

Inotropes and vasopressors in critical care

Hannah Dodwell and Bruce McCormick

Correspondence Email: hannah.dodwell@doctors.net.uk

INTRODUCTION

Shock is present in many patients requiring admission to the intensive care unit. Shock is a clinical syndrome characterised by inadequate tissue perfusion, leading to organ dysfunction. Hypotension is usually present, but is not essential to diagnose shock. Other features include raised lactate levels and increased or decreased mixed venous or central venous saturations (SvO_2), depending on the underlying pathology. Shock has a high mortality.

Shock can be classified as: hypovolaemic, distributive, obstructive and cardiogenic. Patients with all types of shock are admitted to critical care units and inotropes and vasopressors play an important role in their treatment.

Inotropes are endogenous or synthetic agents that elevate the cardiac output by increasing the force of contraction of the heart's ventricles (inotropy). Most are also positive chronotropes, increasing the heart rate.

Vasopressors (again endogenous or synthetic) cause arterial vasoconstriction, tending to elevate the patient's blood pressure. The cardiac output may be increased or decreased.

CARDIOVASCULAR EFFECTS OF INOTROPES AND VASOPRESSORS

Before considering how the different inotropes and vasopressors work, it is useful to revise the relevant physiology of the cardiovascular system. More detail on this is available in a previous *Update* article.¹

Oxygen delivery (DO_2) to tissues is dependent upon cardiac output (CO) and the oxygen content of the arterial blood reaching the tissues (CaO_2):

$$DO_2 \text{ (ml.min}^{-1}\text{)} = CO \text{ (L.min}^{-1}\text{)} \times [CaO_2 \text{ (ml.dl}^{-1}\text{)} \times 10^*]$$

(*Note: the factor of 10 converts the oxygen content from ml per dl to ml per litre)

Cardiac output is the product of heart rate (HR) and stroke volume (SV):

$$CO = HR \times SV$$

Cardiac index is the cardiac output defined by the patient's body surface area.

Stroke volume is the volume of blood ejected from the left ventricle with each contraction and is determined by the preload, afterload and contractility of the ventricle.

The cardiovascular system controls blood pressure and so ensures adequate tissue perfusion by a combination of systems:

- The autonomic nervous system
- Peripheral and central baroreceptors
- The renin-angiotensin-aldosterone system.

There are many important neurotransmitters, hormones, local mediators and receptors involved - inotropes and vasopressors target these sites to exert their effects (see Table 1).

Vasopressors (norepinephrine, phenylephrine, metaraminol and high dose epinephrine) largely work by stimulating alpha-1 adrenergic receptors, causing peripheral vasoconstriction, increasing SVR and elevating the blood pressure. Increasing SVR, raises the left ventricular afterload and so cardiac output may fall, despite an increase in blood pressure. Venoconstriction may contribute by increasing preload and elevating the cardiac output.

CLASSIFICATION OF SHOCK

Shock can have many underlying causes that can be classified as follows.

Hypovolaemic shock

This is most commonly caused by haemorrhage and dehydration.

Haemodynamic parameters

- Low cardiac output with compensatory vasoconstriction causing high systemic vascular resistance.
- Low central venous pressures.
- Likely to improve with intravenous fluid boluses.

Clinical features

- The patient may be hypotensive, tachycardic and peripherally cold due to vasoconstriction.

Summary

This article describes the way in which vasoactive drugs are used in critically ill patients. Typical clinical scenarios are used to demonstrate why we choose certain drugs in certain conditions. The safety aspects of running infusions of highly potent drugs are considered.

Hannah Dodwell
Core Trainee

Bruce McCormick
Consultant
Department of Anaesthesia
Royal Devon and Exeter NHS
Foundation Trust
Barrack Road
Exeter
EX2 5DW
UK

Table 1. Commonly used vasoactive drugs.

