

Shock

Shock is defined in simple terms as a syndrome of impaired tissue perfusion (1) [oxygen delivery (DO_2) fails to meet the metabolic requirements of the tissues (2)]. Shock usually, but not always, accompanied by hypotension (1). Shock is not synonymous with hypotension, which is often a late manifestation (2).

The impairment of tissue perfusion eventually leads to cellular dysfunction, followed by organ damage and death if untreated (1,3).

Classification of shock

Shock may be categorized as either low flow or stroke volume, or low peripheral arteriolar resistance (vasodilatation) (2).

A. Low stroke volume (2)

1. **Hypovolaemic:** any condition provoking a major reduction in blood volume, e.g. internal or external hemorrhage, severe burns, salt and water depletion (2) as in severe diarrhea or severe vomiting or diabetes insipidus (1). The severity of hypovolemic shock depends on the amount and rate of intravascular volume loss and each person's capacity for compensation (1).

2. **Cardiogenic:** result from severe cardiac impairment, e.g. myocardial infarction, acute mitral regurgitation (2) or end stage cardiomyopathy (1). Acute exacerbation of heart failure (1).

3. **Obstructive:** obstruction to blood flow around the circulation, e.g. pulmonary embolism, cardiac tamponade, tension pneumothorax (2).

B. Vasodilatation (2) increased vascular capacitance (1)

1. **Sepsis/SIRS:** mainly due to infection or other causes of a systemic inflammatory response that produce widespread endothelial damage with vasodilatation (2).

2. **Anaphylactic:** inappropriate vasodilatation triggered by an allergen (e.g. bee sting), often associated with endothelial disruption and capillary leak (2).

3. **Neurogenic:** caused by major brain or spinal injury, which disrupts brainstem and neurogenic vasomotor control. High cervical cord trauma may result in disruption of the sympathetic outflow tracts, leading to inappropriate bradycardia due to a combination of loss of noradrenaline mediated vasoconstriction and adrenaline mediated chronotropy (2).

4. **Drug-induced** like Anesthesia, ganglionic and adrenergic blockers, overdoses of barbiturates and narcotics (1)

5. **Acute adrenal insufficiency** (1)

Notes: (1)

1. The distinctions among subtypes of shock only apply, however, in the relatively early stages because the clinical and pathophysiologic features of advanced shock are the same for all.
2. Also, different types of shock can occur at the same time (e.g., a patient with septic shock who is also hypovolemic).

Pathophysiology

Severe metabolic lactic acidosis often develops secondary to tissue ischemia and causes localized vasodilation, which further exacerbates the impaired cardiovascular state (3). Additionally lactic acidosis can alter mitochondrial function and eventually result in cell death (1). In the advanced stages of shock, irreversible cellular damage leads to multiple organ system failure, also known as multiple organ dysfunction syndrome (1).

Regardless of the etiology, fall in blood pressure (BP) is compensated by an increase in sympathetic outflow, activation of the renin–angiotensin system, and other humoral factors that stimulate peripheral vasoconstriction.

Compensatory vasoconstriction redistributes blood away from the skin, skeletal muscles, kidneys, and GI tract toward vital organs (e.g., heart and brain) in an attempt to maintain oxygenation, nutrition, and organ function (3).

Clinical features, clinical assessment and diagnosis

The general diagnosis of shock is based on the finding of impaired tissue perfusion on examination. These findings may include the following (1):

1. **Systolic blood pressure** (SBP) less than 90 mm Hg, or a greater than 40 mm Hg decrease from baseline in a hypertensive patient, or a mean arterial pressure (MAP) less than 65 mm Hg
2. **Tachycardia** (heart rate [HR] >90 beats/minute) (1) or more than 100 (3)
3. **Tachypnea** (respiratory rate [RR] >20 breaths/minute)
4. **Cutaneous** vasoconstriction: cold, clammy, mottled skin (although not typical of distributive shock)
5. **Mental confusion** (agitation, stupor, or coma)
6. **Oliguria**: urine output less than 20 mL/hour (1) or 0.5ml/min (3)

Symptoms and signs of Hypovolemic shock

Patients may present with thirst, anxiousness, weakness, lightheadedness, and dizziness. Patients may also report scanty urine output and dark yellow-colored urine (3). Cold peripheries, reduced or absent peripheral pulses, weak central pulses and evidence of a low cardiac output (2).

