



PREVENTION OF EARLY ONSET NEONATAL GROUP B STREPTOCOCCAL DISEASE

1. Purpose

The purpose of this document is to provide guidance for obstetricians, midwives and neonatologists on the prevention of early-onset neonatal group B streptococcal (GBS) disease.

2. Background

Group B streptococcus (*Streptococcus agalactiae*) is recognised as the most frequent cause of severe early-onset (less than seven days of age) infection in newborn infants. However, there is still controversy about its prevention. A survey in 2001 demonstrated that less than 1% of UK maternity units were performing systematic screening for GBS¹ and, so far, UK clinicians have not generally adopted guidelines from the USA, Australia and Canada that encourage screening.^{2,3} The Public Health Laboratory Service Group B Streptococcal Working Group has produced interim guidelines⁴ but these are based on US data (in the absence of available UK data) and have not been widely adopted in this country. The US Centers for Disease Control and Prevention (CDC) now recommend that all pregnant women undergo bacteriological screening, with vaginal and rectal swabs taken for GBS culture at 35–37 weeks of gestation.⁵ Extrapolation of practice from the USA to the UK may be inappropriate. The incidence of early-onset GBS disease in the UK in the absence of systematic screening or widespread intrapartum antibiotic prophylaxis is 0.5/1000 births,⁶ which is similar to that seen in the USA after universal screening and intrapartum antibiotic prophylaxis, despite comparable vaginal carriage rates.⁷ In 2001 a national UK surveillance study identified 376 cases of early-onset GBS disease, 39 of which were fatal.⁶ There were 2519 neonatal deaths from all causes in the UK in 2000.⁸

The incidence of early-onset disease in the USA has fallen in association with the introduction of screening pregnant women for GBS.² The current US guidelines⁵ advise that all women colonised with GBS at 35–37 weeks (or labouring before this time) should be offered intrapartum antibiotic prophylaxis, usually in the form of high-dose intravenous penicillin or ampicillin. Intrapartum antibiotic prophylaxis has been shown to significantly reduce the risk of early-onset but not late-onset disease (occurring seven or more days after birth). Antenatal screening and treatment have not yet demonstrated an effect on all cause neonatal mortality⁹ and may carry disadvantages for the mother and baby. These include potentially fatal anaphylaxis,¹⁰ the medicalisation of labour and the neonatal period, and infection with resistant organisms.^{11,12}

3. Identification and assessment of evidence

The Cochrane Database of Systematic Reviews and Medline were searched using the terms 'group B streptococcus', '*Streptococcus agalactiae*', 'pregnancy' and 'neonate'.

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.'

4. Population-based screening approaches

Several screening strategies have been proposed to prevent early-onset GBS disease. With risk factor based screening, intrapartum antibiotic prophylaxis is offered to all women with recognised risk factors for early-onset GBS disease. These are:

- previous baby affected by GBS
- GBS bacteriuria detected during the current pregnancy
- preterm labour
- prolonged rupture of the membranes
- fever in labour.

Mathematical modelling in the USA suggests that this approach will result in approximately 25% of women being offered intrapartum antibiotic prophylaxis,^{13,14} with a decrease in the incidence of early-onset GBS disease of 50.0–68.8%.¹⁵

Bacteriological screening involves taking vaginal and rectal swabs from all women between 35–37 weeks of gestation and inoculating the samples into enriched medium. The rate of detection of GBS colonisation can be increased from 22% to 27% by sampling the lower vagina and rectum rather than only the lower vagina.¹⁶ All women carrying GBS and all women who labour before swabs are taken are offered antibiotic prophylaxis. Women who do not have swabs taken, or for whom results are not available at the time of labour, are offered antibiotic prophylaxis if they have any of the clinical risk factors defined above. Bacteriological screening is estimated to result in 26.7% of women in the USA being offered intrapartum antibiotic prophylaxis and to reduce the incidence of early-onset GBS disease by 86%. On the basis of one large, nonrandomised, population-based study¹⁷ the 2002 CDC guidelines⁵ concluded that the risk factor approach to screening was inferior to bacteriological screening and CDC now recommends bacteriological screening for all women.

