South Australian Paediatric Clinical Practice Guidelines

Neonatal Sepsis Presenting from the community

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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.



Cultural safety enhances clinical safety.

To secure the best health outcomes, clinicians must provide a culturally safe health care experience for Aboriginal children, young people and their families. Aboriginal children are born into strong kinship structures where roles and responsibilities are integral and woven into the social fabric of Aboriginal societies.

Australian Aboriginal culture is the oldest living culture in the world, yet Aboriginal people currently experience the poorest health outcomes when compared to non-Aboriginal Australians.

It remains a national disgrace that Australia has one of the highest youth suicide rates in the world. The over representation of Aboriginal children and young people in out of home care and juvenile detention and justice system is intolerable.

The accumulative effects of forced removal of Aboriginal children, poverty, exposure to violence, historical and transgenerational trauma, the ongoing effects of past and present systemic racism, culturally unsafe and discriminatory health services are all major contributors to the disparities in Aboriginal health outcomes.

Clinicians can secure positive long term health and wellbeing outcomes by making well informed clinical decisions based on cultural considerations.

The term 'Aboriginal' is used to refer to people who identify as Aboriginal, Torres Strait Islanders, or both Aboriginal and Torres Strait Islander. This is done because the people indigenous to South Australia are Aboriginal and we respect that many Aboriginal people prefer the term 'Aboriginal'. We also acknowledge and respect that many Aboriginal South Australians prefer to be known by their specific language group(s).



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Purpose and Scope of PCPG

The Management of Neonatal Sepsis Presenting from the Community Clinical Guideline is primarily aimed at medical staff working in any of primary care, local, regional, general or tertiary hospitals. It may however assist the care provided by other clinicians such as nurses. The information is current at the time of publication and provides a minimum standard for the assessment (including investigations) and management neonatal sepsis presenting from the community; it does not replace or remove clinical judgement or the professional care and duty necessary for each specific case.

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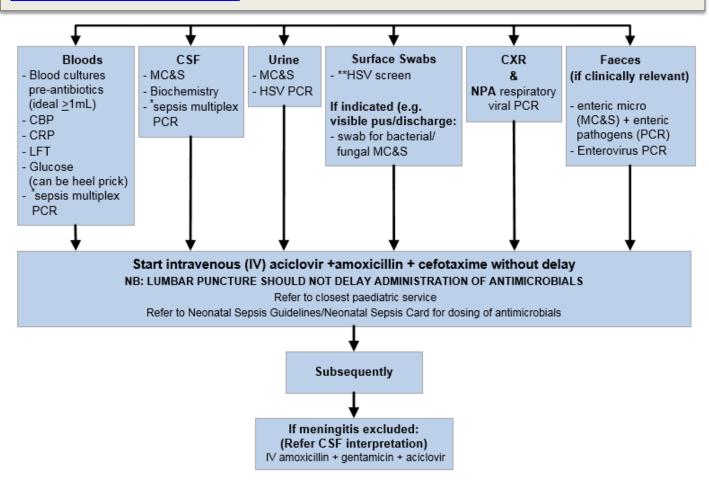
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Flowchart - Neonatal fever/suspected sepsis presenting from the community.

NB: a "neonate" is any baby born at full term who is ≤28 days old.

A premature baby is considered a "neonate" if corrected age ≤44 weeks (see "Neonatal fever/suspected sepsis presenting from the community" guideline for calculation of corrected age, available for download via the SA Health Practice Guidelines website).



* Sepsis multiplex PCR (0.5ml EDTA - separate tube):

· HSV (1+2), VZV, Enterovirus, Parechovirus, S. pneumoniae, N. meningitidis

Ideal total volume for CSF ≥22drops (please collect all CSF in 2 tubes):

- microscopy (50ul= 1drop)
- culture and susceptibility (C&S) (250/500 ul= 10 drops)
- protein, glucose (200 ul= 4 drops)
- *sepsis multiplex PCR (350ul= 7drops)

If <22 drops of CSF obtained:

18-21 drops: protein/glucose will be omitted

<18 drops the priority of testing will be:

- microscopy
- 2. sepsis multiplex PCR
- C&S

If low CSF volume obtained contact SA Pathology Micro lab to discuss priority of test ordering.

