



NCCU CLINICAL GUIDELINES
SECTION: 14

CARDIAC CONDITIONS

Section: 14 Cardiac conditions
Blood pressure in the neonate
Date Revised: 2002

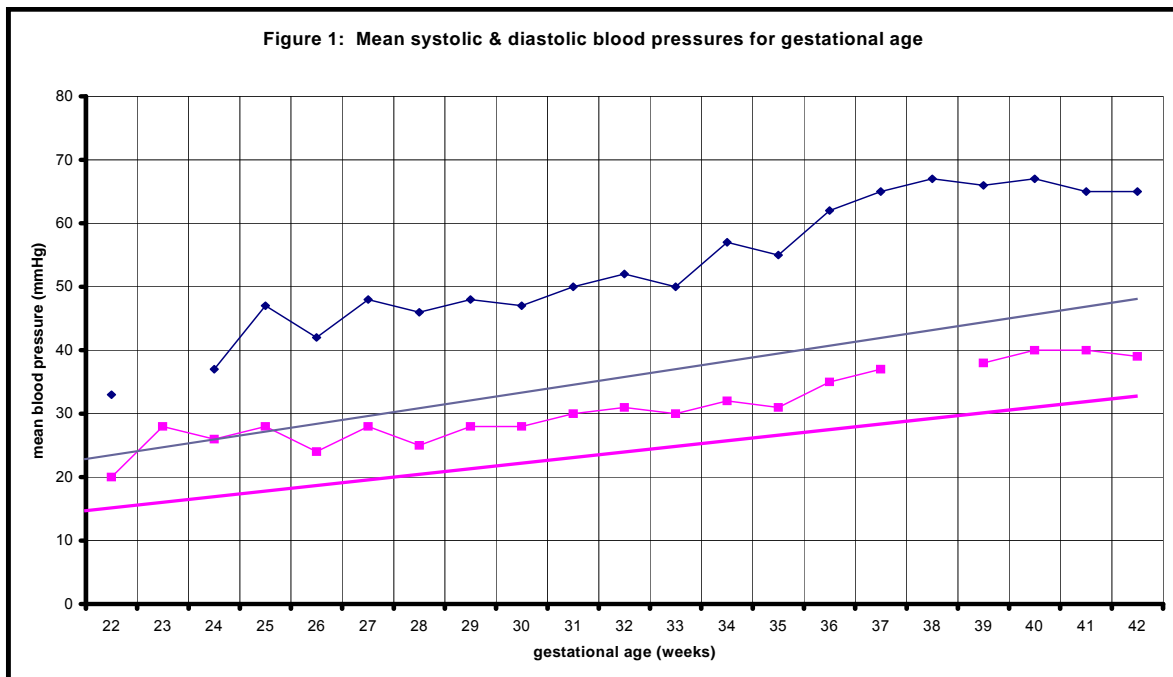
Neonatology Clinical Guidelines
King Edward Memorial/Princess Margaret Hospitals
Perth Western Australia

BLOOD PRESSURE IN THE NEONATE

There is no good evidence for what is a normal blood pressure in a neonate. **A rough rule of thumb is a mean blood pressure equal to the gestational age (in weeks) for the first 24-48 hours.** In addition, if an infant is passing urine adequately and the arterial lactate is normal, that is an indication that perfusion pressure (and blood pressure) is usually adequate.

Some infants require a higher mean blood pressure than normal; for example in persistent pulmonary hypertension of the neonate (PPHN) when pulmonary pressures are equal or greater than systemic pressures. Linear regression graphs (from Philadelphia) for mean systolic and diastolic blood pressures for day 1 taken from 329 infants (Fig 1) and then for the first 5 days of life (Fig 2A & 2B). Small for gestational age infants may have a lower mean blood pressure than a normal-sized infant for the same gestation.

