

Standardised inotrope and vasopressor guidelines

Learning package





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About this document

This learning package outlines the actions, clinical effects, indications and clinical considerations for nine commonly used inotropes and vasopressors in Australia. It has been developed to help nurses, and junior medical and allied health staff transition to areas who use these medications such as intensive care and other critical areas.

Through its Critical Care Clinical Network (CCCN), Safer Care Victoria (SCV) has released standardised clinical guidelines for nine inotropes and vasopressors. This learning package has been designed as an accompanying resource to the guidelines. It provides an introduction to the use of inotropes and vasopressors. It is not meant to replace clinical education.

Section one summarises the nine medications, providing links to our online guidelines.

Section two introduces pharmacodynamics of the medications.

Section three discusses cardiac output and its determinants.

Section four looks at the pathophysiology of shock and sepsis (as the pharmacological actions of inotropes and vasopressors make them the most commonly used tools to maintain blood pressure and cardiac function in patients who are haemodynamically compromised often secondary to sepsis).

Section five guides safe administration of inotropes and vasopressors.

After reading this document, you will be able to:

- explain the actions and clinical effects of the nine inotropes and vasopressors
- understand and list the factors of cardiac output and its determinants
- compare and contrast classifications of shock, including their clinical signs and management
- describe the definition of sepsis and key points when managing septic shock
- describe the administration and monitoring plan to assess the effects of inotropes and vasopressors and relate these effects to clinical end points.

Feedback

This is the first edition of SCV's Standardised inotrope and vasopressor learning package. We appreciate your feedback for ongoing improvement of the package.

Please contact us via email: criticalcare.clinicalnetwork@safercare.vic.gov.au.

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² Safer Care Victoria Standardised inotrope and vasopressor guidelines

1. Introducing the medications

If you care for patients who receive inotropes or vasopressors, you will need to know their specific dosage ranges, the receptors activated, the desired effects and the potential complications. This section summarises the actions and clinical effects of each of the nine medications we provide standardised guidelines for.

ADRENALINE (EPINEPHRINE)

Adrenaline is a non-selective adrenergic agonist with potent beta₁ (β_1) and moderate alpha₁ (α) and beta₂ (β_2) receptor activity.

Increased myocardial force of contraction (positive inotropic effect) and heart rate (positive chronotropic effect) occur as a result of β_1 receptor stimulation.

Systemic vascular resistance is increased overall because the stimulation of α_1 receptors results in peripheral vasoconstriction which counters the vasodilation due to β_2 receptor activation. These β_2 effects also relax bronchial smooth muscle and stabilise mast cells.

Dobutamine is predominantly a β -agonist, resulting in increased myocardial contractility with a variable effect on heart rate.

 β mediated vasodilatation occurs in the skeletal muscle beds – which may result in hypotension.

Dobutamine can be administered by continuous infusion to patients who require short-term treatment of cardiac failure secondary to acute myocardial infarction, or cardiac surgery, as it will increase cardiac output but this occurs at the cost of greater myocardial work.

The administration of dobutamine may worsen myocardial ischaemia and/or infarction due to the increase in myocardial work or due to tachycardia or hypotension.

Dopamine is a naturally occurring catecholamine that acts directly on α , β_1 and dopaminergic receptors and indirectly by releasing noradrenaline. Its actions are described as dose dependent although this distinction is not helpful in clinical practice due to marked individual variation.

- Dopaminergic actions: increased renal and mesenteric blood flow resulting in increased glomerular filtration rate, renal sodium excretion and urine output. Note that dopamine has no "renal protective effect" and administration has NOT been shown to improve renal function or patient outcome.
- B1 actions: increased myocardial contractility resulting in increased stroke volume and cardiac output.
- α actions: vasoconstriction resulting in increased systemic vascular resistance and blood pressure.

Isoproterenol hydrochloride (isoprenaline) is a synthetic sympathomimetic amine that is structurally related to adrenaline but acts almost exclusively on β receptors.

