TURKISH JOURNAL OF EMERGENCY MEDICINE

Review Article

Access this article online

Quick Response Code:

Website: www.turkjemergmed.com

DOI: 10.4103/2452-2473.367400

Circulatory shock in adults in emergency department

Ashok Kumar Pannu*

Department of Internal Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India
**Corresponding author*

Abstract:

Circulatory shock is a common condition that carries high morbidity and mortality. This review aims to update the critical steps in managing common types of shock in adult patients admitted to medical emergency and intensive care units. A literature review was performed by searching PubMed, EMBASE Ovid, and Cochrane Library, using the following search items: ("shock" OR "circulatory shock" OR "septic shock" OR "cardiogenic shock") AND ("management" OR "treatment" OR "resuscitation"). The review emphasizes prompt shock identification with tissue hypoperfusion, knowledge of the underlying pathophysiological mechanism, initial fluid resuscitation with balanced crystalloids, norepinephrine as the preferred vasopressor in septic and profound cardiogenic shock, and tailored intervention addressing specific etiologies. Point-of-care ultrasound may help evaluate an undifferentiated shock and determine fluid responsiveness. The approach to septic shock is improving; however, confirmatory studies are required for many existing (e.g., amount of initial fluids and steroids) and emerging (e.g., angiotensin II) therapies. Knowledge gaps and wide variations persist in managing cardiogenic shock that needs urgent addressing to improve outcomes.

Keywords:

Adults, anaphylactic, cardiogenic, circulatory, management, point-of-care ultrasound, resuscitation, septic, shock, vasopressor

Introduction

Shock is a common life-threatening condition in emergency and critical care, resulting from many heterogeneous disease processes.[1,2] Early management prevents the progression of reversible organ dysfunction to an irreversible state of multiorgan failure. Management of shock can broadly be summarized into four components – (1) prompt recognition of shock; (2) assessment of the type of shock; (3) resuscitation with ventilation, intravenous fluids, and pressor therapy; and (4) diagnosis and treatment of the underlying etiology.

Definition

Shock is a clinical manifestation of circulatory failure causing tissue hypoperfusion and inadequate cellular oxygen supply. Tissue hypoperfusion is central to the definition of shock, which is clinically apparent through the three "windows" of the body – skin, kidney, and brain and biochemically with hyperlactatemia indicating impaired oxidative phosphorylation [Box 1].[1-5] Hypotension is typically present with accompanying tachycardia. Systolic blood pressure (SBP) <90 mmHg or the mean arterial pressure (MAP) <70 mmHg usually defines hypotension, which, however, may not be applied to persons with long-standing hypertension, where the magnitude of reduction in the blood pressure is more important.[1,2,5]

How to cite this article: Pannu AK. Circulatory shock in adults in emergency department. Turk J Emerg Med 2023;23:139-48.

Submitted: 19-09-2022
Revised: 12-11-2022
Accepted: 13-11-2022
Published: 09-01-2023

ORCID:
AKP: 0000-0002-4476-3478

Address for correspondence:
Dr. Ashok Kumar Pannu, 4th Floor, F Block, Nehru Hospital, Postgraduate Institute of Medical Education and Research, Chandigarh - 160 012, India.
E-mail: gawaribacchi@gmail.com

Pathophysiology and Classification of Shock

The major determinants of tissue oxygen supply are cardiac output (CO), which is a product of stroke volume (SV) and heart rate (HR) (i.e., CO = SV x HR), and arterial oxygen content. The SV mainly depends on three parameters – (1) *C*ontractility of cardiac muscles; (2) *A*fterload, i.e., the force against which ventricles must contract (the systemic vascular resistance); and (3) *P*reload, i.e., length of the myocardial muscle at the onset of contraction (the ventricular end-diastolic volume) (can be remembered as an acronym SV-*CAP*). Thus, derangement of one or more of these parameters determining tissue oxygen supply can cause shock and also categorize shock into four major types [Figure 1].[1,2]

Resuscitation

Early resuscitation aiming for adequate hemodynamic stabilization is essential to prevent the progression of tissue hypoperfusion and multiorgan failure. Resuscitation consists of three main components – *V*entilation, *I*ntravenous fluids (IVFs), and *P*ressor therapy, which can be easily remembered as "*VIP* resuscitation."[1,2,6] Ventilation (mask, high-flow nasal cannula, or endotracheal intubation) provides adequate oxygen delivery to the organs, IVF therapy maintains adequate intravascular volume, and pressor support (vasopressors and/or inotropes) increases MAP to improve tissue perfusion.

MAP is the primary driver of CO and remains the essential determinant of mean systemic filling pressure.[2,4] Thus, an increase in MAP usually results in increased tissue perfusion. The measurement using a noninvasive cuff tends to be inaccurate and unreliable. Therefore, invasive arterial blood pressure monitoring with an intra-arterial catheter should be done unless the shock is rapidly reversed.[1,5] The arterial catheter can also facilitate sampling for ABG or lactate. Serial lactate measurement may help in predicting the adequacy of resuscitation.[4,7-9] A central venous catheter (CVC) is frequently required to administer large amounts of IVF, vasoactive drugs, and other medications (e.g., antimicrobial agents in septic shock). The CVC can also monitor central venous pressure (CVP) (to guide fluid therapy) and obtain central venous oxygen saturation (ScvO2). The ScvO2 is a surrogate of mixed venous oxygen saturation; thus, serial monitoring can

Box 1: Parameters for prompt recognition of tissue hypoperfusion for shock

Parameters	Findings
Skin	Cold and clammy skin. Increased capillary refill time (>2 s)
Kidney	Reduced urine output <0.5 mL/kg/h
Brain	Altered mental status, which typically includes drowsiness, disorientation, and confusion
Hyperlactatemia	The cutoff used for an elevated blood lactate level ranges from 1.6-2.5 mmol/L

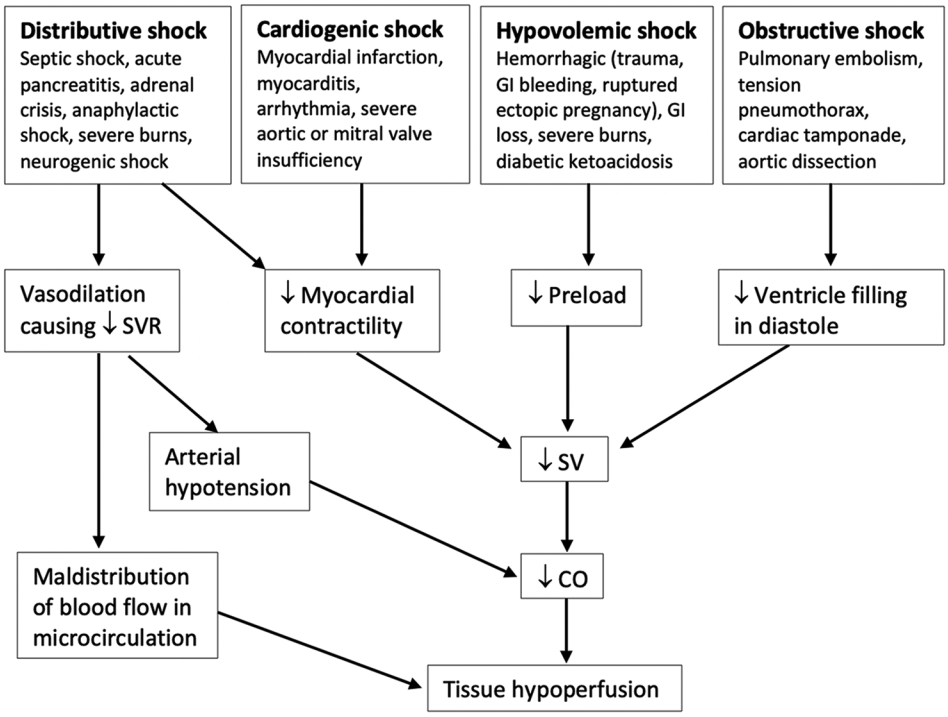

Figure 1: Etiopathogenesis of four major types of shock. CO: Cardiac output, GI: Gastrointestinal, SV: Stroke volume, SVR: Systemic vascular resistance