- Signs of more severe volume loss include tachycardia (>120 beats/min), tachypnea (>30 breaths/min), hypotension (SBP <90 mm Hg), mental status changes or unconsciousness, agitation, and normal or low body temperature (in the absence of infection) with cold extremities and decreased capillary refill (3).

Blood pressure in Hemorrhagic shock

In early haemorrhagic shock, a narrowed pulse pressure, i.e. a raised diastolic (DBP) and reduced systolic (SBP) blood pressure, such as 105/95 mmHg, indicates the combination of hypovolaemia (reduced stroke volume, hence SBP) and activation of the sympathetic nervous system, with noradrenaline (norepinephrine) inducing vasoconstriction and so raising the DBP (2).

In hypovolemic shock decrease blood volume mean decrease in preload which means decrease in stroke volume and thus decrease CO. So oxygen delivery (DO₂) will be reduced. If hypovolemia occur due to hemorrhage a further reduction in DO₂ result due to decrease in O₂ carrying capacity by blood loss (1).

Signs and Symptoms of other forms of shock

Sepsis/SIRS and anaphylactic shock : The BP pattern is again distinctive (e.g. 115/42 mmHg), with a low DBP in the early stages due to peripheral vasodilatation, but a normal systolic BP, as the left ventricular afterload is reduced and stroke volume thus maintained (2).

Neurogenic shock often results in vasodilated hypotension with a paradoxically slow heart rate (2).

Diagnosis and monitoring

Evaluation of past medical history, clinical presentation, and laboratory findings are key components in establishing the diagnosis (3).

Lab data for hypovolemic shock:

Serum sodium and chloride concentrations are usually high with acute volume depletion (3).

The blood urea nitrogen (BUN): creatinine ratio may be elevated initially, but the creatinine increases with renal dysfunction (3).

Metabolic acidosis results in elevated base deficit and lactate conc. with decreased bicarbonate and pH (3).

In hemorrhagic shock, the red cell count, hemoglobin, and hematocrit will decrease (3).

Non invasive monitoring: include (1)

Clinical examination and vital signs (temperature, HR, blood pressure [BP], RR) . Other well-established noninvasive techniques for monitoring

the hemodynamic status of patients include pulse oximetry (for measuring arterial oxygen saturation [Sao₂]) and transthoracic echocardiography, which can estimate the functional status of the heart and heart valves (1).

Invasive monitoring: most importantly by a pulmonary catheter (Swan Ganz) catheter (1), which can be used to determine central venous pressure (CVP); pulmonary artery pressure (PAP); cardiac output (CO); and pulmonary artery occlusion pressure (PAOP), an approximate measure of the left ventricular end-diastolic volume and a major determinant of left ventricular Preload (3). However its use may result in Arrhythmias, thrombotic events, infections, and, very rarely, PA rupture have been reported. (1)

New devices that can measure CO and tissue perfusion noninvasively (or minimally invasively), such as gastric tonometry, esophageal Doppler monitoring, thoracic bioimpedance, and others, have been developed (1).

Tissue perfusion monitoring

The Vo₂ (oxygen consumption): Do₂ (oxygen delivery) ratio (O₂ extraction ratio) can be used to assess adequacy of perfusion and metabolic response. Normal value 25% (1,3)

Blood lactate concentrations may be used as another measure of tissue oxygenation and may show better correlation with outcome than O₂ transport parameters in some patients (3).

Definition of cardiac parameters

Stroke volume (SV) Amount of blood ejected from the ventricle with each systolic contraction. (1)

Cardiac output (CO): Amount of blood ejected from the left ventricle per minute = stroke volume * Heart rate (1).

