The prevention of early-onset neonatal group B streptococcus infection: technical report from the New Zealand GBS Consensus Working Party

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Abstract

Aims Early-onset neonatal group B streptococcus (GBS) is the leading infectious cause of disease in newborn babies. Since intrapartum antibiotics interrupt vertical GBS transmission, this is now a largely preventable public health problem. An important first step is to develop (then implement) nationally, agreed prevention policies.

Methods Representatives from the New Zealand College of Midwives, the Paediatric Society of New Zealand, the New Zealand Committee of the Royal Australian and New Zealand College of Obstetricians and Gynaecologists, the Royal New Zealand College of General Practitioners, and the Homebirth Association met to review evidence that will assist in the formulation of GBS prevention policies that are most suitable for New Zealand.

Results The Technical Working Group noted that (i) no strategy will prevent all cases of early-onset GBS infection, (ii) intrapartum antibiotics are associated with rare, but serious, adverse effects, (iii) concerns remain over developing antibiotic resistance, (iv) an economic analysis is required to help inform policy, (iv) reliable bedside diagnostic tests for GBS in early labour are not yet available and (iv) the most important determinant of effectiveness will be compliance with a single national prevention policy.

Conclusions As an interim measure a GBS risk-based prevention strategy is recommended. This exposes the least numbers of women and their babies to antibiotics, while virtually preventing all deaths from GBS sepsis. Continuing education of health professionals and pregnant women, auditing protocol compliance, tracking adverse events amongst pregnant women, and national surveillance of neonatal sepsis and mortality rates and antibiotic resistance are necessary for the strategy's success.

Group B streptococcus (GBS), *Streptococcus agalactiae*, is part of the rectovaginal flora in 10–30% of pregnant women, and the leading cause of early-onset neonatal sepsis, pneumonia, and meningitis.1,2

The large bowel is the major reservoir for GBS with often-intermittent colonisation of the genital tract. Although maternal intrapartum colonisation is a major risk factor for early-onset neonatal GBS infection, with up to 50% of babies born to colonised women acquiring the organism, only 1–2% of colonised babies become ill from early-onset disease (overall 1–4 cases per 1000 live-births).2–4 Before the introduction of GBS prevention policies as many as 80% of early-onset neonatal GBS cases were associated with one or more obstetric risk factors such as a previously affected baby,
GBS bacteriuria during the current pregnancy and intrapartum risk factors of preterm delivery, maternal fever $\geq 38^\circ\text{C}$ or membrane rupture $\geq 18$ hours. $^5$–$^7$

Despite improvements in perinatal care, the mortality from early-onset neonatal GBS disease is 5–10%, with most deaths being in preterm babies. $^2$–$^8$ Furthermore, of the 10–20% of cases with complicating GBS meningitis, nearly 40% are left with moderate-to-severe neurological disabilities. $^9$ However, reports that high-dose parenteral penicillin or ampicillin administered during labour can interrupt mother to baby GBS transmission, now mean that prevention of early-onset GBS neonatal sepsis is an achievable public health objective. $^{10}$–$^{12}$

It is nevertheless, important to recognise that that this is at best an interim intervention as it does not prevent all cases of early onset GBS infection and has no influence upon late-onset disease. $^{13}$ As many as 30–35% of women during labour may receive antibiotics, the development of antibiotic resistance is concerning and could render current intervention strategies ineffective. $^{14}$ While awaiting the development and implementation of a safe and effective vaccine, GBS prevention strategies should aim to identify those at greatest risk of giving birth to an affected baby while minimising unnecessary antibiotic usage.

**GBS prevention strategies**

In 1996, the Centers for Disease Control and Prevention (CDC) in the United States released consensus guidelines for prevention of early-onset neonatal GBS infection. $^{15}$

These guidelines recommended two strategies to identify women at risk of giving birth to an affected baby, and when intrapartum antibiotics should be offered:

- The first was a universal screening-based strategy that required positive rectovaginal cultures after selective broth enrichment at 35–37 weeks gestation. If taken within 5-weeks before birth, such cultures have positive and negative predictive values of 87% and 96% respectively for the presence of GBS within the birth canal at delivery.

