks)
- Suppressive treatment when needed to be coordinated by obstetric team

- If there are no further issues there is no need at this stage to refer to GUM or Neonatologists
- If there are episodes despite suppression patient can be referred to GUM for review

**Presentation of suspected NEW HSV during pregnancy or within 4 weeks post birth**

- Face to face review by GUM team in Sandyford for GGC residents ideally during clinical episode or as soon as possible. Clinician gain patient consent and to email ggc.sandyfordprofessionalsupport@nhs.scot with patient details
- Testing should be taken as soon as possible from lesion for HSV and Syphilis PCR. If there is diagnostic uncertainty additional tests such as VZV PCR should be taken. Routine STI screening should also be performed even if already done at booking
- GUM team to communicate to GP, obstetric and neonatal team with a birth plan
- Suppressive treatment for remainder of pregnancy

**If <27+6 at presentation**

- HSV 1 and 2 serology should be performed if the person is not known to be positive for both HSV1 and 2 and the result used to inform birth plan
- A discussion should be had around considering avoiding sex in the third trimester, including sex with condoms and oral sex

**If delivery <6 weeks since acquisition**

- Caesarean birth should be the recommended mode of birth as shedding may continue for up to 6 weeks, although it can last for longer than this.

**If >28 weeks at presentation and up to 4 weeks post birth**

- HSV 1 and 2 serology to help identify if initial or recurrent episode
- Caesarean birth should be the recommended mode of birth

**Presentation of suspected recurrence of HSV during pregnancy**

- Can be managed within Obstetric team who will liaise with neonatal team and advise the team of the woman or persons risk profile
- Swabs should be taken for HSV/ syphilis PCR. If diagnostic uncertainty further swabs can be taken and/ or referred to GU clinic for advice
- Where the pregnant woman or person is not known to have both HSV-1 and HSV-2, HSV serology should be performed and if new type found manage as new infection above
- Aciclovir suppression should be given as aciclovir 400 mg three times daily from 32 weeks of gestation or aciclovir 400 mg two times daily from 22 weeks if at risk of preterm birth increasing to TDS at 32 weeks
- If not previously both HSV1 and 2 positive

- a discussion should be had around considering avoiding sex in the third trimester, including sex with condoms and oral sex

**Presentation of suspected HSV primary in labour or up to 4 weeks post partum**

- Caesarean birth recommended to all with first episode of lesions at the time of birth
- PCR and HSV serology to be taken urgently- consideration needed for people who are not known to be positive for both types current episode may be due to a new type and managed as a new/ primary episode
- If in labour, Obstetric team to manage patient and link with neonates. GUM can be liaised with if further support or ongoing care post birth needed.

**Presentation of suspected HSV recurrence in labour or up to 4 weeks post partum**

- Vaginal birth can be offered where there is confidence symptoms are a recurrence

**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) (50). 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 [1D].

## 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) (5).
- 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 (41). 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 national UK-PAS guidelines for when to test and treat 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].

## Summary table

| Risk | Highest | High | Low | Lowest |
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| **Perinatal context** | • All infants with symptoms consistent with HSV infection regardless of delivery method<br>• Babies with <u>any</u> positive HSV test even if this is suspected to be detection of maternal HSV<br>• Babies born by vaginal delivery in the presence of active **primary** herpes lesions<br>• Babies born at <37 weeks by any delivery method with active lesions at delivery and ruptured membranes of any duration<br>• Birthing mother or parent systemically unwell with possible HSV at the time of birth or immediate postpartum period<br><br>• Birthing mother or parent presents post-partum with active primary herpes lesions within 1 weeks of delivery | • Pregnant parent had a **primary** HSV infection within the previous 6 weeks and baby is asymptomatic and born by:<br>– Vaginal delivery<br><br>o **OR**<br><br>– Caesarean section with ruptured membranes regardless of duration | • Asymptomatic babies born by any delivery method in the presence of active **recurrent** herpes lesions<br>• Asymptomatic babies born at >37 weeks by Caesarean section with intact membranes with active **primary** lesions at delivery or within 6 weeks of delivery AND a systemically well mother<br>• Asymptomatic babies born at <37 weeks by Caesarean section with intact membranes with no active lesions at delivery and a history of HSV infection less than 6 weeks previously<br>• Asymptomatic babies born at <37 weeks by any delivery method with no active lesions at delivery, regardless of rupture of membranes, and a history of HSV infection more than 6 weeks previously<br>• Birthing mother or parent presents post-partum with active primary herpes lesions from 1 week to 4 weeks of delivery | • Asymptomatic babies born at >37 weeks by any delivery method with no active lesions in birthing woman or person at delivery **AND a** history of HSV infection more than 6 weeks previously (99) |