Cardiac index = Cardiac output per square meter of body surface area (1)

Mean arterial pressure: $\frac{2}{3}$ Diastolic pressure + $\frac{1}{3}$ Systolic pressure (1)

Central venous pressure (CVP): Measures mean pressure in right atrium and reflects right ventricular filling pressure and volume status. Primarily determined by venous return to the heart (1).

Pulmonary artery pressure PAP: *Systolic* (SPAP): Measures pulmonary artery pressure during systole; reflects pressure generated by the

contraction of the right ventricle. *Diastolic* (DPAP): Measures pulmonary artery pressure during diastole; reflects diastolic filling pressure in the left ventricle (1).

Pulmonary capillary wedge pressure PCWP: Measures pressure distal to the pulmonary artery; reflects left ventricular filling pressures (*preload*). Usually lower than or within 5 mm Hg of pulmonary artery diastolic pressure (DPAP). (1)

Normal values (3): للاطلاع

Parameter	Normal Value ^a
Blood pressure (systolic/diastolic)	100-130/70-85 mm Hg
Mean arterial pressure (MAP)	80-100 mm Hg
Pulmonary artery pressure (PAP)	25/10 mm Hg
Mean pulmonary artery pressure (MPAP)	12-15 mm Hg
Central venous pressure (CVP)	8-12 mm Hg
Pulmonary artery occlusion pressure (PAOP)	12-15 mm Hg
Heart rate (HR)	60-80 beats/min
Cardiac output (CO)	4-7 L/min
Cardiac index (CI)	2.8-3.6 L/min/m ²
Stroke volume index (SVI)	30-50 mL/m ²

Arterial O ₂ saturation (Sao ₂)	97% (range 95-100%)
Mixed venous O ₂ saturation (Svo ₂)	70-75%
Arterial O ₂ content (Cao ₂)	20.1 vol% (range 19-21%)
Venous O ₂ content (Cvo ₂)	15.5 vol% (range 11.5-16.5%)

PCWP = 5-12 mmHg (1)

Ventricular function (Frank-Starling) curve.

In the normal heart, as preload increases, stroke volume increases until the contractile fibers reach their capacity, at which point the curve flattens. A change in contractility causes the heart to perform on a different curve. If the contractile fibers exceed their capacity, as with severe heart failure, the heart will operate on the descending limb of the curve (1).

The primary goals of treatment are to:

- Restore global oxygen delivery (DO_2) by ensuring adequate cardiac output (2).
- Maintain an MAP that ensures adequate perfusion of vital organs. The target pressure will be patient specific, depending on pre-morbid factors (e.g. hypertension or coronary artery disease), and may range from 60 to 90 mmHg (2).

General treatment notes

1. Supplemental O₂ should be initiated at the earliest signs of shock, beginning with 4 to 6 L/min via nasal cannula or 6 to 10 L/min by face mask (3).

2. Adequate fluid resuscitation to maintain circulating blood volume (3) (preload (2)) is essential in managing all forms of shock (3). HR, BP, and urine output have been traditional markers for the adequacy of resuscitation, however we can't depend completely on these parameters, instead measuring bicarbonate and lactate level are essential since Metabolic acidosis can signal that resuscitation is incomplete despite normal vital signs (1).

3. If fluid challenge does not achieve desired end points, pharmacologic support is necessary with inotropic and vasoactive drugs (3).

4. Inotropic agents such as **dobutamine** are preferred if BP is adequate (SBP ≥ 90 mm Hg) because they should not aggravate the existing vasoconstriction. When pressure cannot be maintained with inotropes, or when inotropes with vasodilatory properties can't be used due to concerns about inadequate BP, pressors may be required as a last resort (3).

5. Pressor agents such as **norepinephrine** and **high-dose dopamine** should be avoided if possible because they may increase BP at the expense of peripheral tissue ischemia (3).

Treatment of hypovolemic shock

Once an adequate airway is established and initial vital signs are obtained, the most important therapeutic intervention in hypovolemic shock is the infusion of IV fluids (1).

