

# Clinical Guideline

## Early Onset Neonatal Sepsis

**Objective file number:**

**Policy developed by: SA Maternal, Neonatal & Gynaecology Community of Practice**

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**Summary** The purpose of this guideline is to give clinicians information on the prevention and treatment of early onset neonatal sepsis.

**Keywords** Clinical guideline, Perinatal Practice Guideline, Neonatal Sepsis, early onset neonatal sepsis, GBS prophylaxis, intrapartum antibiotics, risk factors for neonatal sepsis, chorioamnionitis, preterm, PPRM, sepsis, infection, GBS, group B streptococcus

**Policy history** Is this a new policy? **N**  
Does this policy amend or update an existing policy? **Y**  
Does this policy replace an existing policy? **N**  
If so, which policies? **Early Onset Neonatal Sepsis V9.0**

**Applies to** All Health Networks  
CALHN, SALHN, NALHN, CHSALHN, WCHN, SAAS

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All Clinical, Medical, Midwifery, Nursing, Allied Health, Emergency, Mental Health, Pathology, SAAS

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# South Australian Perinatal Practice Guidelines

# Early Onset Neonatal Sepsis

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## Note:

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements

## Explanation of the Aboriginal artwork:

The Aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the Aboriginal culture. The horse shoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant woman. The smaller horse shoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.



***Australian Aboriginal Culture is the oldest living culture in the world yet Aboriginal people continue to experience the poorest health outcomes when compared to non-Aboriginal Australians. In South Australia, Aboriginal women are 2-5 times more likely to die in childbirth and their babies are 2-3 times more likely to be of low birth weight. The accumulative effects of stress, low socio economic status, exposure to violence, historical trauma, culturally unsafe and discriminatory health services and health systems are all major contributors to the disparities in Aboriginal maternal and birthing outcomes. Despite these unacceptable statistics the birth of an Aboriginal baby is a celebration of life and an important cultural event bringing family together in celebration, obligation and responsibility. The diversity between Aboriginal cultures, language and practices differ greatly and so it is imperative that perinatal services prepare to respectively manage Aboriginal protocol and provide a culturally positive health care experience for Aboriginal people to ensure the best maternal, neonatal and child health outcomes.***

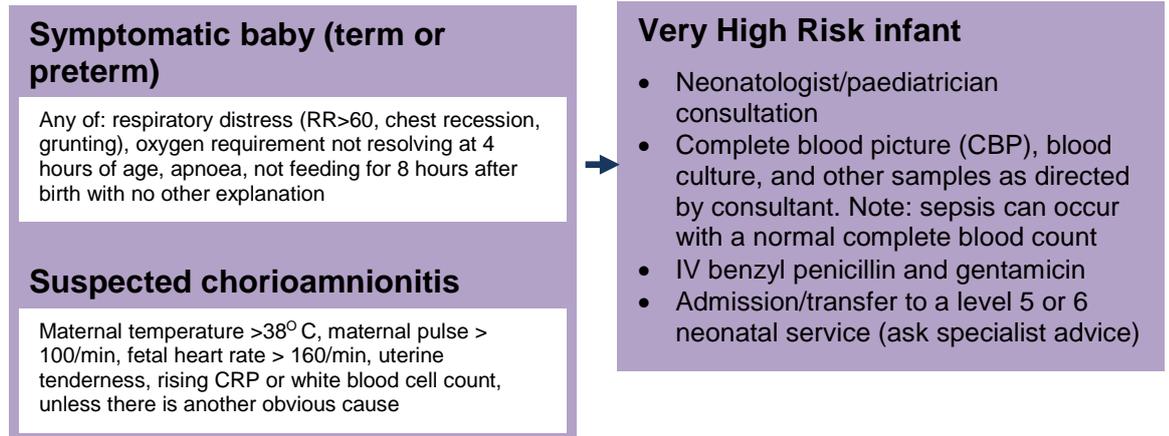
## Purpose and Scope of PPG

The purpose of this guideline is to give clinicians information on the prevention and treatment of early onset neonatal sepsis.