It acts on both β_1 and β_2 receptors causing an increase in heart rate, automaticity, contractility, diastolic blood pressure, systolic blood pressure, and myocardial oxygen demand and, at the same time, causing significant bronchodilation.

Levosimendan enhances the calcium sensitivity of contractile proteins by binding to cardiac troponin C in a calcium-dependent manner.

Levosimendan increases the contraction force but does not impair ventricular relaxation. In addition, levosimendan opens adenosine triphosphate (ATP) sensitive potassium channels in vascular smooth muscle, thus inducing vasodilatation of systemic and coronary arterial resistance vessels and systemic venous capacitance vessels.

In patients with heart failure, the positive inotropic and vasodilatory actions of levosimendan result in an increased contractile force, and a reduction in both preload and afterload, without adversely affecting diastolic function. However, for acute decompensated heart failure there is limited evidence of short or long term benefit.

The use of levosimendan should be guided by heart failure specialists.^{1,2}

Metaraminol bitartrate (metaraminol) is a potent synthetic sympathomimetic amine that acts on both α and β_1 receptors but has no effect on β_2 receptors. It causes peripheral vasoconstriction and has a positive inotropic effect resulting in increased systemic blood pressure (both systolic & diastolic).

The pressor effect begins 1-2 minutes after intravenous injection and 10 minutes after intramuscular injection, and lasts from 20 minutes to 1 hour. It also has a positive inotropic effect upon the heart, as well as being a peripheral vasoconstrictor. It has no chronotropic action and may induce reflex bradycardia.

Milrinone is a positive inotrope and vasodilator, with little chronotropic activity, that also improves left ventricular diastolic relaxation.

It is administered by intravenous infusion. It is a selective inhibitor of peak III phosphodiesterase isoenzyme (phosphodiesterase inhibitor) in cardiac and vascular muscle. It produces slight enhancement of atrioventricular node conduction, but no other significant electro-physiological effects.

NORADRENALINE (NOREPINEPHRINE)

A naturally occurring sympathomimetic agent which acts as an agonist on α_1 , α_2 and β_1 receptors. Its main use is as a vasopressor in hypotensive states associated with an acceptable cardiac index.

Its primary effect is peripheral vasoconstriction. Most vessels constrict, except the brain, the heart (coronary vessels dilate) and the kidneys (unless high doses are used).

VASOPRESSIN (ARGIPRESSIN)

Vasopressin is a potent vasopressor which is an analogue of the posterior pituitary hormone antidiuretic hormone.

Vasoconstrictor effects are through the V_1 vascular receptors. As it acts via different receptors than other vasoconstrictor agents; it may lead to significant reductions in noradrenaline requirements.

2. About inotropes and vasopressors

Due to the frequency with which these drugs are used and the effects they can have on the cardiovascular system, it is essential you understand their actions in order to provide safe, effective care to the critically ill patient.³

Inotropes and **vasopressors** have excitatory and inhibitory actions on the heart and vascular smooth muscle. They also effect the metabolic, central nervous system and presynaptic autonomic nervous system.

They are powerful drugs used in intensive care to regulate a patient's heart rate, blood pressure and the force of the heart's contraction. They do this by working on specific receptors throughout the body.

Small changes in the rate of infusions of these agents may produce a rapid response in the patient's heart rate and blood pressure.

In some intensive care unit patients, the maintenance of blood pressure is extremely dependent on the inotrope and vasopressor infusions and hence careful titration and continuous monitoring is essential.³

USE

Inotropes

Agents that increase myocardial contractility.

Vasopressors

Agents that cause vasoconstriction by stimulating vascular smooth muscle contraction.

Vasodilators

Agents that relax the smooth muscle in blood vessels, causing:

- dilation of arterial (resistance) vessels which reduces systemic vascular resistance, and leads to a fall in arterial blood pressure
- dilation of venous vessels which decreases venous blood pressure.

