Royal College of Obstetricians and Gynaecologists

Setting standards to improve women's health

Clinical Guideline No. 30

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MANAGEMENT OF GENITAL HERPES IN PREGNANCY

1. Purpose and scope

Neonatal herpes is a severe systemic viral infection with a high morbidity and mortality, which is most commonly acquired at or near the time of delivery.[1] It is rare in the UK; the most recent active surveillance data by the British Paediatric Surveillance Unit, obtained between 1986 and 1991, demonstrated an incidence of 1.65 per 100 000 live births annually (95% CI 1.3–2.0).[2] The incidence of neonatal herpes in the UK is considerably lower when compared with that reported from the USA (11–29 per 100 000 live births).[3,4]

Almost all cases of neonatal herpes occur as a result of direct contact with infected maternal secretions, although cases of postnatal transmission have been described.[2] Neonatal herpes may be caused by herpes simplex type 1 (HSV-1) or herpes simplex type 2 (HSV-2), as either viral type can cause genital herpes. The risks are greatest when a woman acquires a new infection (primary genital herpes) during late pregnancy, so that the baby is delivered before the development of protective maternal antibodies.[1,5] Most of these maternal infections are asymptomatic or unrecognised[1,2] and it may be difficult to distinguish clinically between recurrent and primary genital HSV infections.[6]

Type-specific HSV serology has only recently become commercially available and its use for management has not been fully evaluated.[7] Its use should be limited to research settings or where considered appropriate by genitourinary medicine physicians.

Since the severe consequences of neonatal herpes infection are well established, obstetricians need to be aware of interventions that may reduce the risk of perinatal transmission. A survey of Fellows and Members of the Royal College of Obstetricians and Gynaecologists, published in 1995, found that only 31% of those surveyed had a formal policy governing the management of herpes in pregnancy and there was a wide variation in practice.[8] The literature has been reviewed in order to facilitate recommendations for management of genital herpes in pregnancy. Management guidelines of the American College of Obstetricians and Gynecologists[9] and of the UK Herpes Simplex Advisory Panel have also been consulted.[10]

2. Identification and assessment of evidence

A literature search was performed using Medline (1983–2000). The keywords used were 'genital-herpes', 'neonatal-herpes', 'herpes simplex virus', 'pregnancy complications-infectious.' Reference lists of the articles identified were hand searched for additional articles.

The definitions of the types of evidence used in this guideline originate from the US Agency for Health Care Policy and Research. Where possible, recommendations are based on, and explicitly linked to, the evidence that supports them. Areas lacking evidence are highlighted and annotated as 'Good practice points.'

3. Management of women presenting with a first episode of genital herpes during pregnancy

✓ **Referral to a genitourinary physician should be made and management of the woman should be in line with her clinical condition, which will often involve a five-day course of oral aciclovir in standard doses.**

Any woman with suspected first-episode genital herpes should be referred to a genitourinary physician, who will advise on management and arrange a screen for other sexually transmitted infections. Treatment with aciclovir should be considered for all women who develop a first episode of genital herpes in pregnancy. In non-pregnant adults, treatment of first-episode genital herpes is known to reduce the duration and severity of symptoms and decrease the duration of viral shedding. Aciclovir is well tolerated in late pregnancy and there is no clinical or laboratory evidence of maternal or fetal toxicity.[11–13] Aciclovir has been used extensively in pregnancy and the Aciclovir Pregnancy Registry was established in 1984 to collect data on prenatal exposure to the drug. Data from 1207 pregnancies reported prospectively to the Aciclovir Pregnancy Registry between 1984 and 1998 did not demonstrate any increase in the number of birth defects, nor any discernible pattern of defects,[14] and this registry has since been disbanded.

A **Daily suppressive aciclovir in the last four weeks of pregnancy may prevent genital herpes recurrences at term.**

In one double-blind randomised controlled trial,[15] 46 women who presented with their first episode of genital herpes during their current pregnancy were randomised at 36 weeks of gestation to receive either daily suppressive aciclovir or placebo until delivery. No infants in either group developed neonatal herpes. None of the 21 women treated with aciclovir and nine of the 25 women (36%) treated with placebo had clinical evidence of recurrent genital herpes at delivery, necessitating caesarean section (OR 0.04; 95% CI 0.002–0.745). At the time that this study was conducted, it was assumed that all women with recurrent genital HSV lesions should be delivered by caesarean section. However, it is now recognised that women with recurrent HSV at delivery can be delivered vaginally (see below).