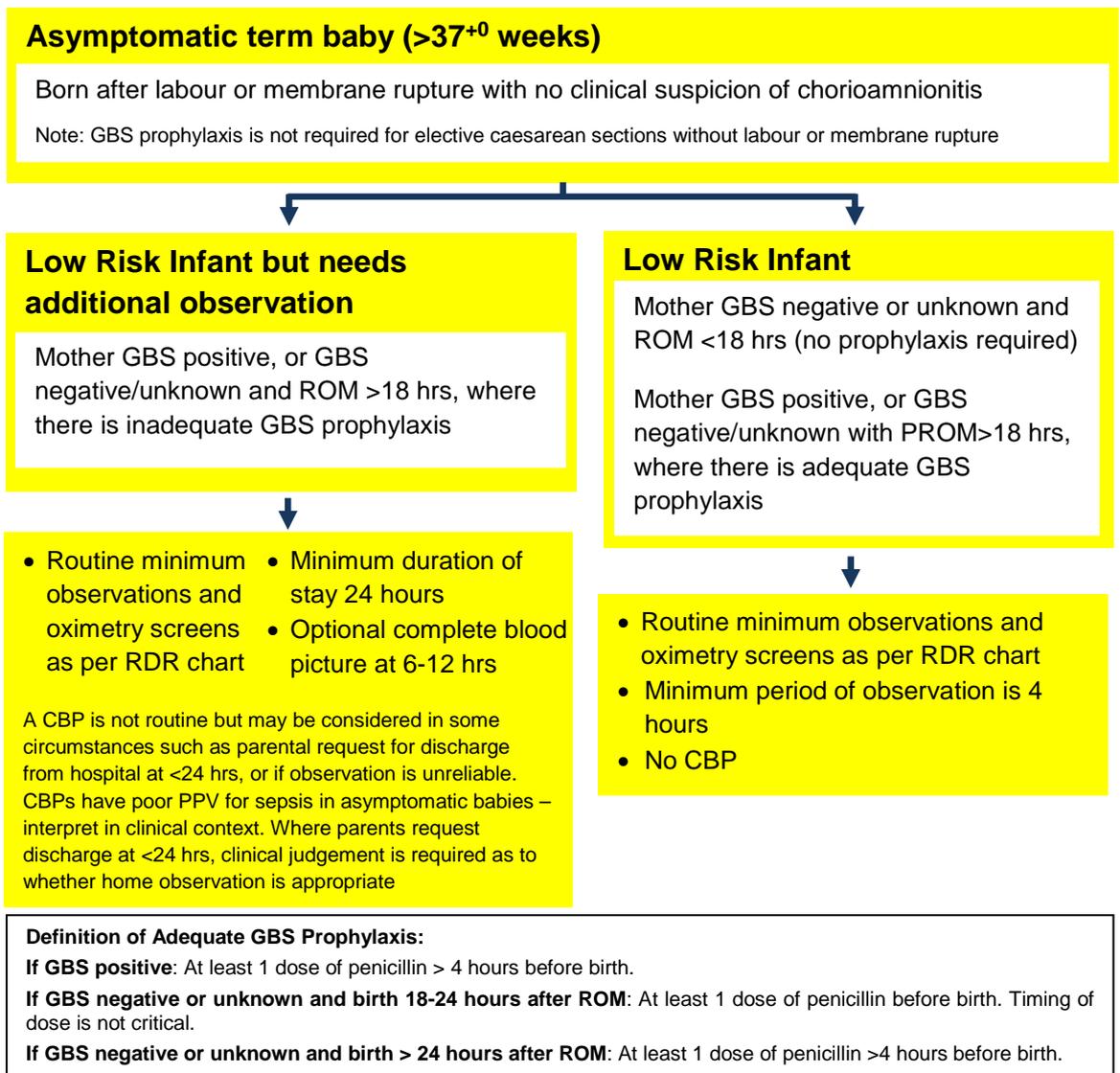
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# Early Onset Neonatal Sepsis

**Flow chart 1:** Neonatal management for prevention and treatment of early onset sepsis – Symptomatic Baby or Suspected Chorioamnionitis



