

Local Guideline



John Hunter
Children's Hospital
CHILDREN, YOUNG PEOPLE AND FAMILIES



Health
Hunter New England
Local Health District

Hypotension and poor circulation in neonates

Sites where Local Guideline applies	Neonatal Intensive Care Unit, JHCH
This Local Guideline applies to:	
1. Adults	No
2. Children up to 16 years	No
3. Neonates – less than 29 days	Yes
Target audience	NICU clinical staff who provide care to neonatal patients
Description	Guideline for clinicians to manage a neonate with hypotension and poor circulation

[Hyperlink to Guideline](#)

Keywords	blood pressure, capillary refill, echocardiogram, haemodynamics, hypotension, inotropes, perfusion, pulmonary hypertension, JHCH, NICU
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Related Legislation, Australian Standard, NSW Ministry of Health Policy Directive or Guideline, National Safety and Quality Health Service Standard (NSQHSS) and/or other, HNE Health Document, Professional Guideline, Code of Practice or Ethics:	<ul style="list-style-type: none"> NSW Health Policy Directive 2007_079 Clinical Procedure Safety NSW Health Policy Directive PD 2007_036 Infection Control Policy
Prerequisites (if required)	N/A
Local Guideline note	This document reflects what is currently regarded as safe and appropriate practice. The guideline section does not replace the need for the application of clinical judgment in respect to each individual patient but the procedure/s require mandatory compliance . If staff believe that the procedure/s should not apply in a particular clinical situation they must seek advice from their unit manager/delegate and document the variance in the patients health record.
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RISK STATEMENT

This local guideline has been developed to provide guidance to clinical staff in NICU to assist in assessment and management of hypotension and poor perfusion in the newborn. It ensures that the risks of harm to the infants whilst caring for an infant being assessed and managed for hypotension are identified and managed.

Any unplanned event resulting in, or with the potential for injury, damage or other loss to infants/staff/family as a result of this management must be reported through the Incident Information management System and managed in accordance with the Ministry of Health Policy Directive: Incident management PD2007_061. This would include unintended injury that results in disability, death or prolonged hospital stay.

Risk Category: Clinical Care & Patient Safety

ABBREVIATIONS & GLOSSARY

Abbreviation/Word	Definition
aEEG	Amplitude-integrated electroencephalography
BP	Blood pressure
NIBP	Non-invasive blood pressure
MBP	Mean blood pressure
PAP	Pulmonary arterial pressure
SAP	Systemic arterial pressure
pCO ₂	Partial pressure of carbon dioxide
PPHN	Persistent pulmonary hypertension
RVO	Right ventricular output
LVO	Left ventricular output
SVC	Superior vena cava

OUTCOMES

1	To use clinical parameters of BP, perfusion and haemodynamics to assess for required cardiovascular support
2	Infants to receive cardiovascular support appropriate to underlying disease process

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GUIDELINE

This Guideline does not replace the need for the application of clinical judgment in respect to each individual patient.

Introduction

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Neonatal hypotension is defined as abnormally low arterial blood pressure affecting perfusion. There is little disagreement that inadequate perfusion or poor circulation should be treated. However, there is uncertainty as to what standards or thresholds should be used to trigger treatment of such infants and which agent or agents should be used.

Poor perfusion and/or hypotension can result from immature myocardium, ischaemic myocardial damage after hypoxic injury, loss of blood and/or as a manifestation of sepsis or underlying heart or endocrine/other diseases. Also, therapy for other complications of prematurity can cause low blood pressure. Medications such as sedatives, opioids or anticonvulsants can reduce vascular tone. High intrathoracic pressures due to over inflation with mechanical ventilation or due to a pneumothorax can reduce preload.

It is not possible to treat all of the above using the same approach and hence the selection of specific cardiovascular support often requires more information than just a blood pressure reading to target the therapy to the underlying problem.

Hypotension as a new clinical feature in a previously stable baby requires immediate attention and investigation into what caused this finding and often cardiovascular supportive treatment will be

needed. However, very preterm infants with transitional hypotension (low blood pressure in the first few hours after birth) pose a specific problem as to when and how to treat. Currently, there is no known blood pressure threshold below which very preterm infants are at an increased risk for a poor outcome and there is little evidence that anti-hypotensive therapy improves outcomes for infants with low blood pressure, however defined.