provide adequacy of oxygen delivery.[2,9] For example, targeting ScvO2 >70% has improved survival in septic shock, but recent data question its compulsory use.[9-13]

Ventilation

Because tissue oxygen supply depends on arterial oxygen content, oxygen supplementation is required in patients with hypoxemia to maintain an arterial saturation of 94-96%.[1,2,5,14-16] Hypoxemia may be related to the cause of shock (e.g., pneumonia, heart failure, pulmonary embolism, or pneumothorax) or the effect of shock (e.g., development of acute respiratory distress syndrome in all types of shock). Endotracheal intubation with mechanical ventilation is required in patients with persistence or worsening of hypoxemia, dyspnea, or metabolic acidosis.[1,2,5] Additionally, invasive ventilation decreases tissue oxygen demand of respiratory muscles and decreases afterload by increasing intrathoracic pressure. The sedative and neuromuscular blocking agents in mechanically ventilated patients should be minimum and intermittent (rather than continuous) to avoid worsening of hypotension.[1,5]

Intravenous Fluids

All types of shock require IVF to restore blood flow in the microvascular bed and intravascular volume.[1,2] Even cardiogenic shock should receive initial IVF to optimize cardiac filling pressures and maintain effective intravascular volume status.[17-19] However, overzealous fluid therapy results in pulmonary and peripheral edema and abdominal and other compartment syndromes and impairs oxygen diffusion.[20,21] Although fluid resuscitation is an essential component of early shock management, there is a lack of universal consensus on the type and dose of IVF and pragmatic endpoints.[20,22] However, these factors may affect patient outcomes.

Fluid resuscitation should begin with a crystalloid solution in most patients with shock.[5,23] Although colloids (e.g., albumin) are theoretically more likely to be physiological (e.g., maintaining oncotic pressure) than crystalloids, they do not offer a substantial hemodynamic benefit, and their routine use is not recommended.[5,20,23-25] Moreover, crystalloids are widely available and inexpensive. The most widely used crystalloid is 0.9% sodium chloride (normal saline). It is slightly hyperosmolar, containing higher sodium and chloride concentrations (both, 154 mEq/L) compared with normal human plasma (sodium, 135-145 mEq/L, and chloride, 94-111 mEq/L). Therefore, a large amount of administration may result in hyperchloremic metabolic acidosis, renal vasoconstriction, and acute kidney injury.[26-31] Balanced crystalloids (e.g., Ringer lactate or Hartmann solution, PlasmaLyte®) have a lower chloride content and better match human plasma. Compared to normal saline, balanced crystalloids have shown better outcomes in patients with distributive shock (septic shock and acute pancreatitis) and hypovolemic shock (gastrointestinal losses and diabetic ketoacidosis).[5,21,32-37] When larger amounts of crystalloids are required, administration of albumin (natural colloid) is suggested to achieve the MAP target early with lower net fluid balance.[5,38] Synthetic colloid (e.g., hydroxyethyl starch and gelatin) use for fluid resuscitation has been associated with increased adverse effects and no conclusive survival benefits in patients with shock.[5,39-43] Box 2 shows current recommendations on initial resuscitation with aggressive fluid therapy in common medical conditions associated with distributive and hypovolemic shock in adults.[5,35-37,43-47]

Following the initial bolus doses, it is important to identify which patients will benefit from further IVF. Dynamic measures are more useful to guide fluid resuscitation than a physical examination or static parameters alone.[5,48-50] Dynamic parameters include response after increasing preload by a passive leg raise (PLR) or an IVF bolus on CO or related parameters or point-of-care ultrasound (POCUS) measurement of inferior vena cava (IVC) diameter variation with respiratory phases. While the patient is resting in semi-recumbent (at 45° angle rather than flat), PLR is performed by placing the bed in Trendelenburg

Box 2: Current recommendations for initial fluid resuscitation in common conditions associated with distributive and hypovolemic shock

Conditions	Rate and type of IVF
Septic shock	30 mL/kg in the first 3 h (weak recommendation). Balanced crystalloids (e.g., RL) are preferred over NS
	If larger amounts of crystalloids are required, consider albumin to achieve mean arterial pressure
Diabetic ketoacidosis	10-20 mL/kg/h of RL or NS in first 1-3 h. Subsequently RL or 0.45% NS at the rate of 5-10 mL/kg/h
Acute pancreatitis	5-10 mL/kg/h targeting mean arterial pressure >65 mmHg, heart rate <100/min, and urine output >0.5 mL/kg/h. RL is preferred over NS
Adrenal crisis	20 mL/kg/h (1 L) of NS bolus, with DNS, added if hypoglycemia is present. Subsequent crystalloid according to volume status
Dengue shock	10-20 mL/kg/h of RL or NS bolus. Monitor hematocrit and volume status
	If improvement, gradually reduce IVF over the next 6 h to a rate of 2-3 mL/kg/h and maintain this infusion rate over next 24-48 h
	If no improvement, repeat a second bolus of 10-20 mL/kg/h of crystalloid or colloid over 1 h. In case of improvement, gradually reduce IVF as mentioned above. If shock persists, repeat a colloid bolus of 10-20 mL/kg/h and look for internal bleeding

DNS: 5% dextrose in normal saline, IVF: Intravenous fluid, NS: Normal saline, RL: Ringer lactate

position with the legs inclined to 45° angle and the upper section flat.[51-53] An immediate (within 60 s) assessment of an increase in CO (e.g., >10%) identifies fluid responders.[48,49,51-53] Transpulmonary thermodilution or transthoracic echocardiography is commonly used for CO or SV measurement in PLR. In resource constraint settings, an increase in pulse pressure (e.g., >15%) could be used to predict an increase in CO after PLR.[53,54] In mechanically ventilated patients, measuring changes in SV (or pulse pressure) variation during the respiratory cycle may also be considered.[48,49,51-53]

POCUS has been used to assess intravascular volume with IVC diameter and its variation with respiratory phases. During inspiration, the IVC collapses in spontaneously breathing patients and distends in patients on invasive ventilation without spontaneous respiration. During inspiration, a >42% reduction in the IVC diameter (collapsibility index) in spontaneously breathing patients, and in mechanically ventilated patients, a >15% increase in the diameter compared to expiration (distensibility index) may help predict fluid responsiveness.[48,55,56] However, the usefulness of the respiratory variation of IVC has been questioned by recent studies.[48,57-60] Alternatively, while the IVF is being administered, a cardiac scan can assess ventricle contractility with ejection fraction, and a lung ultrasound can look for the development of B lines suggesting hemodynamic pulmonary edema.[1,2]

