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Chapter

Shock Pathophysiology: Classifications and Management

Numair Belgaumi, Ahmed Salik and Naveed ur Rehman Siddiqui

Abstract

Shock is a pathological state in which there is an insufficiency in oxygen supply and demand. Ultimately, it results in global hypoperfusion and a resulting increase in anaerobic respiration causing lactic acidosis. Maintaining adequate oxygen delivery in the critical care setting is of primary importance in the management of a critically ill patient. When oxygen supply is inadequate, the body undergoes several physiological changes to maintain the oxygen delivery requirements and perfusion pressure. This stage is referred to as compensated shock, and early signs of shock may be appreciated during this stage. When compensatory mechanisms are inadequate and DO$_2$ begins to fall beyond the critical point, shock has progressed to the uncompensated stage. During this stage, there is rapid deterioration of the patient due to prolonged hypoxia and anaerobic respiration. Multiple Organ Dysfunction Syndrome (MODS) is the development of potentially reversible physiological derangement involving two or more organ systems not involved in the causative disorder, which results in persisting states of shock, sepsis and hypoperfusion and a major cause of high mortality in the intensive care unit reaching a range of 11–54% in septic pediatric patients. The final stage of shock is irreversible shock, which is also referred to as refractory shock. This final stage of shock carries a 96–99% mortality rate.

Keywords: shock, hypovolemic shock, cardiogenic shock, distributive shock, obstructive shock, oxygen delivery, cardiac output, compensated shock, uncompensated shock, resuscitation, management, inotropes

1. Introduction

Shock is a pathological state in which there is an insufficiency in oxygen supply and demand. Ultimately it results in global hypoperfusion and a resulting increase in anaerobic respiration causing lactic acidosis. Adequate oxygen delivery is an essential requirement for the sustenance of every cell in the body, the lack of which can result from a variety of pathological disturbances and can lead to life-threatening alterations. Therefore, maintaining adequate oxygen delivery in the critical care setting is of primary importance in the management of a critically ill patient.
2. Physiological need for oxygen

The requirement for oxygen is as important as a cell’s need for biochemical energy, without which no cellular or biochemical process can occur. Of the various biochemical mediums for energy, ATP is the most crucial due to the inherently high energy stored within the bonds between phosphate groups. Additionally, these bonds are readily and quickly broken to yield energy stored due to their unstable nature [1]. While ATP can be produced by processes such as glycolysis and the Krebs cycle, the amount produced by oxidative phosphorylation during the reactions within the electron transport chain, an oxygen-dependent mechanism, is vastly greater than that which the other two processes can produce. Anaerobic metabolism is an important means by which tissues can continue to produce ATP in oxygen deprived states; however it does not yield enough energy to support the functional requirements of most tissues. Therefore, the need for adequate oxygenation and delivery of oxygen to tissues across the body is essential for normal physiology.

3. Oxygen delivery

For proper oxygenation of tissues, oxygen delivery is essential and is achieved by circulation of oxygenated blood. To understand the mechanisms and factors that influence delivery one must first understand certain terms and their interconnected influence on oxygen delivery.

Firstly, the term oxygen delivery (DO₂) refers to the rate at which oxygen is delivered per unit time to cells, tissues and organs. Oxygen consumption (VO₂) subsequently is the rate at which oxygen is consumed per unit time by a cell, tissue or organ [1]. We’ll begin by discussing oxygen delivery and the essential factors that influence delivery.

Oxygen delivery is dependent on two factors, Cardiac output (CO) and arterial oxygen content (CaO₂). A change in one of these can decrease or increase the amount of global oxygen delivery. Physiologically, these factors are not independent and changes in one will be compensated with changes in the other to maintain adequate DO₂. These components of DO₂ can be expressed (Eq. 1) as:

\[
DO₂ = CO \times CaO₂
\]  

(1)

3.1 Arterial oxygen content

At any given time, blood leaving the left ventricle will be oxygenated to a certain degree expressed as the arterial oxygen content (CaO₂). This term refers both to the amount of hemoglobin saturated with oxygen (SaO₂) and the amount of oxygen dissolved in blood (PaO₂). Furthermore, since hemoglobin accounts for most of arterial oxygenation, the concentration of hemoglobin in blood (Hgb) is also an important determinant of CaO₂ (Figure 1).

These three factors determining arterial oxygen content can be mathematically represented by the following formula (Eq. 2):

\[
CaO₂ = (Hgb \times 1.34 \times SaO₂) + (PaO₂ \times 0.003)
\]  

(2)

As can be appreciated from this equation (Eq. 2) hemoglobin concentration and saturation account for a vast majority of arterial oxygenation with dissolved oxygen only making a fraction of the total oxygen level.
3.2 Cardiac Output

Circulation of oxygenated blood allows for oxygen to reach the most distal parts of the body. Circulation is determined by the heart’s functionality which is represented by cardiac output (CO). Factors that influence cardiac output are the Stroke Volume (SV) and the Heart Rate (HR). The relationship of these measurements to cardiac output is expressed in the equation below (Eq. 3):

\[
CO = SV \times HR
\]

Stroke volume is defined as the amount of blood pumped from the left ventricle into the aorta within a single contraction. Three factors determine stroke volume: Preload, Contractility, and Afterload. These components are often difficult to directly assess clinically and are often estimated using indirect methods and assumptions. Preload refers to the amount of end-diastolic stress or pressure exerted on the walls of the left ventricle influencing myocardial sarcomere length. The major determinant of preload is venous pressure and subsequent venous return. Other factors influencing preload include ventricular wall compliance, atrial contractility and valvular resistance. End-diastolic volume is usually used as an estimate for preload. Contractility refers to the rate of sarcomere shortening during contraction. It represents the functionality of cardiac muscle and is influenced by stimulation via catecholamine and concentration of electrolytes such as calcium, magnesium and potassium. Afterload refers to the force against which the left ventricle contracts and is defined as the left ventricular wall stress.