Haemodynamic assessment of the newborn

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Perfusion is defined as the balance between energy and nutrient delivery to meet cellular demand. The physiology behind adequate perfusion is complex and requires many functions of the body to work together. Arterial oxygen content has to be delivered to organs and tissues using the heart as pump (contractility), sufficient volume to pump around (preload) and a driving pressure difference. Basic principles, pressure = flow x resistance, are neatly tailored to local needs.

An 'ideal' tool for the assessment of perfusion would provide continuous, non-invasive parameters of cellular and organ energy balance. As such a measurement does not exist; we have to rely on alternatives summarised in Table 1. Each diagnostic tool provides unique information on a part of the physiological processes, but none of them can describe all.

Table 1 Haemodynamic assessment tools

	Clinical	Non-invasive	Invasive
Cardiac function	Heart rate	Echocardiogram	Catheterisation
Artery	Pulse volume	Non-invasive blood pressure (NIBP)	Arterial blood pressure
Peripheral blood flow	Capillary refill	Pulse oximetry, laser Doppler	
End organ perfusion	Organ function; urine output, potassium, lactate	Near infrared spectroscopy, aEEG (brain)	Arterial blood gas, mixed venous saturation

Clinical assessment

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Clinical examination is the hallmark of detecting any poor clinical condition. However, all current clinical parameters have significant limitations in predicting poor perfusion. Normal capillary refill in newborn infants is generally less than 3 seconds. However, the diagnostic accuracy of this clinical test to predict low blood flow is limited to significantly increased refill times (> 5 sec). There is no association between heart rate and cardiac output or perfusion. Urine output is low in all newborns in the first day, making interpretation difficult. There are no studies correlating urine output (and cut-off) and cardiac output. A rise in potassium can assist in confirming preceding low flow periods. A serum lactate > 3.0 mmol/L can reasonably predict low blood flow and persistent high values (> 6.0 mmol/L) are associated with morbidity and mortality.

Blood pressure

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Because of the limited techniques and skills available for bedside haemodynamic assessment, blood pressure (BP) remains the most used diagnostic tool to establish perfusion.

The accuracy of BP measurements is dependent on technique (location of measurement, invasive, device) and this aspect deserves attention when considering treatment. The systolic pressure is

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the pressure that blood exerts on arteries and vessels while the heart is beating, whereas the mean pressure (usually calculated as diastolic pressure + $\frac{1}{3}$ (systolic pressure - diastolic pressure) is the average arterial pressure during a single cardiac cycle. Determinants of BP are stroke volume and arterial wall compliance (stiffness) and interactions between the two can vary depending on the physiological situation. Mean BP does not provide information about pulse pressure (systolic pressure - diastolic pressure) and might not reveal clues to certain underlying pathology.

Normal BP values are not easy to obtain in very preterm infants, as many would receive support that could influence cardiovascular function. BP is dependent on gestational age and gradually increases over the first days of life. Table 2 provides a guide to the lowest centiles of BP values found in newborn infants. The rule of thumb 'MBP < GA' is not supported by any high quality evidence, but can help guide the clinician as to indicate when a blood pressure is low and if further action is needed.

Table 2 Lowest percentiles of blood pressure (in mmHg) in newborn infants

Gestation (weeks)	Systolic (mmHg)	Mean (mmHg)	Diastolic (mmHg)
< 28	36–38	24–28	
28–29	42	33	25
30–35	49	35	28
≥ 36	57	40	30

Blood flow

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Adding measurements of blood flow to haemodynamic assessments can significantly increase insight into the pathophysiology at hand. Echocardiography provides detail on cardiac function, volume status and blood flow distribution through the ductus arteriosus and the foramen ovale. Vascular resistance can be calculated and help provide further insight into the cause of the low blood pressure or poor perfusion.

The most commonly used blood flow parameters are RVO, LVO and SVC flow. Although no studies have explored the absolute threshold of low systemic blood flow and whether treatment improves outcome (similar to the situation with hypotension), an SVC flow less than 30 mL/kg/min at 5 h of age and less than 45 mL/kg/min thereafter or a ventricular output (RVO or LVO) less than 150 mL/kg/min is associated with increased morbidity and mortality.