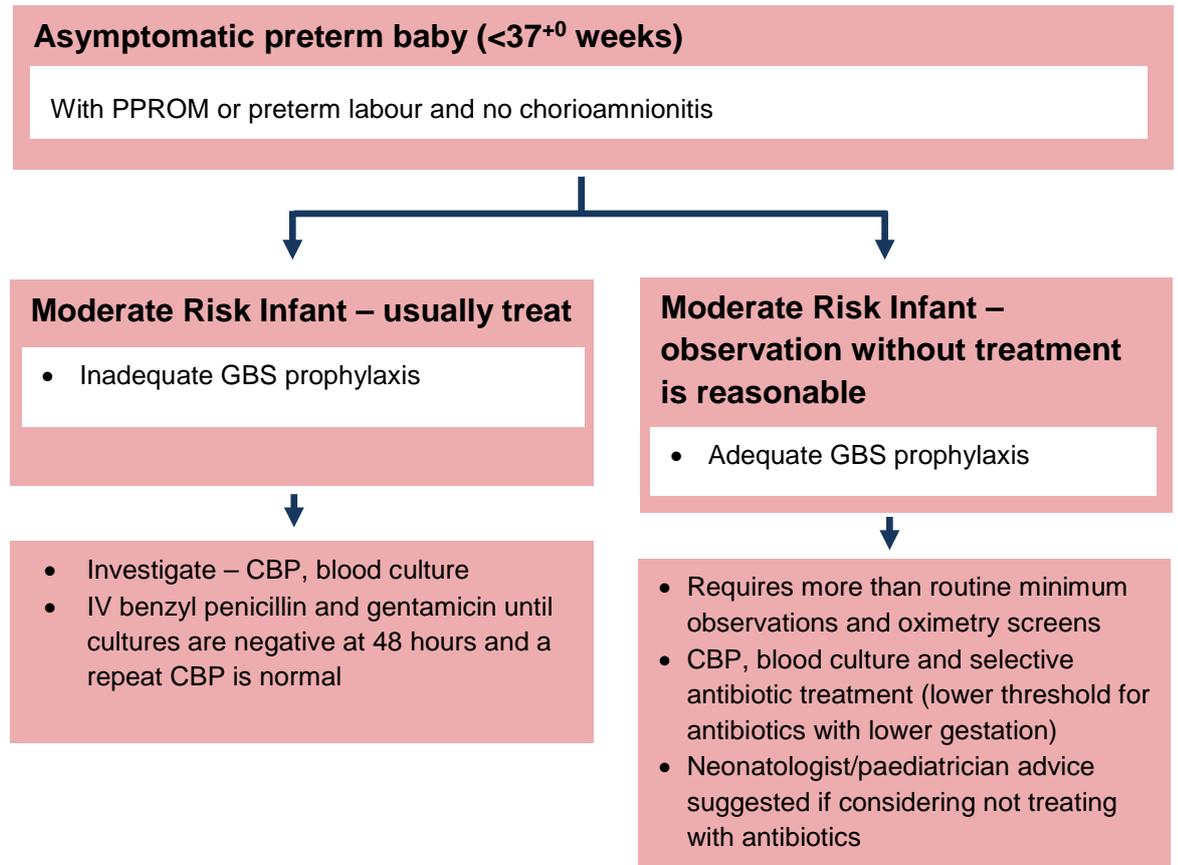
**Flow chart 2:** Neonatal management for prevention and treatment of early onset sepsis – Asymptomatic Baby > 37 weeks



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# Early Onset Neonatal Sepsis

**Flow chart 3:** Neonatal management for prevention and treatment of early onset sepsis – Asymptomatic Baby < 37 weeks



**Definition of Adequate GBS Prophylaxis:**  
**If GBS positive:** At least 1 dose of penicillin > 4 hours before birth.  
**If GBS negative or unknown and birth 18-24 hours after ROM:** At least 1 dose of penicillin before birth. Timing of dose is not critical.  
**If GBS negative or unknown and birth > 24 hours after ROM:** At least 1 dose of penicillin >4 hours before birth.

# Early Onset Neonatal Sepsis

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## Summary of Practice Recommendations

- A policy of screening for GBS and giving intrapartum antibiotic prophylaxis to carrier mothers is the most effective means of preventing early onset GBS
- Any respiratory distress in a preterm infant or respiratory distress not settling by 4 hours of age in a term infant should be investigated and treated as possible sepsis
- The need for positive pressure ventilation during resuscitation at birth, apnoea, poor skin perfusion, and abnormal feeding behaviour (not interested in feeding for 8 hours after birth or the last feed) are other signs of sepsis
- Chorioamnionitis, preterm labour, preterm prelabour rupture of the membranes, ruptured membranes > 18 hours, maternal positive GBS status are risk factors for sepsis
- Careful observation and examination is a key to early detection of sepsis. The extent of observation required will depend on the risk assessment for individual babies
- Routine investigations are a blood culture, and complete blood picture with immature / total neutrophil ratio
- Treat with IV benzyl penicillin and gentamicin: Duration of treatment depends on clinical circumstances but is at least 48 hours. Refer to SA Health Neonatal Medication Guidelines (available at [www.sahealth.sa.gov.au/neonatal](http://www.sahealth.sa.gov.au/neonatal))
- Where symptomatic early onset sepsis is suspected, consult a paediatrician or neonatologist and admit / transfer to level 5 or 6 neonatal service

