

## CMEARTICLE

## Management of circulatory shock and hypotension

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*A 35-year-old man who was admitted to the intensive care unit for dengue fever developed hypotension on Day 2 of hospitalisation. He had no significant past medical history. His height was 1.7 m and weight was 70 kg. In the past 24 hours, he had received 3 L of intravenous normal saline but had passed urine only twice. He was alert and there was no obvious blood loss. His vital signs were as follows: temperature 37°C, pulse rate 120/min, respiratory rate 20/min, blood pressure (by oscillometry in both arms) 80/60 mmHg. Capillary refill time was six seconds, and venous lactate was 5 mmol/L.*

## IDENTIFICATION OF SHOCK

The patient had circulatory shock, marked by a delayed capillary refill time of six seconds (normal  $\leq 3$  seconds).<sup>(1)</sup> Circulatory shock is a state of low tissue oxygenation (tissue hypoxia) owing to oxygen supply-demand mismatch (i.e. oxygen supply is insufficient for end-organ demands) or impaired oxygen utilisation (e.g. due to mitochondrial dysfunction). Persistent circulatory shock will eventually lead to end-organ damage. The patient also had hypotension, which is defined as a systolic blood pressure  $< 90$  mmHg<sup>(2)</sup> or a mean arterial pressure  $< 65$  mmHg.<sup>(1)</sup> Mean arterial pressure is, in turn, defined as the sum of one-third of the systolic blood pressure and two-thirds of the diastolic blood pressure.

Oxygen supply is predominantly determined by cardiac output, haemoglobin concentration and arterial blood oxygen saturation. Blood pressure is determined by both cardiac output and systemic vascular resistance. Given this dual dependency for blood pressure, low blood pressure can occur even in patients with high cardiac output if systemic vascular resistance is very low. Low cardiac output can affect both oxygen supply and blood pressure, and circulatory shock and hypotension can co-exist. However, discordant situations can occur. Circulatory shock can occur in the absence of hypotension (i.e. occult hypoperfusion) if cardiac output is low and systemic vascular resistance is very high. Hypotension can also occur in the absence of circulatory shock if hypotension is solely due to low systemic vascular resistance (i.e. cardiac output is preserved), or if the impact of low cardiac output is counterbalanced by high haemoglobin concentration, high oxygen saturation and low end-organ demand.

## GENERAL APPROACH TO SHOCK MANAGEMENT

The approach to shock management (Fig. 1) comprises four general steps: (1) monitor perfusion; (2) manage cause; (3) maintain blood pressure; and (4) match supply to demand. These four steps can be performed sequentially or concurrently. The steps should be repeated whenever perfusion is impaired and shock persists.

