Pediatric Shock: An Overview

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Abstract: Shock is one of the most frequently diagnosed, yet poorly understood disorders in the pediatric intensive care unit (PICU). The very definition of what constellation of physical signs and symptoms that comprise *shock* remains controversial, in part due to the vast array of disorders that cause shock in critically ill and injured children. Early management and reversal of the shock state is associated with significantly improved outcomes. However, early management is critically dependent upon the early recognition and diagnosis of shock at the bedside. Failure to recognize the signs and symptoms of shock and to institute timely and appropriate care leads to higher mortality rates in both children and adults. Clinical recognition of shock requires a high index of suspicion – as such, all pediatric health care providers should be cognizant of the clinical presentation, pathophysiology, and early management of shock.

INTRODUCTION

Shock is one of the most frequently diagnosed, yet poorly understood disorders in the pediatric intensive care unit (PICU). The very definition of what constellation of physical signs and symptoms that comprise *shock* remains controversial, in part due to the vast array of disorders that cause shock in critically ill and injured children (Table **1**). Early management and reversal of the shock state is associated with significantly improved outcomes [1-6]. However, early management is critically dependent upon the early recognition and diagnosis of shock at the bedside. Failure to recognize the signs and symptoms of shock and to institute timely and appropriate care leads to higher mortality rates in both children and adults [7-11]. Clinical recognition of shock requires a high index of suspicion – as such, all pediatric health care providers should be cognizant of the clinical presentation, pathophysiology, and early management of shock.

HISTORICAL PERSPECTIVE

The French surgeon Henri Francois Le Dran is widely credited with the first use of the medical term *shock* (literally translated from the French verb *choquer*) in 1737 in his textbook, *A Treatise of Reflections Drawn from Experience with Gunshot Wounds* [12]. Le Dran had used the term to describe *a sudden impact or jolt* that often led to death. However, his use of the term referred to the original injury itself, and not the pathologic state that followed. It was actually the English physician Clarke's mistranslation of LeDran's work in 1743 that first introduced the term into the English language to describe the sudden deterioration of a

patient's condition following major trauma [13]. Consistent with these early descriptions was the widespread belief that the pathologic state of shock was due to a nervous condition [14]. For example, the British surgeon Benjamin Travers described shock as *a functional concussion by which the influence of the brain over the organ of circulation is deranged or suspended* in 1826 [15]. He further stated that shock initially manifested as anxiety, altered states of consciousness, and muscle weakness, followed by *a diminution of the power of the heart*, and lastly *the respiratory function becomes impeded, as a necessary consequence of the two first* [15]. Most physicians believed that the nerves were the only anatomic structures found throughout the body – thus, only a condition affecting the nerves could have such widespread effects on the body and explain the wide range of clinical signs and symptoms associated with the shock state. This was the prevailing theory until the time of World War I and led to the widespread use of stimulants, depressants, or in some cases, electrical shock for treating patients with shock [14].

Despite the widespread belief that shock was secondary to a nervous system dysfunction, there were some physicians who believed that shock was due to overt blood or volume loss. For example, William O'Shaughnessy was the first to note that the blood from patients suffering from cholera had *lost a large portion of its water* and later suggested a novel treatment by returning the blood to its *natural specific gravity* by replacing its *deficient saline*. O'Shaughnessy sent a letter to the *Lancet* [16] that included the following description of terminal cholera:

> *On the floor, before the fireplace. . . lay a girl of slender make and juvenile height; with the face of a superannuated hag. She uttered no moan, gave expression of no pain, ... The colour of her countenance was that of lead - a silver blue, ghastly tint; her eyes were sunk*

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Table 1. **Common Causes of Shock in Children (Modified from Thomas NJ, Carcillo JA.** *New Horiz* **1998; 6:120-129)**