** HSV screen

Request HSV PCR (cutaneous virology). Use 1 viral swab from top to bottom:

- · eyes, throat, umbilicus, rectum
- · + extra swab for visible lesions

Important points

This guideline describes the recommended initial investigation and management of neonates presenting from the community with fever or suspected sepsis with the exception of babies admitted under the Neonatology team.

Abbreviations

CRP	C-reactive protein		
CSF	Cerebrospinal fluid		
CXR	Chest X-ray		
DIC	Disseminated Intravascular Coagulation		
EV	Enteroviral		
g/L	gram per litre		
GBS	Group B streptococcus		
HSV	Herpes Simplex Virus		
I/T	immature-to-total ratio		
IV	Intronevous		
kg	kilogram		
LFTs Liver function tests			
LP Lumbar puncture			
MC&S	microscopy and susceptibility		
mL	millilitre		
PCR	polymerase chain reaction		
NPA	Nasopharyngeal aspirate		
NSaline	line Normal Saline		
PCR	Polymerase chain reaction		
SBI	Serious bacterial infections		
SPA	Suprapubic aspiration		
UTIs	S Urinary tract infections		
VZV	Varicella zoster virus		

Definitions

Fever	A "fever" is present when rectal temperature ≥38°C. This correlates with tympanic or axillary temp of 37.5°C.
Neonate	 A "neonate" is any baby born at full term (≥37 weeks' gestation) who is ≤28 days old. A premature baby is considered a "neonate" if their corrected age is ≤44 weeks. Corrected age is the actual age since birth in addition to the gestational age at birth.
Sepsis	For the purpose of these guidelines, a neonate with "sepsis" is any febrile or unwell neonate in whom infection is suspected.



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Differential diagnosis of a critically ill neonate

Sepsis

- > Inborn errors of metabolism
- > Cardiac abnormalities
- > Endocrine crisis
- > Electrolyte abnormalities
- > Trauma accidental or non-accidental
- > Seizure

Note:

- Fever in neonates includes both infectious and non-infectious causes.
- Viral infections are a common cause of fever. However, bacterial coinfection is not uncommon.
- o Incidence of SBI is higher in neonates compared with older children.
- The causative pathogens of sepsis are different in neonates compared with older children.
- It is accepted that the use of antibiotics in all neonates with suspected sepsis will result in neonates without bacterial infection receiving antibiotic therapy. These guidelines emphasise appropriate investigations which will allow the tailoring (or cessation) of antimicrobial therapy further on in the clinical course.

These guidelines refer to neonates who present for medical attention from the community. For guidelines referring to neonates with onset of sepsis prior to leaving hospital (both early and late-onset) please see the SA Perinatal Guidelines at https://extapps2.sahealth.sa.gov.au/PracticeGuidelines/.

Serious Bacterial Infections in neonates

- > SBI include bacteraemia, gastroenteritis, cellulitis, osteomyelitis, septic arthritis, meningitis, pneumonia and, most commonly, UTIs.
- > SBI can occur in the presence of concomitant viral infections, with as many as 10% of patients with confirmed viral infections having UTIs or other SBIs.
- > SBI can be caused by Gram negative bacteria, most commonly Escherichia coli, or Gram positive organisms, most commonly GBS. Other Gram-negative pathogens such as *Klebsiella spp* and *Salmonella spp*, along with Gram-positive pathogens, including *Streptococcus pneumoniae* and *Enterococcus spp*, are less common but may occur.
- > Neisseria meningitidis is a rare cause of bacterial infection in this age group and may signal an underlying complement deficiency or, rarely, asplenia.
- > Staphylococcus aureus is an increasing cause of bacterial infection in this age group and often presents with concomitant skin infection.
- > Listeria monocytogenes, once considered an important neonatal pathogen, has become exceedingly rare in the last two decades.



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Neonatal Herpes Simplex (HSV) infection

Neonatal HSV infection is an important consideration in neonates with suspected sepsis.

Hepatic transaminase levels are elevated with disseminated HSV disease and severe sepsis.

HSV risk factors

*NB. These may not be present in all cases

Maternal:

- > Maternal history of current or past HSV infections
- > Maternal peri partum fever
- > History of prolonged rupture of membranes

Neonatal:

- > History of contact
- > Scalp electrode monitoring
- > Cutaneous vesicles and/or mucosal ulcers
- Seizures particularly focal seizures
- > Elevated transaminases

For guidelines referring to the management of neonates with HSV infection, please see SA Perinatal Practice Guidelines available at

https://extapps2.sahealth.sa.gov.au/PracticeGuidelines/.