Evidence level Ib

B **Caesarean section is recommended for all women presenting with first-episode genital herpes lesions at the time of delivery, but is not indicated for women who develop first-episode genital herpes lesions during the first or second trimesters. For women who present with first-episode genital herpes lesions within six weeks of the expected date of delivery or onset of preterm labour, elective caesarean section may be considered at term, or as indicated, and the paediatricians should be informed.**

Where first-episode genital herpes lesions are present at the time of delivery and the baby is delivered vaginally, the risk of neonatal herpes, calculated from five studies,[1, 16–19] was 19/46 or 41% (95% CI 26–56). In the study by Nahmias *et al.*,[19] the risk of transmission was associated with duration of rupture of the membranes, the risk increasing considerably after the membranes had been ruptured for more than four hours. The risk of perinatal transmission depends on when in pregnancy maternity HSV infection occurs. A large prospective study by Brown *et al.*[1] demonstrated a significant risk of neonatal herpes only when maternal HSV infection was acquired at or just before the onset of labour. In this study of 7046 pregnant women susceptible to infection with either HSV-1 or HSV-2 there were four cases of neonatal herpes among nine women who acquired infection shortly before the onset of labour but no cases among the women who acquired infection prior to this.[1] This study also highlighted the importance of primary, rather than recurrent genital HSV as a risk factor for neonatal herpes; there were no infected babies born to women who had acquired HSV-2 antibodies prior to pregnancy.

Evidence level III

C **For women who develop first-episode genital herpes lesions within six weeks of delivery and who opt for a vaginal birth, invasive procedures should be avoided. For women who develop first-episode genital herpes lesions at or within six weeks of delivery, intravenous aciclovir given intrapartum to the mother and subsequently to the neonate, may reduce the risk of neonatal herpes.**

The use of intravenous aciclovir in this situation may reduce the risk of neonatal herpes by minimising maternal viraemia and reducing exposure of the fetus to HSV.[20] Invasive procedures, such as fetal scalp electrode monitoring, fetal blood sampling, and instrumental deliveries should be avoided, as there have been case reports associating such practices with HSV transmission to the neonate.[21]

Evidence level IV

4. Management of women presenting with a recurrent episode of genital herpes during pregnancy

B **Cultures during late gestation to predict viral shedding at term are not indicated.**

Guidelines from the USA in the 1980s recommended that all women with a history of genital herpes should have weekly viral cultures taken during the last six weeks of pregnancy, with the aim of detecting recurrent herpes episodes, both symptomatic and asymptomatic. Positive cultures near term were an indication for delivery by caesarean section.[22] However, this practice is no longer recommended following a study by Arvin *et al*.,[17] which demonstrated that antenatal swabbing did not predict the shedding of virus at the onset of labour.

Evidence level III

A **Daily suppressive aciclovir in the last four weeks of pregnancy may prevent recurrences of genital herpes at term. However, there is insufficient evidence to recommend this practice routinely.**

Evidence from a small uncontrolled study suggested that taking daily suppressive aciclovir in the last few weeks of pregnancy may prevent recurrences at term in women with a history of recurrent HSV in pregnancy.[23] This was supported by a randomised controlled trial in which 63 pregnant women with recurrent genital herpes were randomised to receive either aciclovir 200 mg four times a day (n = 31) or matched placebo (n = 32) from 36 weeks of gestation.[24] The odds ratio for clinical recurrences during treatment was 0.10 (95% CI 0.00–0.86).

Evidence level Ib

B **For women presenting with recurrent genital herpes lesions at the onset of labour, the risks to the baby of neonatal herpes are small and should be set against the risks to the mother of caesarean section. A recurrent episode of genital herpes occurring at any other time during pregnancy is not an indication for delivery by caesarean section.**

Recurrent genital herpes infection is associated with a much smaller risk of neonatal herpes. Where vaginal delivery is associated with recurrent genital HSV lesions, one study[18] reported a perinatal HSV transmission rate of 3% (1/34) and another study[25] reported a rate of 0% (0/34; 95% CI 0–8%). In the aforementioned study of 7046 pregnant women susceptible to HSV infection,[1] none of the babies diagnosed with HSV was born to a woman who had acquired HSV-2 antibodies prior to pregnancy. A cost-benefit analysis derived from American data has suggested that, if all women with an episode of recurrent genital herpes at the onset of labour were to undergo caesarean section, 1583 (range 632–6340) caesarean sections would be performed to prevent one case of herpes-related mortality or morbidity, at a cost of US$2.5 million per case averted.[26] Moreover, in The Netherlands caesarean sections have not been routinely performed for this indication since 1987 and there has been no increase in the reported incidence of neonatal herpes.[27]