- The second was risk-based assessment, and required intrapartum maternal fever $\geq 38^\circ\text{C}$ or membrane rupture $\geq 18$ hrs to be present before offering chemoprophylaxis.

Both strategies recommended intrapartum antibiotics for women presenting with preterm (<37-weeks gestation) labour, GBS bacteriuria detected during the current pregnancy (of any count as this is a marker for heavy colonisation), or a previous GBS infected baby.

While there was widespread support for the prevention strategies in North America, with 98% of obstetric providers reporting an individual policy, $^{17}$ only about half adhered to their stated preference. $^{18}$

Nevertheless, hospitals that implemented these recommendations experienced a 50% reduction in cases during the following year, whereas those institutions that failed to revise their policies or lacked them completely had no such decrease. $^{19}$ Subsequently, a population-based multi-state surveillance study reported a 65% reduction in attack rates of early-onset GBS disease during the 1990’s from 1.7 to 0.6 per 1000 live-births. $^{13}$
Other countries also adopted the consensus guidelines and, in Canada and Australia, similar reductions in early-onset GBS disease were described. Concomitantly, the incidence of serious post-partum GBS infection among women in the United States declined 21% from 0.29 to 0.23 per 1000 live-births, while rates of late-onset neonatal GBS disease remained unchanged. When the United States consensus guidelines were developed, there was little clinical evidence to support one strategy over the other. While mathematical models predicted the universal screening strategy would prevent more cases, importantly the actual number of deaths averted by both strategies is believed to be comparable. While there have been no comparative randomised controlled trials, observational data now show that each strategy successfully reduces the incidence of early-onset neonatal GBS disease. However, retrospective design, sequential use of strategies, and an inability to control for potential confounding factors have often limited further comparisons being made.

Recently, a CDC-sponsored population-based, retrospective cohort study (involving more than 600,000 live-births) compared the two prevention strategies. The overall attack rate was 0.5 cases per 1000 live-births—but the screening-based approach was at least 50% more effective than the risk-based strategy (0.33 vs 0.59 per 1000 live-births respectively). This was attributed to:

- Identifying (within the cohort) the 18% of GBS-colonised women giving birth at term without obstetric risk factors, and
- Recognising that culture-positive women were more likely to receive intrapartum antibiotics than those managed by risk factors alone.

Unfortunately, no mortality data were reported and, unexpectedly, the anticipated overall rate of antibiotic utilisation was similar (31% vs 29%) for both prevention strategies. This high rate of antibiotic use contrasts with experience in Australia where a risk-based strategy halved the numbers of women receiving intrapartum antibiotics.

Current GBS prevention strategies may also lead to adverse effects. The estimated risk of fatal anaphylaxis to penicillin is 0.001%, although anaphylaxis rates seem much lower in pregnant women—presumably as most are aware of their risk of anaphylaxis and receive alternative medication.

While there are no confirmed reports of GBS becoming resistant to penicillin or ampicillin, there is evidence of increasing GBS resistance to clindamycin and erythromycin—with resistance rates as high as 32% and 15% respectively reported from some North American centres.

There are also reports of increased sepsis from non-GBS neonatal pathogens, particularly ampicillin-resistant strains of Escherichia coli. However, most have been from single hospitals, and limited to preterm, low, or very low birth-weight babies in whom prior maternal exposure to antibiotics during the pregnancy has not been taken into account.

Fortunately, there are reassuring data from several sources. For example, a study involving 11 Australian maternity hospitals showed that over 7 years of intrapartum...
ampicillin prophylaxis early-onset non-GBS sepsis rates fell significantly from 1.2 to 0.5 cases per 1000 live-births. Recently, a nested case-control study from Boston reconfirmed that the current policy of GBS prophylaxis does not confer an increased risk of non-GBS infection.