INDICATIONS

Inotropes are indicated if you think the patient will benefit from increased cardiac output. For example, a patient with cardiogenic shock with acute decompensated heart failure.

Vasopressors are indicated if you think the patient will benefit from vasoconstriction and elevated mean arterial pressure. For example, a patient who is hypotensive due to septic shock and its associated vasodilatation.

Clinical considerations

A tachycardia produced by the B_1 effects of inotropes will increase the workload and myocardial oxygen requirement of the heart.

• In patients who have cardiac disease, the myocardial oxygen demands may exceed the myocardial oxygen supply and myocardial ischemia may result.

 α_1 effects cause vasoconstriction and the systemic vascular resistance or afterload increases.

- This will improve blood pressure, but it also means the heart will have to work a lot harder in order to eject the blood from the ventricle.
- Increased heart workload means increased myocardial oxygen demands.
- If this exceeds myocardial oxygen supply, then ischaemia may occur.
- This could have a significant impact on patients with a cardiac history.

As dobutamine exhibits minimal α properties, blood pressure is only supported by increased myocardial contractility; therefore if hypotension persists an α agonist may be required.

RECEPTORS, AGONISTS AND ANTAGONISTS

Modes of action

- 1. Most drugs produce their effects by acting on specific protein molecules known as **receptors.**
- 2. These receptors are activated by neurotransmitters or hormones. Neurotransmitters are substances that activate a receptor and produce a response.
- 3. Drugs that bind to receptors and produce a response are called **agonists**. Drugs that bind to receptors but do not activate them are called **antagonists**.
- 4. By binding to receptors, antagonists reduce the probability of transmitter substances or hormones binding to the receptor and therefore are often used to block the action of other endogenous transmitters or hormones.

Inotrope/vasopressor, clinical indication, receptor binding

Receptor activity \rightarrow + to +++++ is minimal to maximal.⁴

Drug	Clinical Indication	α ₁	β1	β2	DA	V ₁ /V ₂
Adrenaline (epinephrine)	Shock (cardiogenic, vasodilatory), cardiac arrest, bronchospasm/ anaphylaxis, symptomatic bradycardia	+++++	+++++	+++	N/A	N/A
Noradrenaline (norepinephrine)	Shock (cardiogenic, vasodilatory), low cardiac output with low systemic vascular resistance	+++++	+++	++	N/A	N/A
Dobutamine	Low cardiac output (decompensated heart failure, cardiogenic shock, sepsis induced myocardial dysfunction)	+	+++++	+++	N/A	N/A
Isoprenaline	Heart block and brady arrhythmias	0	+++++	+++++	N/A	N/A
Metaraminol	Acute hypotension	+++++	+	0	N/A	N/A
Vasopressin (argipressin)	Shock (cardiogenic, vasodilatory), cardiac arrest	N/A	N/A	N/A	N/A	+++++
Dopamine	Low cardiac output increases myocardial contractility	+++	+++	+++	+++++	N/A

*Note: DA= dopamine , V_1/V_2 = vasopressin 1/vasopressin 2

Receptor type	Location	Primary action(s) when stimulated
α ₁	Found primarily in vascular smooth muscle	 Vasoconstriction Activation of α1 adrenergic receptors on arterial vascular smooth muscle cells results in smooth muscle contraction and increase in systemic vascular resistance It results in peripheral vasoconstriction
β1	Found in the heart and intestinal smooth muscle	 Increased contractility automatically, atrioventricular conduction and heart rate Stimulation of β1 adrenergic receptors results in enhanced myocardial contractility through calcium mediated facilitation of the actin-myosin complex binding with troponin C It also enhances chronicity through calcium channel activation It results in an increase in heart rate and contractility
β2	Bronchial vascular and uterine smooth muscle	 Vasodilation and bronchial dilation Stimulation of β₂ adrenergic receptors on vascular smooth muscle cells through a different intracellular mechanism results in increased calcium uptake by the sarcoplasmic reticulum and vasodilation This causes bronchodilation and dilation of coronary arteries
DA	Found in the renal and mesenteric vessels	 Increased blood flow to the kidneys and mesentery Stimulation of dopaminergic receptors in the kidney and splanchnic vasculature results in renal and mesenteric vasodilation
V ₁ and V ₂ receptors	V ₁ - found in vascular smooth muscles V ₂ - found in the renal collecting duct	 Stimulation of V₁ receptors in the vascular smooth muscle mediates constriction Stimulation of V₂ receptors in the renal collecting duct, enhances the permeability of the collecting duct and mediates water reabsorption