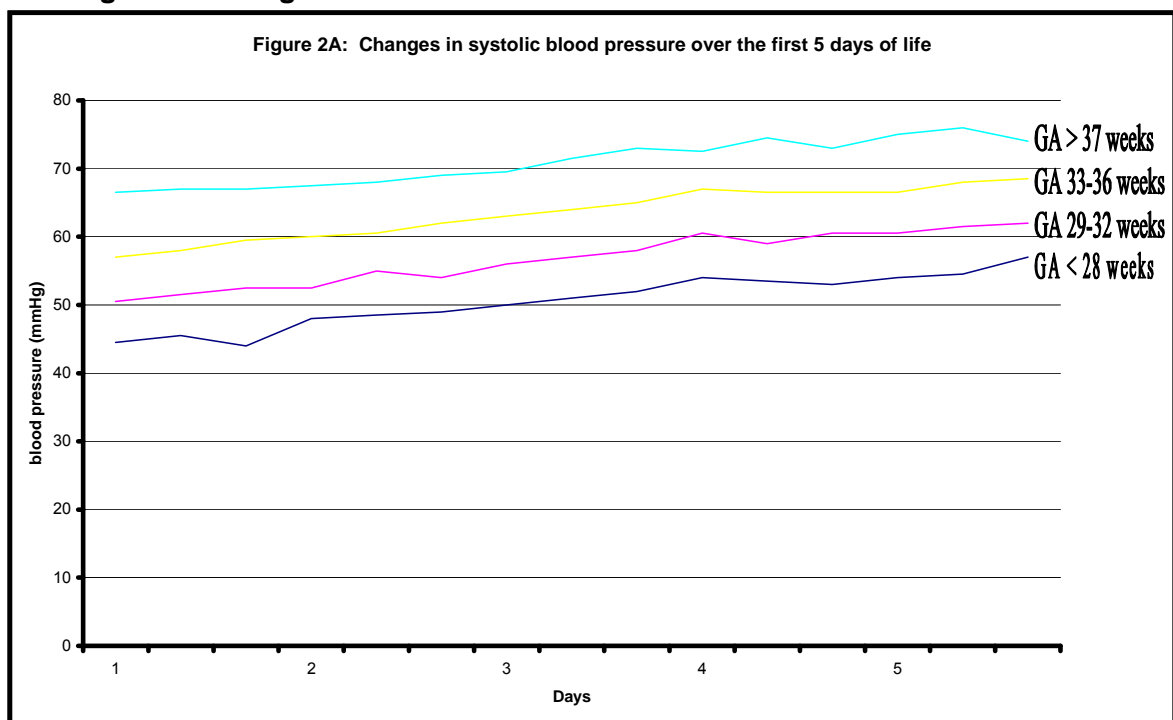
Figure 1. Systolic and Diastolic Blood Pressure: Mean & Standard Deviation

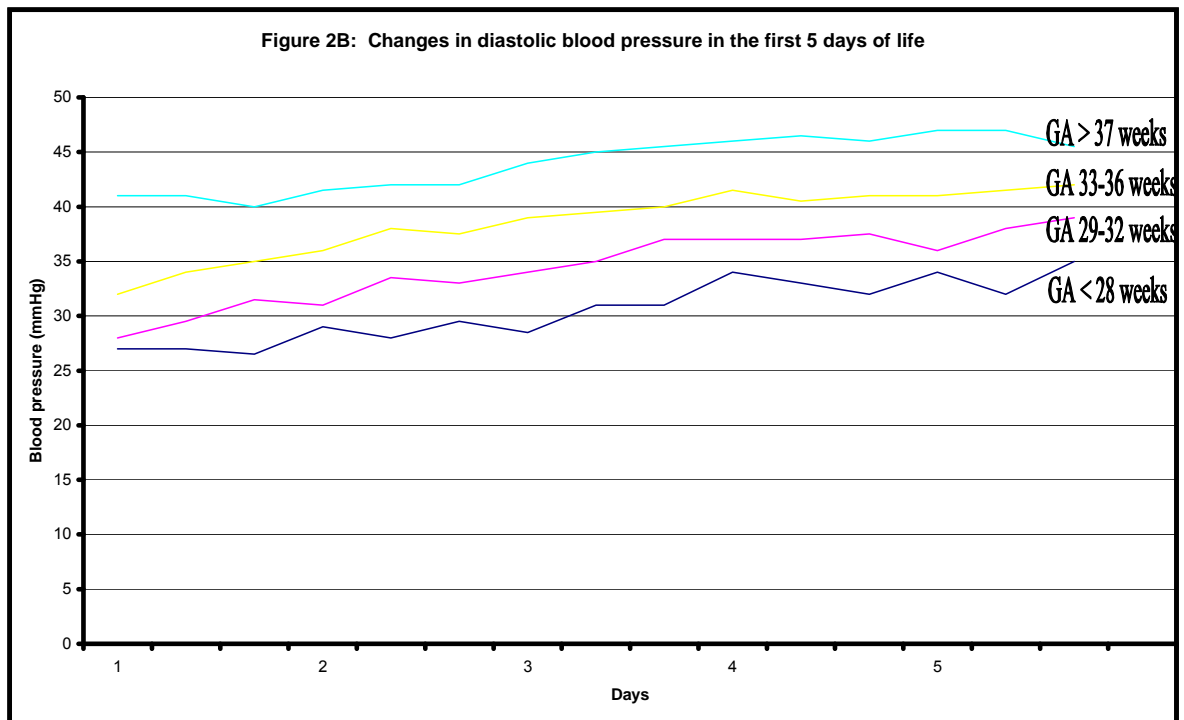


Mean Systolic Blood Pressure ■—■
 Systolic Blood Pressure-2 SD below the mean
 Mean Diastolic Blood Pressure ■—■
 Diastolic Blood Pressure- 2 SD below the mean

Engle WD. Blood pressure in the very low birth weight neonate, Early Human Development 2001; 62:97-130.