**Revised GBS prevention guidelines**

Following publication of the retrospective cohort study in 2002, the CDC revised their guidelines and now recommend universal antenatal screening for rectovaginal GBS colonisation of all pregnant women at 35–37 weeks gestation. Specimens are collected either by health professionals or by women themselves. Revised GBS prevention guidelines

Risk-based intervention is only recommended when the GBS status of pregnant women is unknown. This means that 30–35% of women in labour will potentially receive antibiotics and contrasts with recommendations from countries where the risk-based approach is advocated, and only 15–20% of pregnant women are expected to receive intrapartum antibiotics.

In part, these risk-based policies have arisen out of concerns over rare but potentially serious side effects of antibiotics, the risk of developing antibiotic resistance, results of cost-benefit analyses, resistance by health professionals to obtaining timely rectovaginal samples, and laboratories continuing to employ sub-optimal culture techniques.

**Management of newborn infants after intrapartum prophylaxis**

The CDC guidelines recommend that all newborn babies showing signs of sepsis, or if born to women with chorioamnionitis, should undergo a full diagnostic evaluation and receive empiric antibiotic therapy pending culture results irrespective of whether their mothers had received intrapartum antibiotics.

Maternal chorioamnionitis is a marker for a high-risk of early-onset neonatal GBS disease, even when the mother has received appropriate intrapartum antibiotics, and accounts for most cases of neonatal sepsis when it develops in these circumstances. Nevertheless, early-onset invasive disease remains uncommon in well-appearing babies at birth whose mothers had received intrapartum antibiotics.

One report found only one of 63 asymptomatic babies (born at term to mothers treated with antibiotics for suspected chorioamnionitis) had positive blood cultures. This baby was considered to have bacteraemia rather than ‘full-blown’ sepsis. The CDC recommends that all other babies exposed to maternal intrapartum antibiotics be observed for at least 48-hours. Intrapartum antibiotics do not alter the clinical spectrum of neonatal illness or delay signs of sepsis in newborns ≥35 weeks gestation where more than 90% of affected babies present within 24-hours of delivery.

Moreover, the effectiveness of intrapartum antibiotics (in interrupting vertical transmission of GBS when administered to colonised women and to those with GBS risk factors) approaches 90% when the first dose is given at least 2-hours pre-delivery—with further improvements possible when antibiotics are given more than 4-hours before birth. Thus while close observation in the first 24-hours remains critical, not all babies may need to remain in hospital for the recommended 48-hour period, with many babies being sent home much earlier.
New Zealand data

Until recently, relatively little had been published on maternal GBS carriage and early-onset neonatal GBS infection within New Zealand. Two studies examining GBS colonisation were conducted 20-years apart, each involving 250 pregnant women.\(^47,48\)

To optimise detection, both the distal vagina and rectum were swabbed, and a selective broth enrichment step was included during specimen culture.\(^49\) Each of these studies reported that 22% of women were colonised by GBS late in pregnancy. Carriage was increased by young age, but unaltered by ethnicity. Resistance to clindamycin and erythromycin (in GBS isolates collected from women in Auckland and Wellington between 1998 and 1999) was 15% and 7.5%, respectively.\(^48\)

This rate of resistance was unexpectedly high, as New Zealand generally has lower antibiotic resistance rates than other countries, and (in Australia) only 3% of GBS isolates are resistant to erythromycin.\(^50\) Furthermore, the pattern of resistance was unusual in that the most common resistance phenotype was to ‘clindamycin only’ rather than ‘erythromycin alone’ or to ‘both antibiotics’.

These findings have been recently confirmed by a larger study from Christchurch, indicating that lincosamide and macrolide resistance in GBS isolates is widespread in New Zealand.\(^51\) Consequently, neither erythromycin nor clindamycin can be assumed to be reliable alternatives for empirical intrapartum chemoprophylaxis in women with penicillin allergy.