	Naturally occurring	Synthetic
Catecholamines	Epinephrine (adrenaline) Norepinephrine (noradrenaline) Dopamine	Dobutamine Dopexamine Isoprenaline
Phosphodiesterase (PDE) type 3 inhibitors		Milrinone Enoximone
Increasing ionised calcium		Calcium gluconate / calcium chloride
Increasing sensitivity to calcium		Levosimendan
Na ⁺ /K ⁺ ATPase inhibitor		Digoxin
Increasing intracellular concentrations of cyclic AMP	Glucagon	
Vasopressin		

- The American College of Surgeons Advanced Trauma Life Support classification of haemorrhagic shock severity is useful to assess the severity of shock, in terms of the estimated circulating volume loss (Table 2).²

Distributive shock

This includes septic shock and anaphylaxis. Increased levels of inflammatory mediators cause peripheral vasodilatation; this is sometimes termed relative hypovolaemia, meaning that no fluid has been lost, in contrast to the absolute hypovolaemia of hypovolaemic shock. In addition, capillary beds become more permeable and fluid is lost from the intravascular space into the interstitium.

Haemodynamic parameters

- Initially compensation occurs as a supranormal cardiac output is achieved by a rise in heart rate.
- Cardiac output may fall in the later stages of septic shock due to the presence of a circulating myocardial depressant factor. At this

stage there may be little response seen in haemodynamic parameters on administration of intravenous fluid boluses.

- Note that smaller children show a different response to sepsis, with compensation predominantly manifesting as profound vasoconstriction, often with a low or inappropriately normal cardiac output. This necessitates a different approach to resuscitation in paediatric septic shock.

Clinical features

- Usually includes tachycardia with bounding pulses. The patient may be flushed and be warm to touch.
- Hypotension and pyrexia (or hypothermia) may be present.

Obstructive shock

This follows obstruction of a critical part of the cardiovascular system, for example an embolus in a pulmonary artery or cardiac tamponade.

Haemodynamic parameters

- Low cardiac output, high systemic vascular resistance, high central venous pressures.

Table 2. The American College of Surgeons Advanced Trauma Life Support classification of haemorrhagic shock severity.²

Severity of hypovolaemia	Class 1	Class 2	Class 3	Class 4
Blood loss	< 750ml (0-15%)*	750 – 1500ml (15-30%)	1500 – 2000 (30-40%)	> 2000 (> 40%)
Pulse rate (per minute)	< 100	> 100	> 120	> 140
Blood pressure	Normal	Normal**	Decreased	Decreased
Pulse pressure (mm Hg)	Normal	Decreased	Decreased	Decreased
Respiratory rate (per minute)	14–20	20–30	30–40	> 40
Urine output (ml.h ⁻¹)	> 30	20–30	5–15	Anuric
Central nervous system	+/- slightly anxious	Mildly anxious	Confused	Lethargic

* note that normal blood volume is estimated as about 5000ml for a 70kg patient (~70ml.kg⁻¹)

** Vasoconstriction may cause a rise in the diastolic blood pressure with a normal systolic blood pressure (e.g. 120/90mmHg). This is a useful sign as decompensation is imminent.

- Unlikely to respond to fluid boluses.
- An echocardiogram is very helpful to determine the nature of the obstruction.

Clinical features

Hypotension, vasoconstriction, raised JVP and pulsus paradoxus may be seen.

Cardiogenic shock

This results from failure of the heart to pump blood into the systemic circulation effectively. This can be caused by a myocardial (e.g. myocardial infarction) or valvular defect (e.g. aortic stenosis). The problem may lie within the right or left side of the heart, or both (global).

Haemodynamic parameters

- Cardiogenic shock is defined by a cardiac index less $2.2\text{L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$ and a low SvO_2 despite adequate preload and associated with signs of hypoperfusion.
- An echocardiogram is extremely useful in making this diagnosis.

Clinical features

Hypotension, vasoconstriction and raised JVP.

MANAGEMENT

For all types of shock, an initial rapid assessment using an ABCDE approach, with prompt treatment, is paramount. Where available, transfer to a critical care setting for invasive monitoring and organ support may be necessary and, unless fluid therapy is rapidly effective, this may include the use of inotropes and vasopressors.

Inotropes and vasopressors

Use of inotropes and vasopressors depends upon local availability and local protocols. A recently survey of 263 African healthcare workers regarding the availability of inotropic drugs at their workplace showed that, while the majority had a reliable supply of epinephrine, only half always had norepinephrine and just over one third had access to dobutamine.³ Around one quarter to one third of respondents never had access to these drugs.

