Herpes and Human Papilloma in Pregnancy

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Guideline to be followed by (target staff): Maternity

To be read in conjunction with the following documents:

CQC Fundamental standards:
Regulation 9 – person centred care
Regulation 10 – dignity and respect
Regulation 11 – Need for consent
Regulation 12 – Safe care and treatment
Regulation 17 – Good governance
Regulation 18 – Staffing
Regulation 19 – Fit and proper

Disclaimer

Since every patient's history is different, and even the most exhaustive sources of information cannot cover every possible eventuality, you should be aware that all information is provided in this document on the basis that the healthcare professionals responsible for patient care will retain full and sole responsibility for decisions relating to patient care; the document is intended to supplement, not substitute for, the expertise and judgment of physicians, pharmacists or other healthcare professionals and should not be taken as an indication of suitability of a particular treatment for a particular individual.
The ultimate responsibility for the use of the guideline, dosage of drugs and correct following of instructions as well as the interpretation of the published material **lies solely with you** as the medical practitioner.

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Guideline Statement

To assist midwives and medical staff in the management of herpes and human papilloma in pregnancy.

Executive Summary

Neonatal herpes is a very rare but serious viral infection with a high morbidity and mortality. 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

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.

All immunocompromised women, such as those infected with the human immunodeficiency viruses (HIV) virus, are at increased risk of more severe and frequent symptomatic recurrent episodes of genital herpes during pregnancy and of asymptomatic shedding of herpes simplex virus (HSV) at term.

Definitions

1.0 Roles and Responsibilities:

Doctors – decision making, discussion, planning and providing care.
Midwives and student midwives – decision making, discussion, planning and providing care.

2.0 Implementation and dissemination of document

This guideline is available on the Intranet.

3.0 Processes and procedures

3.1 Herpes Genitalis

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.

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
- The mode of delivery.
- Congenital herpes may occur as a result of transplacental intrauterine infection
- The risks are greatest when a woman acquires a new infection (primary genital herpes) in the third trimester, particularly within 6 weeks of delivery.
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3.1.1 First and Second Trimesters (Until 27 weeks and 6 days)

There is no evidence of an increased risk of spontaneous miscarriage with primary genital herpes in the first trimester.

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

3.1.1.1 Treatment

- Oral (or intravenous for disseminated HSV) Acyclovir in standard doses (400 three times daily, usually for 5 days).
    - The use of Acyclovir is associated with a reduction in the duration and severity of symptoms and a decrease in the duration of viral shedding.
    - Acyclovir 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 has been reported.
    - There is no evidence of an increased risk of birth defects with Acyclovir, famciclovir or valaciclovir if used in the first trimester.
- Paracetamol and topical lidocaine 2% gel can be offered as symptomatic relief

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. These women should have consultant led care in antenatal period and can have midwife led care in labour.

Providing that delivery does not ensue within the next 6 weeks, the pregnancy should be managed expectantly, and vaginal delivery anticipated.

Following first and second trimester acquisition daily suppressive Acyclovir 400mg TDS from 36 weeks reduces HSV lesions at term and need for caesarean section. It also reduces asymptomatic viral shedding.

3.1.2 Third trimester (28 weeks)

There is some evidence of increased perinatal morbidity (preterm labour and low birthweight), together with stillbirth, however the data are conflicting.

No additional monitoring of such pregnancies is recommended.

In the third trimester, treatment will usually continue with daily suppressive Acyclovir 400 mg three times daily until delivery.

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%.

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) Acyclovir in standard doses (400 mg three times daily, usually for 5 days). In the third trimester, treatment will usually continue with daily suppressive Acyclovir 400 mg three times daily until delivery.

In these cases, fetal scalp electrodes should not be used, and fetal blood sampling and instrumental delivery should be avoided.

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

3.2 Recurrent Herpes

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).

Although there is no evidence that Acyclovir 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.

Daily Acyclovir 400mg three times a day from 36 weeks until delivery should be considered to reduce HSV lesions at term as this reduces viral shedding and recurrences at delivery.

There is no increased risk of preterm labour, preterm pre-labour 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.

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

Management is based on clinical assessment as there will not be time for confirmatory laboratory testing.

Detailed history should be taken to ascertain primary or recurrent episode.

Swab from lesions should be taken.

Paediatrician should be informed.

3.3.1 Primary episode

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.