4. Oxygen consumption and oxygen extraction

Oxygen consumption (VO$_2$) by cells and tissues is dependent on their energetic requirements and expenditure. It is defined as the amount of oxygen consumed per minute. The more metabolically active a tissue is the more oxygen it will require to maintain that activity. Therefore, oxygen consumption is a measure of energy expenditure. It can be expressed as the equation (Eq. 4) given below where CmvO$_2$ is the mixed venous oxygen content:

\[
VO_2 = (CaO_2 - CmvO_2) \times CO
\]
From equation 4 it can be appreciated that consumption is an estimate of global oxygen usage calculated using the difference in oxygen content in arterial and venous blood standardized to CO or the cardiac index (cardiac output in relation to body surface area).

At rest, given normal hemoglobin concentration and adequate cardiac output, oxygen delivery exceeds oxygen consumption levels with only 25% consumed of the total oxygen delivered. This number represents an average consumption of all tissues across the body. With adequate oxygen delivery, the central venous oxygen content (ScvO$_2$) is greater than 70%. When metabolic demand increases (e.g., fever, shivering), oxygen extraction increases, and central venous oxygen content may fall.

**Oxygen extraction ratio** (O$_2$ER) represents the amount or fraction of arterial oxygen content that is consumed as blood crosses across a tissue bed [2]. The equation for the oxygen extraction ratio is given below (Eq. 5) and is the difference between arterial O$_2$ content and venous O$_2$ content divided by arterial O$_2$ content.

$$O_2\text{ER} = (\text{CaO}_2 - \text{CvO}_2)/\text{CaO}_2$$

(5)

Normally, this ratio is around 0.2–0.3 which indicates the abundance of delivered oxygen [1]. The actual extraction ratio varies with different tissues depending on the basal metabolic rates. For instance, the brain and myocardial tissue extract the most oxygen when compared to other organs. Conversely, the kidney and liver extract the least oxygen. Tissues such as myocardial tissues are therefore more dependent on oxygen delivery and are more susceptible to ischemia as they are unable to extract more oxygen. Additionally, certain tissues can increase their oxygen extraction (e.g., skeletal muscles during heavy exercise) depending on changes in their metabolic demands.

**Figure 2** summarizes the relationships between oxygen delivery consumption and extraction. As oxygen delivery falls, extraction rises in order to maintain a fixed consumption level required by tissues. With increased extraction, ScvO$_2$ begins to fall. Consumption is maintained by increasing oxygen extraction levels up until the critical point. This phase is termed the supply independent phase as a decrease in delivery will not

![Figure 2. Oxygen delivery and consumption relationship.](image-url)
reduce consumption. Beyond the critical point, extraction can no longer maintain the cells metabolic demands and consumption begins to fall linearly with decreasing oxygen delivery. This phase is termed the supply dependent phase. In this phase ischemia sets in and lactic acid begins to accumulate due to oxygen deprivation and anaerobic respiration.

5. Pathophysiology and progression of shock

As previously defined, shock is a pathological state in which there is an imbalance in oxygen supply and demand. Ultimately it results in global hypoperfusion and a resulting increase in anaerobic respiration causing lactic acidosis (Table 1).

5.1 Compensated shock

When oxygen supply is inadequate, the body undergoes several physiological changes to maintain the oxygen delivery requirements and perfusion pressure. This stage is referred to as compensated shock and early signs of shock may be appreciated during this stage. Findings consistent with compensated shock are briefly mentioned in Table 2. At this point, it is important to identify the underlying cause and correct it to prevent any lasting complications. Homeostatic changes that occur are listen in Table 1 and is stimulated by activation of two pathways. The first is baroreceptor activation. Decreased arterial pressure leads to decreased stretch of the baroreceptors located on the carotid sinus. There is a consequent decrease in afferent baroreceptor firing which increases efferent sympathetic firing and decreases efferent parasympathetic firing. Sympathetic activation results in an increase in CO via an increase in heart rate and stroke volume (increase in contractility). Arteriolar vasoconstiction allows for the redistribution of blood flow to more vital organs such as the brain, heart and kidneys. Additionally, increased sympathetic tone results in constriction of venous circulation thereby increasing venous return. As circulation is a closed system, an increase in venous return or preload brings about an increase in stroke volume and thereby cardiac output. Additionally, the sympathetic nervous system (SNS) directly stimulates the adrenal glands resulting in secretion of epinephrine, norepinephrine and cortisol which also aid in augmenting arteriolar and venous tone. The second pathway is activation of the renin-angiotensin-aldosterone-system (RAAS). A decrease in renal perfusion secondary to systemic hypotension triggers this activation. Aldosterone acts on the

<table>
<thead>
<tr>
<th>Maintaining adequate circulating volume</th>
<th>Vasodilation via ↑ Sympathetic Tone, catecholamine release, angiotensin II release (RAAS) and vasopressin release</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximization of cardiac output</td>
<td>Increase in heart rate</td>
</tr>
<tr>
<td></td>
<td>Increase in contractility</td>
</tr>
<tr>
<td></td>
<td>↑Preload ⇒ ↑CO (Frank-Starling relationship)</td>
</tr>
<tr>
<td>Redirection of blood flow to vital organs</td>
<td>Autoregulation of blood flow to vital organs</td>
</tr>
<tr>
<td>Optimizing oxygen unloaded settings</td>
<td>↑RBC 2-3-DPG concentration</td>
</tr>
<tr>
<td></td>
<td>Bohr Effect (lactic acidosis)</td>
</tr>
</tbody>
</table>

Table 1. Compensatory mechanisms in response to systemic hypotension.
principal cells in the collecting tubules of the kidney to increase sodium reabsorption. This results in fluid retention that ultimately improves cardiac output. The angiotensin II acts on AT1 receptors on vascular endothelial cells causing vasoconstriction. Angiotensin II also preferentially constricts the efferent arteriole maintaining the glomerular filtration rate (GFR) and preventing pre-renal acute kidney injury in the setting of shock. These mechanisms briefly mentioned here all aim to maintain perfusion pressure, direct blood to vital organs (e.g. brain, heart, and kidney) and increase oxygen delivery in the setting of systemic hypoxia. A comprehensive table listing the various compensatory mechanisms in response to hypoxia is given (Table 1).