A third suggested approach is to screen all women with swabs, as in the bacteriological screening approach, and offer antibiotic prophylaxis to the GBS carriers who also have a clinical risk factor. This policy has been suggested by the Canadian Task Force on Preventative Health Care³ and it is estimated to result in 3.4% of women being offered antibiotic prophylaxis and to reduce the incidence of early-onset GBS disease by 51%.¹⁸

There is little organised antenatal screening for GBS carriage in the UK at present. In addition, selective culture media are required for optimal detection of GBS and these media are rarely used in UK laboratories.

There have been no randomised controlled trials (RCTs) comparing antenatal screening, whether bacteriological or risk factor based, with no antenatal screening. No RCTs have compared the different screening strategies. Estimates of the efficacy of the screening strategies are based on observational studies. In addition, the focus of these studies has been the incidence of confirmed early-onset GBS disease. In infants exposed to intrapartum antibiotic prophylaxis, it is possible that the confirmation of GBS disease is made more difficult by the presence of antibiotics effective against GBS in the blood.¹⁹ Studies have not measured the incidence of neonatal sepsis as a whole; a large proportion of this is culture-negative (some of which will be caused by GBS).²⁰ Some studies have suggested that a decreased incidence of neonatal sepsis due to GBS has not been accompanied by a decrease in neonatal sepsis as a whole nor in neonatal mortality; however, findings from other studies have been contradictory.²¹ No study has yet been able to demonstrate that screening for GBS has any impact on neonatal sepsis as a whole.

In order for clear recommendations to be made about the relative benefits and risks of antenatal screening and intrapartum antibiotic prophylaxis for GBS in the UK, further research in the form of an RCT of current clinical practice versus bacteriological screening should ideally be performed.

5. Estimated effects of bacteriological screening

Approximately 25% of mothers in the UK are likely to be GBS carriers.⁷ This estimate is based on a single study performed in the 1980s and it is possible that this study does not reflect the current picture. With the addition of women who present with other clinical risk factors for GBS disease, such as preterm labour, around 30% of all pregnant women would receive intrapartum antibiotic prophylaxis if a bacteriological screening programme were to be introduced in the UK (this is approximately 204 000 women per annum). The current incidence of early-onset GBS disease in the UK and the Republic of Ireland is 0.50/1000 births,⁶ which is equivalent to approximately 340 babies per annum. If we estimate that intrapartum antibiotic prophylaxis is 80% effective at preventing early-onset GBS disease,⁹ then this will decrease the number of affected babies to 68. Therefore each year in the UK 204 000 women will be treated to prevent 272 babies developing early-onset GBS disease. For every 1000 women treated with antibiotic prophylaxis, 1.4 cases of disease may be prevented. However, the numbers of women treated to prevent one case may be higher, as this estimate assumes that antenatal swabs identify all GBS carriers, which is not the case. Also, when applied in practice, 65–70% may be a more reasonable approximation of the effectiveness of intrapartum antibiotic prophylaxis.²² Both of these factors will increase the numbers of women who are treated to prevent one neonatal infection. It is also true that the rate varies within the UK (0.21/1000 births in Scotland, 0.73/1000 births in Northern Ireland).⁶ Where local figures are known, the number needed to treat (NNT) should be adjusted appropriately.

The mortality from early-onset GBS disease in the UK is 6% in term infants and 18% in preterm infants. Intrapartum antibiotic prophylaxis will not prevent all deaths. Even when treated appropriately some infants will still die of early-onset disease, particularly when the disease is well established prior to birth. If one makes the assumption that the effect of antibiotic prophylaxis on neonatal death from GBS is equivalent to its effect on GBS disease, then to prevent one neonatal death from GBS would require at least 7000 colonised women to be given intrapartum antibiotic prophylaxis, which would require at least 24 000 women to be screened.

6. Estimated effects of risk based screening

Information about the UK prevalence of the antenatal risk factors for early-onset GBS disease and data from the cases of early-onset disease in the UK surveillance study⁶ can be used to estimate the risk of the disease developing in the presence of each antenatal risk factor with and without antibiotic prophylaxis. This information is presented in Table 1.