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# Early Onset Neonatal Sepsis

## Abbreviations

AUC	Area under the curve
bpm	Beats per minute
CBP	Complete blood picture
CDC	Centers for Disease Control and Prevention
CRP	C-reactive protein
GA	Gestational age
g	Gram(s)
>	Greater than
<	Less than
GBS	Group B streptococcus
I:T ratio	Immature:total neutrophil ratio
IV	Intravenous
+ve	Positive
-ve	Negative
%	Percentage
mg	Milligram(s)
PROM	Pre-labour rupture of the membranes
PPROM	Premature pre-labour rupture of the membranes
RANZCOG	Royal Australian and New Zealand College of Obstetrics and Gynaecology
RR	Respiratory rate
ROM	Rupture of membranes

## Definitions

Systemic sepsis	A clinical picture consistent with sepsis and either a positive bacterial or fungal culture of blood and/or cerebrospinal fluid
Early onset neonatal sepsis	The presence of systemic bacterial or fungal sepsis with initial symptoms occurring $\leq$ 3 days after birth <sup>9</sup>
Mother is GBS positive	Positive GBS screen < 5 weeks before labour Maternal GBS bacteriuria at any time in the current pregnancy Previous child with early onset neonatal GBS sepsis
Adequate GBS Prophylaxis	If GBS Positive: At least 1 dose of penicillin > 4 hours before birth If GBS Negative or unknown and 18-24 hours after ROM: At least 1 dose of penicillin before birth. Timing not critical. If GBS Negative or unknown: and birth > 24 hours after ROM: At least 1 dose of penicillin > 4 hours before birth

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# Early Onset Neonatal Sepsis

## Important points

Early onset neonatal bacterial sepsis is associated with significant morbidity and mortality. The vast majority of infections are due to Group B Streptococcus (GBS) or Escherichia coli, with other organisms seen less frequently. Other micro-organisms that may be constituents of the normal vaginal flora are potential neonatal pathogens. These include Streptococcus pneumoniae, Haemophilus influenza, Staphylococcus aureus, Clostridia sp., and other Enterobacteriaceae such as Klebsiella.

In 2002 the CDC published detailed consensus guidelines that form the basis for the management of GBS prophylaxis.<sup>1</sup> No published consensus guidelines or evidence based recommendations exist for intrapartum prophylaxis against the other pathogens listed above.

Antibiotic prophylaxis during labour for women with risk factors for GBS has been shown to be effective in preventing GBS transmission to the neonate, and to reduce early onset GBS sepsis.<sup>1</sup> Antibiotic prophylaxis during labour has no effect on late onset neonatal sepsis due to GBS or other organisms.<sup>1</sup>

A policy of screening for GBS and giving intrapartum antibiotic prophylaxis to carrier mothers is the most effective means of preventing early onset GBS.<sup>2</sup> Prospective surveillance for cases of early onset GBS has shown a reduction from 0.47 cases/1,000 livebirths to 0.34 cases/1,000 livebirths following the publication of the 2002 CDC guidelines and widespread implementation of universal GBS screening and intrapartum chemoprophylaxis.<sup>3</sup>

A retrospective cohort study evaluating universal GBS screening using culture has shown that for 116/189 (61.4 %) term infants with early onset GBS the antenatal screen, as a guide to GBS status at birth, was falsely negative.<sup>4</sup> This emphasises the importance of not relying solely on a negative maternal swab. False negative rates for GBS PCR are less well defined.

Neonatal sepsis can also occur due to organisms other than GBS where a mother is GBS positive or negative. Where another organism is known to be a part of the ambient vaginal flora, specific prophylaxis may be considered although there is limited evidence to guide practice. Treatment of suspected neonatal sepsis must include both gram positive (GBS) AND gram negative antibiotic coverage.

The recognition of symptoms of neonatal sepsis and treatment on clinical grounds is critical. Respiratory distress due to congenital pneumonia is the most common presentation of early onset sepsis. Any respiratory distress in a preterm infant or respiratory distress not settling by 4 hours of age in a term infant should be investigated and treated as possible sepsis, unless the baby has been delivered from a sterile uterus by elective caesarean section.

Other clinical findings that should raise suspicion of sepsis include a need for positive pressure ventilation during resuscitation at birth, apnoea, poor skin perfusion, and abnormal feeding behaviour (not interested in feeding for 8 hours after birth or the last feed) where another cause is not immediately apparent.