CVC and pulmonary artery catheter (PAC , Swan-Ganz catheter) have traditionally been used for invasive hemodynamic assessment in shock.[61] Although CVC placement with a low CVP (usually <8 mmHg) is frequently used for fluid responsiveness, recent evidence finds it a poor predictor.[48,61-63] Its accuracy is further compromised by ventilator settings and lung compliance. A PAC allows direct measurement of CVP, pulmonary artery, and pulmonary capillary wedge pressure (a measure of left atrial pressure). Despite the absence of benefits from its routine use, PAC may be required in selected patients with cardiogenic shock or mixed distributive and cardiogenic shock.[64-67] Static measures such as CVP, SBP, or HR alone are poor indicators of volume status.[5] Similarly, besides capillary refill time as an adjunctive measure for septic shock, physical examination findings are not predictive of fluid responsiveness.[5,48] A shock index, the HR to SBP ratio of > 0.9 (normal range 0.5-0.7), may predict a transfusion requirement in hemorrhagic shock.[2,68] The shock index may also indicate a decrease in BP after the initiation of invasive mechanical ventilation.[69,70] Postintubation hypotension usually reflects hypovolemia and a reduction in preload.[1]

Vasoactive Drugs

Vasopressor or inotropic support is indicated if shock persists despite initial fluid resuscitation or is profound at presentation. Vasoactive drugs are used to increase MAP.[71] An initial target MAP of 65 mmHg is recommended in shock requiring vasoactive medications.[1,2,5,19] A higher target is associated with no survival benefits and increased adverse effects.[72] A CVC is usually indicated to administer vasoactive drugs as peripheral administration may cause extravasation or local tissue injury. However, the initiation of vasoactive agents should not be delayed while waiting for a CVC placement.[5,73] Table 1 shows the usual recommended dose of commonly used vasoactive agents in circulatory shock.

Vasopressors

Catecholamines or adrenergic agonists are the first-line pressor agents, given their rapid onset and short duration of action. Because stimulation of each adrenergic receptor causes both therapeutic and adverse effects, pressor therapy should be targeted to the primary pathophysiologic mechanism.[74,75] Norepinephrine remains the first-choice vasopressor in septic shock because of its predominant α-effects (increases systemic vascular resistance) and modest β1-adrenergic activity (maintains CO).[1,5,74,76] Epinephrine has potent β-effects at low doses and with higher doses, causes α-effects (similar to norepinephrine), but also increases the risk of arrhythmia, reduced splanchnic circulation, and metabolic acidosis.[77-80] Dopamine has β-effects at low doses and additional α-effects at high doses; however, these effects are weaker than norepinephrine and epinephrine. Studies have found that dopamine use increases the risk of arrhythmia and overall mortality in patients with cardiogenic and septic shock.[76,81,82] Septic shock may cause a "relative vasopressin deficiency" state.[83,84] Vasopressin acts on the vasopressin (V1)

Table 1: The usual dose of commonly used vasoactive agents in shock

Vasopressor	Usual infusion dose	Infusion rate
Norepinephrine	0.05-0.5 μg/kg/min	1-12 mL/h with 8 mg in 50 mL NS or D5
Epinephrine	0.05-0.5 μg/kg/min	1-12 mL/h with 8 mg in 50 mL NS or D5
Vasopressin	0.01-0.04 units/min (usually 0.03 units/min)	1.5-6 mL/h (usually 4.5 mL/h) with 20 U in 50 mL NS or D5
Dobutamine	5-20 μg/kg/min	2.5-10 mL/h with 500 mg in 50 mL NS or D5
Dopamine	5-20 μg/kg/min	1.2-4.8 mL/h with 800 mg in 50 mL NS or D5

D5: 5% dextrose, NS: Normal saline

receptors on vascular smooth muscle, and it reverses vasodilation and increases splanchnic blood flow. Vasopressin is recommended as a second agent for septic shock requiring a norepinephrine dose above 0.25-0.5 μg/kg/min [Figure 2].[5,84-86] Vasopressin is usually administered at a fixed dose of 0.03 units/min without titrating to the response. Doses above 0.04 units/min increase the risk of cardiac, splanchnic, and digital ischemia.[87] Other selective V1 agonists, e.g., selepressin and terlipressin, are associated with increased adverse effects and thus not indicated.[88,89] Epinephrine has been suggested as a second- or third-line vasopressor for septic shock.[5,90,91] Angiotensin II, a natural hormone, exerts marked vasoconstrictor effects by stimulating the renin–angiotensin–aldosterone system.[92] Recent trials find an adjunctive role of angiotensin II in managing distributive shock, but strong evidence for its routine clinical use is lacking.[5,92-94]

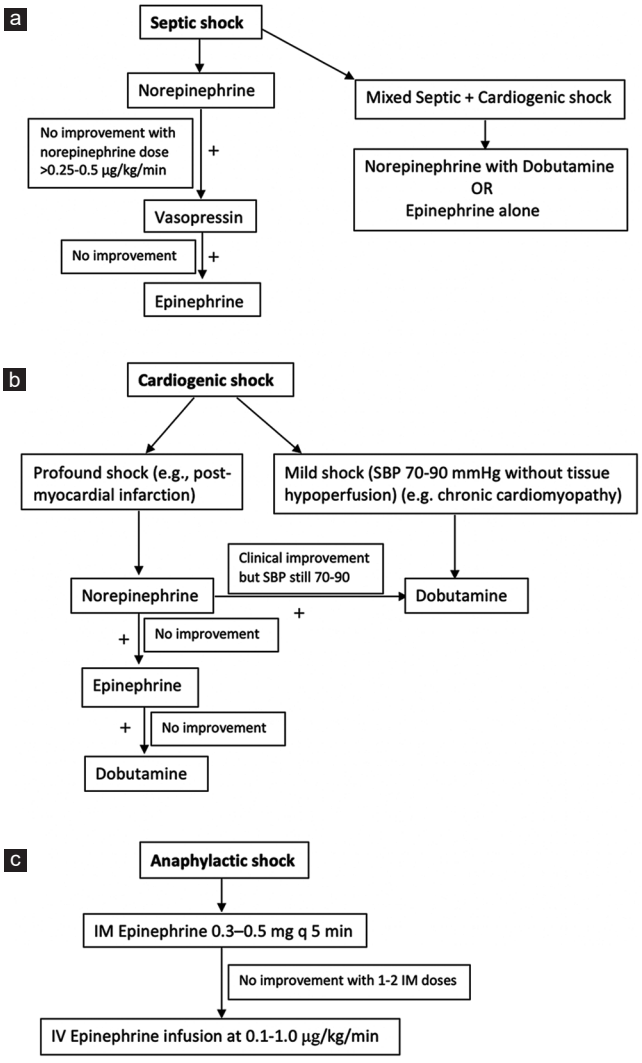

Figure 2: Recommended use of vasoactive drugs in shock - (a) septic, (b) cardiogenic, and (c) anaphylactic