HYPOVOLEMIC SHOCK
  FLUID AND ELECTROLYE LOSSES
    VOMITING
    DIARRHEA
    NASOGASTRIC TUBE DRAINAGE
    RENAL LOSSES (*VIA* EXCESSIVE URINARY OUTPUT)
      DIURETIC ADMINISTRATION
      DIABETES MELLITUS
      DIABETES INSIPIDUS
      ADRENAL INSUFFICIENCY
    FEVER
    HEAT STROKE
    EXCESSIVE SWEATING
    WATER DEPRIVATION
    SEPSIS
    BURNS
    PANCREATITIS
    SMALL BOWEL OBSTRUCTION
  HEMORRHAGE
    TRAUMA
      FRACTURES
      SPLEEN LACERATION
      LIVER LACERATION
      MAJOR VESSEL INJURY
      INTRACRANIAL BLEEDING (ESPECIALLY NEONATES)
    GASTROINTESTINAL BLEEDING
    SURGERY
CARDIOGENIC SHOCK
  MYOCARDITIS
  CARDIOMYOPATHY
  MYOCARDIAL ISCHEMIA (E.G. KAWASAKI'S DISEASE, ANOMALOUS ORIGIN OF THE LEFT CORONARY
    ARTERY, ETC)
  VENTRICULAR OUTFLOW TRACT OBSTRUCTION
  ACUTE DYSRHYTHMIAS
  POST CARDIOPULMONARY BYPASS
OBSTRUCTIVE SHOCK
  TENSION PNEUMOTHORAX
  CARDIAC TAMPONADE
  PULMONARY EMBOLISM
DISTRIBUTIVE SHOCK
  SEPSIS
  ANAPHYLAXIS
  NEUROGENIC SHOCK

deep into the sockets, as though they had been driven in an inch behind their natural position; her mouth was squared; her features flattened; her eyelids black; her fingers shrunk, bent, and inky in their hue. All pulse was gone at the wrist, and a tenacious sweat moistened her bosom. In short, Sir, that face and form I never can forget, were I to live to beyond the period of man's natural age.

The astute clinician will appreciate O'Shaughnessy's apt description of the late stages of uncompensated and irreversible shock here. Ironically, O'Shaughnessy received a knighthood for his later work on the electric telegraph and not for his work on cholera. Unfortunately, it was not until 1832 that Thomas Latta followed O'Shaughnessy's advice and first attempted intravenous fluid resuscitation.

Shock has been called a lot of things over the years. Samuel Gross called shock *the rude unhinging of the machinery of life* in 1872 [17]. John Warren called shock *a momentary pause in the act of death* in 1895 [18]. Blalock defined shock as *a peripheral circulatory failure, resulting from a discrepancy in the size of the vascular bed and the volume of the intravascular fluid* in 1940 [19]. Finally, the

famed physiologist Carl Wiggers offered the following definition in 1942:

> *Shock is a syndrome resulting from a depression of many functions but in which reduction of the effective circulating blood volume is of basic importance and in which impairment of the circulation steadily progresses until it eventuates into a state of irreversible circulatory failure* [20].

While all of these descriptions are appropriate, shock is now commonly defined as a clinical state characterized by an inadequate delivery of oxygen and metabolic substrates to meet the metabolic demands of the cells and tissues of the body. We now recognize Gross' *machinery of life* as the mechanisms that assure adequate oxygen delivery and utilization at the cellular level. Inadequate oxygen delivery results in cellular hypoxia, anaerobic metabolism and resultant lactic acidosis, activation of the host inflammatory response, and eventual vital organ dysfunction.

Although significant progress has been made in elucidating the molecular and cellular basis of shock, morbidity and mortality from shock remain unacceptably high. Orr and colleagues evaluated a 5,000 patient database of children referred from the community setting to five separate pediatric hospitals in 2000 [2]. Shock, defined in this report by the presence of either hypotension or a capillary refill > 2 seconds was the leading cause of death in these children, regardless of trauma status. Although head trauma was more common among patients who died, shock at the outside community hospital was a major predictor of subsequent death. Of major concern, only 7% of the 5,000 patients were referred for a diagnosis of *shock*, yet more than 40% of these children did, in fact, meet the prospectively defined criteria for the diagnosis of shock. Community physicians were more likely to refer these children for respiratory distress when shock was present, even though the presence of shock was a significant risk factor for subsequent mortality. Therefore, despite the dramatic advances in the care of children with shock over the last 50 years, shock remains both common and often underappreciated in children, even in tertiary care pediatric hospitals.