Clinical features of sepsis

The clinical features of sepsis may be nonspecific and subtle. Neonates may present unwell with one or more of the following symptoms and signs:

- > Hypothermia, fever or temperature instability <36oC or >38oC
- > Lethargy, poor cry or inconsolable crying feeding difficulties
- > Altered behaviour/responsiveness
- > Poor perfusion
- > Altered muscle tone (e.g. floppiness)
- Not moving a limb
- > Abnormal heart rate (bradycardia, tachycardia)
- > Respiratory distress, apnoea
- > Hypo or hyperglycaemia
- Metabolic acidosis
- > Feed intolerance, including vomiting (bilious and non-bilious), abdominal distension
- > Unexplained jaundice
- > Umbilical flare or skin rashes
- > Conjunctivitis
- > Oliguria persisting >24 hours
- > Unexplained excessive bleeding /abnormal clotting



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Assessment and Diagnosis

Clinical Assessment

- ABC Treat any septic shock with sodium chloride 0.9% boluses up to 40 mL/kg, obtain at least 2 vascular accesses, monitor urine output and assess conscious level. Contact MedSTAR for retrieval/advice if in Rural Hospital. Once sepsis is suspected, the IV antibiotics should be given within an hour.
- 2. Temperature measurement can be axillary, rectal or tympanic. Rectal temperature is the gold standard to establish fever ≥38°C. This correlates with tympanic or axillary temp of 37.5 °C.

Note:

- A response to antipyretic medication does not change the likelihood of an infant having a serious bacterial infection.
- A fever documented at home by thermometer should be approached in the same manner as fever recorded in hospital.
- 3. A thorough history and physical examination is required.

Note:

- Include questions about recent exposures, maternal risk factors at the time of delivery, child's birth history and recent symptoms.
- Review any available microbiological results for mother (eg vaginal/placental swabs, urine cultures) in case of resistant organisms.
- Clinical features of sepsis may be non-specific and subtle (see above).

Laboratory studies

It is recommended that the following studies be performed in neonates with suspected sepsis, (with or without fever):

Blood

- > Glucose.
- > Blood cultures- ideally at least 1mL of blood.
- Sepsis multiplex PCR (HSV (1and 2), VZV, Enterovirus, Neisseria meningitides, Streptococcus pneumoniae and Parechovirus).
- > Complete blood count, differential and I/T ratio. An increase in the band count (>2) or I/T ratio ≥ 0.2 (or 20%) is moderately predictive of sepsis.
- > A low white cell count with neutropenia is also suspicious of sepsis.
- CRP has been studied in infants less than 90 days presenting with fever of unknown source. A low CRP does not improve the confidence of ruling out SBI.
- > Liver function tests.
- > Lactate & acid base status
- > Coagulation to check for DIC



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Cerebrospinal fluid

An LP should be performed to obtain CSF prior to starting antibiotics if it is thought safe to do so. **Antimicrobial therapy should not be delayed in order to perform an LP.**

Request: microscopy (including Gram stain), culture and susceptibility, sepsis multiplex PCR, which includes HSV (1 and 2), VZV, *Enterovirus, Neisseria meningitides and Streptococcus pneumoniae and Parechovirus*. Protein, glucose (only if sufficient sample volume).

Note:

- The ideal volume of CSF is greater than 22 drops. This should be collected into 2 tubes.
- If less than 22 drops are obtained, contact microbiology to discuss priority of test ordering.
- A suggested priority is: microscopy (1 drop required), then sterile site PCR (7 drops required), then culture and susceptibility (10 drops required). Biochemistry (protein and glucose) requires 4 drops and should be omitted if <22 drops obtained.

Interpretation of CSF

١		Neutrophils (x 10 ⁶ /L)	Lymphocytes (x 10 ⁶ /L)	Protein (g/L)	Glucose (CSF: blood ratio)
	Normal term neonate	0*	< 20	< 1.0	≥ 0.6 (or ≥ 2.5 mmol/L)
	Bacterial meningitis	100-10,000 (but may be normal)	Usually < 100	> 1.0 (but may be normal)	< 0.4 (but may be normal)
	Viral meningitis	Usually <100	10-1000 (but may be normal)	0.4-1 (but may be normal)	Usually normal

* Some studies have found up to 5% of white cells in neonates without meningitis comprise neutrophils.