Inotropes

Dobutamine, a synthetic catecholamine, is considered the inotropic agent of choice due to its predominant β1-adrenergic effects. However, its β2-adrenergic effects may worsen hypotension. Therefore, dobutamine is usually considered a first-line agent for mild cardiogenic shock without severe tissue hypoperfusion (e.g., in patients with chronic cardiomyopathy).[1,19,95,96] A vasopressor remains the first-line agent for profound cardiogenic shock (e.g., after myocardial infarction) [Figure 2].[1,19,67,95] Norepinephrine is preferred over epinephrine in cardiogenic shock.[1,96-98] Dobutamine may improve tissue perfusion and splanchnic blood flow in septic shock, but these effects may not be predictable.[99-101] In patients with septic shock and cardiac dysfunction with persistent hypoperfusion, the addition of dobutamine to norepinephrine or the use of epinephrine alone is suggested by recent guidelines.[5] Thus, it is a phosphodiesterase-3 inhibitor that increases inotropy without significant chronotropic effects and also causes vasodilation in pulmonary and systemic circulations.[102] It has a slow-onset action and long-half life, and the doses require renal modifications. It may increase the risk of arrhythmia and hypotension. Milrinone is primarily used to increase CO in patients who are not critically unstable and without profound hypotension.[19,103] Levosimendan is a calcium-sensitizing drug with both inotropic and vasodilatory properties which has been recently used in septic shock. However, it did not improve outcomes and had a risk of tachyarrhythmia.[104]

Specific Treatment of the Underlying Etiology

Specific forms of shock require therapy directed to the underlying cause. The diagnostic evaluation must begin in all patients while "VIP" resuscitation is ongoing. An initial practical approach is to make a rapid evaluation with limited clinical history, physical examination, and basic laboratory investigations directed to determine the cause and severity of shock. Basic laboratory testing may include complete blood count (with differential), biochemistry with renal and liver functions, arterial blood gas, lactate, electrocardiography, chest radiograph, and coagulation profile.[1,2] POCUS has a diagnostic value in undifferentiated shock (i.e., when the shock is recognized but the cause is not apparent) with a rapid assessment of myocardial function, intravascular volume status, and fluid collections in serous cavities.[2,105] The Rapid Ultrasound in SHock examination is an easy and widely used three-step shock ultrasound protocol [Table 2].[106] However, a recent trial did not find to improve outcomes using POCUS in patients with

undifferentiated shock.[107] The potential diagnostic clues, based on the initial evaluation, should tailor further comprehensive diagnostic testing after an early clinical stabilization.

Distributive shock secondary to sepsis remains the most common cause of shock. Recent guidelines recommend initiating broad-spectrum antimicrobials immediately, preferably within 1 h, in all patients with potential septic shock.[5] Empirical antimicrobial agents should be directed against the likely causative organism (e.g., based on the specific risks for multidrug-resistant Gram-negative bacilli, methicillin-resistant *Staphylococcus aureus*, or fungal infections) and ideally be administered after obtaining appropriate cultures. The dosing of antibiotics should be optimized based on pharmacokinetic/pharmacodynamic principles.[5,108] Table 3 shows the usual dosing of commonly used antibiotics in adult patients with septic shock. Adjunctive steroids have been widely used in septic

Table 2: Rapid Ultrasound in SHock (RUSH) protocol summary for diagnosing four major types of shock

RUSH exam steps	Hypovolemic shock	Cardiogenic shock	Obstructive shock	Distributive shock
Step 1: *Pump* - Cardiac status (LV function, RV function, pericardium)	Preserved LVEF	Reduced LVEF, dilated LV, regional wall motion abnormalities	Pericardial effusion, RV strain	LVEF may be reduced in advanced septic shock
Step 2: *Tank* - Effective intravascular volume (IVC, lung scan, pleural or peritoneal fluid)	Small and collapsible IVC, no "B" lines on lung scan (no pulmonary edema)	Distended IVC, "B" lines present (pulmonary edema), pleural effusion, or ascites	Distended IVC, no lung sliding (pneumothorax)	Normal or small IVC, pleural effusion, or ascites may suggest a source of sepsis
Step 3: *Pipes* - Large vessels (thoracic and abdominal aorta, femoral and popliteal veins)	Aortic aneurysm and dissection	-	Deep venous thrombosis (source of pulmonary embolism)	-

IVC: Inferior vena cava, LV: Left ventricle, LVEF: Left ventricular ejection fraction, RUSH: Rapid Ultrasound in SHock, RV: Right ventricle

Table 3: Usual dosing of commonly used antibiotics in septic shock

Antibiotics	Usual intravenous dose	Infusion[a]	Dose adjustment in renal dysfunction (CrCl[b] in mL/min is given in parenthesis)
Piperacillin-tazobactam	4.5 g QID	4 h	4.5 g TDS (20-40), 4.5 g BD (<20 or HD)
Meropenem	1 g TDS	3 h	1 g BD (25-50), 500 mg BD (10-25), 500 mg OD (<10 or HD)
Imipenem (-cilastatin)	1 g TDS	3 h	500 mg TDS (30-60), 500 mg BD (15-30), 250 mg BD (5-15 or <5[c] and undergoing HD)
Cefoperazone (-sulbactam)	2 g BD	3 h	1 g BD (15-30), 500 mg BD (<15)
Cefepime	2 g TDS	3 h	2 g BD (30-60), 1 g BD (10-30), 1 g OD (<10 or HD)
Ceftazidime	2 g TDS	3 h	2 g BD (30-50), 1 g BD (15-30), 1 g OD (<15 or HD)
Amikacin	15-30 mg/kg OD	30 min	Administer usual dose every 36 h (40-60), every 48 h (20-40), single dose[d] with monitoring levels (<20)
Tobramycin	5-7 mg/kg OD	30 min	Administer usual dose every 36 h (40-60), every 48 h (20-40), single dose[d] with monitoring levels (<20)
Gentamicin	5-7 mg/kg OD	30 min	Administer usual dose every 36 h (40-60), every 48 h (20-40), single dose[d] with monitoring levels (<20)
Levofloxacin	750 mg OD	1 h	750 mg every 48 h (20-50), 750 mg loading followed by 500 mg every 48 h (<20 or HD)
Ciprofloxacin	400 mg TDS	1 h	400 mg BD (10-30), 400 mg OD (<10 or HD)
Vancomycin	20-30 mg/kg loading, 15-20 mg/kg BD maintenance	4 h	Maintenance dose OD (15-50), every 72 h (<15 or HD)
Teicoplanin	12 mg/kg loading, 6 mg/kg OD maintenance	4 h	Maintenance dose 3 mg/kg OD (40-60), 2 mg/kg OD (<40 or HD)
Linezolid	600 mg BD	30 min	No dose adjustment required
Colistin (CBA 1 mg=CMS 30,000 U)	CBA 5 mg/kg loading, 2.5 mg/kg BD maintenance	2 h	Maintenance dose 1.5-2.0 mg/kg BD (30-50), 1.25-1.5 mg/kg BD (10-30), 1 mg/kg BD (<10), for HD-1.5 mg/kg BD on dialysis days and 1 mg/kg BD on other days
Polymyxin B	20,000-25,000 U/kg loading, 125,000-15,000 U/kg BD maintenance	2 h	No dose adjustment required
Tigecycline	100 mg loading, 50 mg BD	30 min	No dose adjustment required
Minocycline	200 mg loading, 100 mg BD	30 min	No dose adjustment required