THE PATHOPHYSIOLOGY OF SHOCK

Shock is characterized by a relative imbalance between the delivery of oxygen and metabolic substrates and the metabolic demands of the cells and tissues of the body. While the shock state most commonly occurs in the setting of decreased oxygen delivery, it is certainly feasible that excessive metabolic demands could produce a similar pathologic state. However, the body's compensatory mechanisms are able to adjust to meet even incredibly high metabolic demand, so that a state of shock will usually only occur in the setting of decreased oxygen and substrate delivery.

Under resting conditions, with normal distribution of cardiac output, oxygen delivery (DO_2) is more than adequate to meet the total oxygen requirements of the tissues needed to maintain aerobic metabolism, referred to as oxygen consumption (VO_2). This excess delivery or *oxygen reserve* serves as a buffer, such that a modest reduction in oxygen delivery is more than adequately compensated by increased extraction of the delivered oxygen, without any significant reduction in oxygen consumption. During stress or vigorous exercise, oxygen consumption markedly increases, as does oxygen delivery. Therefore, in the majority of circumstances, the metabolic demands of the cells and tissues of the body dictate the level of oxygen delivery. However, very little oxygen is stored in the cells and tissues of the body. As oxygen delivery falls with the shock state, oxygen extraction must necessarily increase to meet metabolic demands, and oxygen consumption remains relatively constant (i.e., so-called *delivery-independent* oxygen consumption) (Fig. **1**). However, there is a critical level of oxygen delivery at which the body's compensatory mechanisms are no longer able to keep up with metabolic needs (i.e. the point at which oxygen extraction is maximal). This point is often referred to as the *anaerobic threshold*. Once oxygen delivery falls below this level, oxygen consumption must also fall and is said to become *delivery-dependent*. Notably, lactate production increases significantly beyond this critical point and may often be detected in the peripheral blood.
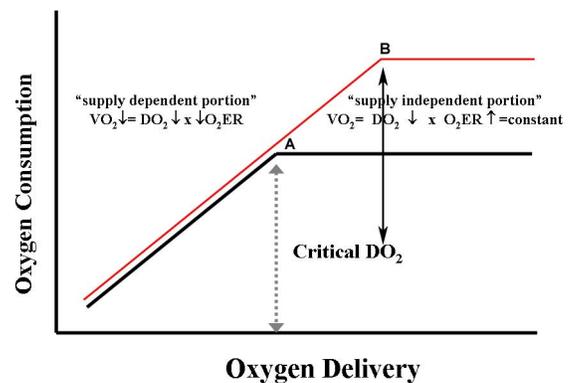

Fig. (1). The oxygen delivery – oxygen consumption relationship.

For many years, many investigators believed that a so-called pathologic supply-dependency existed in critical illness. Experimental models of sepsis [21-23] and clinical data [24] both reported that the critical oxygen extraction ratio was lower than normal during critical illness - that is oxygen consumption became *delivery-dependent* at a higher critical DO_2 in critically ill patients. This observation implied an intrinsic defect at the cellular level in oxygen extraction. While an attractive hypothesis, most of the clinical data on which this concept was based are suspect due to the fact that the formulas for DO_2 and VO_2 share common variables:

$DO_2 = CO \times (Hb \times 1.34 \times SaO_2) + (0.003 \times PaO_2)$ (Eq 1)

$VO_2 = CO \times (Hb \times 1.34 \times (SaO_2 - SvO_2) + 0.003 \times (PaO_2 - PvO2)$ (Eq 2)

As can be easily identified in the equations above, the calculation of DO_2 and VO_2 both share the measurements of cardiac output and arterial oxygen content (CaO_2). The potential for computation error arises because the measurements of these variables in the calculation of DO_2

and VO_2 result in a mathematical coupling of measurement errors in the shared variables resulting in false correlation between oxygen delivery and consumption. In order to avoid potential mathematical coupling, oxygen consumption and delivery should be determined independent of each other. Studies in which VO_2 was directly measured (rather than calculated) have largely disproved this pathologic supply dependency hypothesis. Regardless, during the shock state, the body's compensatory mechanisms, as well as our therapeutic efforts, are largely directed at optimizing the balance between oxygen delivery and consumption.

