UK NATIONAL SCREENING COMMITTEE

Antenatal Screening for Group B Streptococcus Carriage
Policy Position Statement

13 November 2012

Aim

1. This paper is an update report following the consultation on the review of antenatal screening for group B streptococcus (GBS) carriage.

Current policy

2. The last time the policy was reviewed was 2009 and the current policy is:

‘Screening for GBS should not be offered to all pregnant women. This is because there is insufficient evidence to demonstrate that the benefits to be gained from screening all pregnant women and treating those carrying the organism with intravenous antibiotics during labour would outweigh the harms.’

Background

3. The rationale for the current policy was multifactorial:

- The natural history of transmission of GBS from the intestine and the genital tract to the baby is poorly understood, this includes the mechanisms by which some colonised newborns are affected while others are not.
- The rate of early onset GBS is comparable to those countries in which screening is recommended and benefits of screening are uncertain.
- Screening at 35 – 7 weeks will not impact on a significant burden of early onset GBS disease. For example premature deliveries account for about 30% of cases and 65% of deaths to early onset GBS. Late onset GBS is not reduced by screening and accounts for the majority of GBS meningitis.
- The test cannot distinguish between the majority of low risk women and the minority whose baby will be affected, this results in over-detection and over-treatment of a very large number of women at very low risk.
- The limitations / problems relating to the treatment can be summarised as:

  - effectiveness - evidence, from a study in Spain, considered in the last UK National Screening Committee (UK NSC) review, suggested that the treatment may not be as effective as suggested in an Health Technology Assessment (HTA) study. This is difficult to quantify as there have been no RCTs but creates uncertainty about the additional benefit of screening over the current prevention strategy in the UK,
  - long term effect – a screening approach would expand the use of the antibiotics into a low risk population and there have been no studies of the long term effects of this. The ORACLE study used different combinations of antibiotics to prevent preterm labour, the seven year follow up showed an
increased rate of cerebral palsy associated with the use erythromycin and co-
amoxiclav. The regimens were different to the GBS context but the study
illustrated a general point that there may be a long term negative effect from
antibiotic use in labour,

- impact on sepsis as a whole – the UK NSC review considered reports that
other causes of severe neonatal sepsis (such as E Coli sepsis) may be increased
thereby resulting in no overall reduction in neonatal sepsis. These reports are
conflicting but again illustrate a general concern about uncertainty,

- antibiotic resistance – expansion of antibiotic use on this scale may promote
antibiotic resistance. This has not been reported for penicillin but has been for
antibiotics used as second line regimens e.g. clindamycin

- anaphylaxis – there is a small but real risk of maternal reactions to antibiotics
in labour. This is poorly studied but there are some reports of babies being
adversely affected by maternal anaphylaxis e.g. in France five cases in one
hospital were identified resulting in death or brain damage,

- increasing medicalisation of labour – which may result in women at low risk
being unable to give birth at home,

UK NSC review

4. The immediate background to initiation of the UK NSC review was the momentum
of pressure to introduce screening in Northern Ireland. Additionally, within the UK NSC, there
was a felt need to undertake the review because of an increasing number of publications
discussing the limitations of culture testing. As a result, the review was brought forward by
six months.

5. Bazian were asked to consider the evidence published between 2008 – 2012 with particular
reference to the factors informing the current policy and to publications addressing culture
testing at 35 – 7 weeks. Professor Peter Brocklehurst and Professor Catherine Peckham
provided expert advice on the review.

Group B Strep Support (GBSS) campaign and pre-consultation exercise

6. There is a highly committed user group who have been pressing publically for screening of
GBS at 37 weeks. They have used a variety of mechanisms to raise the issue with the public
and with MPs. Part of this is a report (attached) and a website encouraging wider engagement
with the UK NSC review and also encouraging responses. However they have circulated their
report and a template for people to use when responding to the issue of screening for GBS in
pregnancy. This has meant that a number of responses are very similar. 31 Parliamentary
Questions have been submitted in England during the review period to date (as of 26/10/12). The
GBSS also provided a standard response template for those wishing to submit comments
to the UK NSC consultation.