Figure 2A, 2B. Changes in Systolic and Diastolic Blood Pressure in the first 5 days of life, based on gestational age.





Engle WD. Blood pressure in the very low birth weight neonate, *Early Human Development* 2001; 62:97-130.

HYPERTENSION

Hypertension is rare in the neonate. Infants may be asymptomatic or may have the following:

- Respiratory distress and / or congestive cardiac failure – tachpnoea, apnoea, cyanosis
- Seizures / lethargy
- Mottling
- Fever

CAUSES (MOST COMMON)

1. Renal artery thrombosis (related to placement of a UAC)
2. Renal failure (polycystic kidneys, obstructive uropathy)
1. Pain
2. Coarctation of the Aorta
3. Drug withdrawal
4. Seizures
5. Initial closure of abdominal wall defects
6. Medications (dopamine, adrenaline)

HYPOTENSION

There are no studies demonstrating the incidence of hypotension in neonates. Low systemic blood flow as opposed to low blood pressure is common in the first 24hrs in preterm infants and also in more mature infants with respiratory problems. The causes of both are complex. The treatment of hypotension in the neonate is controversial as there is only a weak association between blood pressure and systemic blood flow.

PATHOPHYSIOLOGY

Arterial pressure is determined by propulsion of blood by the heart (pump) and resistance to flow of this blood through the blood vessels. As it is impractical to measure flow or resistance, we rely on blood pressure to gauge the adequacy of the circulatory system.

Physiological variables affecting blood pressure include:

Cardiac output: This is a product of heart rate and stroke volume. Stroke volume is dependent on preload (filling volume of the heart), contractility, and the afterload (resistance to emptying of the ventricle during systole). Therefore volume loss (blood loss or excessive diuresis) and peripheral vasodilation will contribute to hypotension.

Neural regulation: This involves arterial baroreceptors (carotid sinus and aortic arch), other cardiorespiratory reflexes (great veins & lungs), the autonomic nervous system, smooth muscle, and humoral mechanisms (release of adrenaline, noradrenaline, and adrenal steroids, renin-angiotensin system, and vasopressin).

Gestational age: (see Figures 1, 2A & 2B) This rise in blood pressure with increasing gestational age is thought to be due to maturation in vascular tone and increased vascular reactivity, in addition to increased response to adrenaline and noradrenaline.

Medication: Sedation may cause hypotension due to decreased movement (decrease venous return) or poor gas exchange (inadequate oxygenation). In addition muscle relaxants will decrease the effort of breathing and result in poor gas exchange unless artificial ventilation is instituted. Vasodilators used in pulmonary hypertension or as afterload reducers will also decrease systemic blood pressure.

Asphyxia/PPHN: Usually due to adrenal haemorrhage, direct myocardial compression, or too much volume following resuscitation (further impeding myocardial function).

Patent Ductus Arteriosis: Diastolic blood pressure decreases with a left-to-right shunt. One group suggested that systolic pressure may also decrease in this situation in very low birth weight infants.

Over-distension of the lungs during mechanical ventilation: If the mean airway pressure is too high, venous return will be impaired and hence cardiac output decreased.

Type of measurement:

The “gold standard” of measuring blood pressure in the neonate is through an indwelling arterial catheter. A few small studies have demonstrated Doppler or oscillometric techniques to be relatively accurate but continuous measurements are impractical. Inappropriate cuff size is the main cause of inaccurate measurements. The width of the cuff should be a ratio of width-to arm circumference of 0.5-0.7. There is no difference between umbilical and peripheral arterial blood pressures. Damping of the blood pressure may occur if there are air bubbles or a clot in the line.

CLINICAL PRESENTATION

An infant with inadequate blood pressure may present with:

- Hypovolaemia
- Poor urine output.
- Poor perfusion and capillary refill.
- Apnoea.
- Lethargy or decreased conscious state.

- Poor gas exchange either due to the direct effects of respiratory failure or pulmonary hypertension.
- Acidosis secondary to poor organ perfusion.
- Sepsis - NEC, pneumonia, septicemia.