[a]Extended infusion method. First dose may be given over 30 min to rapidly achieve therapeutic drug levels, [b]CrCl (in ml/min) may be estimated using Cockcroft-Gault formula=([140-age in years] × weight in kg)/(72 x serum creatinine in mg/dl) (for women, multiply by 0.85), [c]Do not administer in patients with CrCl ≤5 unless HD is started within 48 h, [d]Subsequent doses based on the serum levels. CBA: Colistin base activity, CMS: Colistimethate sodium, CrCl: Creatinine clearance, HD: Hemodialysis (intermittent, thrice weekly), BD: every 12 h, OD: every 24 h, TDS: every 8 h, QID: every 6 h

shock with persisting hypoperfusion; however, many large trials and meta-analyses have divergent mortality results.[109-111] The recent sepsis guidelines suggest initiating intravenous hydrocortisone at a dose of 200 mg/day if the shock requires norepinephrine or epinephrine at a dose ≥0.25 μg/kg/min for at least 4 h (weak recommendation; moderate quality of evidence).[5]

Distributive shock secondary to anaphylaxis requires removing the inciting allergen, administering epinephrine, and IVF resuscitation. Intramuscular epinephrine (0.3-0.5 mg q 5 min in the outer middle third of thigh or deltoid) is recommended as the first-line treatment.[112] However, if the shock is refractory to 1-2 doses of intramuscular epinephrine and fluid boluses, epinephrine infusion remains the mainstay of treatment [Figure 2].[112,113] Intravenous bolus of epinephrine is associated with a high risk of arrhythmia; however, it may be given as 10-20 μg q 2-5 min in profound shock while the infusion is being prepared.[113] Acute adrenal insufficiency requires steroid therapy, i.e., intravenous hydrocortisone with an initial bolus of 100 mg followed by daily doses of 200 mg in 2-3 divided doses.[45]

Myocardial infarction remains the most common cause of cardiogenic shock, which requires reperfusion therapy with percutaneous coronary intervention or coronary artery bypass grafting. Mechanical circulatory support devices (e.g., intra-aortic balloon pump, percutaneous ventricular assist device, and venoarterial extracorporeal membrane oxygenation) are increasingly used for temporary hemodynamic support in cardiogenic shock.[19,64] However, consensus on the indication and timing of their use remains poorly defined.[64] Management of the primary disease process is critical for obstructive shocks, such as thrombolysis or thrombectomy for pulmonary embolism, decompression of pneumothorax, or drainage of pericardial effusion.[1,2] Hemorrhagic shock requires blood product resuscitation and surgical interventions to achieve hemostasis (surgical, interventional radiology, or endoscopic).[114]

Conclusion

This review highlights recent advances in caring for adult patients with circulatory shock. Early management in the reversible phase requires rapid shock identification with clinical signs of tissue hypoperfusion ("three windows - skin, kidney and brain") and hyperlactatemia. Knowledge of underlying physiologic derangement (and classification) of shock is essential for appropriate treatment, including "*VIP*" resuscitation. Balanced crystalloids are preferred IVF for initial resuscitation. Dynamic measures, most notably PLR, should guide further fluid therapy. POCUS may have a role in diagnostic evaluation, fluid resuscitation, and treatment. Norepinephrine remains the first-line vasopressor in septic shock (strong recommendation) and profound cardiogenic shock (weak recommendation). Dopamine is no longer used in most patients with shock. Specific forms of shock require therapy directed to the underlying cause.

Acknowledgment

The author (AKP) is grateful to Mrs. Sunaina Verma for her timely intellectual assistance.

Author contributions

AKP: Conceptualization; Literature search; Writing-original draft, review and editing. The corresponding author is responsible for ensuring that the descriptions are accurate and agreed upon by all authors.

Conflicts of interest

None declared.

Funding

None declared.

References

1. Vincent JL, De Backer D. Circulatory shock. N Engl J Med 2013;369:1726-34.
2. Massaro AF. Approach to the patient with shock. In: Loscalzo J, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL, editors. Harrison's Principles of Internal Medicine. 21st ed. New York, NY: McGraw-Hill Education; 2022. p. 2235-41.
3. Vincent JL, Ince C, Bakker J. Clinical review: Circulatory shock – An update: A tribute to Professor Max Harry Weil. Crit Care 2012;16:239.
4. Vincent JL, Quintairos E Silva A, Couto L Jr., Taccone FS. The value of blood lactate kinetics in critically ill patients: A systematic review. Crit Care 2016;20:257.
5. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, *et al.* Surviving sepsis campaign: International guidelines for management of sepsis and septic shock 2021. Intensive Care Med 2021;47:1181-247.
6. Weil MH, Shubin H. The "VIP" approach to the bedside management of shock. JAMA 1969;207:337-40.
7. Jansen TC, van Bommel J, Schoonderbeek FJ, Sleeswijk Visser SJ, van der Klooster JM, Lima AP, *et al.* Early lactate-guided therapy in Intensive Care Unit patients: A multicenter, open-label, randomized controlled trial. Am J Respir Crit Care Med 2010;182:752-61.
8. Bakker J, Postelnicu R, Mukherjee V. Lactate: Where are we now? Crit Care Clin 2020;36:115-24.
9. Hallisey SD, Greenwood JC. Beyond mean arterial pressure and lactate: Perfusion end points for managing the shocked patient. Emerg Med Clin North Am 2019;37:395-408.
10. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, *et al.* Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345:1368-77.
11. ProCESS Investigators, Yealy DM, Kellum JA, Huang DT, Barnato AE, Weissfeld LA, *et al.* A randomized trial of protocol-based care for early septic shock. N Engl J Med 2014;370:1683-93.
12. ARISE Investigators, ANZICS Clinical Trials Group, Peake SL, Delaney A, Bailey M, Bellomo R, *et al.* Goal-directed resuscitation for patients with early septic shock. N Engl J Med 2014;371:1496-506.
13. Mouncey PR, Osborn TM, Power GS, Harrison DA, Sadique MZ, Grieve RD, *et al.* Trial of early, goal-directed resuscitation for septic