Neonatologist or paediatrician consultation and transfer/retrieval to a Level 5 or 6 neonatal service (previously Level 3) are necessary where symptomatic early onset sepsis is suspected.

For a baby with respiratory distress there is a narrow window for withholding antibiotics based on clinical judgment, restricted to babies born by caesarean section without labour or membrane rupture and where respiratory distress is improving with time. Neonatal practitioners should pay careful regard to all risk factors and the clinical condition of babies before withholding antibiotics.

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For term babies who appear well at birth but are 'at risk' of early onset sepsis due to inadequate antibiotic prophylaxis

- Observation and treatment on clinical grounds is emphasised. Total white blood cell counts, total neutrophil counts, and neutrophil indices have poor positive predictive accuracy (high false positive rate) for detecting sepsis in this clinical context.<sup>5,6,7,8,9</sup>
- A raised immature:total neutrophil ratio and neutropenia based on age specific cut-offs are the most sensitive indicators of sepsis.<sup>5</sup> Normal ranges for neonatal CBPs vary with population, gestation and postnatal age.<sup>5,7</sup> In term infants according to Manroe, neutropenia is  $<1800/\text{mm}^3$  at birth,  $< 5400$  at 6 hours, and  $<7800$  at 12 hours.<sup>5</sup> An I:T ratio of  $> 0.2$  is a suggested cut-off for abnormality.<sup>5</sup>
- The sensitivity of a CBP for detecting sepsis is higher if taken 6-12 hours after birth.<sup>9</sup>
- A normal CBP at 6-12 hours has a high negative predictive value for sepsis in a well baby, but continued observation is required.<sup>5,6,7,8,9</sup>
- Well 'at risk' babies do not need a routine CBP even if antibiotic prophylaxis is inadequate, A CBP may be considered at 6-12 hours in some circumstances at clinician discretion, such as parental request for discharge from hospital at  $<24$  hours or if observation is unreliable. Where parents request discharge at  $<24$  hours, clinical judgement is required as to whether home observation is appropriate.
- Observation is recommended for 48 hours by the American Academy of Pediatrics.<sup>9</sup> This PPG however recommends a 24 hour period of observation because approximately 75% of cases of early onset GBS sepsis (in the first 3 days) occur within 24 hours of birth.<sup>10</sup> Parental observation at home after this period is likely to be safe if a discharge examination occurs at 24 hours and parents are aware of symptoms that require immediate medical review.
- Where symptoms of sepsis develop the baby should be treated regardless of the CBP result
- Asymptomatic term at-risk babies who are treated with antibiotics based on a CBP and who remain well at 24 hours can reasonably have antibiotics ceased at 24 hours where blood cultures are also negative and the CBP has normalised
- The risk of early onset GBS in a term baby of a GBS unknown mother with ROM $<18$  hours is approximately 2/1000 (assuming a 20-25% GBS carrier rate), compared to 0.9/1000 for a baby of a GBS negative mother with ROM $<18$  hours.<sup>11</sup> This risk is reduced further with good postnatal observation, and discharge after a minimum of 4 hours observation is reasonable.

## Risk factors for neonatal sepsis

An infant is considered at risk for early onset neonatal sepsis (GBS or other organisms) if any of the following apply:

- Evidence of maternal chorioamnionitis. Assume chorioamnionitis if maternal temperature above 38.0 C, maternal pulse  $> 100$  / min, fetal heart rate  $> 160$  bpm, uterine tenderness, rising CRP or white blood cell count, unless there is another obvious cause
- Preterm labour at less than 37+0 weeks gestation
- Preterm prelabour rupture of membranes
- Prolonged rupture of membranes greater than 18 hours at term (greater than 36 completed weeks gestation) with or without labour, irrespective of GBS status
- Mother is GBS positive, defined as:
  - Maternal GBS vaginal colonisation during this pregnancy based on a swab taken less than 5 weeks before labour
  - Maternal GBS bacteriuria in the current pregnancy
  - Early onset neonatal GBS sepsis in a previous pregnancy

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# Early Onset Neonatal Sepsis

## Management of the neonate in the postnatal period

### Term or preterm baby with symptoms possibly due to early onset sepsis, or born after suspected chorioamnionitis

Careful observation and examination is a key to early detection of sepsis. The extent of observation required will depend on the risk assessment for individual babies. The complete blood picture should be considered as an adjunct, and the limitations of the test appreciated by clinicians.