The main mechanism by which inotropes improve tissue perfusion is by increasing cardiac contractility by increasing intracellular calcium. This can be facilitated by:

- *Increasing cyclic AMP (cAMP)*
This is a second messenger which causes increased calcium ion mobilisation.
- *Inhibition of phosphodiesterase (PDE) type 3*
This is normally responsible for breakdown of cAMP, therefore inhibiting PDE 3 increases cAMP levels.
- *Directly increasing the amount of ionised calcium available in plasma.*
- *Increasing myocardial cell sensitivity to calcium.*
- *Inhibition of Na^+/K^+ ATPase*
This causes slowing of the heart rate which allows further

diastolic filling, thus increasing stroke volume. It also increases calcium availability.

- *Others mechanisms*
Glucagon, for example, stimulates adenylate cyclase, increasing calcium flux into myocardial muscle.

PRACTICAL USE OF INOTROPES AND VASOPRESSORS

The following clinical scenarios demonstrate how to use different inotropes and vasopressor in common clinical situations. In all cases basic resuscitation (guided by an ABC approach) should be the highest priority and in some cases other treatments should precede administration of vasoactive drugs (for example prompt administration of antibiotics in septic shock). Appropriate monitoring should be in place and, where available, this will include invasive blood pressure measurement and a monitor of cardiac output.

Mean arterial pressure is a useful target, with 65mmHg commonly used as an estimated adequate value. This should tailored to the response (e.g. urine output), and may need to be higher in patients with pre-existing hypertension. Other special situations are outlined within the scenarios.

It is also important to remember that patients may present with more than one type of shock, and each case must be assessed and managed on an individual basis. Further information, including doses, for each drug is found in Box 1 at the end of the article..

SCENARIO 1

A 56-year-old female presents with community-acquired right upper lobe pneumonia. She has a heart rate of 140bpm, a BP of 75/30mmHg, she is oliguric and has a temperature of 38.7°C. She feels warm to touch with a bounding pulse.

Interpretation

This patient has met the criteria of systemic inflammatory response syndrome (see page 145). The cause is infective and so she has sepsis. Her haemodynamic profile is profound vasodilatation and increased capillary leakage.

Management

She should be treated according to the 'Surviving Sepsis' care bundle, that involves taking blood cultures, giving appropriate antibiotics and administering a fluid bolus of $20\text{ml}\cdot\text{kg}^{-1}$ of crystalloid.⁴

If she remains hypotensive after 'adequate' fluid resuscitation, she has septic shock, and administration of a vasopressor agent is indicated. Norepinephrine is the drug of choice,⁵ although dopamine and epinephrine are popular worldwide. An infusion of vasopressin may be added if high doses of norepinephrine fail to achieve a target blood pressure. Steroids (hydrocortisone 50mg 6 hourly) are indicated for patients on high or rapidly escalating doses of vasopressor drugs.

Cardiac output may fall due to a circulating myocardial depressant factor. This may be present from the outset or develop later in the course of the illness. This may be evident clinically or using

cardiac output measurement. Inadequate oxygen delivery is indicated by a high or rising arterial lactate level or a low $S_{cv}O_2$ level (see Figure 1). At this point supplementation of the cardiac output, using an inotrope is appropriate, typically dobutamine, but dopamine and epinephrine are alternatives. The other way to improve oxygen delivery is to increase the haemoglobin level (and so oxygen content of blood) by transfusion.

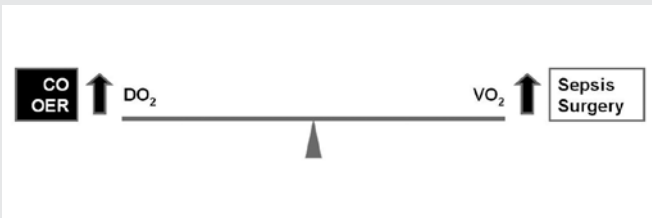


Figure 1. Organs depend on adequate delivery of oxygen (DO_2) for their oxygen consumption (VO_2). VO_2 is increased by stresses such as sepsis or surgery. DO_2 can be improved by increasing cardiac output (CO) and then, if delivery is inadequate, by the organ increasing its oxygen extraction ratio (OER). At this point delivery becomes supply-dependant - if supply falls, anaerobic metabolism increases and lactate rises. Increased OER causes venous desaturation, and so a low $S_{cv}O_2$ indicates impaired oxygen delivery.