INVESTIGATIONS

This is dependent on the cause of the hypotension.

In general exclude:

- Medications.
- Blood loss (FBC, PCV, U&E, Cr, lactate).
- Volume loss (U&E, Cr, FBC, PCV, osmolality, lactate).
- Sepsis (septic work-up-blood, urine \pm CSF, \pm viral studies).
- Cardiac lesion: Duct dependent lesion, or heart failure (examination, CXR, lactate \pm cardiac echo).
- Respiratory failure (ABG, lactate, CXR, septic work-up).
- Tension pneumothorax.
- Renal failure-acute tubular necrosis secondary to hypoxaemia (U&Es, lactate, urine osmolality, urine sodium/creatinine ratio, urine dip-stick, renal ultrasound). This is usually secondary to hypotension. Primary renal failure invariable causes hypertension.
- Head injury (head ultrasound, coagulation).

MANAGEMENT

Attention to the clinical situation: any reversible problems should be attended to; ie decrease sedation as much as possible, support ventilation, drain a pneumothorax.

Volume: The neonatal myocardium has decreased ability to deal with volume load and unless there is obvious blood loss or profound peripheral vasodilation due to sepsis, should not be given in excess immediately after delivery. Crystalloid is as effective, cheaper, and safer than colloid for hypovolemia. In addition, some investigators have reported an increased risk of periventricular and intraventricular haemorrhage with too much volume administration. In general not more than 20 ml/kg should be given without considering inotrope support.

Assess the type of fluid loss:

Blood- crystalloid first, then blood.

Urine-test the urine electrolytes and replace with required saline concentration (usually half normal saline is adequate).

Insensible (transepidermal) losses-usually need to replace water with less saline, but the urine electrolytes should still be measured. Check serum osmolality to assist in calculating the volume of fluid to be replaced.

Inotrope support: The use of inotropes in neonates is also controversial. A number of small studies have been performed comparing dopamine and dobutamine in preterm infants, but none in term infants, and none have been completed to compare adrenaline with dopamine or noradrenaline. Neonates are thought to have a more resistant myocardium and hence require higher doses of dobutamine and dopamine.

The effects of each inotrope are tabled below.

AGENT	CARDIAC RECEPTORS			Peripheral vascular receptors		
	α_1	$\beta_1(\beta_2)$	Dopamine	α_1/α_2	β_2	Dopamine
	renal contractility mesenteric, &	rate conduction contractility	contractility	peripheral vasoconstriction	peripheral vasodilation	vasodilation: coronary
Adrenaline	++	++++	+		++++	
NORADRENALI	+	++++				
Dobutamine	++	++++	∅		++++	+
	++	∅				

Re-landscape

Inotropes

Greater response to hypotension in preterms may be due to enhanced α -adrenergic sensitivity of a more immature cardiovascular system.

The use of dopamine together with dobutamine is not proven but practised widely. In general, when dopamine is not effective, the next step is addition of adrenaline or noradrenaline to increase afterload, rather than add dobutamine, which causes peripheral vasodilation and decreases afterload. In specific situations, afterload reduction may be appropriate (post-operative cardiac surgery), but this must be discussed with a consultant.

Dopamine

Pharmacology:

- Endogenous catecholamine.
- Acts via dose-dependent stimulation of dopaminergic, α & β adrenergic cardiovascular and peripheral receptors.
- Requires the release of endogenous noradrenaline to exert its effect on myocardial contractility (a problem at high doses).
- May have an action on renal rather than mesenteric vessels.
- [Start at 2-4 \$\mu\text{cg}/\text{kg}/\text{min}\$ for a renal dose effect, but increase as needed for inotropic effect.](#)
outdated
- May need higher doses due to insensitivity and down regulation of adrenergic receptors.

Pathophysiology:

- Improves preload- decreases venous capacitance.
- Improves myocardial contractility- α & dopaminergic receptors.
- Increases afterload- α & β adrenergic effects and conversion to noradrenaline.

Complications:

- May cause tissue necrosis when used in peripheral veins.
- Theoretical risk of causing cerebral vasoconstriction.
- Hypertension.
- Renal salt wasting.
- Inhibits prolactin (increases oedema).
- Inhibits thyrotropin, therefore repeat Guthrie when off dopamine.

Dobutamine

Pharmacology:

- Synthetic cardioselective catecholamine.
- Action is dependent on dobutamine metabolites.
- α & β adrenergic inotropic effects with little chronotropy.
- Most effective dose is 2-15 $\mu\text{cg/kg/min}$.