5.2 Uncompensated shock

When compensatory mechanisms are inadequate and DO$_2$ begins to fall beyond the critical point, shock has progressed to the uncompensated stage. During this stage there is rapid deterioration of the patient due to prolonged hypoxia and anaerobic respiration. When this state persists, a cascade of events occurs resulting in various pathophysiological outcomes outlined in Figure 3.

Lactic acid accumulation has an effect on several organs systems. Cardiac contractility has been shown to be reduced in states of acidosis further worsening DO$_2$. Acidosis also causes a predisposition to ventricular arrhythmias. At the cellular level, the function of pH dependent enzymes such as 6-phosphofructokinase, essential in glycolysis, are compromised further retarding ATP production. As hypoxia progresses, cells begin to deplete their ATP stores resulting in the dysfunction of various ATP dependent enzymatic reactions. Of key importance is the dysfunction of ion pumps which maintain membrane potential and cellular fluid dynamics. About 70 percent of ATP produced by cells is used to maintain sodium-potassium ATPase pumps. In the setting of hypoxemia there is decreased ATP production resulting in Na$^+$/K$^+$ ATPase pumps failure. Improper functioning ion pumps results in an influx of sodium and efflux of potassium altering the osmotic equilibrium between extracellular and intracellular fluids. This results in cellular edema leading to cell dysfunction and rupture. This is the underlying issue of all types of shock and leads to the most damaging outcome of hypoxia. Cellular hypoxia also activates monocytes which result in the release of cytokines. This triggers a cascade

![Figure 3. Cellular response to hypoxia.](image)
ultimately leading to more vasodilation and increased vascular permeability further contributing to reduced tissue perfusion and hypotension. Additionally, lysosomal ion channel dysfunction disrupts lysosomal membrane potential leading to their dysfunction and release of contents. Both lysosome and cellular rupture lead to the release of toxic substances into extracellular fluids and circulation resulting in a cascade of capillary endothelial damage and cell death. Ultimately, these events produce findings such as hyperkalemia, hyponatremia, prerenal azotemia and lactic acidosis.

Clinical findings for both compensated and uncompensated shock are contrasted on Table 2.

### 5.3 Irreversible shock

The final stage of shock is irreversible shock which is also referred to as refractory shock. This final stage of shock carries a 96–99% mortality rate. There is loss of almost all compensatory mechanisms. Decreased perfusion exacerabtes anaerobic metabolism processes due to lack of oxygen delivery to end-organs. Vasodilation and increased vascular permeability results in plasma leaving the vascular space, contributing to profound interstitial edema and loss of intravascular volume. This results in refractory hypotension, end organ ischemia, Multiple Organ Dysfunction Syndrome (MODS) and ultimately death.

### 6. Systemic inflammatory response syndrome (SIRS)

One complication that may arise as shock progresses is the development of Systemic Inflammatory Response Syndrome (SIRS). While SIRS may not always be present in the progression of shock, its presence heralds the onset of a more serious syndrome mentioned earlier; Multiple Organ Dysfunction Syndrome (MODS). SIRS is defined as an “exaggerated defense response to a noxious stressor” and can be due to

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<table>
<thead>
<tr>
<th>System</th>
<th>Compensated shock</th>
<th>Uncompensated shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurological</td>
<td>Alert and oriented. Irritable</td>
<td>Altered mental status, Decreased responsiveness</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Tachycardia</td>
<td>Tachycardia, Hypotension (MAP &lt; 60 mmHg)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Tachypnea, Increased Work of Breathing</td>
<td>Tachypnea, Decreased oxygen saturation, ARDS</td>
</tr>
<tr>
<td>Renal/GU</td>
<td>Decreased urine output (&lt;0.5 mL/kg/h)</td>
<td>Prerenal azotemia, Metabolic acidosis, Anuria</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Nausea, Anorexia</td>
<td>Absence/Hypoactive bowel sounds, Ischemic bowel</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Hyperglycemia</td>
<td>Hypoglycemia</td>
</tr>
<tr>
<td>Integumentary</td>
<td>Warm extremities with normal capillary refill time</td>
<td>Cold extremities with slow capillary refill time</td>
</tr>
<tr>
<td>Labs</td>
<td>Decreased venous PO$_2$</td>
<td>Elevated lactate</td>
</tr>
</tbody>
</table>

*Increased work of breathing is evident by findings such as subcostal recessions, sternal recession and nasal flaring.*

Table 2. Findings in compensated and uncompensated shock.
Management of Shock - Recent Advances

insults such as infection, trauma, surgery, acute inflammation, and ischemia or reperfusion injury [3]. The relationship between shock and SIRS is not linear and one does not necessarily arise from the other. Shock may progress in the absence of SIRS depending on the etiology and type of shock. Infection is the most common cause of SIRS and is termed sepsis. In the early phases of septic shock, a cause of distributive shock discussed later, pathological stimuli result in cellular and immunological activation. This cellular activation leads to the release of a variety of chemokines including histamine, kinin, prostaglandins, leukotrienes and complement. Over activation of this system results in an imbalance between pro-inflammatory and anti-inflammatory mechanisms. Diagnostic criteria for determining SIRS are outlined in Table 3.