STAGES OF SHOCK

During the shock state, the body's compensatory mechanisms (summarized in Table **2**) attempt to maintain vital organ function. The progression of the shock state is commonly divided into three phases: compensated, uncompensated, and irreversible shock [25, 26] (Table **3**). During compensated shock, oxygen delivery to the brain, heart, and kidney is maintained at the expense of *less vital* organs. Signs and symptoms of the shock state, though often subtle, may be apparent even at this early stage. Notably, hypotension is not a feature during this stage – rather, increased peripheral vascular tone and increased heart rate maintain a normal cardiac output and a normal blood

pressure. As shock progresses to the *uncompensated stage*, the body's compensatory mechanisms eventually contribute to the further progression of the shock state (e.g., blood is shunted away from the skin, muscles, and gastrointestinal tract in order to maintain perfusion of the brain, heart, and kidneys, leading to ischemia in these vascular beds with subsequent release of toxic substances, further perpetuating the shock state). Cellular function deteriorates further, culminating in end-organ dysfunction. The *terminal* or *irreversible stage* of shock implies irreversible organ injury, especially of the vital organs (brain, heart, and kidneys). Intervention at this late stage is unsuccessful, and death occurs even if therapeutic intervention restores cardiovascular measurements such as heart rate, blood pressure, cardiac output, and oxygen saturation to normal or even supranormal levels.

THE FUNCTIONAL CLASSIFICATION OF SHOCK

Hinshaw and Cox [27] proposed a classification scheme for shock in 1972 that is still useful today. The four major categories of shock (Table **4**) include (i) hypovolemic shock (shock as a consequence of inadequate circulating volume), (ii) obstructive shock (shock caused by obstruction of blood flow to and from the heart), (iii) cardiogenic shock (shock caused by primary pump failure), and (iv) distributive shock

Table 2.   Compensatory Responses to the Shock State

Compensatory Mechanisms to Maintain Effective Blood Volume
1.   Decreased venous capacitance (*via* venoconstriction)
a.   Increased sympathetic tone
b.   Increased circulating epinephrine (secondary to release from the adrenal medulla)
c.   Increased circulating angiotensin II (secondary to activation of the renin-angiotensin-aldosterone axis)
d.   Increased circulating vasopression (secondary to release from the posterior pituitary gland)
2.   Decreased renal losses of fluid
a.   Decreased Glomerular Filtration Rate (GFR)
b.   Increased circulating aldosterone (secondary to activation of the renin-angiotensin-aldosterone axis)
c.   Increased circulating vasopressin (anti-diuretic hormone)
3.   Fluid re-distribution to the vascular space
a.   Starling effect (fluid redistribution from the interstitial space)
b.   Osmotic effect (fluid redistribution from the intracellular space)
Compensatory Mechanisms to Optimize Cardiac Performance
1.   Increased Heart Rate
a.   Increased sympathetic tone
b.   Increased circulating epinephrine (secondary to release from the adrenal medulla)
2.   Increased Contractility
a.   Increased sympathetic tone
b.   Increased circulating epinephrine (secondary to release from the adrenal medulla)
3.   Increased Frank-Starling Mechanism (Increased Preload = Increased Cardiac Output)
a.   Decreased venous capacitance (see above)
b.   Decreased renal losses of fluid (see above)
c.   Fluid redistribution to the vascular space (see above)
Compensatory Mechanisms to Preferentially Maintain Perfusion of Vital Organs ("Dive Reflex")
1.   Extrinsic regulation of systemic arterial tone
2.   Auto-regulation of vital organs (Brain, Heart, Kidneys)
Compensatory Mechanisms to Optimize Oxygen Unloading at the Tissue Level
1.   Increased RBC 2,3-DPG
2.   Tissue Acidosis (Bohr Effect)
3.   Decreased tissue PO2