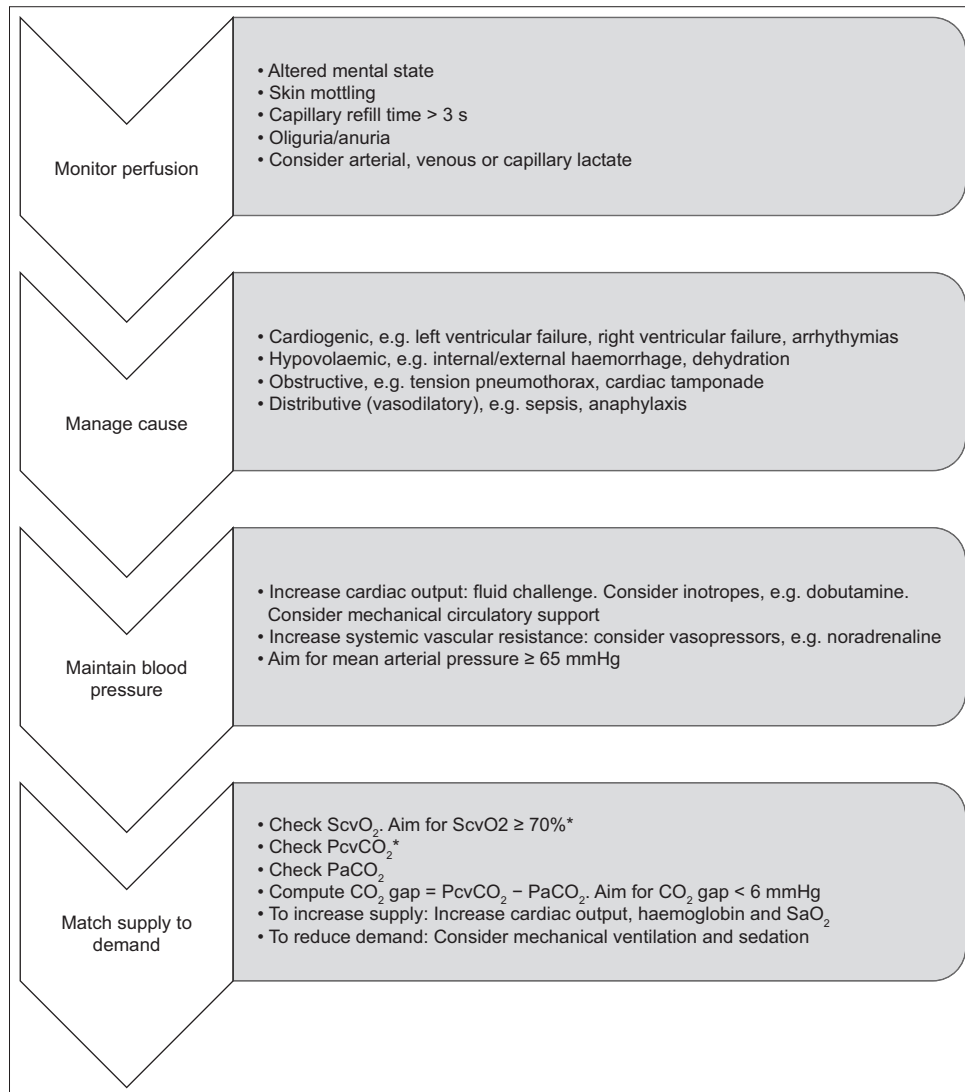
The first step involves identification of hypoperfusion, which can be detected clinically (altered mental state, delayed capillary refill time, skin mottling, oliguria) or via lactate testing (Table I).<sup>(3)</sup> To quantify the degree of hypoperfusion, either capillary refill time or lactate measurements should be carried out. Capillary refill time is particularly valuable for frontline clinicians who do not have access to lactate testing.

The second step for shock management involves uncovering and treating the cause of circulatory shock. The same aetiological framework also applies to hypotension. Four broad pathophysiological causes may be present, namely cardiogenic, hypovolaemic, obstructive and distributive (vasodilatory).<sup>(2)</sup> These causes can coexist, such as in sepsis, where septic cardiomyopathy, dehydration and vasodilatation can all contribute to shock. It might be difficult to assess the aetiology based on clinical examination alone. At the bedside, history-taking and physical examination should be supplemented by point-of-care echocardiography and lung ultrasonography (Table II).<sup>(4)</sup> Owing to the possibility of diagnostic uncertainty, repeated evaluation should be performed.

The third step for shock management involves maintaining adequate blood pressure. A systolic blood pressure of at least 90 mmHg<sup>(2)</sup> and a mean arterial pressure of at least 65 mmHg should be targeted.<sup>(1)</sup> Blood pressure can be measured in a non-invasive or invasive manner (Key Clinical Tool 1). To boost blood pressure, fluids should be given to patients who are fluid responsive (i.e. stroke volume should increase by at least 10% when a fluid bolus is given). Stroke volume needs to be measured accurately using either transthoracic echocardiography (measuring the left ventricular outflow tract velocity-time integral) or thermodilution methods (e.g. using a pulmonary artery catheter). If stroke volume cannot be measured, a surrogate measure may be pulse pressure (difference between systolic blood pressure and diastolic blood pressure).<sup>(5)</sup>

The probability of being fluid responsive can be tested by relying on cardiopulmonary interaction (e.g. inferior vena cava