The outcomes of this imbalance occur globally, are a result of increased pro-inflammatory activity and are listed below:

a. Peripheral Vasodilation
b. Endothelial dysfunction \(\rightarrow\) Increase capillary permeability
c. Cellular activation \(\rightarrow\) neutrophils, macrophages, mast cells, platelets, endothelial cells
d. Microvascular coagulation \(\rightarrow\) end-organ micro thrombosis
e. Loss of circulatory integrity

7. Multiple organ dysfunction syndrome

Multiple Organ Dysfunction Syndrome (MODS) is a potentially life-threatening condition and is a major cause of high mortality in the intensive care unit reaching a range of 11–54% in septic pediatric patients [4]. It is defined as the ‘development of potentially reversible physiological derangement involving two or more organ systems not involved in the disorder that resulted in ICU admission” and is a result of persisting states of shock, sepsis and hypoperfusion [4]. Most often, it is the end stage in the progression of septic shock and commonly affects the lungs, myocardium and
brain before other organs. It is believed that the role of pro-inflammatory cytokines is key in inducing damage. Increased capillary leakage in the lungs causing pulmonary edema and surfactant loss, increased circulating nitrous oxide causing myocardial dysfunction and disturbances in the blood–brain barrier are all mechanisms thought to induce damage to these organs [4].

8. Types of shock

Shock can be broadly classified into four different types based on the pathological mechanism resulting in impaired oxygen delivery to the tissues. When dealing with a patient presenting with shock, it is important to identify the type of shock as all of them are treated differently. The four types of shock are:

1. Hypovolemic Shock
2. Cardiogenic Shock
3. Distributive Shock
4. Obstructive Shock

8.1 Hypovolemic shock

Hypovolemic shock occurs due to loss of intravascular volume. This is the most common type of shock. Loss of intravascular volume can be in the form of loss of blood or loss of fluids from the body other than blood. Causes of blood loss can include trauma, gastrointestinal bleeding, postpartum hemorrhage, esophageal varices and ruptured abdominal aortic aneurysm. Causes of non-blood fluid losses can include diarrhea, vomiting, reduced intake, third degree burns and diabetic ketoacidosis. Hypovolemic shock can be further classified according to the amount of volume loss. The classes of hypovolemic shock are given in Table 4.

8.2 Cardiogenic shock

Cardiogenic shock occurs due to inability of the heart to pump blood adequately to the peripheral circulation as a result of impaired contractility. This leads to end-organ

<table>
<thead>
<tr>
<th>Class</th>
<th>Volume loss</th>
<th>Pulse</th>
<th>Blood pressure</th>
<th>Capillary refill</th>
<th>Respiratory rate</th>
<th>Urine output (mL/kg/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0–15%</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>1–2</td>
</tr>
<tr>
<td>II</td>
<td>15–30%</td>
<td>Mild Tachycardia</td>
<td>Mildly Low</td>
<td>Mildly Prolonged</td>
<td>Mild Tachypnea</td>
<td>0.5–1</td>
</tr>
<tr>
<td>III</td>
<td>30–40%</td>
<td>Tachycardia</td>
<td>Low</td>
<td>Prolonged</td>
<td>Tachypnea</td>
<td>0.25–0.5</td>
</tr>
<tr>
<td>IV</td>
<td>&gt;40%</td>
<td>Tachycardia, Bradycardia or absent</td>
<td>Very Low</td>
<td>Greatly Prolonged</td>
<td>Severe Tachypnea</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 4. Classes of hypovolemic shock.
hypoxia and shock. Causes of cardiogenic shock can be myocardial infarction, myocarditis (secondary to Coxsackie B virus), dilated cardiomyopathy, and congenital heart disease, valvular dysfunction like aortic valve stenosis or mitral valve stenosis and arrhythmias. Both tachy-arrhythmias and brady-arrhythmias can lead to cardiogenic shock. Tachy-arrhythmias cause the heart to beat abnormally fast which impairs the filling ability of the heart, hence decreasing the preload and subsequently decreasing the cardiac output. Brady-arrhythmias decrease the heart rate and since CO = SV x HR, this also causes the cardiac output to decrease.

8.3 Distributive shock

Distributive shock occurs due to inappropriately distributed blood volume. Under normal physiology, vascular tone is under control of the autonomic nervous system. Sympathetic stimulation causes vascular smooth muscle to contract and vasoconstrict, while the parasympathetic nervous system causes vascular smooth muscle to relax and vasodilate. Distributive shock occurs when the sympathetic nervous system is unable to maintain the tone of the vascular system, allowing abnormal vasodilation of blood vessels. This allows pooling of blood and decreases preload. This also leads to increased vascular permeability and third-space fluid loss. This in turn causes intravascular hypovolemia and decreased end-organ perfusion. Distributive shock can have different etiologies like septic shock, anaphylactic shock and neurogenic shock.

Septic shock is the most common cause of distributive shock [5]. It can be defined as “sepsis-induced hypotension (systolic blood pressure <90 mm Hg or a reduction of 40 mm Hg from baseline) despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include, but are not limited to, lactic acidosis, oliguria, or an acute alteration in mental status.” Septic shock results from an overwhelming systemic inflammatory response which leads to vasodilation and subsequent hypotension. Most common causes of septic shock are gram negative bacteria like Escherichia coli, Proteus species, Klebsiella pneumoniae which release endotoxins which are responsible for activation of the immune system.