3. Cardiac output and its determinants

CARDIAC OUTPUT

The amount of blood ejected from the heart in litres/minute.

Normal cardiac output = 4-8 L/min

The determinants of cardiac output are:

- heart rate
- stroke volume

The determinants of stroke volume are:

- preload
- afterload
- contractility

Cardiac Output = Heart Rate x Stroke Volume

Mechanisms that regulate cardiac output are:

- the autonomic nervous system by altering the heart rate, contractility, preload and afterload
- the parasympathetic nervous system by slowing down the heart rate
- the sympathetic nervous system innervates the conduction system of the heart, the arterioles and veins.

Stimulation produces an increase in heart rate, contractility, preload (venous constriction) and afterload (arterial vasoconstriction).

CARDIAC INDEX

Cardiac index is calculated by dividing the cardiac output by body surface area, thus correcting cardiac output for the size of the patient.

Body surface area can be calculated using the patient's height and weight (the patient's cardiac monitor will usually calculate this for you).⁵

The normal range for cardiac index is 2.5–4.0 L/min/m²

HEART RATE

Number of beats per minute.

Optimal heart rate balances coronary blood flow (which takes place mainly during diastole) with cardiac output and is usually between 80 and 100 beats per minute.

Normal sinus rhythm indicates atrioventricular synchrony and maximises cardiac efficiency.

STROKE VOLUME

The amount of blood ejected from the heart with each beat.

Determined by preload, afterload and myocardial contractility.

Can be manipulated by fluids, inotropes, vasopressors and vasodilators.

CONTRACTILITY

The ability of the myocardial muscle fibres to shorten independent of preload and afterload.

It is the ability of the heart to contract and the force at which it does so.

The force of contraction is determined by the concentration of calcium ions in the cells

Increase contractility can be increased by flooding cell with more calcium (β agonist) or by keeping more calcium in the cell and not letting it escape.

Myocardial contractility is enhanced if necessary by using inotrope pharmacological agents, such as adrenaline, dobutamine, milrinone and levosimendan. The choice of agent is individualised to the specific clinical situation. ⁵

PRELOAD

Pressure or stretch exerted on the walls of the ventricle by blood filling at end diastole.

'The heart will pump what it receives': Starling's law of the heart.

The Frank-Starling mechanism describes the ability of the heart to change its force of contraction (and hence stroke volume) in response to changes in end-diastolic myocardial fibre length.

In other words, if the end diastolic volume increases, there is potential for a corresponding increase in stroke volume.

Preload = reflects volume status

Increases with hypervolaemia

Decreases in hypovolaemia - may result from bleeding, fluid loss or vasodilation

AFTERLOAD

Resistance to left ventricular contraction.

It is assessed by measuring systemic vascular resistance.

It is the degree of constriction or dilatation of the arterial circulation.

High afterload increases myocardial work load and oxygen demand and decreases cardiac output.

Afterload = the resistance left ventricle must overcome to circulate blood

Increases with:

- Hypothermia
- Hypertension
- Vasoconstriction
- Aortic valve stenosis
- Left ventricular dilatation

4. Shock

Shock is a state of cellular and tissue hypoxia due to reduced oxygen delivery and/or increased oxygen consumption or inadequate oxygen utilisation. This ultimately results in organ failure. Many of the patients in intensive care present with or develop different types of shock.