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**Fig. 1** Diagram shows circulatory shock management. \*If ScvO<sub>2</sub> and PcvCO<sub>2</sub> measurements are not available, then one should at least meet the conventional targets for blood pressure (mean arterial pressure 65 mmHg or systolic blood pressure 90 mmHg), haemoglobin (7–9 g/dL) and SaO<sub>2</sub> (94%–98%). CO<sub>2</sub>: carbon dioxide; PaCO<sub>2</sub>: arterial carbon dioxide partial pressure; PcvCO<sub>2</sub>: central venous carbon dioxide partial pressure; SaO<sub>2</sub>: arterial oxygen saturation; ScvO<sub>2</sub>: central venous oxygen saturation

variability, pulse pressure variation and stroke volume variation) or by using functional haemodynamic tests (e.g. end-expiratory occlusion, passive leg raising). However, all of these methods are imperfect and may not be available outside of intensive care units.<sup>(6)</sup> If fluid responsiveness cannot be assessed with confidence, a fluid challenge should be performed, using a fast bolus of a crystalloid solution (e.g. 500 mL of normal saline for < 30 minutes).<sup>(7)</sup> The fast fluid infusion rate can be assured if fluid is administered using an infusion pump; for example, setting the pump at 1,200 mL/h would mean that 500 mL of fluid will be given over 25 minutes. After volume expansion has been attempted, continued hypotension should be treated with a vasopressor (e.g. noradrenaline). If cardiac contractility is known to be low, inotropes (e.g. dobutamine) can be considered. Early use of vasopressors and inotropes can be facilitated by peripheral administration before a central venous catheter is available.<sup>(8)</sup> At the earliest opportunity, a central venous line should be inserted for further monitoring and resuscitation.

The final step for shock management involves matching oxygen supply to end-organ demand. This step requires a central venous catheter or peripherally inserted central catheter with its tip around the junction of the superior vena cava and the right atrium. In this position, blood drawn from the catheter would be the ‘central venous’ blood; blood gas analysis would yield the central venous oxygen saturation (ScvO<sub>2</sub>) and the central venous carbon dioxide partial pressure (PcvCO<sub>2</sub>). Paired assay of arterial blood would provide the arterial carbon dioxide partial pressure (PaCO<sub>2</sub>) and CO<sub>2</sub> gap (Key Clinical Tool 2). In general, oxygen supply can be improved via increases in stroke volume (via volume expansion in fluid-responsive patients and inotropes in patients with low cardiac contractility), haemoglobin and arterial oxygen saturation (SaO<sub>2</sub>). Oxygen demand can be reduced via mechanical ventilation and sedation. If ScvO<sub>2</sub> and PcvCO<sub>2</sub> measurements are not available, then the conventional targets for blood pressure (mean arterial pressure 65 mmHg or systolic blood pressure 90 mmHg), haemoglobin (7–9 g/dL)<sup>(9)</sup> and SaO<sub>2</sub> (94%–98%) should at least

**Table I. Methods to assess perfusion.**

Method	Performance	Interpretation	Limitations
Capillary refill time	Measured by applying firm pressure to blanch the ventral surface of a finger's distal phalanx for 10 s	Normal: $\leq 3$ s Abnormal: $> 3$ s	Inter-observer variability. Falsely abnormal due to cold environment
Skin mottling	Assessed visually as discoloration of the skin due to reduced skin blood flow	Normal: No mottling Less severe: Skin mottling restricted to the knee cap More severe: Skin mottling extending beyond the knee cap	Cutaneous vasculitis can result in skin mottling without shock. Falsely abnormal due to cold environment
Urine output	Measured via an indwelling urinary catheter	Oliguria: $< 0.5$ mL/kg/h	Advanced kidney disease can result in oliguria without hypoperfusion
Lactate	Point-of-care or laboratory testing of arterial, venous or capillary blood	Abnormal: $> 2$ mmol/L Severe elevation: $> 4$ mmol/L	Beta-agonist use, metformin use and malignancy can elevate lactate without hypoperfusion