Anaphylactic shock occurs due to type 1 hypersensitivity reaction to any foreign antigen. Antigens bind to IgE molecules on pre-sensitized mast cells and cause mast cell degranulation and release of inflammatory mediators like histamine. Histamine causes vasodilation and increased capillary permeability. This causes severe hypovolemia and cardiovascular collapse leading to shock.

Neurogenic shock results from the inability of the sympathetic nervous system to maintain the tone of blood vessels. In most cases, this is a result of trauma to the brain or spinal cord above the level of T6 [6]. The trauma leads to a loss of background sympathetic stimulation to the vascular smooth muscles. This causes vasodilation resulting in a sudden decrease in blood pressure (secondary to a decrease in peripheral vascular resistance).

8.4 Obstructive shock

Obstructive shock occurs when there is a barrier to the flow of blood or a barrier which impairs proper filling of the heart. There are several conditions which can cause obstructive shock. These include cardiac tamponade, tension pneumothorax and pulmonary embolism.

Cardiac tamponade is the result of fluid in the pericardial space which impairs the filling ability of the heart during diastole. This reduces the preload and subsequently
decreases cardiac output. This is similar in presentation to constrictive pericarditis in which the pericardium shrinks and hardens.

Tension pneumothorax is the presence of air in the pleural cavity under positive pressure. The elevated intrathoracic pressure leads to decreased venous return to the heart as it compresses the inferior vena cava, thus leading to reduced cardiac output.

Pulmonary embolism is an embolus (usually dislodged from the proximal deep veins of the lower limb) lodged in the vasculature of the lungs. This obstructs blood flowing to the lungs and the blood coming from the lungs to the heart. There is a decrease in end-diastolic volume which leads to a decreased stroke volume and hence decreased cardiac output and oxygen delivery to the peripheral tissues resulting in shock.

9. Resuscitation goals

When approaching a patient in shock, management requires attaining physiological normalcy and hemodynamic stability. In the clinical setting, the progress of treatment is measured by achieving certain goals. These clinical goals help ascertain improvement in global perfusion and oxygenation. Factors measured are included in Table 5 and are used clinically to determine a patient’s response to the management of shock. While these conditions are useful in measuring response, the use of only one or two as an indicator for improvement will lead to shortcomings and mislead a physician regarding the actual response to management.

One goal used to assess treatment is normalcy in heart rate and perfusion pressure representing adequate perfusion and venous return/cardiac output. Perfusion pressure is determined by subtracting the central venous pressure (CVP) by the mean arterial pressure (MAP); MAP-CVP. These parameters can be used to measure hemodynamic stability and are also used to assess response to fluid therapy. With administration of a fluid bolus, heart rate should ideally decrease and MAP-CVP should increase. Another measurement that can be used to assess response to fluid therapy and inotrope therapy response is the shock index (HR/SBP). Calculated by dividing

<table>
<thead>
<tr>
<th>Indicators of therapeutic responsiveness</th>
<th>Normal value/Prognostic value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Mental Status</td>
<td>GCS = 15/15</td>
</tr>
<tr>
<td>Normal pulse quality and rate</td>
<td>Palpable in all extremities; Rate varies with age</td>
</tr>
<tr>
<td>Difference in Central and peripheral temperatures</td>
<td>36.1–37.2°C; equal centrally and peripherally</td>
</tr>
<tr>
<td>Normal Capillary Refill</td>
<td>≤ 2 seconds</td>
</tr>
<tr>
<td>Adequate Urine Output</td>
<td>&gt;1 mL/kg/h</td>
</tr>
<tr>
<td>Lactate Trends</td>
<td>≥0.75 mmol/L/h, associated with bad prognosis</td>
</tr>
<tr>
<td>Normal Superior Vena Cava Oxygen Saturation (SVC O₂)</td>
<td>≥ 70%</td>
</tr>
<tr>
<td>AVDO₂</td>
<td>≤5 mL O₂/100 mL of blood</td>
</tr>
</tbody>
</table>

Table 5. Resuscitative goals and normal values.
heart rate (HR) by systolic blood pressure (SPB), the shock index should ideally decrease as fluid therapy is directed at improving stroke volume, thereby decreasing HR, and inotropic therapy improves vascular tone and SBP.

As mentioned earlier, during shock states compensatory mechanisms redirect blood to vital organs such as the brain, heart and kidneys. Consequently, as shock progresses from compensated to uncompensated phase, these organs will begin to show signs of dysfunction. Mental status of a patient is therefore a parameter which should be assessed to determine improvement in a patient’s condition. While improvement is a good sign, not all patients will have altered mental status and, when present, is often a late manifestation of shock. Relying on altered mental status as an indicator of shock and its improvement as good response to therapy is not a reliable approach and should be taken with caution and in combination with other factors. The kidney is another organ which can be used to assess response to therapy. A normal urine output of >1 mL/kg/h represents adequate renal perfusion and perfusion pressure. However, urine output only represents the improvement in renal perfusion and does not provide a picture of global perfusion status.

Systemic vascular tone and cardiac output can both be determined by assessing peripheral temperatures, capillary refill and distal pulse qualities. Normal capillary refill is <2 seconds and coupled with normal peripheral temperature and distal pulses correlates with adequate perfusion to the peripheries. However, these parameters do not provide indication of oxygenation. Cases such as anemia or hemodilution may have normal peripheral temperature, pulses and capillary refill but oxygen delivery is still impaired.

As shock is defined as impaired systemic oxygen delivery, lactate levels are a good indicator of global oxygenation. Lactate trends should be observed rather than single serum lactate measurements as a single measurement does not indicate the progression of disease. Increases of lactate levels of ≥70 mmol/L/h. is associated with worsening oxygen delivery and outcomes.