CLASSIFICATION OF SHOCK⁶

- a) Hypovolaemic
- b) Cardiogenic
- c) Obstructive
- d) Distributive

Shock is a dynamic process, and more than one classification can contribute at any one time.

Figure 1⁷ outlines an initial assessment of a patient in shock (Panel A), relative frequencies of the main shock types (Panel B) and a schematic representation of the four shock classifications.

The algorithm used for the initial assessment of a patient in shock starts with the most common presentation (i.e. arterial hypotension), but hypotension can be minimal or absent. CVP is central venous pressure and SvO_2 is mixed venous oxygen saturation.



Figure 1: Initial assessment of shock states⁷

DETERMINE THE AETIOLOGY OF SHOCK⁸

History

The history will often reveal valuable information to narrow down the possible causes, not forgetting that treatment is a priority in a patient with shock.

In particular, ask about previous cardiac disease, medications (especially those recently started or stopped), existing allergies and possible exposure to allergens, existing conditions such as abdominal aortic aneurysm and any recent illness or hospitalisation (which may increase the risk of sepsis or pulmonary embolism).

Examination

Rapid assessment and treatment usually occur concurrently. Cognition, pulse rate, blood pressure, and respiratory rate will reveal if a patient is improving or deteriorating with treatment

Key findings on examination:

Obstructive

- Tension pneumothorax: Jugular vein distension, tracheal deviation, difference in chest excursion, resonance to percussion and absent breath sounds in the area of the pneumothorax.
- Cardiac tamponade: Jugular vein distension, pulsus paradoxus, muffled heart sounds.
- Pulmonary embolus: tachypnoea, hypoxia, sinus tachycardia (can be difficult to differentiate clinically from other causes of shock).

Cardiogenic

- Acute myocardial infarction is the most common cause, clinical signs usually non-specific.
- New or changed murmur if valve abnormality is the cause, jugular vein distension, signs of pulmonary oedema, skin mottled and diaphoretic.

Distributive

- Spinal shock: flaccid paralysis below the motor level of the spinal lesion, palpable bladder due to urinary retention.
- Anaphylaxis: tongue and facial swelling (urgent airway control required), rash, wheeze on auscultation of lung fields.
- Septic shock: evidence of infection and hypotension, fever or hypothermia, signs specific to the area of infection, warm peripheries, petechial rash characteristic of meningococcal sepsis.

Hypovolemia

• Bleeding may be obvious or suggested by signs of trauma. Tender abdomen may be present with intra-abdominal bleeding, extensive burns can cause hypovolaemia.

Urgent investigations

- Electrocardiography to look for signs of cardiac ischaemia and potentially critical arrhythmias.
- Full blood count, serum chemistries, C-reactive protein, and lactate for evidence of sepsis, acute kidney injury, and tissue hypoperfusion; blood cultures should be taken when sepsis is suspected.
- Focused ultrasound of the abdomen and chest to demonstrate or exclude critical bleeding (e.g. tamponade, free abdominal fluid, or aortic aneurysm), evaluate cardiac function and cardiac cavity enlargement (particularly of the right ventricle in massive pulmonary embolism), assess for pneumothorax and pulmonary consolidation, and assess the diameter and filling of the inferior vena cava to determine vascular volume status.
- Arterial blood gas to assess acid-base status and oxygenation is useful in all causes of shock. The base deficit may help guide fluid resuscitation.
- Blood glucose for evidence of hypoglycaemia or hyperglycaemia, which may be a cause or a consequence of shock (e.g. diabetic ketoacidosis).
- Rapid urine pregnancy testing for women of childbearing age and pelvic ultrasound if a ruptured ectopic pregnancy is suspected.
- Chest x-ray is easily obtainable and may offer clues to the aetiology, such as a widened mediastinum in aortic disruption, haemothorax, or a globular cardiac shadow suggestive (but not diagnostic) of cardiac tamponade. Pneumonia can usually be confirmed by chest x-ray, but in early pneumonia or hypovolaemic states there is potential that an existing pneumonia will not be detected with conventional x-ray.
- Further investigations are likely to identify precise aetiology and may include ultrasound or computed tomographic scanning depending on the likely aetiology. Ultrasound and echocardiography can be performed at the bedside, whereas a patient must be stabilised before attempting to transfer to a computed tomographic scanner.