**Table II. Causes of circulatory shock or hypotension.**

Pathophysiological mechanism	Causes	Selected point-of-care ultrasonography features*
Cardiogenic	Left ventricular failure	Poorly contracting left ventricle
	Right ventricular failure	Poorly contracting right ventricle
	Valvular rupture	Valvular regurgitation demonstrated by color Doppler
	Ventricular septal rupture	Shunt flow through the interventricular septal defect demonstrated by color Doppler
	Severe tachy-arrhythmia or brady-arrhythmia	Abnormal cardiac contractions (better diagnosed using an electrocardiogram)
Hypovolemic	Dehydration; external haemorrhage; internal haemorrhage	Small left ventricle at end-diastole. Narrow and collapsible inferior vena cava (non-ventilated patient). Narrow and distensible inferior vena cava (positive pressure ventilation)
Obstructive	Pericardial tamponade	Large pericardial effusion ( $> 2$ cm in thickness) with diastolic collapse of the right ventricle
	Massive pulmonary embolism	Severely dilated right ventricle (right ventricle-to-left ventricle end-diastolic area ratio $\geq 1$ ). Occasionally, a thrombus in transit is seen in the right heart
	Tension pneumothorax	A-profile on lung ultrasonography (horizontal repetitions of the pleural line) <i>and</i> no lung sliding <i>and</i> no lung pulse (no cardiac pulsations transmitted to the pleura) <sup>†</sup>
Distributive (vasodilatory)	Sepsis; anaphylaxis; adrenal crisis; myxoedema; neurogenic shock; liver failure	No specific features

\*These selected ultrasonography features should be identifiable by most ultrasonography operators, and are not meant to be comprehensive. †Chest radiography may be performed where feasible to confirm the presence of pneumothorax.

be met.<sup>(10)</sup> Mechanical circulatory support (e.g. veno-arterial extracorporeal membrane oxygenation) may be required as a last resort for refractory shock.

**Key clinical tool 1: blood pressure measurement**

Blood pressure should be measured using a sphygmomanometer or an oscillometric device, using an appropriately sized cuff. This cuff is most commonly applied at the brachial artery, although ankle or thigh blood pressure measurements will be necessary if satisfactory cuff placement is not possible in the arms.<sup>(11)</sup> For accurate and continuous blood pressure monitoring in critically ill patients, invasive blood pressure measured via an arterial line is the reference standard. Although the more distal positions of arterial line sites give higher systolic blood pressure readings, the mean arterial

pressure is similar across sites and is the preferred metric for blood pressure evaluation.

For accurate invasive blood pressure measurement, care should be taken with regard to three technical details.<sup>(12)</sup> Firstly, the arterial line must be zeroed by transiently opening the line to atmospheric pressure and pressing the 'zero' button on the monitoring device. Secondly, the arterial line must be levelled by placing the transducer at the level of the aortic root (i.e. phlebostatic axis), which is marked by the intersection of the fourth intercostal space and the mid-axillary line. Thirdly, the arterial line must be appropriately damped, which can be checked by performing a saline flush and looking for 1–2 oscillations of the arterial line waveform after the fast flush. If no oscillations are present, the arterial line is over-damped and any line obstruction by air bubbles, clots and kinks must be fixed. If  $> 2$  oscillations

**Table III. Oxygen supply and demand analysis in shock.**

ScvO <sub>2</sub>	CO <sub>2</sub> gap*	Interpretation	Treatment
< 70%	Not needed†	Supply < demand	Improve supply by increasing cardiac output, haemoglobin or arterial oxygen saturation. Consider mechanical ventilation and sedation to reduce demand.
≥ 70%	≤ 6 mmHg	Supply > demand	Treat causes of mitochondrial dysfunction (e.g. sepsis, cyanide poisoning).
≥ 70%	> 6 mmHg	Preserved metabolism in ischaemic tissue; low cardiac output	Improve cardiac output by volume expansion in fluid-responsive patients. For patients with low cardiac contractility, consider inotropes (e.g. dobutamine).