Indications for cardiovascular support

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Hypotension and/or poor perfusion are clinical signs due to underlying disease processes and pathology. Treating the underlying cause of poor perfusion and/or hypotension is the primary goal. Until such treatment is deemed effective, cardiovascular supportive treatment might be needed. Cardiovascular support should be targeted towards the underlying pathophysiology.

A. Hypotension in a baby with previous normal cardiovascular status

Hypotension as a new clinical feature in a previously stable baby requires immediate attention. The commonest cause is sepsis and early intervention with volume and inotropes can reduce morbidity and mortality.

B. Transitional hypotension or low blood flow in very preterm infants If low blood pressure or low blood flow is the only sign (i.e., normal clinical assessment of perfusion, normal lactate, normal urine output) and there are no significant risk factors for the immediate development of poor

perfusion (peri-partum haemorrhage, sepsis, significant perinatal hypoxia), current evidence does not support the use of inotropes as this does not improve short-term (cerebral perfusion) or long-term (neurodevelopment) outcomes. However, with persistent (> 3 hours) or very low blood pressure or very low blood flow, many clinicians feel increasingly obliged to start supportive measures.

C. Cardiovascular support in specific clinical situations

Poor perfusion and hypotension after perinatal hypoxia and/or PPHN require a tailored approach to support the heart and optimise afterload without creating increased pulmonary vascular resistance.

Vasoactive medications

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Inotropes that can be used in newborns include dopamine, dobutamine, adrenaline (epinephrine), and noradrenaline (norepinephrine). Milrinone and vasopressin are also currently being looked at as drugs to assist in circulatory disturbances in newborns. Before prescribing, it is important to consider the underlying pathophysiology of the cardiovascular compromise as well as the pharmacokinetics and pharmacodynamics of the drug you want to prescribe (Table 3).

Table 3 Cardiovascular support agents, mechanism of action and physiological targets

Cardiovascular support agent	Expected actions	Comments	Physiological target
Volume	Improves cardiac input		Low preload, collapsed systemic veins
Dopamine	Pressor	Increases afterload May increase PAP/SAP ratio	Systemic hypotension, normal blood flow
Dobutamine	Pressor, improves contractility	Tachycardia May decrease PAP/SAP ratio	Low contractility, low blood flow
Adrenaline (epinephrine)	Pressor, improves contractility	Tachycardia Beta-adrenergic stimulation with hyperglycemia and increased lactate May decrease PAP/SAP ratio	Low contractility, low blood flow, systemic hypotension
Noradrenaline (norepinephrine)	Pressor, improves contractility	Increases afterload Can decrease PAP/SAP ratio No reports of use in preterm infants	Low contractility, systemic hypotension
Milrinone	Phosphodiesterase inhibitor, improves contractility	Reduces afterload Tachycardia, systemic hypotension May exacerbate right-to-left shunting	Low contractility, low blood flow, high afterload
Vasopressin	Pressor, no effect on contractility	Increases afterload	Systemic hypotension refractory to catecholamine

PAP/SAP – pulmonary to systemic arterial pressure ratio

Although much supportive data on pharmacodynamics (how the drug works) are available from animal and adult studies, limited data are available on inotropic action in newborn infants and even less on use in very preterm infants. The expected action (e.g., vasoconstriction with dopamine) does not always happen and this is reflected in a 10–20% non-responder rate for commonly used inotropes. Continuous monitoring, including echocardiography, with adjustment of therapy if the patient does not respond is needed to optimise cardiovascular support.

There is considerable controversy as to whether dopamine or dobutamine should be the first-line pharmacological agent for the treatment of neonatal hypotension. The goal in treating poor perfusion and/or hypotension would be to increase tissue perfusion. Proponents of dopamine often argue that it brings about a faster and more effective increase in blood pressure. This is not surprising, since it is a potent vasoconstrictor. However, proponents of dobutamine argue that because of this intense vasoconstriction, tissue perfusion is further compromised because of decreased blood flow.