The combined risk factor approach recommended by CDC may also be analysed in the same way. Approximately 15% of all UK pregnancies have one or more of the following risk factors:

- intrapartum fever
- prolonged rupture of membranes (PROM) greater than 18 hours
- prematurity less than 37 weeks
- previous infant with GBS.^{23,24}

Approximately 60% of UK early-onset GBS cases have such risk factors.^{6,23,24} Thus, two cases of disease and 0.21 deaths from GBS disease occur for every 1000 pregnancies with one or more of these factors. Approximately 625 women with one or more of these risk factors need to be treated to prevent one case of disease and 5882 women need to be treated to prevent one death. This can be compared with prophylactic corticosteroids given prior to preterm birth when the number of women needed to treat to prevent one neonatal death is 23.²⁵

Risk factor	EOGBS cases/ 10 000 untreated women with risk factor	EOGBS deaths/ 10 000 untreated women with risk factor	NNT with IAP to prevent one case of EOGBS	NNT with IAP to prevent one death from EOGBS	EOGBS cases prevented/ year in UK	EOGBS deaths prevented / year in UK
Intrapartum fever (> 38°C)	60	6.3	208	1984	52	5.5
Prematurity (< 35 weeks)	35	8.0	357	1562	61	14.0
Prematurity (< 37 weeks)	25	4.6	500	2717	101	18.5
Prolonged rupture of membranes (≥ 18 hours) at term	21	1.2	595	10416	91	5.2

EOGBS = early-onset group B streptococcus; IAP = intrapartum antibiotic prophylaxis; NNT = number needed to treat

Assumptions

- Live birth rate UK = 680 000 (Office for National Statistics).
- Prevalence of risk factors in pregnancy:
 - 1.6% intrapartum fever > 38°C²³
 - 8% PROM at term²⁶
 - 7.4% < 37 weeks of gestation
 - 3.2% < 35 weeks of gestation.²⁷
- Prevalence of risk factors in babies with EOGBS disease:
 - 19% intrapartum fever > 38°C²⁴
 - 34% PROM at term²⁴
 - 37% < 37 weeks
 - 22% < 35 weeks of gestation.²⁸
- Incidence of early-onset GBS in the UK is 0.5/1000.⁶
- Mortality of early-onset GBS in the UK is:
 - 10.6% overall
 - 18.3% < 37 weeks
 - 22.8% < 35 weeks
 - 5.7% ≥ 37 weeks.²⁸
- 80% effectiveness of intrapartum antibiotic prophylaxis in preventing early-onset GBS.⁹

7. Potential risks of screening

In addition to the possible benefits of antenatal GBS screening and intrapartum antibiotic prophylaxis, there are also possible risks.

The incidence of severe anaphylaxis associated with the use of penicillin in labour has been estimated at 1/10 000 women treated. Fatal anaphylaxis has been estimated to occur in as many as 1/100 000 women treated.¹⁰ If 30% of the UK pregnant population is treated with penicillin, this might result in two deaths a year as a consequence of penicillin anaphylaxis. The fetal effects of severe anaphylaxis have not been well reported.

The widespread use of antibiotics is known to contribute to the development of resistant organisms. This is a particular risk when broad-spectrum antibiotics such as ampicillin are used^{11,12} but should not be ignored as a possibility when using penicillin.

There is also a possibility that exposure to antibiotics in the neonatal perinatal period may affect neonatal faecal flora, with a subsequent impact on immune development and later allergy.²⁹

8. Antenatal screening

C Routine screening (either bacteriological or risk based) for antenatal GBS carriage is not recommended.

Until it is clear that antenatal screening for GBS carriage does more good than harm and that the benefits are cost effective, there seems little justification at present for recommending routine screening in the UK.

Initiating national swab-based screening for antenatal GBS carriage would have a substantial impact on the provision of antenatal care within the UK. Major organisational changes and new funding would be required to ensure an equitable and quality assured service.

Evidence level IV

9. Prophylaxis

9.1 Should women be treated antenatally, if GBS is detected incidentally?

B Antenatal treatment with penicillin is not recommended.

Antenatal prophylaxis with oral penicillin does not reduce the likelihood of GBS colonisation at the time of delivery³⁰ and so is not indicated in this situation.

Evidence level IIa

9.2 Should women receive intrapartum antibiotic prophylaxis, if GBS detected incidentally?

C Intrapartum antibiotic prophylaxis should be considered if GBS is detected incidentally.

If GBS is present in a vaginal swab as an incidental finding, it is difficult to quantify the risk of neonatal disease. If swabs have been taken from the rectum and lower vagina and inoculated into enriched medium at 35–37 weeks, a risk of disease of 1/500 may be assumed (UK incidence 0.5/1000; approximately 25% women are carriers). The risk will probably be greater if a positive swab is obtained from the upper vagina or has been cultured using non-enriched medium. If a positive swab is obtained at an earlier stage of pregnancy, the risk is probably lower. Incidental carriage and GBS bacteriuria should be considered as additional risk factors to those listed in Table 1.