shock. N Engl J Med 2015;372:1301-11.
14. Cumpstey AF, Oldman AH, Martin DS, Smith A, Grocott MP. Oxygen targets during mechanical ventilation in the ICU: A systematic review and meta-analysis. Crit Care Explor 2022;4:e0652.
15. ICU-ROX Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group, Mackle D, Bellomo R, Bailey M, Beasley R, Deane A, *et al.* Conservative oxygen therapy during mechanical ventilation in the ICU. N Engl J Med 2020;382:989-98.
16. Girardis M, Busani S, Damiani E, Donati A, Rinaldi L, Marudi A, *et al.* Effect of conservative versus conventional oxygen therapy on mortality among patients in an Intensive Care Unit: The oxygen-ICU randomized clinical trial. JAMA 2016;316:1583-9.
17. Nativi-Nicolau J, Selzman CH, Fang JC, Stehlik J. Pharmacologic therapies for acute cardiogenic shock. Curr Opin Cardiol 2014;29:250-7.
18. Thiele H, Ohman EM, Desch S, Eitel I, de Waha S. Management of cardiogenic shock. Eur Heart J 2015;36:1223-30.
19. Tewelde SZ, Liu SS, Winters ME. Cardiogenic shock. Cardiol Clin 2018;36:53-61.
20. Myburgh JA, Mythen MG. Resuscitation fluids. N Engl J Med 2013;369:1243-51.
21. Cordemans C, De Laet I, Van Regenmortel N, Schoonheydt K, Dits H, Huber W, *et al.* Fluid management in critically ill patients: The role of extravascular lung water, abdominal hypertension, capillary leak, and fluid balance. Ann Intensive Care 2012;2:S1.
22. Myburgh J. Patient-centered outcomes and resuscitation fluids. N Engl J Med 2018;378:862-3.
23. Lewis SR, Pritchard MW, Evans DJ, Butler AR, Alderson P, Smith AF, *et al.* Colloids versus crystalloids for fluid resuscitation in critically ill people. Cochrane Database Syst Rev 2018;8:CD000567.
24. Caironi P, Tognoni G, Gattinoni L. Albumin replacement in severe sepsis or septic shock. N Engl J Med 2014;371:84.
25. Rochwerg B, Alhazzani W, Gibson A, Ribic CM, Sindi A, Heels-Ansdell D, *et al.* Fluid type and the use of renal replacement therapy in sepsis: A systematic review and network meta-analysis. Intensive Care Med 2015;41:1561-71.
26. Curran JD, Major P, Tang K, Bagshaw SM, Dionne JC, Menon K, *et al.* Comparison of balanced crystalloid solutions: A systematic review and meta-analysis of randomized controlled trials. Crit Care Explor 2021;3:e0398.
27. Waters JH, Gottlieb A, Schoenwald P, Popovich MJ, Sprung J, Nelson DR. Normal saline versus lactated Ringer's solution for intraoperative fluid management in patients undergoing abdominal aortic aneurysm repair: An outcome study. Anesth Analg 2001;93:817-22.
28. Kellum JA. Fluid resuscitation and hyperchloremic acidosis in experimental sepsis: Improved short-term survival and acid-base balance with Hextend compared with saline. Crit Care Med 2002;30:300-5.
29. Kellum JA, Song M, Almasri E. Hyperchloremic acidosis increases circulating inflammatory molecules in experimental sepsis. Chest 2006;130:962-7.
30. Chowdhury AH, Cox EF, Francis ST, Lobo DN. A randomized, controlled, double-blind crossover study on the effects of 2-L infusions of 0.9% saline and plasma-lyte® 148 on renal blood flow velocity and renal cortical tissue perfusion in healthy volunteers. Ann Surg 2012;256:18-24.
31. Yunos NM, Bellomo R, Hegarty C, Story D, Ho L, Bailey M. Association between a chloride-liberal versus chloride-restrictive intravenous fluid administration strategy and kidney injury in critically ill adults. JAMA 2012;308:1566-72.
32. Young P, Bailey M, Beasley R, Henderson S, Mackle D, McArthur C, *et al.* Effect of a buffered crystalloid solution vs. saline on acute kidney injury among patients in the Intensive Care Unit: The SPLIT randomized clinical trial. JAMA 2015;314:1701-10.
33. Semler MW, Wanderer JP, Ehrenfeld JM, Stollings JL, Self WH, Siew ED, *et al.* Balanced crystalloids versus saline in the Intensive Care Unit. The SALT randomized trial. Am J Respir Crit Care Med 2017;195:1362-72.
34. Semler MW, Self WH, Wanderer JP, Ehrenfeld JM, Wang L, Byrne DW, *et al.* Balanced crystalloids versus saline in critically Ill adults. N Engl J Med 2018;378:829-39.
35. Boxhoorn L, Voermans RP, Bouwense SA, Bruno MJ, Verdonk RC, Boermeester MA, *et al.* Acute pancreatitis. Lancet 2020;396:726-34.
36. Iqbal U, Anwar H, Scribani M. Ringer's lactate versus normal saline in acute pancreatitis: A systematic review and meta-analysis. J Dig Dis 2018;19:335-41.
37. Catahay JA, Polintan ET, Casimiro M, Notarte KI, Velasco JV, Ver AT, *et al.* Balanced electrolyte solutions versus isotonic saline in adult patients with diabetic ketoacidosis: A systematic review and meta-analysis. Heart Lung 2022;54:74-9.
38. Martin GS, Bassett P. Crystalloids versus. Colloids for fluid resuscitation in the Intensive Care Unit: A systematic review and meta-analysis. J Crit Care 2019;50:144-54.
39. Myburgh JA, Finfer S, Bellomo R, Billot L, Cass A, Gattas D, *et al.* Hydroxyethyl starch or saline for fluid resuscitation in intensive care. N Engl J Med 2012;367:1901-11.
40. Perner A, Haase N, Guttormsen AB, Tenhunen J, Klemenzson G, Åneman A, *et al.* Hydroxyethyl starch 130/0.42 versus Ringer's acetate in severe sepsis. N Engl J Med 2012;367:124-34.
41. Haase N, Perner A, Hennings LI, Siegemund M, Lauridsen B, Wetterslev M, *et al.* Hydroxyethyl starch 130/0.38-0.45 versus crystalloid or albumin in patients with sepsis: Systematic review with meta-analysis and trial sequential analysis. BMJ 2013;346:f839.
42. Moeller C, Fleischmann C, Thomas-Rueddel D, Vlasakov V, Rochwerg B, Theurer P, *et al.* How safe is gelatin? A systematic review and meta-analysis of gelatin-containing plasma expanders versus crystalloids and albumin. J Crit Care 2016;35:75-83.
43. Crockett SD, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN, American Gastroenterological Association Institute Clinical Guidelines Committee. American Gastroenterological Association institute guideline on initial management of acute pancreatitis. Gastroenterology 2018;154:1096-101.
44. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. Diabetes Care 2009;32:1335-43.
45. Rushworth RL, Chrisp GL, Bownes S, Torpy DJ, Falhammar H. Adrenal crises in adolescents and young adults. Endocrine 2022;77:1-10.
46. World Health Organization. Handbook for Clinical Management of Dengue. Geneva: WHO Press; 2012.
47. Pan American Health Organization. Dengue: Guidelines for Patient Care in the Region of the Americas. 2nd ed. Washington, DC: PAHO; 2016.
48. Bentzer P, Griesdale DE, Boyd J, MacLean K, Sirounis D, Ayas NT. Will this hemodynamically unstable patient respond to a bolus of intravenous fluids? JAMA 2016;316:1298-309.
49. Fleischmann-Struzek C, Mellhammar L, Rose N, Cassini A, Rudd KE, Schlattmann P, *et al.* Incidence and mortality of hospital and ICU-treated sepsis: Results from an updated and expanded systematic review and meta-analysis. Intensive Care Med 2020;46:1552-62.
50. Messina A, Calabrò L, Pugliese L, Lulja A, Sopuch A, Rosalba D, *et al.* Fluid challenge in critically ill patients receiving haemodynamic monitoring: A systematic review and comparison of two decades. Crit Care 2022;26:186.
51. Monnet X, Rienzo M, Osman D, Anguel N, Richard C, Pinsky MR, *et al.* Passive leg Raising predicts fluid responsiveness in the critically ill. Crit Care Med 2006;34:1402-7.
52. Cavallaro F, Sandroni C, Marano C, La Torre G, Mannocci A, De Waure C, *et al.* Diagnostic accuracy of passive leg raising for prediction of fluid responsiveness in adults: Systematic