\*CO<sub>2</sub> gap = PcvCO<sub>2</sub> – PaCO<sub>2</sub>. †If this is measured, a high CO<sub>2</sub> gap > 6 mmHg indicates low cardiac output, which should then be improved. CO<sub>2</sub>: carbon dioxide; PaCO<sub>2</sub>: arterial carbon dioxide partial pressure; PcvCO<sub>2</sub>: central venous carbon dioxide partial pressure

are present, the arterial line is under-damped (e.g. due to stiff non-compliant tubing), leading to falsely high systolic blood pressure and falsely low diastolic blood pressure, although the mean arterial pressure will remain accurate.

**Key clinical tool 2: ScvO<sub>2</sub> and CO<sub>2</sub> gap**

These clinical tools are key for assessing oxygen supply and demand.<sup>(13)</sup> When end-organs undergo aerobic metabolism, oxygen is taken up from blood and CO<sub>2</sub> is released into blood. Venous blood returning to the heart would then have lower oxygen content and higher CO<sub>2</sub> content compared to that of the arterial blood being supplied to the end-organs. Venous blood returning to the heart is assayed around the junction of the superior vena cava and the right atrium, via central venous catheters or peripherally inserted central catheters, allowing measurements of ScvO<sub>2</sub> and PcvCO<sub>2</sub>. Arterial blood can be simultaneously sampled via an invasive arterial cannula or via intermittent arterial blood draws, allowing measurement of arterial PaCO<sub>2</sub>.

High demand compared to supply would render the ScvO<sub>2</sub> lower than 70%. When such a patient has circulatory shock, efforts to increase supply or reduce demand are warranted. A low demand compared to supply would mean that the ScvO<sub>2</sub> would be 70% or higher. When such a patient has circulatory shock, two possibilities could exist. Firstly, oxygen demand is low owing to damaged tissue metabolism, which is, in turn, due to mitochondrial dysfunction (e.g. sepsis, cyanide poisoning), necessitating treatment of the underlying cause. Secondly, oxygen demand is low owing to reduced oxygen extraction by ischaemic tissue in the setting of poor blood flow into end-organs, which can be reversed by improving cardiac output. Differentiating these two possibilities requires the CO<sub>2</sub> gap, which is the difference between PcvCO<sub>2</sub> and PaCO<sub>2</sub>. The CO<sub>2</sub> gap would be 6 mmHg or less if tissue metabolism is damaged, while it would be > 6 mmHg if tissue metabolism is preserved within ischaemic tissues. The widened CO<sub>2</sub> gap in the context of poor blood flow into end-organs is due to continued diffusion of CO<sub>2</sub>, which has higher blood solubility than O<sub>2</sub>, from ischaemic tissues into the venous blood. Table III summarises the interpretation of the ScvO<sub>2</sub> and CO<sub>2</sub> gap.

**TAKE HOME MESSAGES**

1. Circulatory shock is the state of low tissue oxygenation (tissue hypoxia) due to oxygen supply-demand mismatch (i.e. oxygen supply is insufficient for end-organ demands) or impaired oxygen utilisation (e.g. due to mitochondrial dysfunction).
2. Hypotension is defined as a systolic blood pressure

- < 90 mmHg or a mean arterial pressure < 65 mmHg. Circulatory shock can occur in the absence of hypotension (i.e. occult hypoperfusion).
- 3. Oxygen supply is predominantly determined by cardiac output, haemoglobin concentration and arterial blood oxygen saturation. Blood pressure is determined by cardiac output and systemic vascular resistance.
- 4. The approach to shock management comprises four general steps: monitor perfusion, manage cause, maintain blood pressure and match supply to demand.
- 5. Four broad pathophysiological causes may be present and may coexist: cardiogenic, hypovolaemic, obstructive and distributive (vasodilatory).