Notes on vasoactive drugs used in sepsis

Norepinephrine (noradrenaline)

- Noradrenaline is predominantly a vasopressor agent, acting on α_1 adrenoceptors, causing peripheral vasoconstriction. It does have some β_1 -agonist effects causing positive inotropic effects.
- Restoration of blood pressure may stimulate the baroreceptor reflex causing compensatory bradycardia.
- Noradrenaline may exhibit tachyphylaxis (i.e. it becomes less potent with prolonged therapy).

Dopamine

- Dopamine acts at α_1 , and D1 (dopamine) receptors.
- Lower doses tending to have β_1 effects and stimulate endogenous noradrenaline production.
- Higher doses elicit effects at α_1 adrenoceptors and have a role in low cardiac output states, particularly in children.
- There is no evidence that dopamine a significant reno-protective role.
- Side effects include gastric stasis, arrhythmias (making it inferior to norepinephrine in this setting⁵) and anaphylaxis due to sodium metabisulphite.

Vasopressin

- This is an endogenous peptide (also known as antidiuretic hormone), usually produced in the hypothalamus. It is released in response to increased plasma osmolality and has its effects at V1, V2, V3 and OTR (oxytocin-type) receptors.

- V1 receptors are found on vascular smooth muscle of the systemic, splanchnic, renal, and coronary circulations. V2 receptors are located in the distal tubule and collecting ducts of the kidney and, when stimulated, increase water reabsorption.
- Vasopressin levels fall dramatically in septic shock and it was postulated that replacing it would improve survival in patients with septic shock. However, a large randomised controlled trial failed to show any difference in survival between treatment with vasopressin compared to noradrenaline⁶ and it is used as a catecholamine-sparing agent in septic patients on high or escalating doses of catecholamines.
- It may have a role in renal resuscitation for patients with impending acute kidney injury.
- Side effects include myocardial ischaemia at high dose, reduced splanchnic circulation and skin necrosis.

Epinephrine (adrenaline)

- Adrenaline stimulates both α - and β -adrenoceptors, with different effects depending on the dose administered.
- At low dose, there are mostly β effects; increased inotropy and chronotropy and also bronchodilatation.
- At high dose, alpha effects predominate, resulting in peripheral vasoconstriction.
- Side effects include lactic acidosis. One of its constituents (sodium metabisulphite) can cause allergic-type reactions, including anaphylaxis and life-threatening asthmatic episodes in susceptible individuals.

SCENARIO 2

A 62-year-old man presents to the Emergency Department after being stung by a wasp. He has a widespread rash, is hypotensive, tachycardic and finding it difficult to breathe. On auscultation of his chest he has widespread wheeze.

Interpretation

This patient has anaphylaxis, an IgE mediated type 1 hypersensitivity reaction. Exposure to an allergen causes widespread mast cell degranulation, resulting in the release of vasoactive substances such as histamine, prostaglandins and tryptase. These cause the clinical picture of vasodilatation, increased capillary permeability and bronchospasm.

Management

Immediate management involves an ABC approach and may necessitate tracheal intubation. Epinephrine should be administered as soon as possible in repeated boluses of 50 micrograms intravenously or 500 micrograms intramuscularly. Intravenous chlorphenamine 10mg and hydrocortisone 200mg should be administered early. Nebulised salbutamol may help

bronchodilatation. Serum tryptase levels should be taken as per published recommendations.⁷

If the patient remains cardiovascularly unstable, an epinephrine or norepinephrine infusion should be considered.

SCENARIO 3

A 70-year-old man presents with an acute anterior myocardial infarction. He has received immediate conservative treatment for this from the medical team, but has become tachycardic, hypotensive, peripherally cold due to vasoconstriction and is oliguric.

Interpretation

This patient is likely to have cardiogenic shock. After initial ABC assessment, where available, invasive arterial monitoring will be helpful.

Several drugs are available to help augment cardiac output and blood pressure. Dobutamine, levosimendan and milrinone all increase contractility and cause vasodilatation, which reduce the afterload to the heart.