Superior vena cava oxygen saturation (SVCO2) of ≥70% is a good therapeutic endpoint in the management of shock. As mentioned earlier in the chapter, when there is good oxygen delivery, SVCO2 should be maintained above 70% representing no increase in oxygen extraction during the compensatory phase of shock. Measuring SVCO2 can be done via central venous catheters with venous oximetry or, more recently, with the use of near-infrared spectroscopy, a less invasive method. One can also calculate the difference in arterial and venous oxygen content (AVDO2) to assess the degree of oxygen extraction during this phase of shock. Normal values show a difference of ≤5 mL O2/100 mL of blood and increases in AVDO2 indicate increases in oxygen extraction.

10. General principles in the treatment of shock

In order to provide a patient with the benefit of rational and effective treatment, it is critical to identify the specific cause of shock in each case. Although treatment should be aimed at the underlying etiology of shock, the most critical aspect of treatment is the prompt restoration of normal hemodynamics.

From a hemodynamic perspective, there are three main categories in the management of shock:
Intravenous fluids, which act by increasing central venous pressure and downstream left ventricular end-diastolic volume (EDV)

- Vasopressors which act by increase systemic vascular resistance (SVR)

- Inotropes which act by increasing contractility and thus increase cardiac output

In hypovolemic shock, the primary derangement is low central venous pressure (CVP) so therefore IV fluids are the cornerstone of therapy. If the patient is profoundly hypotensive, vasopressors are sometimes used temporarily but only while definitive access is obtained, and fluids are pushed as quickly as possible. If a patient in hypovolemic shock is requiring vasopressors to maintain enough perfusion pressure to stay conscious, they are in critical need for more fluid. Since these patients are already extremely hyper dynamic, there are no benefits of inotropes which will only risk worsening tachycardia to the point that diastolic filling time is too short for the left ventricle to fill.

In distributive shock, the primary derangement is low SVR. Vasopressors are therefore almost always necessary. Since most of these patients are also hypovolemic, or at the very least, have fluid maldistributed to the extravascular space rather than central circulation, IV fluids are also used in every case. Because of sepsis induced cardiomyopathy, some patients with sepsis may also benefit from inotropes but identifying those patients can be a challenge.

In cardiogenic shock, the primary problem is low cardiac output, thus inotropes are the mainstay therapy. Both fluids and vasopressors are not only unnecessary but contraindicated. In fact, reduction in preload by using diuretics, and reducing the afterload helps in augmenting the cardiac output in patients with cardiogenic shock.

Finally, in obstructive shock, it is impossible to generalize about the appropriateness of fluids, vasopressors and inotropes and if there is a response to any of those, it is likely only temporary. Definitive relief of the obstruction is still critical. For pneumothorax (PTX), this is either chest tube or needle thoracostomy which consists of a needle placed into the pleural space via the second intercostal space in the midclavicular line. For cardiac tamponade, pericardiocentesis can be performed, a procedure in which a needle is placed in the pericardial space most commonly via a subxiphoid approach. In case of massive pulmonary embolism, depending on the circumstances, this may require systemic thrombolysis or embolectomy.

General treatment principles are summarized in Table 6.

<table>
<thead>
<tr>
<th>Type of shock</th>
<th>IV Fluids (↑ CVP)</th>
<th>Vasopressors (↑ SVR)</th>
<th>Inotropes (↑ Contractility)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypovolemic</td>
<td>+</td>
<td>Temporary use only</td>
<td>-</td>
</tr>
<tr>
<td>Distributive</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
</tr>
<tr>
<td>Cardiogenic</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Obstructive</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
</tr>
</tbody>
</table>

Table 6.
General approach to therapy with regards to type of shock.
10.1 Fluid therapy

Fluid resuscitation is the rapid delivery of fluids to patients who have acutely impaired hemodynamics. Resuscitative fluids are given universally to patients in hypovolemic shock and lesser forms of dehydration, as well as to almost all patients with severe sepsis and septic shock. In these situations, the preload to the heart is not enough for adequate cardiac output. To understand why these patients are given fluids we need to review the Frank-Starling curve as shown in Figure 4. According to the Frank-Starling Law, the length of myocardial tissue is directly related to the force of the subsequent contraction. The more myocardial fibers are stretched, the more they contract. Preload determines the degree of myocardial fiber stretching. Therefore, as shown in Figure 4, an increase in preload results in a responsive increase in stroke volume. Patients on the left side of the curve are those who are preload dependent. Towards the right, the curve flattens and increases in preload are met with a reduced rate of increase in stroke volume until we see no change in stroke volume with increasing preload. These patients are preload independent. Essentially, only if the patient is preload dependent will we see benefits to stroke volume if given fluid. Preload independent patients will not benefit from fluids. It is important to note that the shape and position of the curve will vary between individuals, and it is important to identify where on the curve the patient lies to determine whether it is suitable to give fluids.

Once we have decided which patient needs to be given fluids, we need to decide which fluids to give. The first decision to make is whether to give crystalloid or colloid. Crystalloids are fluids which contain water and various electrolytes and other small water-soluble molecules. Colloids are large, insoluble molecules and oftentimes proteins. Theoretically, colloid should be superior to crystalloid as it has an increased tendency to stay intravascular. However, a 2013 Cochrane review found no evidence from randomized controlled trials that resuscitation with colloids reduces the risk of death, compared to resuscitation with crystalloids, in patients with trauma, burns or following surgery [7]. Therefore, given their decreased cost and increased availability,
as well as the low immunogenic response, crystalloids are almost always favored over colloids.