Evidence level IV

9.3 Should women receive intrapartum antibiotic prophylaxis if GBS was detected in a previous pregnancy?

C There is no good evidence to support the administration of intrapartum antibiotic prophylaxis to women in whom GBS carriage was detected in a previous pregnancy.

Evidence level IV

9.4 Should women with a previous baby with neonatal GBS disease be offered intrapartum antibiotic prophylaxis?

C Intrapartum antibiotic prophylaxis should be offered to women with a previous baby with neonatal GBS disease.

Subsequent infants born to these women are probably at increased risk of GBS disease, although this has not been accurately quantified. The probable increase in risk may be due to low levels of maternal anti-GBS antibodies.³¹ Vaginal or rectal swabs are not helpful, as intrapartum antibiotic prophylaxis would be recommended even if these swabs were negative for GBS.

Evidence level IV

9.5 Intrapartum antibiotic prophylaxis for other groups

C Clinicians should use the table above to inform discussions with women regarding the use of intrapartum antibiotic prophylaxis in the presence of known risk factors including incidental carriage. The argument for prophylaxis becomes stronger in the presence of two or more risk factors.

Evidence level IV

A If chorioamnionitis is suspected, broad-spectrum antibiotic therapy including an agent active against GBS should replace GBS-specific antibiotic prophylaxis.

Evidence level Ib

B IAP should be offered to women with GBS bacteriuria in the current pregnancy after discussion.

GBS bacteriuria is associated with a higher risk of neonatal disease.³² Again, it is not possible to quantify this increased risk. These women should be offered antibiotic prophylaxis after appropriate discussion. Women with GBS urinary tract infection during pregnancy should receive appropriate treatment at the time of diagnosis as well as antibiotic prophylaxis.

Evidence level III

C Antibiotic prophylaxis is not required for women undergoing planned caesarean section in the absence of labour and with intact membranes.

Women undergoing planned caesarean delivery in the absence of labour or membrane rupture do not require antibiotic prophylaxis for GBS, regardless of GBS colonisation status. The risk of neonatal GBS disease is extremely low in this circumstance.³³

Evidence level IV

C Antibiotic prophylaxis for GBS is unnecessary for women with preterm rupture of membranes unless they are in established labour.

Antibiotic administration specifically for GBS colonisation is not necessary prior to labour. If these women are known to be colonised with GBS, antibiotic prophylaxis should be considered, especially if labour occurs prior to 37 weeks (see Table 1).

Evidence level IV

9.6 Which antibiotics should be given?

B Penicillin should be administered as soon as possible after the onset of labour. Clindamycin should be administered to those women allergic to penicillin.

It is recommended that intravenous penicillin 3 g be given as soon as possible after the onset of labour and 1.5 g four-hourly until delivery. Clindamycin 900 mg should be given intravenously eight-hourly to those allergic to penicillin. It should be noted that these doses are based on tradition rather than good evidence. Broad-spectrum antibiotics such as ampicillin should be avoided if possible, as concerns have been raised regarding increased rates of neonatal Gram-negative sepsis.¹¹ To optimise the efficacy of antibiotic prophylaxis, the first dose should be given at least two hours prior to delivery.^{34,35}

Evidence level III

10. Management of the newborn infant

The evidence base upon which to make treatment decisions for newborn infants is weak. Few RCTs have been performed.³⁶⁻³⁸ Unlike some other countries, the UK does not have a well-established neonatal surveillance network. The establishment of such a network would facilitate the prospective collection of data on GBS disease. Previous guidelines have largely been based on consensus rather than evidence. However, study data permit risk estimates to be made which can be used to inform decision making.

10.1 Sick infants

C Newborn infants with clinical signs of early-onset GBS disease should be treated promptly with the necessary antibiotics.

Many infants with early-onset GBS disease have symptoms at or soon after birth.⁶ Neonatal sepsis can progress rapidly to death. Whether they received intrapartum antibiotics or not, any newborn infant with clinical signs compatible with infection should be treated promptly with broad-spectrum antibiotics, which provide cover against early-onset GBS disease and other common pathogens. Blood cultures should always be obtained before antibiotic treatment is commenced, and CSF cultures should be considered.