Dobutamine is the first line inotropic agent in many countries, however it does increase myocardial oxygen consumption. In contrast to its use in sepsis (where a vasopressor is usually also required) it can often be infused as a sole agent in patients with pure cardiogenic shock

Levosimendan is a relatively new drug which does not increase myocardial oxygen consumption.

The patient's haemodynamic performance after acute myocardial infarction is dictated by a number of factors:

- Site of the infarct - a predominantly left ventricular infarct is likely to cause left ventricle impairment, with pulmonary oedema and low cardiac output. A blockage of the right coronary circulation may predominantly affect the right ventricle, causing right ventricular failure, with pulmonary oedema less likely, but still a low cardiac output state.
- Coronary intervention - emergency angioplasty or stent insertion may prevent, reduce or reverse myocardial damage and is offered in many well-resourced centres.

Remember that an acute deterioration should prompt a thorough reassessment of the patient:

- **Pulmonary oedema may indicate sudden onset of severe mitral regurgitation (MR) following infarction and rupture of a papillary muscle - listen for the pan-systolic murmur of MR.**
- **Sudden loss of cardiac output or reduced blood pressure, may be due to cardiac tamponade due to ventricular rupture after MI or coronary graft leak after grafting. Echocardiography is useful to confirm or exclude tamponade.**

Notes on vasoactive drugs used in cardiogenic shock

Dobutamine

- This is a potent β_1 -agonist. It also causes some β_2 -mediated vasodilatation, but this is usually counteracted by α -mediated vasoconstriction.
- It is useful in low cardiac output states.
- It is less arrhythmogenic than isoprenaline and dopamine.

Milrinone

- Milrinone is a PDE-3 inhibitor, with use limited to specialist cardiac centres. It is useful in promotion of diastolic function in patients with poorly compliant ventricles.

Levosimendan

- Levosimendan has some benefits when compared to placebo and dobutamine in reducing mortality in acute decompensated heart failure.
- At low doses it causes an improvement in microcirculation in severe septic shock, however its use in this role remains controversial.
- It is an 'inodilator' that works by increasing troponin C sensitivity to calcium. In the heart this causes positive inotropy, while causing vasodilatation of both the peripheral and coronary circulations. Use is generally restricted to a 24-hour infusion - because of its relatively long half-life the benefits on myocardial function persist for several days.
- As it improves myocardial contractility but not oxygen demand, it can help prevent cardiac ischaemia.
- Side effects include hypotension due to vasodilatation.

SCENARIO 4

An elderly patient on the medical ward is hypotensive, bradycardic and confused. His ECG shows complete heart block with ST depression in the inferior leads.

Interpretation

This patient has complete block with adverse signs.

Management

Follow the Advanced Life Support (ALS) algorithm (see page 178). After initial assessment using an ABC approach, atropine 500mcg should be administered intravenously, repeated up to a dose of 3mg. If this fails, isoprenaline 5mcg.min⁻¹ IV or epinephrine 2-10mcg.min⁻¹ IV can be given as a bridge to transvenous pacing. Dopamine may also be considered.

Notes on vasoactive drugs used in bradycardia/complete heart block

Isoprenaline

- This is a β -adrenoceptor agonist that is used in the

management of bradyarrhythmias as a bridge to transvenous or permanent pacing.

- It has a greater chronotropic than inotropic effect.
- Side effects include angina in patients with ischaemic heart disease secondary to coronary artery hypoperfusion.

SCENARIO 5

A 23-year-old girl is brought to the Emergency Department. She is hypotensive, bradycardic and says she has taken an overdose of her father's atenolol.

Management

Beta blocker overdose is treated according to the ALS algorithm for bradycardia (page 180). However, a glucagon infusion is also used to counteract the effects of beta blockers.

Glucagon

- This is an endogenous hormone released from pancreatic alpha cells, important in blood glucose homeostasis.
- It is positively inotropic and chronotropic. It acts by increasing intracellular concentrations of cyclic AMP, resulting in an increase in calcium influx. It is also useful in calcium channel blocker overdose.

SCENARIO 6

You are asked to review a 22-year-old male motorcyclist who was involved in vehicle accident 12 hours ago. He was stable on presentation, but complained of left upper quadrant pain and was admitted to the surgical ward for observation. His heart rate is now 105bpm, his blood pressure is 125/92, he has cool hands and feet and he is extremely anxious.