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| **Clinical assessment** | Urgently inform the neonatal team<br><br>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<br><br>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.<br><br>Ophthalmology review. | Urgently inform the neonatal team<br><br>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.<br><br>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<br><br>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<br><br>No investigations required<br><br>Normal postnatal care |
| **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 hours of life) | 24 hours post-delivery (note maternal or birth parent HSV may still be detected on surface swabs, and therefore should be repeated if taken <24 hours of life) | 24 hours post-delivery (note maternal or birth parent HSV may still be detected on surface swabs taken <24 hours of life) | |
| **HSV PCR swab** | Any visible lesions<br>Throat swab<br>Nose swab<br>Conjunctival swabs<br>Rectal swab | Throat swab<br>Nose swab<br>Conjunctival swabs<br>Rectal swab | Throat swab<br>Nose swab<br>Conjunctival swabs<br>Rectal swab | |
| **Bloods** | HSV PCR (1mL EDTA required) (note may take >24 hours 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) (106) | HSV PCR (1mL EDTA required) (note may take >24 hours for sufficient HSV replication to occur for a positive result to occur, and so a negative test does not exclude | HSV PCR (1mL EDTA required) (note may take >24 hours for sufficient HSV replication to occur for a positive result to occur, and so a negative test does not exclude | |

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| | Full blood count<br>Liver function tests<br>Coagulation screen | infection, may need to be repeated) (106)<br><br>Full blood count<br>Liver function tests<br>Coagulation screen | infection, may need to be repeated) (106) | |
| **Lumbar puncture for CSF** | If clinically safe, undertake lumbar puncture for CSF and send for:<br>• HSV PCR<br>• Protein<br>• Glucose<br>• Cell count, microscopy and culture | If clinically safe, undertake lumbar puncture for CSF and send for:<br>• HSV PCR<br>• Protein<br>• Glucose<br>• Cell count, microscopy and culture | | |
| **Other tests** | As guided by the infant's clinical condition (for example chest X-ray)<br><br>In cases where drug resistance is a concern, discuss with a virologist and consider sending samples for drug resistance testing (available at the UKHSA laboratory at Colindale) | | | |
| **Management** | Urgently start aciclovir 20mg/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.<br><br>Duration of treatment:<br>• All results are negative, and no other cause identified: 10 days<br>• Skin, eye and mouth disease only: 14 days | Urgently start aciclovir 20mg/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.<br><br>Duration of treatment:<br>• All results are negative, and baby remains asymptomatic: 10 days | If any HSV test is positive, manage as per highest risk | |

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| | • CNS or disseminated disease, or no CNS obtainable but other positive HSV tests: 21 days. 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.<br><br>A long line may be considered to avoid extravasation of IV aciclovir.<br><br>Oral aciclovir prophylaxis at 300mg/$m^3$ 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. | • If baby becomes symptomatic or if any test is positive manage as per highest risk<br><br>A long line may be considered to avoid extravasation of IV aciclovir. | | |
| **Advice to parents and carers from discharging team** | Practice good hand hygiene and take care to reduce risk of postnatal infection from maternal genital secretions or other sources including anyone with oral herpetic lesions (cold sores).<br>Seek urgent medical help if they have concerns regarding their baby in the next 6 weeks, in particular:<br>• Skin, eye and mucous membrane lesions<br>• Lethargy/irritability<br>• Poor feeding<br>• Fever | | | |

**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 post-natal 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 (4,9,10,22).

Mothers and pregnant people diagnosed with HSV at least three 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 (106).

- Efforts to prevent postnatal transmission of HSV are important and advice should be given to the parents regarding this [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 [IV, C]:
    - 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.

**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 (107–110) [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 (111–113). The presence of aciclovir or valaciclovir in breast milk has not been demonstrated to be harmful to infants (111). Furthermore, aciclovir given orally to infants (at therapeutic doses) rarely causes serious side effects (114). The manufacturer advises caution with use of aciclovir or valaciclovir when breastfeeding, but this is not based on evidence of harm (115).

- 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 (1) [1D].
- There are no human data on famciclovir in breastfeeding in humans (116), and famciclovir should therefore not be used [1D].

**Breastfeeding with <u>current or previous</u> herpetic ulcers on the breast**

Herpes DNA is detectable in breast milk (117), 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 **<u>on</u>** 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 six 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 (118–120) [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 (1) [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 three months following herpes acquisition (121).

Mothers and pregnant people diagnosed with HSV at least three 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 (106). 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 (122). 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 (1), for at least six 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 (1), until the infant reaches the age of 6 weeks of life [1D].