review and meta-analysis of clinical studies. Intensive Care Med 2010;36:1475-83.
53. Cherpanath TG, Hirsch A, Geerts BF, Lagrand WK, Leeflang MM, Schultz MJ, *et al.* Predicting fluid responsiveness by passive leg raising: A systematic review and meta-analysis of 23 clinical trials. Crit Care Med 2016;44:981-91.
54. Misango D, Pattnaik R, Baker T, Dünser MW, Dondorp AM, Schultz MJ, *et al.* Haemodynamic assessment and support in sepsis and septic shock in resource-limited settings. Trans R Soc Trop Med Hyg 2017;111:483-9.
55. Airapetian N, Maizel J, Alyamani O, Mahjoub Y, Lorne E, Levrard M, *et al.* Does inferior vena cava respiratory variability predict fluid responsiveness in spontaneously breathing patients? Crit Care 2015;19:400.
56. Barbier C, Loubières Y, Schmit C, Hayon J, Ricôme JL, Jardin F, *et al.* Respiratory changes in inferior vena cava diameter are helpful in predicting fluid responsiveness in ventilated septic patients. Intensive Care Med 2004;30:1740-6.
57. Charbonneau H, Riu B, Faron M, Mari A, Kurrek MM, Ruiz J, *et al.* Predicting preload responsiveness using simultaneous recordings of inferior and superior vena cavae diameters. Crit Care 2014;18:473.
58. Kory P. COUNTERPOINT: Should acute fluid resuscitation be guided primarily by inferior vena cava ultrasound for patients in shock? No. Chest 2017;151:533-6.
59. Vignon P, Repessé X, Bégot E, Léger J, Jacob C, Bouferrache K, *et al.* Comparison of echocardiographic indices used to predict fluid responsiveness in ventilated patients. Am J Respir Crit Care Med 2017;195:1022-32.
60. Orso D, Paoli I, Piani T, Cilenti FL, Cristiani L, Guglielmo N. Accuracy of ultrasonographic measurements of inferior vena cava to determine fluid responsiveness: A systematic review and meta-analysis. J Intensive Care Med 2020;35:354-63.
61. Magder S. Invasive hemodynamic monitoring. Crit Care Clin 2015;31:67-87.
62. Marik PE, Cavallazzi R. Does the central venous pressure predict fluid responsiveness? An updated meta-analysis and a plea for some common sense. Crit Care Med 2013;41:1774-81.
63. Eskesen TG, Wetterslev M, Perner A. Systematic review including re-analyses of 1148 individual data sets of central venous pressure as a predictor of fluid responsiveness. Intensive Care Med 2016;42:324-32.
64. Tehrani BN, Truesdell AG, Sherwood MW, Desai S, Tran HA, Epps KC, *et al.* Standardized team-based care for cardiogenic shock. J Am Coll Cardiol 2019;73:1659-69.
65. Basir MB, Kapur NK, Patel K, Salam MA, Schreiber T, Kaki A, *et al.* Improved outcomes associated with the use of shock protocols: Updates from the national cardiogenic shock initiative. Catheter Cardiovasc Interv 2019;93:1173-83.
66. Taleb I, Koliopoulou AG, Tandar A, McKellar SH, Tonna JE, Nativi-Nicolau J, *et al.* Shock team approach in refractory cardiogenic shock requiring short-term mechanical circulatory support: A proof of concept. Circulation 2019;140:98-100.
67. Tehrani BN, Truesdell AG, Psotka MA, Rosner C, Singh R, Sinha SS, *et al.* A standardized and comprehensive approach to the management of cardiogenic shock. JACC Heart Fail 2020;8:879-91.
68. Vang M, Østberg M, Steinmetz J, Rasmussen LS. Shock index as a predictor for mortality in trauma patients: A systematic review and meta-analysis. Eur J Trauma Emerg Surg 2022;48:2559-66.
69. Lee K, Jang JS, Kim J, Suh YJ. Age shock index, shock index, and modified shock index for predicting postintubation hypotension in the emergency department. Am J Emerg Med 2020;38:911-5.
70. Althunayyan SM. Shock index as a predictor of post-intubation hypotension and cardiac arrest; a review of the current evidence. Bull Emerg Trauma 2019;7:21-7.
71. LeDoux D, Astiz ME, Carpati CM, Rackow EC. Effects of perfusion pressure on tissue perfusion in septic shock. Crit Care Med 2000;28:2729-32.
72. Asfar P, Meziani F, Hamel JF, Grelon F, Megarbane B, Anguel N, *et al.* High versus low blood-pressure target in patients with septic shock. N Engl J Med 2014;370:1583-93.
73. Delaney A, Finnis M, Bellomo R, Udy A, Jones D, Keijzers G, *et al.* Initiation of vasopressor infusions via peripheral versus central access in patients with early septic shock: A retrospective cohort study. Emerg Med Australas 2020;32:210-9.
74. Wieruszewski PM, Khanna AK. Vasopressor choice and timing in vasodilatory shock. Crit Care 2022;26:76.
75. Wieruszewski ED, Jones GM, Samarin MJ, Kimmons LA. Predictors of dysrhythmias with norepinephrine use in septic shock. J Crit Care 2021;61:133-7.
76. Avni T, Lador A, Lev S, Leibovici L, Paul M, Grossman A. Vasopressors for the treatment of septic shock: Systematic review and meta-analysis. PLoS One 2015;10:e0129305.
77. Annane D, Vignon P, Renault A, Bollaert PE, Charpentier C, Martin C, *et al.* Norepinephrine plus dobutamine versus epinephrine alone for management of septic shock: A randomised trial. Lancet 2007;370:676-84.
78. Myburgh JA, Higgins A, Jovanovska A, Lipman J, Ramakrishnan N, Santamaria J, *et al.* A comparison of epinephrine and norepinephrine in critically ill patients. Intensive Care Med 2008;34:2226-34.
79. De Backer D, Creteur J, Silva E, Vincent JL. Effects of dopamine, norepinephrine, and epinephrine on the splanchnic circulation in septic shock: Which is best? Crit Care Med 2003;31:1659-67.
80. Levy B, Perez P, Perny J, Thivilier C, Gerard A. Comparison of norepinephrine-dobutamine to epinephrine for hemodynamics, lactate metabolism, and organ function variables in cardiogenic shock. A prospective, randomized pilot study. Crit Care Med 2011;39:450-5.
81. De Backer D, Biston P, Devriendt J, Madl C, Chochrad D, Aldecoa C, *et al.* Comparison of dopamine and norepinephrine in the treatment of shock. N Engl J Med 2010;362:779-89.
82. De Backer D, Aldecoa C, Njimi H, Vincent JL. Dopamine versus norepinephrine in the treatment of septic shock: A meta-analysis*. Crit Care Med 2012;40:725-30.
83. Landry DW, Levin HR, Gallant EM, Ashton RC Jr., Seo S, D'Alessandro D, *et al.* Vasopressin deficiency contributes to the vasodilation of septic shock. Circulation 1997;95:1122-5.
84. Holmes CL, Patel BM, Russell JA, Walley KR. Physiology of vasopressin relevant to management of septic shock. Chest 2001;120:989-1002.
85. Russell JA, Walley KR, Singer J, Gordon AC, Hébert PC, Cooper DJ, *et al.* Vasopressin versus norepinephrine infusion in patients with septic shock. N Engl J Med 2008;358:877-87.
86. Sacha GL, Lam SW, Wang L, Duggal A, Reddy AJ, Bauer SR. Association of catecholamine dose, lactate, and shock duration at vasopressin initiation with mortality in patients with septic shock. Crit Care Med 2022;50:614-23.
87. Dünser MW, Mayr AJ, Tür A, Pajk W, Barbara F, Knotzer H, *et al.* Ischemic skin lesions as a complication of continuous vasopressin infusion in catecholamine-resistant vasodilatory shock: Incidence and risk factors. Crit Care Med 2003;31:1394-8.
88. Laterre PF, Berry SM, Blemings A, Carlsen JE, François B, Graves T, *et al.* Effect of Selepressin versus placebo on ventilator and vasopressor-free days in patients with septic shock: The SEPSIS-ACT randomized clinical trial. JAMA 2019;322:1476-85.
89. Liu ZM, Chen J, Kou Q, Lin Q, Huang X, Tang Z, *et al.* Terlipressin versus norepinephrine as infusion in patients with septic shock: A multicentre, randomised, double-blinded trial. Intensive Care Med 2018;44:1816-25.
90. Belletti A, Benedetto U, Biondi-Zoccai G, Leggieri C, Silvani P, Angelini GD, *et al.* The effect of vasoactive drugs on mortality in patients with severe sepsis and septic shock. A network meta-analysis of randomized trials. J Crit Care 2017;37:91-8.