Interpretation

This man has deteriorated, with hypovolaemia due to haemorrhage the most likely cause. Although his systolic blood pressure is maintained, the raised diastolic blood pressure (and lowered pulse pressure) indicates that he is maintaining his blood pressure by vasoconstriction. He has class 2 shock indicating that he has lost up to about 1500ml of blood. As a young fit man, his physiological compensation masks the fact that he is close to profound haemodynamic decompensation.

Management

We should check his airway and breathing, administer high flow oxygen, check his intravenous access and administer intravenous fluids. His haemoglobin level should be measured (although this may only fall after appropriate administration of fluid) and crossmatch 4-6 units of blood. At present there is no need for vasopressors or inotropes. Full examination shows that he is markedly tender in his abdomen, in the left upper quadrant. It is likely that he has lacerated his spleen and the surgical team should be called to assess him immediately.

Excessive fluid resuscitation may increase mortality, since full restoration of normal blood pressure may further exacerbate bleeding. It is recommended that in the short term a target mean arterial pressure of 40mmHg is appropriate or that palpation of central pulses is an acceptable end point.⁸ The concept of *talking hypovolaemia* describes resuscitation end points that target cerebral perfusion, rather than a certain blood pressure.

This man should respond well to fluid administration, but probably needs an exploratory laparotomy. Inotropes and vasopressors are not likely to be needed and if fluid therapy is insufficient, other causes of hypotension should be sought (e.g. myocardial contusion causing cardiogenic shock, anaphylaxis to an administered drug).

SAFETY ASPECTS

Vasoactive drugs are life saving therapies but also highly potent agents that should be administered by nursing and medical staff with appropriate experience and training. Preparation and checking of calculations, dosages and dilutions should be undertaken by two members of staff. A major limitation to use in poor resource settings is the unavailability of reliable infusion devices. Where available, syringe pumps are used to infuse high concentration solutions. More dilute preparations may be infused from a bag of fluid, but this should always be via an infusion device, where available. There is a significant risk of inadvertent infusion of high doses of the agent, if the infusion is run without an infusion device.

The half-life of catecholamines is 1-2 minutes and so patients receiving high doses of these drugs will tolerate interruption of delivery of the agent during syringe changes poorly. 'Double pumping' may be used - two infusions are run together into a two-way tap; the new infusion is increased as the old infusion is weaned off.

Ensure that the infusion line is clamped as the syringe is loaded into the driver, as the agent may inadvertently be administered during this process.

Most agents must be administered through a central vein, although dobutamine is generally well tolerated via a peripheral vein in adults and children.

SUMMARY

Shock is a common cause of admission to critical care units and can occur for a variety of reasons.

Inotropes are used to manipulate critically ill patients' physiology, to maintain tissue perfusion and prevent end organ damage. Most inotropes work by increasing intracellular calcium and therefore myocardial contractility. Inotropes should be used in appropriately monitored and adequately fluid resuscitated patients. In all cases, it is essential that the underlying cause of the clinical presentation is sought and addressed as soon as possible.

Box 1. Doses of commonly used inotropes and vasopressors

This chart is for example only. Doses quoted are adult doses. Please refer to local policies and check all doses prior to administration. Remember that the patient should be adequately fluid resuscitated and monitored, before starting inotropes and vasopressors. Most inotropes require central venous access for their administration and should be given through pumps to ensure accuracy.