7. GBSS have suggested that the UK NSC is biased in its review and treatment of the issue. They
have focussed their criticism on Professor Peter Brocklehurst and Bazian. As the UK NSC
process allows for extensive consultation this possibility is minimised but to further reassure
stakeholders a number of individuals and organisations were asked to comment on the draft
review prior to consultation. This included GBSS and those recommended by GBSS as unbiased
and knowledgeable. Some of GBSS’s comments were incorporated into the review prior to the
consultation opening.
Professor David Taylor (obstetrics) – excellent
Professor Helen Spiby (midwifery) – well argued and suitable for a scientific audience
Jim Gray (microbiology) - excellent and fair
Mark Turner (neonatology / National Institute for Health and Clinical Excellence (NICE)
Management of Early Onset Infections GDG) – no substantive comments
Mary Newburn (National Childbirth Trust) – fit for consultation purposes
Joe Kearney (Health Protection Agency) – no comments at this stage
Theresa Lamagni (Health Protection Agency Surveillance) – suggested cosmetic changes about
the Health Protection Agency method of quantifying under-reporting in Health Protection
Agency laboratory reports
GBSS – unfit for consultation purposes and a process which continues on its basis is invalid
because:
• review methodology – does not meet the standard of a systematic review or a peer
reviewed publication.
• presentation of the studies considered in the document is biased. A key issue in this
respect was the test.
• exclusion of key messages – because the review’s conclusions conflicted with those of
the authors of some of the papers on the test.
• arbitrary choice of papers and quotations – there was a further criticism that the review
should have had a different focus eg test sensitivity and specificity not ppv and npv.

8. Unstated implication relating to UK NSC reviews - that the type of document produced by
Bazian is insufficiently robust to support policy making decisions.

9. The review was considered at the July meeting of the Fetal, Maternal and Child Health Co-
ordinating Group (FMCH) and a consultation began shortly after that.

10. The document is attached.

Wider context of recent guideline development

11. The Royal College of Obstetricians and Gynaecologists (RCOG) issued a revised
guideline in June 2012. This recommends an approach to antibiotic administration based on
maternal risk factors. This recommends a very conservative approach to intrapartum
antibiotic usage.

12. NICE issued a guideline on the management of early onset infections in August 2012.
This did not assess screening directly but the guideline development group did assess whether
maternal GBS carriage was a useful predictor of early onset infection. This is an important
issue as a screening programme would test all women at 35 – 37 weeks as a means of
identifying a group of women who would be eligible for intravenous antibiotic prophylaxis
during labour. The conclusion of the assessment was that maternal GBS carriage was not a
useful predictor of disease.

Consultation

13. The consultation period ran from 16th July 2012 to October 23rd 2012. The following
stakeholders were contacted directly: RCOG, Royal College of Midwives (RCM), Royal
College of Paediatrics and Child Health (RCPCH), GBSS, National Childbirth Trust (NCT),
Health Protection Agency, Association for Improvements in the Maternity Services (AIMS),
British Maternal and Fetal Medicine Society (BMFMS), British Infection Association, the four Departments of Health.

14. As the UK NSC process allows discretion in areas where there is controversy a workshop to clarify concerns with the report was held with some of the pre-consultation group towards the end of the consultation period. The note of this meeting is attached. GBSS were concerned that, in focusing on the USA, the review had not adequately addressed the international experience of screening. It was agreed that GBSS would submit a list of publications which would be considered for inclusion in the review. The list is attached as an appendix with comments on the individual papers.

15. In total 212 written responses were received. All responses are attached.

- 175 responses were received from individual members of the public who had experience of early onset GBS, stillbirth, late onset GBS, intrapartum antibiotic prophylaxis to prevent GBS or who knew friends or relatives who had experience of the condition. These responses all advocate screening and are, to a greater or lesser degree, informed by themes found within the GBSS report.
- 16 responses were received from individual professionals the majority of which were supportive of screening.
- 16 responses were received from national professional bodies, charities and international organisations. Of these organisations RCOG, RCM, NCT, BMFMS and Public Health Agency (Northern Ireland), DHSSP Northern Ireland considered the report’s conclusion to be appropriate. The Health Protection Agency made no overall comment on the conclusion. Meningitis UK commented that vaccination is would be the appropriate solution. Responses from GBS International, GBS Association, Action on Pre-eclampsia, Miscarriage Association, Twin and Multiple Births Association and the Foundation for Families considered that screening should be introduced.
- The most sustained critique came from GBSS. The response runs to over 80 pages and makes many detailed points which have been addressed with the reviewers. The main themes are highlighted in the summary document. These relate to the review methodology, its handling of papers relating to the test, UK incidence data, international reports of falling incidence as a consequence of screening, cost effectiveness studies, issues relating to antibiotic use in labour, missed data on acceptability of screening and the emphasis given to the importance of RCT evidence. GBSS considered that a decision made on the basis of the review would not be valid.
- Two responses were received from MPs and three from commercial organisations.