*Given the presence of circulatory shock, the patient underwent a thorough physical examination, which revealed cool peripheries and mild peripheral oedema. Point-of-care echocardiography using a handheld device demonstrated poor biventricular contraction and no large pericardial effusion. A fluid challenge with 500 mL of normal saline over 25 minutes did not improve blood pressure. Low-dose noradrenaline was started, targeting a mean arterial pressure of 65 mmHg. The ScvO<sub>2</sub> was 60% despite an oxygen saturation of 96% on pulse oximetry and a haemoglobin level of 12 g/dL. Troponin I was elevated, and an electrocardiogram demonstrated sinus tachycardia and nonspecific ST/T-wave changes. An urgent bedside echocardiogram by the on-call cardiologist showed a left ventricular ejection fraction of 15%, suggesting dengue with cardiac involvement. Low-dose dobutamine was administered intravenously at 5 mcg/kg/min, after which the ScvO<sub>2</sub> increased to 70% and the CO<sub>2</sub> gap was 5 mmHg. The patient was transferred from the medical intensive care unit (ICU) to the cardiothoracic ICU for potential institution of mechanical circulatory support. Fortunately, with careful titration of fluids and dobutamine, he did not require mechanical ventilation or extracorporeal membrane oxygenation. His perfusion and left ventricular function gradually improved over the next five days, allowing him to be weaned off dobutamine.*

## REFERENCES

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## SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME (Code SMJ 202205A)

	True	False
1. Low tissue oxygenation (tissue hypoxia) can occur even when the oxygen supply exceeds tissue demand.	<input type="checkbox"/>	<input type="checkbox"/>
2. Mean arterial pressure is defined as the average of the systolic blood pressure and the diastolic blood pressure.	<input type="checkbox"/>	<input type="checkbox"/>
3. Tissue oxygen supply is predominantly determined by blood pressure, haemoglobin concentration and arterial blood oxygen saturation.	<input type="checkbox"/>	<input type="checkbox"/>
4. Circulatory shock can occur in the absence of hypotension.	<input type="checkbox"/>	<input type="checkbox"/>
5. A capillary refill time of six seconds always indicates circulatory shock.	<input type="checkbox"/>	<input type="checkbox"/>
6. Skin mottling limited to the knee caps excludes circulatory shock.	<input type="checkbox"/>	<input type="checkbox"/>
7. In fluid-responsive patients, systolic blood pressure should increase by at least 10% following a fluid bolus.	<input type="checkbox"/>	<input type="checkbox"/>
8. A fluid challenge consists of 500 mL of crystalloid solution given over < 30 minutes.	<input type="checkbox"/>	<input type="checkbox"/>
9. Noradrenaline is a medication that can improve blood pressure.	<input type="checkbox"/>	<input type="checkbox"/>
10. Noradrenaline is a medication that must be given only via central lines.	<input type="checkbox"/>	<input type="checkbox"/>
11. In a patient with circulatory shock, a central venous oxygen saturation of 60% indicates inadequate oxygen supply to satisfy tissue demand.	<input type="checkbox"/>	<input type="checkbox"/>
12. In a patient with circulatory shock, a central venous oxygen saturation of 80% excludes the possibility of inadequate oxygen supply.	<input type="checkbox"/>	<input type="checkbox"/>
13. In a patient with septic shock, a central venous oxygen saturation of 70% indicates haemodynamic optimisation.	<input type="checkbox"/>	<input type="checkbox"/>
14. CO <sub>2</sub> gap is computed as PaCO <sub>2</sub> – PcvCO <sub>2</sub> , where PaCO <sub>2</sub> is arterial carbon dioxide partial pressure and PcvCO <sub>2</sub> is central venous carbon dioxide partial pressure.	<input type="checkbox"/>	<input type="checkbox"/>
15. A CO <sub>2</sub> gap of 8 mmHg indicates low cardiac output.	<input type="checkbox"/>	<input type="checkbox"/>
16. A CO <sub>2</sub> gap of 8 mmHg indicates anaemia.	<input type="checkbox"/>	<input type="checkbox"/>
17. In a patient with circulatory shock, the haemoglobin target should be at least 10 g/dL.	<input type="checkbox"/>	<input type="checkbox"/>
18. Ankle blood pressure may be used to detect hypotension.	<input type="checkbox"/>	<input type="checkbox"/>
19. An over-damped arterial line system will lead to falsely low mean arterial pressure.	<input type="checkbox"/>	<input type="checkbox"/>
20. An under-damped arterial line system will lead to falsely low diastolic blood pressure.	<input type="checkbox"/>	<input type="checkbox"/>

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