Note:

If CSF is abnormal, or unable to be obtained, the safest course is to treat as if there is bacterial or HSV meningitis.

- > Gram stain may be negative in up to 60% of cases of bacterial meningitis even without prior antibiotics.
- > Neither a normal Gram stain, nor a lymphocytosis excludes bacterial meningitis.
- > Neutrophils may predominate in viral meningitis even after the first 24 hours.
- > CSF findings in bacterial meningitis may mimic those found in viral meningitis (particularly early on).
- Prior antibiotics usually prevent the culture of bacteria from the CSF. Antibiotics are unlikely to significantly affect the CSF cell count or biochemistry in samples taken <24 hours after antibiotics. PCR may be useful in this situation.
- > Recent studies do not support the earlier belief that seizures can increase cell counts in the absence of meningitis. It is safest to assume that seizures do not cause an increased CSF cell count.
- Some guidelines suggest that in traumatic taps 1 white blood cell can be allowed for every 500 to 700 red blood cells and 0.01g/L protein for every 1000 red cells. However, rules based on a 'predicted' white cell count in the CSF are not reliable.



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Urine

SPA or urethral catheterisation is recommended for obtaining urine specimens. There is a high rate of contamination of bag specimens.

Request: Urinalysis, urine culture, MC&S and urine HSV PCR.

Swabs

Swabs (1 swab from top to bottom) including eyes, throat, umbilicus and rectum and a separate swab for any visible vesicles or lesions. Place in viral transport medium.

Request: HSV PCR

Faeces

To be collected depending on clinical context.

Request: Enteric micro (MC&S), enteric pathogens (PCR), EV PCR.

NPA or High Nasal Swab / Posterior pharyngeal throat swab

Request: respiratory viral PCR (also includes *Bordetella pertussis* and *Mycoplasma pneumoniae* PCR).

Radiological studies

- It is recommended that a Chest X-ray is performed as part of the sepsis work-up. Consider Neuroimaging if there is an encephalitic picture or if suspected meningitis which isn't improving with recommended antibiotic regime, as may be a cerebral abscess
- > ECHC
- > Enteroviral infection may be associated with a myocarditis so arrange echo if clinically suspicious.

Further management

- > It is recommended that all neonates presenting from the community with suspected sepsis be admitted to hospital for further evaluation and management.
- > Empiric antimicrobial therapy should be initiated as soon as possible (see below).
- > If there are signs consistent with a specific pathogen, e.g. skin infection suggestive of *Staph aureus*, directed therapy may be appropriate. Discuss with specialist.

Empiric Antimicrobials

> Modify according to clinical picture, specimen culture and susceptibility results.

Note:

- It is recommended that, if a lumbar puncture has not been performed prior to antibiotic therapy, it is performed as soon as is safely possible afterwards.
- Note there are reports that EV and bacterial meningitis can co-exist.

Community-onset sepsis (meningitis not excluded):

IV cefotaxime PLUS IV amoxicillin PLUS IV aciclovir

Duration of treatment depends on organisms isolated and clinical presentation.

Community-onset sepsis (meningitis excluded):

IV amoxicillin PLUS IV gentamicin PLUS consider adding IV aciclovir if clinically indicated.



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For neonates at increased risk of MRSA infection add IV vancomycin to the above regimens. Duration of treatment depends on organisms isolated and clinical presentation

Antimicrobial Doses

Cefotaxime

Refer to Neonatal Medication Guidelines for dose regimens www.sahealth.sa.gov.au/neonatal

Amoxicillin

> Refer to Neonatal Medication Guidelines for dose regimens www.sahealth.sa.gov.au/neonatal

Gentamicin

Refer to Neonatal Medication Guidelines for dose regimens www.sahealth.sa.gov.au/neonatal

Aciclovir

> Refer to Neonatal Medication Guidelines for dose regimens www.sahealth.sa.gov.au/neonatal

Vancomycin

Refer to Neonatal Medication Guidelines for dose regimens www.sahealth.sa.gov.au/neonatal

References

Several Guideline sites were consulted for existing guidelines regarding neonatal sepsis presenting from the community, including:

- Royal Children's Hospital. 2017 Clinical Practice Guidelines Sepsis assessment and management. [ONLINE] Available at: https://www.rch.org.au/clinicalguide/guideline_index/SEPSIS_assessment_and_management/. [Accessed 4 July 2018]
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