A) HYPOVOLEMIC SHOCK

Causes

Hypovolaemic shock results from intravascular fluid loss, which may be caused by:

- blood loss
- gastrointestinal loss (vomiting, diarrhoea, pancreatitis, peritonitis, etc.)
- renal (diuretics, sodium losing nephropathy)
- surface losses (burns, sweat, respiration)
- maldistribution or third space fluid sequestration "third spacing" (anaphylaxis, sepsis, crush syndrome, etc).

Figure 2: Pathophysiology of hypovolemic shock



Clinical signs

Decreased cardiac output, low blood pressure, peripheral vasoconstriction and/or tachycardia

Management

A - Maintain **airway**

- B Optimise **breathing** and **oxygenation**
- C Restore and maintain circulation
- Stop any ongoing bleeding.
- Insert two large bore cannulas.
- Fluid boluses to resuscitate intravascular space.
- Whole blood, packed cells, fresh frozen plasma, platelets if indicated and patient is bleeding or has lost blood.
- Ongoing fluid therapy to maintain circulating volume.
- Consider vasopressors, e.g. noradrenaline/norepinephrine if not responsive to fluid resuscitation; look for ongoing bleeding.⁷

B) CARDIOGENIC SHOCK

Causes

- Myocardial infarction/ischaemia.
- Trauma (including tamponade).
- Cardiomyopathy.
- Myocarditis.
- Dysrhythmia.
- Valvular/septal defects.
- Post cardiac surgery/transplantation.
- Drugs/poisons.

Pathophysiology of cardiogenic shock

There is myocardial dysfunction that leads to decreased cardiac output because of impaired contractility and stroke volume.

The compensatory mechanisms put further strain on the impaired myocardium and can increase the workload of the heart and worsen existing myocardial ischemia.

Clinical signs

Decreased cardiac output, moderate tachycardia or severe bradycardia, jugular venous pressure/central venous pressure raised or normal, peripherally cold.

Management

A - Maintain **airway**.

B - Optimise **breathing** and give high flow oxygen. Non-invasive ventilation with continuous positive airway pressure will assist/alleviate respiratory distress and treat cardiogenic pulmonary oedema.

C - Ensure that there is good access, assess and aim to treat/reverse the cause of shock.

Administer vasodilating agents and inotropes such as dobutamine that improve contractility without increasing heart rate and systemic vascular resistance.

- Administer diuretics if there are signs of heart failure and fluid overload.
- Consider intravenous glyceryl trinitrate if pulmonary oedema is present and the blood pressure is relatively stable.
- Aim is to reduce myocardial workload and oxygen demand and improve oxygen supply.

C) OBSTRUCTIVE SHOCK

Obstructive shock is characterised by obstruction of circulation in the⁹⁻¹⁰:

- great veins tension pneumothorax
- heart cardiac tamponade
- pulmonary arteries pulmonary embolism
- aorta aortic dissection.

Clinical signs

Decreased cardiac output, peripheral vasoconstriction, tachycardia, jugular venous pressure/central venous pressure often raised.

Always consider cardiac tamponade when the blood pressure is low and central venous pressure is high, pulsus paradoxus.

Management

Identify aetiology – Pulmonary computed tomographic angiography, echocardiograph, point of care ultrasound.