Step wise approach to cardiovascular support

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Review and document all clinical and physiological parameters available. Clinical appearance, capillary refill, blood pressure (including how and where measured), current respiratory support and settings, oxygenation index, lactate, pH, echocardiography findings if available.

Document your working diagnosis (most likely cause of the poor perfusion and/or hypotension) and describe the expected underlying physiology.

Choose your cardiovascular supportive treatment and document expected action. Pre-defining 'success' can help direct escalation of therapy.

After starting therapy, monitor response. If not successful, consider changing inotropes and repeat diagnostic assessment (clinical, echocardiography).

Too much inotrope can negatively affect cardiac function. Replacing one supportive treatment for another instead of adding them together should be considered to prevent catecholamine overload.

Sepsis with cardiovascular compromise or systemic inflammatory response syndrome after major surgery

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1. Early fluid expansion (20 mL/kg bolus in 30 minutes, up to 60 mL/kg)
2. If unsuccessful in restoring blood pressure, start dopamine 5 microg/kg/min and increase by 5 microg/kg/min until effect
3. If dopamine > 10 microg/kg/min is needed, consider echocardiography to evaluate blood flow, preload, contractility and blood flow distribution
4. If dopamine > 10 microg/kg/min is needed, also consider hydrocortisone 1 mg/kg per dose every 8 hours
5. Preterm infants with sepsis present with high central blood flow but with (initial) good contractility. Persistent acidosis can induce changes in cardiac function that may respond to dobutamine
6. Rescue therapy with adrenaline (epinephrine), noradrenaline (norepinephrine) and/or vasopressin can be considered for refractory hypotension and persistent acidosis

Transitional hypotension in the very preterm infant[Top](#)

1. Fluid expansion (10 mL/kg bolus over 60 minutes, up to 20 mL/kg).
2. If normal blood flow or blood flow is unknown, start dopamine 5 microg/kg/min and increase by 5 microg/kg/min until effect
3. If dopamine > 10 microg/kg/min is needed, consider echocardiography to evaluate blood flow, preload, contractility and blood flow distribution
4. If dopamine > 10 microg/kg/min is needed, also consider hydrocortisone 1 mg/kg per dose every 8 hours
5. If low blood flow, start dobutamine 10 microg/kg/min
6. Adrenaline (epinephrine) can be considered for refractory hypotension and persistent acidosis

Cardiovascular support in infants with pulmonary hypertension[top](#)

1. Cardiovascular support may be needed for left ventricular dysfunction (often early) and/or right ventricular dysfunction (often later, after ductal constriction)
2. Noradrenaline (norepinephrine) as the first-line drug has the best pharmacodynamics for treatment of low blood pressure (increased systemic vascular resistance >> pulmonary vascular resistance) and left ventricular dysfunction (positive inotropy) in term infants with PPHN. Experience in preterm infants is limited.
3. As discussed previously, dopamine has poor pharmacodynamics, and should be avoided when possible
4. Milrinone can be used to treat low systemic blood flow due to cardiac dysfunction, but can cause significant systemic hypotension in preterm infants
5. Low-dose vasopressin as an additive agent has been shown to be effective in improving oxygenation
6. Increasing inotropic support until so-called supra-systemic pressures are reached is not recommended, as it will increase the pulmonary pressure as well and does not restore the systemic to pulmonary pressure imbalance
7. Careful management of mean airway pressure can assist in optimising cardiac function. Continuous distending pressure can significantly increase right atrial pressure. Pump function can (in theory) be optimised with conventional ventilation strategies if lung parenchymal disease allows

Cardiovascular support after significant perinatal hypoxia[Top](#)

1. Use volume for hypovolaemia
2. If significant cardiovascular compromise, obtain a cardiac ultrasound to determine cardiac function and target treatment appropriately. Hypotension due to depressed cardiac function with low blood flow will respond best to dobutamine; hypotension due to loss of vascular tone with normal blood flow to dopamine.
3. Pulmonary hypertension after hypoxic-ischaemia responds to normalising pCO₂, acidosis and blood pressure

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FEEDBACK

Any feedback on this document should be sent to the Contact Officer listed on the front page.