Initially, crystalloids or colloids are used to restore blood volume as blood products may not be immediately available and are frequently unnecessary to manage mild shock (10%–20% blood loss). (1)

IV fluids

Initial fluid resuscitation consists of isotonic crystalloid (0.9% sodium chloride or lactated Ringer solution), colloid (5% albumin and 6% hetastarch, dextran or gelatin), or whole blood (1,3).

Effectiveness of crystalloids

Isotonic crystalloid solutions freely distribute within the extracellular fluid compartment, which is divided between the interstitial and intravascular spaces at a ratio of 3:1. So this mean large volumes of crystalloid fluid is required to expand the intravascular space during resuscitation (1). However they have the advantage of correcting the deficit of fluids not only in the intravascular but also in the interstitium (1).

Effectiveness of colloids

While colloids effectively expand the intravascular space with little loss into the interstitium since intact capillary membranes are relatively impermeable to colloids. Thus smaller volumes of colloids than of crystalloids are thus required for resuscitation, and because these large molecules persist intravascularly, their duration of action is longer (1).

Crystalloid versus colloid (Advantages and disadvantages)

There is a large controversy in considering whether colloids or crystalloids are better (1).

Given the lack of evidence for a significant clinical difference between crystalloids and colloids and the greater expense of using albumin (1)

Most clinicians agree that crystalloids should be the initial therapy of circulatory insufficiency, since crystalloids with many advantages like rapidity and ease of administration, compatibility with most drugs, absence of serum sickness, and low cost (3). Additionally Many of the colloidal agents, however, can cause hypersensitivity or allergic reactions as well as coagulopathic effects, and colloids are much more expensive than crystalloids (1). Furthermore crystalloids are preferred over colloids as initial therapy for burn patients because they are less likely to cause interstitial fluid Accumulation (3) because in these patients burns cause an increase in pulmonary capillary and vascular permeability, resulting in extravasation of the colloid into the interstitium, which further worsens the effective vascular volume and pulmonary edema (1). If volume resuscitation is suboptimal following several liters of crystalloid, colloids should be considered (3). The only problem with Crystalloids is that if they infused in large amounts may cause pulmonary edema but only in patients at risk for such resuscitation (1). Some patients may require

blood products to ensure maintenance of O₂-carrying capacity, as well as clotting factors and platelets for blood hemostasis (3). Blood should only be used if there is ongoing blood loss demonstrated by a decreasing hematocrit or hemoglobin (1).

Crystalloids

Lactated Ringer solution may be preferred because it is unlikely to cause the hyperchloremic metabolic acidosis seen with infusion of large amounts of normal saline (3). Which thereby worsens the tissue acidosis that occurs in the setting of hypovolemic shock (1). The likelihood is increased in those with renal impairment (1). However in patients with liver impairment lactate metabolism decreased and unmetabolized lactate can be converted to lactic acid, prolonged infusion of LR could cause tissue acidosis in predisposed patients (1). In practice, normal saline and LR solutions typically are used interchangeably because neither solution appears to be superior to the other (1).

Dosing of crystalloids in the resuscitation of patients with hemorrhagic shock: 1 to 2 L of fluid as an initial bolus as rapidly as possible for an adult or 20mL/kg for a pediatric patient. Additional fluid boluses may be necessary, depending on the patient's response. Between boluses, fluids are slowed to maintenance rates (150–200 mL/hour), with ongoing evaluation of the patient's physiologic response for signs of continued blood loss or inadequate perfusion that would indicate the need for additional volume replacement (1).

Monitoring response to fluid resuscitation

Indications that circulation is improving include normalization of BP, pulse pressure, and HR. Signs that actual organ perfusion is normalizing and that fluid resuscitation is adequate include improvements in mental status, warmth and color of skin, improved acid–base balance, and increased urinary output to at least 0.5ml/kg. Serum lactate and base deficit are important values to monitor to determine that the patient is receiving adequate resuscitation (1). Persistent metabolic acidosis in a normothermic shock patient usually indicates the need for additional fluid resuscitation; Sodium bicarbonate is not recommended unless the pH is less than 7.2 (1).