91. Akinaga J, Lima V, Kiguti LR, Hebeler-Barbosa F, Alcántara-Hernández R, García-Sáinz JA, *et al.* Differential phosphorylation, desensitization, and internalization of α1A-adrenoceptors activated by norepinephrine and oxymetazoline. Mol Pharmacol 2013;83:870-81.
92. Chawla LS, Busse L, Brasha-Mitchell E, Davison D, Honiq J, Alotaibi Z, *et al.* Intravenous angiotensin II for the treatment of high-output shock (ATHOS trial): A pilot study. Crit Care 2014;18:534.
93. Khanna A, English SW, Wang XS, Ham K, Tumlin J, Szerlip H, *et al.* Angiotensin II for the treatment of vasodilatory shock. N Engl J Med 2017;377:419-30.
94. Wieruszewski PM, Wittwer ED, Kashani KB, Brown DR, Butler SO, Clark AM, *et al.* Angiotensin II infusion for shock: A multicenter study of postmarketing use. Chest 2021;159:596-605.
95. Amado J, Gago P, Santos W, Mimoso J, de Jesus I. Cardiogenic shock: Inotropes and vasopressors. Rev Port Cardiol 2016;35:681-95.
96. Tarvasmäki T, Lassus J, Varpula M, Sionis A, Sund R, Køber L, *et al.* Current real-life use of vasopressors and inotropes in cardiogenic shock – Adrenaline use is associated with excess organ injury and mortality. Crit Care 2016;20:208.
97. Levy B, Clere-Jehl R, Legras A, Morichau-Beauchant T, Leone M, Frederique G, *et al.* Epinephrine versus norepinephrine for cardiogenic shock after acute myocardial infarction. J Am Coll Cardiol 2018;72:173-82.
98. van Diepen S. Norepinephrine as a first-line inopressor in cardiogenic shock: Oversimplification or best practice? J Am Coll Cardiol 2018;72:183-6.
99. Cunha-Goncalves D, Perez-de-Sa V, Larsson A, Thörne J, Blomquist S. Inotropic support during experimental endotoxemic shock: Part II. A comparison of levosimendan with dobutamine. Anesth Analg 2009;109:1576-83.
100. De Backer D, Creteur J, Dubois MJ, Sakr Y, Koch M, Verdant C, *et al.* The effects of dobutamine on microcirculatory alterations in patients with septic shock are independent of its systemic effects. Crit Care Med 2006;34:403-8.
101. Dubin A, Lattanzio B, Gatti L. The spectrum of cardiovascular effects of dobutamine from healthy subjects to septic shock patients. Rev Bras Ter Intensiva 2017;29:490-8.
102. Alousi AA, Johnson DC. Pharmacology of the bipyridines: Amrinone and milrinone. Circulation 1986;73:III10-24.
103. Shah P, Cowger JA. Cardiogenic shock. Crit Care Clin 2014;30:391-412.
104. Gordon AC, Perkins GD, Singer M, McAuley DF, Orme RM, Santhakumaran S, *et al.* Levosimendan for the prevention of acute organ dysfunction in sepsis. N Engl J Med 2016;375:1638-48.
105. Wacker DA, Winters ME. Shock. Emerg Med Clin North Am 2014;32:747-58.
106. Perera P, Mailhot T, Riley D, Mandavia D. The RUSH exam: Rapid ultrasound in shock in the evaluation of the critically lll. Emerg Med Clin North Am 2010;28:29-56, vii.
107. Atkinson PR, Milne J, Diegelmann L, Lamprecht H, Stander M, Lussier D, *et al.* Does point-of-care ultrasonography improve clinical outcomes in emergency department patients with undifferentiated hypotension? An international randomized controlled trial from the SHoC-ED investigators. Ann Emerg Med 2018;72:478-89.
108. Guilhaumou R, Benaboud S, Bennis Y, Dahyot-Fizelier C, Dailly E, Gandia P, *et al.* Optimization of the treatment with beta-lactam antibiotics in critically ill patients-guidelines from the French Society of Pharmacology and Therapeutics (Société Française de Pharmacologie et Thérapeutique-SFPT) and the French Society of Anaesthesia and Intensive Care Medicine (Société Française d'Anesthésie et Réanimation-SFAR). Crit Care 2019;23:104.
109. Annane D, Renault A, Brun-Buisson C, Megarbane B, Quenot JP, Siami S, *et al.* Hydrocortisone plus fludrocortisone for adults with septic shock. N Engl J Med 2018;378:809-18.
110. Venkatesh B, Finfer S, Cohen J, Rajbhandari D, Arabi Y, Bellomo R, *et al.* Adjunctive glucocorticoid therapy in patients with septic shock. N Engl J Med 2018;378:797-808.
111. Fang F, Zhang Y, Tang J, Lunsford LD, Li T, Tang R, *et al.* Association of corticosteroid treatment with outcomes in adult patients with sepsis: A systematic review and meta-analysis. JAMA Intern Med 2019;179:213-23.
112. Muraro A, Worm M, Alviani C, Cardona V, DunnGalvin A, Garvey LH, *et al.* EAACI guidelines: Anaphylaxis (2021 update). Allergy 2022;77:357-77.
113. McHugh K, Repanshek Z. Anaphylaxis: Emergency department treatment. Emerg Med Clin North Am 2022;40:19-32.
114. Cannon JW. Hemorrhagic shock. N Engl J Med 2018;378:370-9.