Studies conducted during the 1980s and early 1990s, well before GBS prevention policies were introduced into New Zealand, estimated attack rates of early-onset neonatal GBS disease at 1–2 cases per 1000 live-births.\(^4,21,52\) However, by the late 1990s, three-quarters of New Zealand's largest public hospital maternity units had a GBS prevention policy, and a recent study reported that attack rates had fallen to 0.5 cases per 1,000 live-births.\(^53\)

The reduced incidence may have resulted from methodological differences as earlier studies involved small numbers from single regions or institutions. Nevertheless, the most likely explanation is the introduction of GBS prevention strategies in most maternity units, especially as a later sub-analysis found rates of early-onset GBS infection were significantly greater in hospitals without such policies.\(^54\)

Importantly, nearly 60% of GBS infected babies in the 1998–1999 study had mothers with GBS risk factors who did not receive intrapartum antibiotics.\(^53\) Thus, allowing for the 10% chance that antibiotics may be ineffective,\(^25\) complete implementation of the risk-based GBS prevention strategy could have further halved the national attack rate to only 0.24 cases per 1000 live-births. Nonetheless, deviations from GBS prevention protocols may result from factors beyond the control of healthcare professionals—such as the unavailability of GBS culture results, women refusing antibiotics, precipitous labour before antibiotics can be given, or women just barely meeting criteria before giving birth.

However, within New Zealand, lead maternity carers (LMCs) also show incomplete knowledge of GBS preventive strategies.\(^55\) Furthermore, although most public maternity units in New Zealand have a prevention protocol, a recent survey found that less than half of the centres (using risk-based assessment) administered antibiotics for
all high-risk criteria—while inadequate specimen collection and culture methods meant no centre maximised the culture-based screening strategy.\textsuperscript{54}

Despite incomplete implementation of prevention strategies, the attack rate of early-onset neonatal GBS disease within New Zealand seems to have been reduced.\textsuperscript{53} Nonetheless, GBS remains the leading infectious cause of early-onset neonatal disease, and each case represents missed opportunities, protocol failures, or the unavoidable consequences of using an imperfect prevention strategy.

Therefore, further improvements are possible. An important first step is to develop and then implement nationally agreed guidelines.

**Consensus Group**

Consequently, representatives of the New Zealand College of Midwives, the Paediatric Society of New Zealand, the New Zealand Committee of the Royal Australian and New Zealand College of Obstetricians and Gynaecologists, the Royal New Zealand College of General Practitioners, and a consumer representative from Homebirth Aotearoa met in February 2003.

MEDLINE databases were searched from January 1966 to February 2003 for subject headings (\textit{group B streptococcus}, \textit{Streptococcus agalactiae}, \textit{newborn}, \textit{chemoprophylaxis}, \textit{chemoprevention}, and \textit{intrapartum antibiotics}); and the Cochrane database was also accessed using these headings. As the number of references that could be cited was limited, review articles and original articles were provided to each of the participants.

The Consensus Group reviewed the available evidence and formulated a technical working paper from which to develop consensus recommendations for a New Zealand context. The first draft of the technical working paper recommendations was circulated to all participants, and revisions (including updated references) were incorporated into subsequent drafts. The draft and final consensus documents were developed from the working paper and circulated to each of the relevant colleges, professional societies, and consumer groups for their endorsement.

This report represents the final consensus recommendations accompanied by the levels of evidence and consensus achieved (Table 1).

**Table 1. Evidence-based rating system and degree of consensus**

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- **Quality of evidence**
  - A: At least one well-designed randomised-controlled trial
  - B: At least one well-designed, non-randomised clinical trial; cohort, or case-control studies; or multiple time series experiments
  - C: Large observational studies
  - D: Expert opinion based upon clinical or laboratory experience

- **Strength of consensus**
  - 1: Complete consensus of entire working group
  - 2: Near complete consensus (90%) of entire working group
  - 3: No consensus
The technical working group agreed upon the following:

- GBS infection in women and their newborn babies remains an important and largely preventable public health problem in New Zealand.
- Implementation of any one of several strategies to deliver intrapartum antibiotics to women at risk of delivering a GBS affected baby has proven to be effective in reducing attack rates of early-onset neonatal GBS infection.
- No strategy, even if perfectly implemented, will prevent all early-onset neonatal GBS infection.
- The most important determinant of effectiveness is likely to be compliance with a nationally agreed, single prevention strategy.
- Intrapartum antibiotics are associated with rare, but potentially serious, side effects; and there remain concerns over selection of antibiotic resistant bacteria. Strategies should therefore seek to limit the number of women exposed to antibiotics.
- Recognition of the signs of sepsis and early treatment of affected babies remains crucial for further reducing morbidity and mortality from early-onset neonatal GBS disease.
- Cost-effectiveness and cost-benefit analyses should be undertaken to help determine which GBS prevention strategy is most suitable for New Zealand.

The working group also observed that:

- While attack rates during the 1990s of early-onset neonatal GBS disease amongst New Zealand babies have fallen,\textsuperscript{4,21,53} further improvements are possible. This could be best achieved by:
  - Adopting nationally agreed guidelines to minimise confusion over the multiple existing policies.
  - Ensuring that these are implemented by educating LMCs and pregnant women,
  - Conducting audits of policy compliance with cumulative feedback of results to inform LMCs,
  - Undertaking national surveillance of early-onset neonatal GBS and non-GBS cases and monitoring antibiotic resistance.
- Available evidence suggests that late antenatal GBS culture screening will prevent most cases.\textsuperscript{26} However, in this large American retrospective cohort study there were significant differences in ethnicity, rates of preterm delivery and adequacy of antenatal care between the groups, as well as geographic differences in approach and rates of antibiotic prescribing.\textsuperscript{26} Additionally, babies were assigned by default to the risk-based group if evidence of culture screening was lacking. Despite these limitations, the findings are consistent with those of other studies and while such a strategy is unlikely to substantially prevent more deaths it will help protect the 20–40% of cases currently born to mothers at term who lack GBS risk factors.\textsuperscript{38,53}
The latest CDC guidelines recommending universal late antenatal screening may not be the most suitable policy for current New Zealand practice. This is because:

- It is the prevention strategy least utilised in New Zealand’s public hospitals, and
- When used, practitioners usually do not comply with either the recommended sites or timing of sample collection, while laboratories often fail to include a selective broth enrichment step.

This means that GBS detection rates and the likelihood of accurately predicting the presence of GBS at birth are reduced by approximately 50%. Moreover, such a strategy poses several logistic and economic challenges, including the absolute requirement for robust systems that ensure culture results are available to the LMC at the time of labour. Finally, with a maternal GBS carriage rate of 22%, nearly one-third of women would be expected to be eligible for intrapartum antibiotics as determined by culture screening results (22%), preterm birth (7.5%), or other risk factors when culture results are unknown (~3%).

In contrast, risk-based prevention is the most common strategy used in New Zealand maternal facilities. Compared with universal screening, there is greater compliance with recommendations of a risk-based policy. Moreover, while both strategies prevent similar numbers of GBS-related deaths, risk-based prevention requires fewer women to be exposed to antibiotics at birth.

Experts in other countries have raised similar concerns over the CDC guidelines. In the United Kingdom, the Royal College of Obstetricians and Gynaecologists recently recommended that women should not be offered antenatal GBS screening. The National Institute for Clinical Excellence (NICE) guidelines on routine antenatal care for healthy pregnant women also recommend against routine antenatal GBS screening. In contrast, in Australia the Royal Australian and New Zealand College of Obstetrics and Gynaecology has advocated that whenever possible obstetric providers should follow a culture-based strategy.

Notwithstanding the above considerations, it is recognised that (because of the CDC recommendations) some maternity hospitals, LMCs, and pregnant women may opt for universal GBS screening at 35–37 weeks.

The preferred prevention policy needs to be re-evaluated following an economic analysis or future developments that would allow for more accurate and effective intrapartum prophylaxis—such as rapid bedside diagnostic tests for GBS during labour.