16. While recognising that screening for GBS carriage continues to attract interest, particularly amongst those affected by the condition, it is also significant that major stakeholders in this area continue to have concerns about screening.

Recommendation

17. The UK NSC is asked to agree that

i) the current policy statement should be retained

Screening for GBS should not be offered to all pregnant women. This is because there is insufficient evidence to demonstrate that the benefits to be gained from screening all pregnant
women and treating those carrying the organism with intravenous antibiotics during labour would outweigh the harms.'."

ii) the following text should be added to the policy statement

18. The current UK rate of early onset GBS is comparable to that in countries in which screening is recommended. A significant burden of disease is found in risk groups whose management would not be affected by a screening programme. The ability of screening to significantly impact on mortality and long term morbidity caused by GBS is uncertain.

19. Systematic reviews of culture testing suggest that many screen positive women may no longer be carriers at the point of treatment. In the absence of a diagnostic test, current screening strategies are unable to distinguish between carriers whose babies will be affected by early onset GBS and those which would not. As a result many thousands of low risk women would receive intravenous antibiotic prophylaxis during labour. The consequences of expanding antibiotic usage in this way are unknown.

20. The UK NSC is asked to agree that the policy should be reviewed in three years’ time unless there is significant new peer reviewed evidence in the meantime.

21. It is recommended that:

- the Director of Programmes’ office should work to develop a communications strategy to promote understanding of the policy, perhaps in collaboration with RCOG and NICE.
- a detailed modelling exercise based on assumptions arising from the review,
- a national surveillance study should be encouraged to generate up to date epidemiological data,
- a review of issues relating to antibiotic use in pregnancy and labour should be commissioned given the evolving context of work on the microbiome and the National Perinatal Epidemiology Unit’s study of anaphylaxis in pregnancy and labour,
- the possibility of natural history studies exploring vertical transmission of GBS and development of early onset GBS in the newborn
- work should be undertaken with the HTA to explore the possibility of studies of rapid testing in high risk groups (for example prolonged rupture of the membranes or preterm deliveries) as a means of targeting antibiotics in these populations
## Appendix 1: Papers submitted by GBSS for additional consideration of the international experience of screening.

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<tr>
<th>Paper details</th>
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<tr>
<td>3 Berardi A et al, Group B Streptococcus Early-Onset Disease in Emilia-Romagna: Review After: Introduction of a Screening-Based Approach, The Pediatric Infectious Disease Journal Volume 29, Number 2, February 2010</td>
<td>Consider inclusion in addendum to the review. This study was highlighted in GBSS’s formal submission in response to the consultation.</td>
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<td>5 Daley AJ, Isaacs D. Ten-year study on the effect of intrapartum antibiotic prophylaxis on early onset group B streptococcal and</td>
<td>Outside literature search limits, looked at early onset disease less than 48 hours, no follow up since and was in the Lancet systematic review of global prevalence described in the NSC review</td>
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<td>6</td>
<td>Escherichia coli neonatal sepsis in Australasia. Pediatr Infect Dis J 2004; 23(7):630-634.</td>
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<td>7</td>
<td>Eberly MD, Rajnik M. The effect of universal maternal screening on the incidence of neonatal early-onset group B streptococcal disease. Clinical Pediatrics. 48(4):369-75, 2009 May.</td>
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<td>8</td>
<td>Elvedi-Gasparović V. Peter B. Maternal group B streptococcus infection, neonatal outcome and the role of preventive strategies. Collegium Antropologicum. 32(1):147-51, 2008 Mar.</td>
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<td>9</td>
<td>Hafner E, Sterniste W, Rosen A et al. Group B streptococci during pregnancy: a comparison of two screening and treatment protocols. American journal of obstetrics and gynecology. 1998;179(3 Pt 1):677-81.</td>
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<tr>
<td>10</td>
<td>Jordan HT, Farley MM, Craig A, Mohle-Boetani J, Harrison LH, Petit S et al. Revisiting the need for vaccine prevention of late-onset neonatal group B streptococcal disease: a multistate, population-based analysis. Pediatr Infect Dis J 2008; 27(12):1057-1064.</td>
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This is a Czech language paper.