There is some evidence to suggest that the benefit of caesarean section reduces if the membranes have been ruptured for greater than 4 hours.

However, there may be some benefit in performing a caesarean section even after this time interval.

3.3.2 Mother opting for vaginal delivery/ mothers who delivered quickly

Intravenous Acyclovir given intrapartum to the mother (5 mg/kg every 8 hours) and subsequently to the neonate (intravenous Acyclovir 20 mg/kg every 8 hours) may be considered

It is unknown whether intrapartum Acyclovir reduces the risk of neonatal HSV infection. When primary herpes lesions are present at the time of vaginal delivery, the risk of neonatal herpes is estimated to be 41%.

Invasive procedures (application of fetal scalp electrodes, fetal blood sampling, artificial rupture of membranes and/or instrumental deliveries) should be voided.

3.3.3 Recurrent genital Herpes at the time of labour

Risk to the baby of neonatal herpes is low (0–3% for vaginal delivery).

Vaginal delivery should be offered to women with recurrent genital herpes lesions at the onset of labour

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

Women should be managed in accordance with standard National Institute for Health and Care Excellence (NICE) intrapartum guidelines.

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.

Use of invasive procedures in women with recurrent herpes

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.

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**.

3.3.4 Genital Herpes in preterm pre-labour rupture of membranes (PPROM)

There is limited evidence to inform best obstetric practice when PPROM 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 PPROM 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 Acyclovir 5 mg/kg every 8 hours.

Prophylactic corticosteroids should be considered to reduce the implications of preterm delivery upon the infant.

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

3.3.4.1 Recurrent genital herpes in PPROM

When PPROM 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.

In the case of PPROM before 34 weeks there is evidence to suggest that expectant management is appropriate, including oral Acyclovir 400 mg three times daily for the mother.

After this gestation, it is recommended that management is undertaken in accordance with relevant RCOG guidelines on PPROM and antenatal corticosteroid administration to reduce neonatal morbidity and mortality and is not materially influenced by the presence of recurrent genital herpes lesions.

3.4 Women who are HIV positive with HSV infection

3.4.1 Primary Infection with HIV

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.

3.4.2 Recurrent infection with HIV

Women who are HIV antibody positive and have a history of genital herpes should be offered daily suppressive Acyclovir 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.

3.5 Management of the neonate

Paediatrician registrar should be informed in all cases and baby alert form should be sent in antenatal period.

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

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.

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.

3.5.1 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 Acyclovir (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 the baby.

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

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

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.

Inform the paediatric registrar on call.

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, and poor feeding

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

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 Acyclovir (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.

3.5.4 Prevention of postnatal transmission

In 25% of cases a possible source of postnatal infection is responsible, usually a close relative of the mother.

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

3.6 Herpes Labialis ("Cold Sores")

- Any member of staff with herpetic lesions should avoid contact with babies.
- Mothers should be advised not to kiss the baby, and to wash their hands thoroughly before any contact with the baby.

3.7 Human Papillomavirus (HPV) is the causative agent of condylomata acuminata (genital warts)

HPV in pregnancy is important for 3 reasons.

- Genital warts may rapidly enlarge during pregnancy.
- The association with cervical intra epithelial neoplasia
- Perinatal exposure may result in the development of juvenile laryngeal papillomatosis

3.7.1 Management in Pregnancy

Most cases of HPV infection are sub-clinical. If lesions are obvious it is rarely necessary to treat them during pregnancy. Often, they will regress post-delivery. The options for the treatment of anogenital warts during pregnancy are limited by potential teratogenicity of some modalities such as podophylline.

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- TCA (Trichloroacetic acid) can be used safely.
- Imiquimod not licensed for use in pregnancy.
- Ablative techniques, such as cryotherapy can be used safely in pregnancy.
- Treatment of the warts is not always needed but may reduce transmission of the HPV to the fetus during vaginal delivery.
- Caesarean section is not indicated to prevent vertical transmission of HPV infection.
- The only serious, rare complication is recurrent respiratory papillomatosis in the infant, which occurs in about 4/100,000 births .
- Review result of woman's most recent cervical smear report and if any concerns about cytological abnormalities refer for colposcopy.
- If women present in labour, with large obstructive vulval lesions or gross cervical warts, Caesarean Section may be necessary.