Evidence level III

5. Prevention of acquisition of genital herpes infection during pregnancy

C **All women should be asked at their first antenatal visit if they or their male partner have ever had genital herpes. Female partners of men with genital herpes, who themselves give no history of genital herpes, should be advised about reducing their risk of acquiring this infection.**

Women who report a history of genital herpes can be reassured that, in the event of an HSV recurrence during pregnancy, the risk of transmission to the neonate is very small, even if genital lesions are present at delivery.[18–25] Women with no history of genital herpes may reduce their risk of acquiring herpes during pregnancy by avoiding sexual intercourse at times when their partner has an HSV recurrence. However, the impact of this intervention is limited because sexual transmission of HSV commonly results from sexual contact during periods of asymptomatic viral shedding.[28] Use of condoms throughout pregnancy has also been proposed.[29]

Evidence level IV

C **Identifying women susceptible to acquiring genital herpes in pregnancy by means of type-specific antibody testing has been evaluated in the UK in terms of costs and benefits and is not indicated, except in the context of further research.**

Asking a pregnant woman at her screening visit whether she or her male partner has ever had genital herpes is not an accurate way of determining her risk of acquiring primary HSV infection in pregnancy, because of the prevalence of asymptomatic or unrecognised HSV infection. Type-specific HSV serology is thought to be a more accurate way of detecting women susceptible to HSV infection in pregnancy. As the greatest risk of neonatal herpes occurs when women acquire genital herpes at or near the time of delivery, it has been proposed that serological testing should be undertaken in the latter half of pregnancy in order to identify susceptible women.[1,30] The partners of these women could then be tested and couples discordant for HSV infection could be counselled about ways of reducing the risk of maternal HSV acquisition in pregnancy (abstinence and/or condom use). One study from the USA[31] used a decision-analysis model to assess the potential cost-effectiveness of type specific HSV antibody screening in pregnancy. It concluded that such an intervention could not be recommended. A UK study[32] evaluating the knowledge and attitudes of women to antenatal serum screening for genital herpes found that the population surveyed had a good knowledge about genital herpes and would accept antenatal testing. However, given the current low incidence of neonatal herpes in the UK,[2] it would seem unlikely that such a screening programme would be cost-effective. This has been confirmed by one UK study.[33]

Evidence level IV

6. Prevention of postnatal HSV transmission to the neonate

C **Healthcare workers and family members with active HSV infection, such as orolabial herpes or herpetic whitlow, should avoid direct contact between lesions and the neonate.**

Neonatal herpes may occur as a result of nosocomial or community-acquired infection.[34,35] Mothers, family members and healthcare workers should be aware of the risk of neonatal transmission from active HSV lesions.

Evidence level IV

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Further reading

National Guidelines for the Management of Genital Herpes' Clinical Effectiveness Group (Association of Genitourinary Medicine and the Medical Society for the Study of Venereal Diseases). *Sex Transm Infect* 1999;73 Suppl 1:S24–8.

Helpful address

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APPENDIX

Clinical guidelines are: 'systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions'. Each guideline is systematically developed using a standardised methodology. Exact details of this process can be found in Clinical Governance Advice No 1: *Guidance for the Development of RCOG Green-top Guidelines* (available on the RCOG website http://www.rcog.org.uk/medical/greentopguide.html). These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference to individual patient needs, resources and limitations unique to the institution and variations in local populations. It is hoped that this process of local ownership will help to incorporate these guidelines into routine practice. Attention is drawn to areas of clinical uncertainty where further research may be indicated.

The evidence used in this guideline was graded using the scheme below and the recommendations formulated in a similar fashion with a standardised grading scheme.

Classification of evidence levels

Ia	Evidence obtained from meta-analysis of randomised controlled trials.
Ib	Evidence obtained from at least one randomised controlled trial.
IIa	Evidence obtained from at least one well-designed controlled study without randomisation.
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study.
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.

Grades of recommendations

A Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. (Evidence levels Ia, Ib)

B Requires the availability of well-controlled clinical studies but no randomised clinical trials on the topic of recommendations. (Evidence levels IIa, IIb, III)

C Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV)

Good practice point

✓ Recommended best practice based on the clinical experience of the guideline development group.

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The final version is the responsibility of the Guidelines and Audit Committee of the RCOG.
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Association for Improvements in the Maternity Services; Association of Community Health Councils; Family Planning Association; Maternity Alliance; Maternity and Health Links; National Childbirth Trust; National Council for Women; Women's Health

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