Crystalloid replacement is usually sufficient in hypovolemic shock caused by vomiting and diarrhea. The presence or absence of associated electrolyte disturbances (e.g., hypo- or hypernatremia) determines the type of crystalloid. The use of albumin as a replacement fluid for hypovolemic shock is probably best reserved for situations involving direct albumin loss (e.g., burns, open wounds, protein-losing enteropathies). Volume replacement with crystalloid or albumin may be appropriate in cases of hemorrhagic shock, but with significant blood loss, replacement of red blood cell mass will eventually become necessary.

While the majority of patients with hypovolemic shock tolerate relatively rapid correction of intravascular volume depletion, there are a few notable exceptions that may require slower correction. For example, in cases of hypovolemic shock accompanied by significant metabolic/electrolyte derangements (e.g., hypernatremia or diabetic ketoacidosis), volume deficit correction must be tempered so that the accompanying metabolic/electrolyte abnormalities are not corrected too quickly. Rapid correction of hypernatremia can lead to cerebral edema while rapid correction of hyponatremia can lead to central pontine myelinolysis.

Correction of hypovolemic shock in patients with underlying myocardial dysfunction must be done with greater caution than in patients with normal myocardial function to avoid further compromising myocardial function. Finally, in trauma-specific situations, very aggressive volume resuscitation for hemorrhagic shock may not be appropriate until surgical hemorrhage control is achieved.

10.2 Blood products

Oxygen delivery, as described in the first section, is dependent on two factors: cardiac output and arterial oxygen content. Vasoactive and fluid therapy both aim to enhance cardiac output and global perfusion to enhance oxygen deliver. In both these therapies the arterial oxygen content remains the same. The use of blood products aims to increase arterial oxygen content (CaO₂) by infusing packed red blood cells (PRBC) thereby increasing hemoglobin levels, the main parameter determining arterial oxygen content. The use of PRBC is therefore most useful in situations where shock is caused or worsened by decreasing hemoglobin concentration such as in patients with hemolytic anemia. The goal of blood product therapy is to return hemoglobin concentrations to normal values with regards to age. Approximately 10 mL/kg of PRBC should increase hemoglobin concentration by 2 g/dL. A 20 kg child with an Hb concentration of 5 g/dL would therefore require 500 mL of PRBC to reach an Hb concentration of 10 g/dL. When considering blood transfusion, it is important to consider the hemodynamic changes that occur with increasing hematocrit. Experimentally it has been shown that a hematocrit of 30% is optimal for oxygen delivery while hematocrit levels exceeding 40% increase viscosity and hinder oxygen delivery [8].

10.3 Vasoactive therapy

Vasoactive drugs used in the management of shock can be divided into inotropic, vasoconstrictive and vasodilative medication. The main goals of employing these medications are to increase cardiac output, decrease vascular resistance and increase
perfusion pressure. The administration of these drugs usually come after initial use of fluid and blood product therapies fail to produce adequate improvement.

**Inotropes:** Inotropes are generally used to increase cardiac output and stroke volume. Their mechanism of action usually involves stimulation of adrenergic receptors and includes endogenous catecholamines such as dopamine, epinephrine and norepinephrine and exogenous catecholamines such as dobutamine and phenylephrine. These drugs work to stimulate $\alpha$-adrenergic, $\beta$-adrenergic and dopaminergic receptors which subsequently alter conditions such as contractility and systemic vascular resistance (vasodilation or vasoconstriction) thereby influencing cardiac output and perfusion pressures. In the setting of shock, the use of these drugs helps enhance cardiac function to improve oxygen delivery.

Aside from drugs such as phenylephrine, most inotropic drugs will stimulate multiple receptor types with varying selectivity. For example, as shown in Table 7, dopamine will preferentially stimulate dopaminergic receptors but will also stimulate $\beta$- and $\alpha$-adrenergic receptors and will therefore exhibit varying and multiple physiological changes in a dose dependent manner. It is therefore important to know drugs selectivity and the physiological response of each receptor type. $\beta_1$-adrenergic receptors are primarily expressed in myocardial tissue and have positive inotropic and chronotropic activity when stimulated. Stimulation of this receptor directly enhances cardiac output by increasing heart rate and contractility (stroke volume). $\beta_2$-adrenergic receptors act on smooth muscle of vascular tissue and bronchial tissue and produce vasodilation and bronchodilation respectively. $\alpha_1$-adrenergic receptors work mainly on vascular smooth muscles contraction and cause peripheral vasoconstriction. $\alpha_2$-adrenergic receptors on the other hand causes vasodilation via the inhibition of norepinephrine secretion from presynaptic sympathetic neurons. Dopaminergic receptors (DA) receptors act on renal vasculature and causing renal arterial vasodilation.

**Dopamine**, in terms of inotropic therapy, displays dose-dependent activity on dopaminergic, $\beta$- and $\alpha$-adrenergic receptors. At low doses (0-3 $\mu$g/kg/min) dopamine acts as a mild vasodilator in peripheral vasculature by stimulating the release of norepinephrine [9]. Additionally, it inhibits norepinephrine reuptake in presynaptic sympathetic neurons indirectly enhancing contractility and heart rate [9]. Activation of dopaminergic receptors at low doses also improves renal and splanchic perfusion via $D_2$ presynaptic receptors potentially providing renal protective activity [8, 9], but it remains matter of debate. Stimulation of $D_2$ presynaptic receptors enhances vasodilation in coronary, renal, mesenteric and cerebral vasculature promoting improved blood flow to these organs [9]. While inhibition of norepinephrine reuptake in sympathetic neurons does have vasoconstrictive activity, the direct vasodilatory effects in peripheral vasculature offsets the level of constriction resulting in mild elevation of SVR. Ultimately, dopamine has the combined effect of significantly improving contractility and heart rate with only mild changes in SVR resulting in effective improvement in cardiac output. At higher doses (>10 $\mu$g/kg/min) $\alpha$-adrenergic activity is stimulated causing vasoconstriction and aids in increasing blood pressure [8, 9].