Further evaluation of prevention policies may also be required if improved culture techniques find, as recently shown in Denmark, a more than two-fold increased GBS detection rate and if almost half of all women are colonised during pregnancy.
The working group noted the following simplified model:

- At present, as imperfect implementation of both risk- and antenatal culture-based strategies occurs in New Zealand, each year there are approximately 30 proven cases of early-onset neonatal GBS disease.\(^{53,63}\)

- Assuming that:
  - The underlying attack rate of early-onset neonatal GBS disease in New Zealand is 1.0 per 1000 live-births,\(^{52,53}\)
  - Without prevention strategies, 80% of mothers who give birth to GBS-infected babies have identifiable clinical risk-factors,\(^{5–7}\)
  - The positive predictive accuracy of antenatal culture-based screening is 90%,\(^{16}\) and
  - Antibiotic efficacy is 90%,\(^{24}\)

  Then perfect implementation of a national risk-based GBS prevention policy would further reduce the number of early-onset GBS cases to 16 per year \([0.001 \times 56,000 \times (1-0.8\times0.9)]\)—just five more than the 11 cases expected following full implementation of universal screening \([0.001 \times 56,000 \times (1-0.9\times0.9)].\)

- While the overall case fatality rate is 5–10%,\(^{2–8}\) 90% of deaths are in babies whose mothers have identifiable risk factors.\(^{22}\) Furthermore, those babies with GBS sepsis that are not identified by a risk-based approach (term, no maternal fever or prolonged membrane rupture) have mortality rates of only 2%.\(^{64}\) Consequently, there is unlikely to be any material difference between the two strategies on the numbers of babies dying from early-onset GBS sepsis.

- Although the risk-based strategy is likely to expose approximately 9,000 (16%) women each year to intrapartum antibiotics and the small risk of fatal anaphylaxis (1 in 100,000), it is anticipated that almost 18,000 (32%) women would receive antibiotics should a universal culture-based screening strategy be implemented.\(^{27}\)

  (In other words, for every 1,000 women receiving intrapartum antibiotics, 4.4 cases of early-onset neonatal GBS disease would be prevented by a nationally implemented risk-based strategy, compared with 2.5 cases prevented per 1,000 treated women following universal antenatal screening.)

Recommendations

New Zealand has a unique maternity service. Within this framework, the importance of the Code of Health and Disability Services Consumer's Rights (The Health and Disability Commissioner Regulations 1996) must be recognised. This Code of Rights outlines consumers’ rights and responsibilities as well as providing a guide for the health professionals who provide those patients with care—specifically, what is a reasonable expectation of the care, and the information they receive for which they give consent.

While awaiting the development of bedside diagnostic testing of GBS (and cost-effectiveness and cost-benefit analyses to determine which prevention strategy is best suited for New Zealand conditions), the following is recommended:
GBS prevention

- In New Zealand, the risk-based approach (Figure 1) should be used to identify those women at risk of giving birth to GBS-affected babies [B2—see Table 1 for interpretation].

- Women require quality information from which to understand the significance of GBS infection and the reason for the risk-based approach in New Zealand. This information also needs to assist women to understand why it may be recommended they receive antibiotics during labour. This is essential for women to understand so that they are fully informed when they consent to this treatment as required under the Code of Health and Disability Services Consumer's Rights [D1].

- In women with preterm labour or preterm premature rupture of membrane, antibiotics for GBS prevention are only administered to those at significant risk of imminent birth [D1].

- Intrapartum penicillin G (1.2 g intravenously as the initial dose, then 0.6 g intravenously every 4-hours until birth) is the intrapartum antibiotic of choice [A1]. Penicillin is recommended because of its narrow spectrum of activity. An alternative is amoxycillin (2 g intravenously initially, then 1 g every 4-hours until birth occurs) [A1].