Epinephrine (adrenaline)	
Preparation	Available as 1 in 10 000 or 1 in 1 000 dilution in ampoules or pre-filled syringes. For infusion: 1 ampoule contains 5mg of epinephrine in 5ml to be diluted in 5% dextrose to total 50ml (100mcg.ml ⁻¹)
Administration	Intravenous or intramuscular injection or infusion Cardiac arrest: 1mg (10ml of 1 in 10 000) Anaphylaxis: 50mcg bolus IV, 500mcg bolus IM
Infusion	0.01-0.15mcg.kg.min ⁻¹ increasing as required. Start at 1-5ml.h ⁻¹ and titrated according to effect
Norepinephrine (noradrenaline)	
Preparation:	1 ampoule contains 4mg of norepinephrine tartrate in 4ml to be diluted in 5% dextrose to total 40ml (100mcg.ml ⁻¹)
Administration	Intravenous infusion 0.05-0.5mcg.kg.min ⁻¹ . Start at 1-5ml.h ⁻¹ and titrated according to effect
Dopamine	
Preparation	200mg (40mg.ml ⁻¹) or 800mg (160mg.ml ⁻¹) in 5ml water with the additive sodium metabisulphite. Dilute to 50ml in 5% dextrose
Administration	Either low dose (<10mcg.kg.min ⁻¹) or high dose (>10mcg.kg.min ⁻¹) depending on desired effect
Vasopressin	
Preparation	20 units in 1ml glass vial. To be diluted with 5% dextrose
Administration	Surviving Sepsis Bundle recommends infusion of 0.03units.min ⁻¹
Dobutamine	
Preparation	250mg dobutamine in 5ml ampoule. To be diluted in either 50ml or 500ml 5% dextrose to give a 5000mcg.ml ⁻¹ or 500mcg.ml ⁻¹ dilution respectively
Administration	2.5-10mcg.kg.min ⁻¹ , higher rate if required
Milrinone	
Preparation	1mg.ml ⁻¹ in 10, 20 and 50ml vials. To be diluted in either 0.9% saline or 5% dextrose to give a 200mcg.ml ⁻¹ dilution
Administration	A loading dose of 50 mcg.kg ⁻¹ over 10mins is administered intravenously, followed by an infusion at 0.3-0.75mcg.kg.min ⁻¹
Isoprenaline	
Preparation	Isoprenaline hydrochloride 1mg in 5ml ampoule, dilute up to 50ml in 5% dextrose (20mcg.ml ⁻¹) or up to 500ml in 5% dextrose (2mcg.ml ⁻¹)
Administration	At a cardiac arrest or peri-arrest situation, infusion at 5mcg.min ⁻¹ Reduce to 0.02-0.2mcg.kg.min ⁻¹ . Reduce rate or stop infusion once the heart rate > 80bpm
Levosimendan	
Presentation	2.5mg.ml ⁻¹ solution, diluted in 5% dextrose for infusion
Administration	Initial IV bolus of 12 mcg.kg ⁻¹ over 10 minutes, followed by an infusion of 1mcg.kg.min ⁻¹ , which can be reduced to 0.05 or increased to 0.2 mcg.kg.min ⁻¹ for 24 hours
Glucagon	
Preparation	1mg of freeze-dried glucagon per ampoule . Dilute 25mg in 25ml 5% dextrose (1mg.ml ⁻¹)
Dose	An IV loading dose of 50-150 mcg.kg ⁻¹ is administered, then 0.8-1.6 mcg.kg.min ⁻¹ infusion

REFERENCES

1. Rogers J. An introduction to cardiac physiology. *Update in Anaesthesia* 2008; **27,2**: 6-10. Available at: <http://update.anaesthesiologists.org/2008/12/01/an-introduction-to-cardiovascular-physiology/>
2. ACS/ATLS, American College of Surgeons/Advanced Trauma Life Support.
3. Baelani J. et al. Availability of critical care resources to treat patients with severe sepsis or septic shock in Africa: a self-reported, continent-wide survey of anaesthesia providers. *Critical Care* 2011; **15**: R10doi:10.1186/cc9410.
4. Surviving sepsis Campaign. Sepsis Resuscitation Bundle. Available at: <http://www.survivingsepsis.org/Bundles/Pages/default.aspx>
5. De Backer D. Comparison of dopamine and norepinephrine in the treatment of shock. *N Engl J Med* 2010; **362**: 779-89.
6. Russell JA et al. Vasopressin versus norepinephrine infusion in patients with septic shock (VASST trial). *N Engl J Med* 2008; **358**: 877-87.
7. Xin Xin, Zhao Jing, Shen Le and Huang Yu-guang. Management of a patient with suspected anaphylaxis during anaesthesia. *Update in Anaesthesia* 2009; **25,2**: 26-30. Available at: <http://update.anaesthesiologists.org/2009/12/01/update-in-anaesthesia-volume-25-number-2-2009/>
8. Bickell WH, Wall MJ, Pepe PE, et al. Immediate versus delayed resuscitation for hypotensive patients with penetrating torso injuries. *N Engl J Med* 1994; **331**: 1105-9