**Epinephrine** is a nonselective catecholamine stimulating both adrenergic receptors of all types. Therefore, is produces both increases in CO and increases in SVR. When administered at a low dose at an infusion rate of 0.03-0.3 $\mu$g/kg/min, epinephrine mostly exhibits inotropic activity via $\beta$-adrenergic receptors increasing cardiac output. As higher infusion rates >0.3 $\mu$g/kg/min are used, $\alpha$-adrenergic activity is also activated resulting in vasoconstriction and an increase in SVR. Because of its selective inotropic activity at low doses, epinephrine is reliable choice in patients with
hypotension without myocardial dysfunction. In high doses epinephrine has also been seen to cause atrial and ventricular arrhythmias [9]. One aspect of inotropic therapy using epinephrine is its administration in correlation with elevated lactate levels. Studies have shown that epinephrine may elevate lactate levels, interfering with lactate trends. It is therefore important to interpret lactate trends with skepticism when assessing response to therapy and concomitant resuscitation goals should be viewed when using epinephrine.

**Norepinephrine** preferentially binds $\alpha_1$-adrenergic receptors over $\beta$-adrenergic receptors resulting in more vasoconstrictive activity than inotropic activity. Because of its potent $\alpha$-receptor stimulation, norepinephrine is the vasopressor drug of choice in distributive shock with hypotension [9]. At low doses of 0.01–0.05 $\mu$g/kg/min its inotropic activity can be appreciated with an improvement in cardiac output. However, at higher doses, its affinity for $\alpha$-adrenergic receptors takes over, vastly increasing vasoconstriction and blood pressure. This shift in receptor activity can impede cardiac output especially in patients with cardiac dysfunction.

**Dobutamine** is a synthetic catecholamine that has mixed $\beta$- and $\alpha$-adrenergic stimulation at varying dosages. It primary acts as an inotrope increasing contractility with minimal increases in SVR indicating its use in patients with cardiogenic shock. Additionally, at infusion rates $>10$ $\mu$g/kg/min dobutamine can reduce afterload by stimulating $\alpha_2$-adrenergic stimulation causing vasodilation [8]. In this setting dobutamine can improve cardiac output [8]. At low doses of $<5$ $\mu$g/kg/min, dobutamine can exhibit $\alpha_1$-adrenergic antagonism resulting in vasodilation and decreased afterload.

**Phenylephrine** is a pure $\alpha_1$-adrenergic agonist and has strong vasoconstrictor activity. It can be used as an additional therapy where an increase in vascular tone is needed without changes in cardiac function.

**Phosphodiesterase inhibitors (Milrinone)** work as an inotrope via a different mechanism than the catecholamines described above. By inhibiting phosphodiesterase, it causes an increase in intracellular cAMP levels thereby increasing intracellular Ca$^{2+}$. These changes subsequently increase both inotropic activity in myocytes and

<table>
<thead>
<tr>
<th>Drug</th>
<th>Receptor/mechanism</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine</td>
<td>Dopaminergic (DA) $&gt;\beta$-adrenergic $&gt;\alpha$-adrenergic</td>
<td>Low doses (DA) $\rightarrow$ ↑ renal artery vasodilation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mod/high. Doses (DA + $\beta$) $\rightarrow$ ↑ renal blood flow, HR, contractility, CO</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>$\alpha$ &amp; $\beta$-adrenergic</td>
<td>↑ CO with minimal effects on BP</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>$\alpha_1$ &amp; $\beta$-adrenergic</td>
<td>↑ SVR, HR, CO, BP</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>Pure $\alpha_1$-adrenergic</td>
<td>Peripheral arterial vasoconstriction $\rightarrow$ ↑ BP, MAP, SVR</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>Mixed $\alpha_1$ &amp; $\beta$-adrenergic ($\alpha_1 &gt; \beta_1 &gt; \beta_2$)</td>
<td>Significant ↑ BP + MAP, SVR, CO, HR</td>
</tr>
<tr>
<td>Vasopressin</td>
<td>V-1 &amp; V-2 receptors</td>
<td>↑ BP, SVR; anti-diuretic action via V-2</td>
</tr>
<tr>
<td>Phosphodiesterase Inhibitor (Milrinone)</td>
<td>↑ cAMP</td>
<td>↑ CO + vasodilation $\rightarrow$ ↓ BP</td>
</tr>
</tbody>
</table>

Table 7.  
Mechanism of action and effects of inotropes and vasopressors.
Vasodilation in vascular smooth muscle. It has the advantage of achieving these results without acting on adrenergic receptors and is therefore ideal in situations where receptor downregulation has developed due to chronic inotrope usage such as in those patients with chronic heart failure [9].

**Vasopressin** maintains perfusion pressure through two main mechanisms. Firstly, it acts on blood vessels to produce vasoconstriction via the activation of \( \text{V}_1 \)-receptors. This causes an increase in SVR and thereby increases arterial pressure. Secondly, it stimulates \( \text{V}_2 \)-receptors on renal tubular cells to enhance fluid reabsorption via aquaporin channels. Vasopressin is also known to stimulate CRH release from the hypothalamus, thereby increasing downstream ACTH and cortisol secretion. Cortisol in turn enhances vasoconstriction and inhibits secretion of vasodilators such as PGE2 and nitric oxide.

Mechanisms of these drugs and their effect on the cardiovascular system are summarized in Table 7.

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References