Hypertonic saline solution

The advantage of HS solution as a resuscitative fluid is the smaller volume of fluid required to expand the intravascular compartment compared with isotonic solutions. This could be a particular advantage in the prehospital setting (1). HS solution may be safe and effective for the

initial resuscitation of hemorrhagic shock and may help prevent the development of posttraumatic multiple system organ failure and sepsis. Despite these positive findings, HS solutions are not widely used. (1)

Blood transfusion

Because it takes at least 24 hours for all fluid compartments to come to equilibrium, a normal hematocrit (or hemoglobin concentration) in the setting of hemorrhagic shock does not rule out significant blood loss or indicate adequacy of transfusion (1).

Which patients require blood transfusion?

- Patients who are not acutely bleeding and who do not respond to initial volume resuscitation or who transiently respond but remain tachycardic, tachypneic, and oliguric clearly are underperfused and will likely require blood transfusion. (1)
- Trauma patients who have acute bleeding issues or who demonstrate signs of underperfusion should be considered for transfusion much sooner; (1)

Complication of blood transfusion

Electrolyte abnormalities, hemolytic reactions, transmission of infectious disease, coagulopathies (because transfused blood does not contain platelets because platelets do not survive at the temperatures required for red blood cell storage), and immunosuppression (it is most likely caused by the infusion of donor white blood cells (WBCs), which create a competition between the donor and recipient leukocytes.). Banked blood is stored with a citrate anticoagulant additive, with multiple transfusions, the large amount of citrate can cause hypocalcemia and acid–base abnormalities. Hyperkalemia also can occur because transfusion of stored blood causes the release of potassium from hemolyzed (ruptured) red blood cells (1).

Coagulation problems are primarily associated with low levels of clotting factors in stored blood, as well as dilution of endogenous clotting factors and platelets following administration of the blood. As a result, a coagulation panel (PT, international normalized ratio, and aPTT) should be checked in patients undergoing replacement of 50% to 100% of blood volume in 12 to 24 hours (3).

Other blood products

Packed red blood cells: contain hemoglobin that increases the O₂-carrying capacity of blood, thereby increasing O₂ delivery to tissues. This is a function not performed by crystalloids or colloids. Packed red cells are usually indicated in patients with continued deterioration after volume replacement or obvious exsanguinations (3).

Fresh frozen plasma replaces clotting factors. It is indicated if there is ongoing hemorrhage in patients with a prothrombin time (PT) or activated partial thromboplastin time (aPTT) >1.5 times normal, severe hepatic disease, or other bleeding disorders (3). fresh-frozen plasma (containing all clotting factors) (1), **Platelets** are used for bleeding due to severe thrombocytopenia (3).

Cryoprecipitate and **factor VIII** are generally not indicated in acute hemorrhage but may be used once specific deficiencies have been identified (3).

Cryoprecipitate (containing factor VIII and fibrinogen) (1).

Colloidal solutions

Albumin

On infusion, 5% albumin increases plasma volume by approximately half the volume infused, with an initial duration of action of 16 hours. Substantial side effects primarily involve transient clotting abnormalities and anaphylactic (1). Albumin is available as a 5% solution which used for volume expansion and it is isotonic with the plasma and a 25% solution that is hypertonic which is used for hypoproteinemia (1). It may cause anaphylactic reaction (3).

Hydroxyethyl starch has comparable plasma expansion to 5% albumin solution but is usually less expensive (3). HES should not be used because of the potential adverse effects and that other alternatives are available (1). Like bleeding, increase amylase level and renal dysfunction (3).

Dextran 40, dextran 70, and dextran 75 are available for use as plasma expanders (the number indicates the average molecular weight \times 1,000). These solutions are not used as often as albumin or hetastarch for plasma expansion, possibly due to concerns related to aggravation of bleeding (i.e., anticoagulant actions related to inhibiting stasis of microcirculation) and anaphylaxis, which is more likely to occur with the higher molecular weight solutions (3).

References

1. Applied therapeutics 2013;
2. Davidson 2014; 3.Pharmacotherapy handbook 2011