Supportive therapy

- Cautious fluid therapy.
- Vasoconstriction, with noradrenaline (increases mean arterial pressure and right ventricular coronary perfusion (for pulmonary embolus).⁹

Definitive management

- Needle thoracocentesis for tension pneumothorax.
- Pericardiocentesis or surgery for cardiac tamponade.
- Thrombolysis for pulmonary thrombo-embolism with hemodynamic instability (unless contraindicated).

D) DISTRIBUTIVE SHOCK

Characterised by a maldistribution of circulation from sepsis, anaphylaxis or neurogenic shock

Pathophysiology of distributive shock

The main deficit lies in the periphery, with decreased systemic vascular resistance and altered oxygen extraction. Typically, cardiac output is high, although it may be low as a result of associated myocardial depression.¹¹

Of these, the focus will now be on septic shock as it is the most common type of shock and continues to be associated with a high mortality especially in critically ill patients.

Clinical signs

- Distributive shock impacts cardiovascular system differently to other forms of shock.
- Increased pulse pressure, increased capillary return and warm peripheries.

SEPSIS DEFINITIONS

(Revised in 2016 – SEPSIS 3)

Sepsis is defined as 'life threatening organ dysfunction caused by the dysregulated host response to infection'.¹²

- Organ dysfunction can be represented by an increase in the Sequential (Sepsis-related) Organ Failure Assessment (SOFA) score of 2 points or more.
- Associated with an in-hospital mortality of greater than 10 per cent.

Septic shock is a more severe subset of sepsis.

Patients with septic shock are identified by:

- a vasopressor requirement to maintain a mean arterial pressure of 65 mmHg
- a serum lactate greater than 2 mmol/L
- no evidence of hypovolemia

Associated in-hospital mortality in patients with septic shock is greater than 40 per cent.

²⁰ Safer Care Victoria Standardised inotrope and vasopressor guidelines

Role of quickSOFA

- Patients with suspected infection who are likely to have a prolonged ICU stay or to die in hospital can be identified with a simple screening tool (qSOFA).
- If the patient has at least two of the following criteria then he/she is identified as being high risk: Altered mentation (Glasgow Coma Scale (GCS) <15), systolic blood pressure (SBP) < 100 mmHg, respiratory rate ≥ 22.
- The qSOFA is a prognostic indicator, not a diagnostic tool, it can be assessed quickly and repeatedly and should prompt the clinician to investigate, initiate or escalate therapy as appropriate.
- qSOFA provides simple bedside criteria to identify adult patients with suspected infection who are likely to have poor outcomes.¹²

qSOFA

- Sepsis with SBP <100 mmHg
- Respiratory rate ≥22
- Altered mentation (GCS<15)

SEPSIS INDUCED ORGAN DYSFUNCTION

Organ dysfunction secondary to sepsis may not be immediately obvious due to compensatory mechanisms, therefore any patient presenting with infection should be considered to be at risk for sepsis. Conversely unrecognised infection may be the cause of new onset organ dysfunction.





MANAGEMENT OF SEPSIS AND SEPTIC SHOCK

Hour 1 – Bundle¹³

Resuscitation and management must begin **immediately**.

A - maintain **airway**.

B - Optimise **breathing** and oxygenation (including strategies to optimize oxygen delivery and match this to consumption).

C - Ensure there is good access. Administer fluid boluses to compensate for vasodilation and decreased circulatory volume.

- Source identification culture to determine the causative organism.
- Source control remove and treat the source of infection. Administer antibiotic therapy early and in a timely manner (within one hour, as per the sepsis bundle guidelines).
- For blood pressure not responding to fluid therapy commence inotropic support and administer infusion of vasopressors to maintain systolic blood pressure and mean arterial pressure and hence prevent organ ischaemia and injury.
- Obtain blood cultures prior to antibiotic administration.
- Administer broad spectrum antibiotics.
- Measure lactate level. Remeasure if lactate > 2 mmol/L.
- Begin rapid administration 30 ml/kg crystalloid for hypotension or lactate > 4 mmol/L.
- Apply vasopressors if patient hypotensive during or after fluid resuscitation to maintain mean arterial pressure > 65 mmHg.