Evidence level IV

10.2 Low-risk term infants

B Postnatal antibiotic prophylaxis is not recommended for low-risk term infants.

The incidence of early-onset GBS disease in term infants without antenatal risk factors in the UK is 0.2 cases/1000 births.⁶ No RCT has investigated treatment in this group. If postnatal antibiotic treatment was completely effective and there were no adverse effects, 5000 infants would need to be treated to prevent a single case and at least 80 000 infants would have to be treated to prevent a single death from early-onset GBS disease.

Evidence level III

Routine postnatal antibiotic prophylaxis is not recommended.

10.3 Well infant with risk factor, including incidental finding of maternal GBS carriage, with or without intrapartum antibiotics

C RCTs have not provided a sufficient evidence base for clear treatment recommendations in well newborn infants.

Estimates of the risk of early-onset GBS disease in the presence of individual antenatal risk factors, before and after antibiotic prophylaxis, are shown in Table 2. Some clinicians will recommend treatment of the infants, while others will prefer to observe them because the balance of risks and benefits of treatment is uncertain. Because 90% of cases present clinically before 12 hours of age,^{28,34,39} the risk of disease in infants who remain well without treatment beyond this time may not be substantially elevated above that of the infant with no risk factors. Prolonged observation of well infants is therefore not indicated. The argument for using prophylactic treatment in well infants is stronger in the presence of multiple risk factors but is still unproven.

Evidence level IV

Risk factor	Risk of EOGBS disease if IAP were not given	Risk of EOGBS disease if full IAP were given	Risk of death from EOGBS disease if IAP were not given	Risk of death from EOGBS disease if full IAP were given	Risk of EOGBS if infant remains well at 12 hours in absence of IAP and neonatal treatment
Intrapartum fever (> 38°C)	1:167	1:1572	1:1572	1:7861	1:1670
Prolonged rupture of membranes (≥ 18 hours) at term	1:476	1:8351	1:8351	1:41,771	1:4760
Prematurity (< 37 weeks)	1:400	1:2186	1:2186	1:10,929	1:4060
Prematurity (< 35 weeks)	1:286	1:1253	1:1253	1:6266	1:2860

EOGBS = early-onset group B streptococcus; IAP = intrapartum antibiotic prophylaxis

Assumptions

- As for Table 1, plus
- 90% of cases of early-onset GBS disease present by 12 hours of age^{28,34,39}

10.4 Previous infant with GBS disease

C For an infant, whose mother had a previous infant with GBS disease, either clinical evaluation after birth and observation for at least twelve hours are necessary, or blood cultures should be obtained and the infant treated with penicillin until the culture results are available.

The risk of GBS disease is unquantified but is probably significantly increased.²⁷ The infant should be evaluated clinically soon after birth and observed for at least twelve hours. An alternative approach would be to obtain blood cultures and treat with penicillin until the culture results are available. There is insufficient evidence to suggest that neonatal treatment should be given if antibiotic prophylaxis has been administered.

Evidence
level IV

10.5 Routine neonatal surveillance cultures

It is not necessary to perform routine surface cultures or blood cultures on well infants.

Most infants who develop early-onset GBS disease present with illness soon after birth and 90% have presented clinically by 12 hours of age, before culture results become available.^{28,34,39} Postnatal antibiotic treatment has not been shown to eradicate carriage of GBS or to influence the risk of late-onset GBS disease. It is therefore unnecessary to perform routine surface cultures or blood cultures on well infants, whether they received antibiotic prophylaxis or not.

Evidence
level III

10.6 Breastfeeding

C Breastfeeding does not increase the risk of neonatal GBS disease and women concerned about late-onset disease should be given the usual advice about breastfeeding.

Evidence
level IV

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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 at www.rcog.org.uk/clingov1). 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		Grades of recommendations	
Ia	Evidence obtained from meta-analysis of randomised controlled trials.	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)
Ib	Evidence obtained from at least one randomised controlled trial.		
IIa	Evidence obtained from at least one well-designed controlled study without randomisation.	B	Requires the availability of well controlled clinical studies but no randomised clinical trials on the topic of recommendations. (Evidence levels IIa, IIb, III)
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.	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)
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.		
		Good practice point	
		<input checked="" type="checkbox"/>	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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unless otherwise indicated