- As part of antenatal assessment, a history of penicillin allergy should be sought—including details of immediate (within 24-hours) hypersensitivity reactions (eg, anaphylaxis, angioedema, laryngospasm, bronchospasm, or urticaria). Women not at high-risk of anaphylaxis should receive cephazolin (2 g intravenously initially, then 1 g intravenously every 8-hours until birth) [C1]. The small group of women with a definite history of immediate hypersensitivity reactions can receive vancomycin. This should be only after seeking clinical microbiology or infectious diseases advice. The recommended dose is 1 g intravenously every 12-hours until the baby is born [D1].

- Neither penicillin G nor amoxycillin alone are adequate treatment for maternal chorioamnionitis (intrapartum fever with ≥2 of the following signs: fetal tachycardia, uterine tenderness, offensive vaginal discharge, or maternal leucocytosis) [A1]. As *E. coli*, anaerobes, and GBS can all cause chorioamnionitis, this requires immediate aggressive management with broad-spectrum antibiotics [C1].
Figure 1. Risk-based group B streptococcus (GBS) prevention strategy

Any of the following present?
- Previous GBS-infected baby
- GBS bacteriuria (of any count) this pregnancy
- Preterm (<37 weeks) labour and imminent birth *
- Intrapartum fever ≥ 38°C †
- Membrane rupture ≥ 18 hrs
**OR** A positive maternal screening test for GBS at 35-37 weeks of the current pregnancy ‡

**YES**

Give intrapartum penicillin or amoxycillin intravenously

**NO**

No intrapartum antibiotics

*Except in women with intact membranes undergoing pre-labour elective caesarean section and who lack other GBS risk factors. †If chorioamnionitis is suspected, GBS chemoprophylaxis is insufficient and aggressive treatment with broad-spectrum antibiotics is required. ‡Optimal antenatal GBS screening requires collection of anogenital swabs at 35-37 weeks gestation and a selective broth incubation step. Intrapartum antibiotics are not indicated when a GBS culture positive woman with intact membranes undergoes pre-labour elective caesarean section. Similarly, intrapartum chemoprophylaxis is not required for culture negative women (after optimal screening at 35-37 weeks gestation), regardless of intrapartum risk factors. All women with a previous GBS-infected baby or GBS bacteriuria in the current pregnancy are offered intrapartum antibiotics and do not need to undergo antenatal culture screening.
Figure 2. Management of newborn babies

All newborn babies

Symptoms/signs of sepsis*  Asymptomatic

Full sepsis evaluation and empiric antibiotics for ≥ 48 hrs†

‡GBS risk factors [OR: Positive GBS screen at 35-37 wks]

Antibiotics ≥4 hrs before delivery  Routine care
Figure 2. Management of newborn babies (continued)

≥35 wks gestation      <35 wks gestation   <35 wks gestation      ≥35 wks gestation

No tests                    No tests             Consider FBC\(^{\ddagger}\),
No antibiotics              No antibiotics         blood cultures and
Observe ≥24 hrs in hospital  Observe >48 hrs in hospital

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* Signs of sepsis include respiratory distress (tachypnoea, grunting, subcostal recession), apnoea, an oxygen requirement, pallor with poor peripheral perfusion, fever > 38°C or an unstable temperature, and acidosis.

† At least a full blood count, blood cultures and, when feasible, a lumbar puncture. A penicillin and an aminoglycoside are the antibiotics of choice.

‡ Group B streptococcus risk factors (see Fig. 1).

‡‡ There are insufficient data upon which to base a single management strategy for situations where intrapartum antibiotics are indicated but not given.

¶ FBC, full blood count.
Newborn babies (Figure 2)

- All newborn babies showing signs of sepsis should undergo immediate evaluation (at least a full blood count and blood cultures), and pending culture results should receive empiric therapy for at least 48-hours [B1]. The antibiotics are usually a penicillin and an aminoglycoside as this combination is active against common early-onset neonatal pathogens, such as GBS, *E. coli* and *Listeria monocytogenes* [C1]. When feasible a lumbar puncture should be performed on all septic newborn babies (and especially when blood cultures are positive or, because of clinical instability, therapy is continued beyond 48-hours) [C1]—as 10–15% of neonates with meningitis will have sterile blood cultures.