Pathophysiology:

- Causes increases in cardiac output by increasing stroke volume.
- It's vasodilatory effects mean that it decreases peripheral vascular resistance and is beneficial in cardiomyopathy when inotropy with afterload reduction is required.
- Does not cause tissue necrosis (vasodilation rather than vasoconstriction) and therefore may be used safely in peripheral intravenous lines (and arterial lines in an emergency).

Complications:

Tachycardia, arrhythmia, hypo or hypertension.

Adrenaline

Reserved for situations where the failing myocardium is unresponsive to other inotropic drugs.

Pharmacology:

- Endogenous catecholamine.
- α & β adrenergic effects: vasodilation of splanchnic bed and skeletal muscle at low doses (β_2 effect).

Pathophysiology:

- Major metabolic effects-increases free fatty acids, and glucose.
- Higher doses ($>1.6 \mu\text{cg/kg/min}$) may lead to renal, mesenteric, and myocardial ischaemia.
- Diastolic pressure is less affected because of vasodilation (β_2 effect) of muscle beds, therefore less effective in sepsis.

Noradrenaline

Used only in situation in which arterial pressure has decreased to levels in which acutely jeopardise coronary & cerebral perfusion.

Pharmacology:

- Endogenous catecholamine.
- Predominant α adrenergic stimulation overshadows the β effects on the myocardium.

- Does not effectively stimulate peripheral β receptors, therefore does not cause vasodilation.

Pathophysiology:

- Both systolic and diastolic arterial pressure is increased by vasoconstriction of arteriolar and venous smooth muscle.
- Useful in sepsis where there is marked peripheral vasodilation and hypotension from cytokine release.
- More effective than adrenaline in the setting of sepsis because of the powerful α effect (increases peripheral vascular resistance).

COMPLICATIONS OF ADRENALINE AND NORADRENALINE

ADRENALINE AND NORADRENALINE

Unpredictable, and inappropriate episodes of increased peripheral vascular resistance which may cause:

- Tachycardia.
- Arrhythmias.
- Decreased cardiac output and tissue perfusion.
- Decreased myocardial oxygen perfusion.

NORADRENALINE

May cause hypocalcemia, hypoglycaemia, ischaemic dysrhythmias & ischaemia of renal & splanchnic beds at high doses.

There is no evidence for adrenaline or noradrenaline use in neonates. There is a theoretical concern that their use may exacerbate or cause cerebral vasoconstriction. High doses ($>0.5-1 \mu\text{cg/kg/min}$) cause vasoconstriction of all organ vascular beds and therefore may cause oliguria. High doses ($>1 \mu\text{cg/kg/min}$) may also cause endocardial necrosis.

STEROIDS

In shock, adrenergic receptors are down-regulated. In addition there is usually a state of adrenal insufficiency.

Steroids:

- Induce the expression of cardiovascular adrenergic receptors and some components of the second messenger systems.
- Inhibit catecholamine metabolism and release of vaso-active factors.
- Increase intracellular calcium availability, and therefore myocardium and vascular smooth muscle responsiveness to catecholamines.
- Have a rapid action.

TREATMENT

Small dose of 1-2 mg/kg hydrocortisone 6-8 hourly should be sufficient.

A serum cortisol should always be measured prior to commencing treatment with hydrocortisone to eliminate primary adrenal insufficiency

COMPLICATIONS

- Glucose intolerance.
- Immune dysfunction (fungal infection).
- Hypertension.
- Intestinal perforations.
- Cerebral function.
- No studies reported complications with single dose or 1-3 day course.

EVIDENCE FOR USING SPECIFIC INOTROPES

Dopamine versus Dobutamine

Four small randomised controlled trials demonstrated no difference in periventricular leukomalacia, grade III or IV intraventricular haemorrhage, or mortality. Dopamine was more effective at increasing blood pressure than dobutamine. Long term outcomes were not measured.

Dopamine versus Adrenaline

One small study demonstrated adrenaline to be more efficient at increasing left ventricular output (LVO) than dopamine. Dopamine caused a secondary drop in LVO due to decreased stroke volume, whereas adrenaline increased stroke volume. One small study suggested that adrenaline added to dopamine, improved urine output compared to dopamine alone.

Noradrenaline

Descriptive studies only.

Investigations are dependent on the aetiology of the hypotension.

If hypotension is resistant to 2 inotropes, serum cortisol and ACTH should be measured before a dose of hydrocortisone is given.

PROGNOSIS

This is also dependent on the aetiology of the hypotension. Sepsis resistant to 2 inotropes for support is invariably fatal in neonates. Volume loss is dependent on the speed at which volume may be replaced. In every condition, outcome is dependent on the extent of end-organ damage.