Key points to remember when managing a patient with shock

- Time is of the essence, intensive therapy and monitoring is essential.
- Identify cause, treat and prevent further losses.
- Assess extent of physiological disturbance.
- Identify 'deficiency' and 'replenish'.
 - Intravascular volume.

Contractility.

- Capillary permeability.
- Monitor therapy and adjust accordingly.

5. Safe administration of inotropes and vasopressors

Small changes in the rate of infusions of these agents may produce a rapid response in patients' heart rate and blood pressure. In some ICU patients, the maintenance of blood pressure is extremely dependent on the inotrope and vasopressor infusions and hence careful titration and continuous monitoring is essential.

The above drugs must always be administered via a central venous catheter (CVC) (the only exception being during an emergency situation).

Inotropes and vasopressors should never be purged or bolused. Purging results in uneven doses of the drug being given to the patient and as a result the patient can have huge changes in their haemodynamic parameters.

Inotropes and vasopressors need to be regulated by continuous infusion to maintain a consistent dose delivery and haemodynamic control. Continuous monitoring of blood pressure with arterial lines is necessary to help close monitoring and titration of therapy.

ICU patients commonly require multiple drug infusions together with intermittent drug administration. These infusions and drugs need to be distributed amongst the available lumens according to safe administration, drug compatibilities and the number of lumens available.¹⁴

Issues to consider in safe administration

- How 'secure' the lumen is, with the more distal lumens being the most secure (i.e. drug delivery is less likely to be affected if the line migrates outwards). In general, the most distal lumen should be reserved for emergency drug access and the second most distal lumen reserved for vasoactive drugs.
- The use of double/multiple concentrations with inotropes and vasopressors is not considered best practice. For patients on fluid restrictions, aim to optimise their fluid management in other ways.
- The rate of administration of drugs on the same lumen (co-administration of a fast-running drug can increase the delivery of a slow running drug through the venturi effect. This can result in unexpected cardiovascular changes if a drug is bolused through a lumen through which a vasoactive drug is also being delivered).

Drug administration is also limited by drug compatibilities. All lines should be monitored for the formation of precipitates when more than one drug is delivered to a lumen.

The ongoing need for a central venous catheter should be reviewed daily and the central venous catheter removed if it is no longer necessary.

USING THE CENTRAL VENOUS CATHETER

The distal lumen

- Opens at the catheter tip and is the most secure lumen.
- Reserved for central venous catheter measurements, blood specimen collection and emergency drug administration.

May be used for intermittent drug administration if there is no other option.

Medial lumen/s

Second most distal lumen (opening 2 cm from the tip) and is the second most secure lumen.

Vasoactive drugs should be infused via this lumen (depending on compatibilities):

- Adrenaline (epinephrine)
- Dopamine
- Dobutamine
- Isoprenaline
- Milrinone
- Noradrenaline (norepinephrine)
- Vasopressin (argipressin)

Proximal lumen

If limited access, other infusions may run through this lumen provided they are physically compatible and will not be bloused.⁴

Not appropriate for infusing vasopressors or inotropes due to the risk for extravasation of drug into tissue.

Figure 4: Four lumen central venous catheter



Worksheet

1. Discuss the response elicited when the following receptors are activated:

- α₁
- β1
- β₂
- V₁ & V₂

2. Why is dobutamine a useful inotrope for patients in cardiogenic shock?

- 3. List the actions and usages for adrenaline.
- 4. Why is noradrenaline useful drug for septic shock?

5. What is the dose in mcg/min of a noradrenaline infusion (concentration 6 mg/100 ml) running at 10 mls/hr for a 70 kg patient?

6. What is the maximum infusion rate for vasopressin when used for shock?

7. What are some of the safety considerations when caring for patients with inotrope and vasopressor or vasodilator infusions?

8. Define shock. How is shock classified into four different types?

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