- All babies born to women with suspected chorioamnionitis (irrespective of their gestation, condition at birth, or exposure to intrapartum antibiotics) require careful evaluation. Antibiotic therapy (as outlined above) is not recommended unless the baby shows signs of sepsis [B1].

- Healthy-appearing babies born at ≥35-weeks gestation to women with GBS risk factors and who have received appropriate antibiotics ≥4-hours before birth require no investigations or treatment, but should be observed closely for at least 24-hours post-partum [B1]. This could include close observation at home after an early discharge [D1].

- Well-appearing babies born at ≥35-weeks gestation to women with GBS risk factors who have received either no or inadequate (<4-hours) chemoprophylaxis should be observed closely in hospital for at least 24-hours [B1].

- Well-appearing babies born at ≤35-weeks gestation to women with GBS risk factors, who have received appropriate antibiotics ≥4 hours before birth, should be observed in hospital for at least 48-hours. When such babies have been born to women who have not received antibiotics ≥ 4 hours before delivery, then a full blood count, blood cultures and antibiotics should be considered [D1].

Other issues identified by the technical working party

- Women who opt for a screening-based approach should have the benefits of this strategy optimised. The LMC should ensure that samples are collected from the correct anatomical sites at the recommended time of 35–37 weeks gestation, laboratories need to employ correct culture methods and systems must be in place to make sure that results are available when the woman is in labour. Intrapartum antibiotics are only administered when a positive GBS culture result is obtained or if there has been a previous GBS-infected baby [B1].

- It is important that when rectovaginal specimens are collected they are taken from the distal vagina and rectum (ie, through the anal sphincter), before placing the swab(s) in non-nutritive transport media and requesting the laboratory performs an enrichment step in selective broth media [B1]. Specimens collected between 35–37 weeks gestation best predict the presence of GBS at term. In contrast, those collected more than 5 weeks before the onset of labour do not [B1].
• Women can be shown (in the clinic) how to obtain their own rectovaginal samples [B1].

• As an alternative to prescribing vancomycin for women at high risk of penicillin-related anaphylaxis, consideration should be given to late antenatal culture screening. Under these circumstances, GBS isolates are tested for their susceptibility to clindamycin and erythromycin [D1]. If susceptible to these antibiotics, intravenous doses of either clindamycin (900 mg every 8-hours), or erythromycin (500mg every 6-hours), are administered intrapartum until the baby is born [C1].

• Currently available rapid GBS detection techniques (during labour) are either unreliable (eg, antigen assays) or impractical (eg, 24 hour, 7 days a week molecular diagnostic testing) in the New Zealand healthcare setting [D1].

• National compliance with a single strategy is likely to be the major determinant in making further reductions in early-onset neonatal GBS disease [D1]. To achieve this, there must be ongoing education programmes for all LMCs and information developed for pregnant women using written and web-based material [D1]. Audits of policy compliance with cumulative data feedback for providers should also be introduced [D1].

• When necessary, microbiology and infectious diseases experts can further advise on optimal sampling and diagnostic testing, emerging antibiotic resistance, and treating women with penicillin allergies [D1].

Future directions in New Zealand

• To undertake rigorous cost-effectiveness and cost benefit analyses (including sensitivity analyses around estimates of the proportions of women with clinical risk-factors), antibiotic effectiveness, and mortality rates [D1].

• To produce consumer information about GBS to increase awareness among pregnant women [D1].

• To monitor early-onset neonatal GBS and non-GBS disease, detect emerging antibiotic resistance, and track serious maternal adverse effects from chemoprophylaxis that may herald a change in prevention strategy [D1].

• Await a safe, effective vaccine that offers additional opportunities of preventing GBS-related stillbirths, preterm deliveries, late-onset neonatal disease and maternal infection [D1].

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- Brian Darlow
- Keith Grimwood

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists
- Alistair Haslam
- Peter Stone

The Royal New Zealand College of General Practitioners
- Tim Cookson

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