Breastfeeding

Imiquimod: no quantifiable levels (>5 ng/ml) of Imiquimod are detected in the serum after single and multiple topical doses, however no specific advice is given in the summary of product characteristics on whether to use or not, in lactating mothers

Podophyllotoxin: there is insufficient information on the excretion of topically applied podophyllotoxin in human milk. A risk to breastfed infants cannot be excluded and use is not recommended

4.0 Statement of evidence/references

British Association for Sexual Health and HIV (2015) *UK National Guidelines on the management of anogenital warts 2015.* [Online]. Available from: https://www.bashhguidelines.org/media/1075/uk-national-guideline-on-warts-2015-final.pdf [Accessed 1 November 2018]

British Association for Sexual Health and HIV and the Royal College of Obstetricians and Gynaecologists (2014) *Management of genital herpes in pregnancy.* [Online]. Available from: https://www.rcog.org.uk/globalassets/documents/guidelines/management-genital-herpes.pdf [Accessed 1 November 2018]
Note: Due for review "by 2018".

British HIV Association (2014) British HIV Association guidelines for the management of HIV infection in pregnant women 2012 (2014 interim review). *HIV Medicine*, 15 (Suppl. 4), 1–77. DOI: 10.1111/hiv.12185
https://www.bhiva.org/file/FCUcXrfVgWsYl/BHIVA-Pregnancy-guidelines-update-2014.pdf
Note: The guidelines were due to be fully updated and revised in 2017. There is a 'Consultation version 2018' available from: https://www.bhiva.org/file/WrhwAPoKvRmeV/BHIVA-Pregnancy-guidelines-consultation-draft-final.pdf

National Institute for Health and Care Excellence (2011, last updated Aug 2012) *Caesarean section.* [CG132]. [Online]. Available from: https://www.nice.org.uk/guidance/cg132 [Accessed 1 November 2018]

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5.0 Governance

5.1 Document review history

Version number	Review date	Reviewed by	Changes made
6.0	10/2023	Anu Ram Mohan	Updated, references updated. Breastfeeding section added.
5.2	07/2020	N Gupta	Audit Criteria Amended
5.1	Sept 2019	Anu Ram Mohan	1. New Trust Template 2. section 3.1.1.1 added for consultant led care 3. section 3.5 addition to adding baby alert 4. references updated 5.

5.2 Consultation History

Stakeholders Name/Board	Area of Expertise	Date Sent	Date Received	Comments	Endorsed Yes/No
Jane Plant	Library	October 2018	November 2018	Comments Received	Yes
Women's Health Guideline Review group meeting		20/09/2019	20/09/2019	Comments received	Yes
Women's Health Guideline Review group meeting	Maternity	10/2023	10/2023	No comments received	Yes

5.3 Audit and monitoring

How will compliance of this Guideline be evidenced?.

Audit/Monitoring Criteria	Tool	Audit Lead	Frequency of Audit	Responsible Committee/Board
Audit not required	N/A	N/A	N/A	N/A

5.4 Equality Impact Assessment

As part of its development, this Guideline and its impact on equality has been reviewed. The purpose of the assessment is to minimise and if possible remove any disproportionate impact on the grounds of race, gender, disability, age, sexual orientation, religion or belief, pregnancy and maternity, gender reassignment or marriage and civil partnership. No detriment was identified. Equality Impact assessments will show any future actions required to overcome any identified barriers or discriminatory practice.

Equality Impact Assessment			
Division	Women and Children's Health	Department	Maternity
Person completing the EqIA	Anu Ram Mohan	Contact No.	
Others involved:		Date of assessment:	10/2023
Existing policy/service	Yes	New policy/service	No

Will patients, carers, the public or staff be affected by the policy/service?	Yes
If staff, how many/which groups will be affected?	Maternity Staff

Protected characteristic	Any impact?	Comments
Age	NO	Positive impact as the policy aims to recognise diversity, promote inclusion and fair treatment for patients and staff
Disability	NO	
Gender reassignment	NO	
Marriage and civil partnership	NO	
Pregnancy and maternity	NO	
Race	NO	
Religion or belief	NO	
Sex	NO	
Sexual orientation	NO	

What consultation method(s) have you carried out?
Guideline Review Group
How are the changes/amendments to the policies/services communicated?
Email
What future actions need to be taken to overcome any barriers or discrimination?

What?	Who will lead this?	Date of completion	Resources needed
Review date of EqIA			