Routine investigations are a blood culture, and complete blood picture with immature / total neutrophil ratio

Treat with IV benzylpenicillin and gentamicin: Duration of treatment depends on clinical circumstances but is at least 48 hours (see [www.sahealth.sa.gov.au/neonatal](http://www.sahealth.sa.gov.au/neonatal))

Admit / transfer to level 5 or 6 neonatal service

There should be a low threshold for lumbar puncture in symptomatic babies. However, a lumbar puncture should never delay initiation of antibiotics, nor cardio-respiratory stabilisation where this is required. A lumbar puncture is always required where there are neurological symptoms or if a blood culture returns positive after commencement of antibiotics.

An endotracheal aspirate for culture should be taken if intubated

Gastric aspirate or surface swabs (e.g. ear) may be useful to determine colonising flora if taken soon after birth, but have a poor correlation with invasive sepsis

### Term baby, asymptomatic, mother GBS positive, or GBS negative/unknown and ROM > 18 hours, where mother received inadequate intrapartum antibiotic prophylaxis

Adequate antibiotic prophylaxis for a GBS positive mother is at least one dose of antibiotic given >4 hours before birth. For a GBS negative/unknown mother adequate antibiotic prophylaxis is at least one dose of antibiotic given between 18 and 24 hours (time not critical), or at least one dose given >4 hours before birth is the duration of ROM is >24 hours

Observe for 24 hours in hospital. Observation is the key to early detection of sepsis.

Optional CBP, at clinician discretion. Sensitivity and specificity are improved if this is delayed for 6-12 hours.

### Term baby, asymptomatic, mother GBS positive, or GBS negative/unknown and ROM >18 hours; mother received adequate intrapartum antibiotic prophylaxis

This is a low risk situation. Adequate antibiotic prophylaxis is at least one dose >4 hours before birth in a GBS positive woman. However this strict definition in GBS unknown/negative women with ROM 18-24 hours leads to excessive investigation and treatment of babies, despite a lower sepsis risk. The strict definition of at least one dose >4 hours before birth is applied to GBS negative/unknown women where ROM is >24 hours as sepsis risk is higher for babies born to these mothers.

No investigations

Observe. Minimum period of observations is 4 hours after birth

### Term baby, asymptomatic, mother GBS negative or unknown with ROM < 18 hours

No investigations

Observe. Minimum period of observations is 4 hours after birth

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## Management of early discharge home (<48 hours after birth) of the term asymptomatic infant with risk factors

Term, asymptomatic infants at risk for sepsis and with inadequate intrapartum antibiotic prophylaxis should be observed in hospital for at least 24 hours. Clinical circumstances may indicate a longer period of observation

Term asymptomatic babies at risk for sepsis but with adequate intrapartum antibiotic prophylaxis, and those where mother is GBS unknown but with no other risk factors, may be discharged after a minimum observation period of 4 hours. If discharged, parents should be advised to seek immediate medical attention if their baby develops breathing difficulty or poor feeding over the following 24 hours.

## Preterm baby, asymptomatic, mother received inadequate intrapartum antibiotics

Investigate with a blood culture, and complete blood picture with immature / total neutrophil ratio. Treat with penicillin and gentamicin (or other antibiotics based on results of preterm cultures)

## Preterm baby, asymptomatic, mother received adequate intrapartum antibiotics

Investigate with a blood culture, and complete blood picture with immature / total neutrophil ratio. Observe closely, consider selective antibiotics (e.g. based on results of preterm cultures or degree of prematurity)

## References

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## Useful Websites

Courts Administration Authority South Australia

<http://www.courts.sa.gov.au/index.html>

South Australia Coroners findings for 2009

[http://www.courts.sa.gov.au/courts/coroner/findings/findings\\_2009/content\\_2009.html](http://www.courts.sa.gov.au/courts/coroner/findings/findings_2009/content_2009.html)

[http://www.courts.sa.gov.au/courts/coroner/findings/findings\\_2009/linnell\\_sienna\\_jools.pdf](http://www.courts.sa.gov.au/courts/coroner/findings/findings_2009/linnell_sienna_jools.pdf)

South Australia Coroner's findings 2012

<http://www.courts.sa.gov.au/CoronersFindings/Lists/Coroners%20Findings/Attachments/469/KISON%20Trinity%20Isabel.pdf>

Centers for Disease Control and Prevention (CDC). Patient information leaflet on Group B Streptococcus

[http://www.cdc.gov/groupbstrep/docs/GBS\\_Patient\\_Info.pdf](http://www.cdc.gov/groupbstrep/docs/GBS_Patient_Info.pdf)

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