Table 3.   Stages of Shock

Organ System	Compensated Shock	Uncompensated Shock	Irreversible Shock
Central Nervous System	Agitation Anxiety ↓ Lethargy Somnolence	Altered mental status Encephalopathy Hypoxic-ischemic injury	Hypoxic-ischemic injury and cell necrosis
Heart	Tachycardia	Tachycardia ↓ Bradycardia	Myocardial ischemia Cell Necrosis
Lungs	Tachypnea Increased WOB	Acute Respiratory Failure	Acute Respiratory Failure
Kidneys	Oliguria ↑ urinary osmolality ↑ urinary sodium $FE_{Na} < 1$	Acute Tubular Necrosis Acute Renal Failure	Tubular necrosis
Gastrointestinal Tract	Ileus Feeding intolerance Stress gastritis	Pancreatitis Acalculouscholecystitis GI Bleeding Gut Translocation	GI Bleeding Sloughing
Liver	Centrilobular injury Elevated transaminases	Centrilobular necrosis *Shock Liver*	Hepatic Failure
Hematologic	Endothelial activation Platelet activation (Pro-coagulant, Hypofibrinolytic)	DIC	DIC
Metabolic	Glycogenolysis Gluconeogensis Lipolysis Proteolysis	Glycogen depletion Hypoglycemia	Hypoglycemia
Immune System	Immunoparalysis	Immunoparalysis	Immunoparalysis

(shock caused by maldistribution of the circulating volume). Notably, distributive shock encompasses anaphylactic shock, septic shock, and neurogenic shock. A system containing a reservoir tank, pump, and a set of pipes is a useful analogy in further explaining the classification (and pathophysiology of shock). In this system, a hydraulic pump distributes water through a network of pipes, returning to a reservoir tank. The heart is the pump, the vascular blood volume is the reservoir, and the network of pipes are analogous to the vascular system. Hypovolemic shock is analogous to an empty reservoir tank ("the tank is empty"). Cardiogenic shock is analogous to a broken pump. Obstructive shock analogous when there is a blockage in the network of pipes, such that water cannot return to the reservoir. Finally, distributive shock is analogous to a situation in which the network of pipes have become quite leaky or, in some cases, stretched or bent beyond repair [28]. Notably, children sufferingfrom distributive shock are often further classified into *cold shock* or *warm shock*;the difference being the integrity of the systemic vascular endothelium (the "pipes"). With too little resistance to blood flow, patients present in *warm shock* (hypotensive, flash capillary refill, bounding pulses, warm extremities), while too much resistance or leakage in the

pipes leads to *cold shock* (hypotensive, delayed capillary refill, poor pulses, mottled and cool extremities).

Table 4.   Classification of Shock

Type of Shock	Preload	Afterload	Contractility
Hypovolemic	↓	↑	N
Cardiogenic	↑	↑	↓
Obstructive	↓	↑	N
Distributive	↑, ↓, or N	↓	↑

While relatively arbitrary, especially when viewed in the context that different features of each category may be present at the same time (e.g. septic shock is often characterized by manifestations of hypovolemic shock, cardiogenic shock, and distributive shock at the same time), this classification scheme provides valuable information about the physiological alterations involved, including changes in preload ("the tank"), contractility ("the pump"), and afterload ("the pipes"). Knowledge of these physiological alterations can then be used to guide

Table 5.   Vasoactive Pharmacologic Agents Commonly Used in the Management of Pediatric Shock

Agent	Dose Range	Comments
Dopamine[1,2,3]	3-5 µg/kg/min	*Renal-dose dopamine* (primarily dopaminergic agonist activity); increases renal and mesenteric blood flow, increases natriuresis and urine output
	5-10 µg/kg/min	Inotropic (β_1 agonist) effects predominate; increases cardiac contractility, heart rate, and blood pressure
	10-20 µg/kg/min	Vasopressor (α_1 agonist) effects predominate; increases peripheral vascular resistance and blood pressure
Dobutamine[1,2]	5-10 µg/kg/min	Inotropic effects (β_1 agonist) predominate; increases contractility and reduces afterload
Epinephrine[1,2]	0.03-0.1 µg/kg/min	Inotropic effects (β_1 and β_2 agonist) predominate, increases contractility and heart rate; may reduce afterload to a slight extent *via* β_2 effects
	0.1-1 µg/kg/min	Vasopressor effects (α_1 agonist) predominate; increases peripheral vascular resistance and blood pressure
Norepinephrine[1,2]	0.1-1 µg/kg/min	Potent vasopressor (α_1 and β_1 agonist); increases heart rate, contractility, and peripheral vascular resistance; absent β_2 effect distinguishes it from epinephrine
Phenylephrine[1,2,4]	0.1-0.5 µg/kg/min	Potent vasopressor with primarily α_1 agonist effects; indicated in tetralogy of Fallot hypercyanotic spells (*tet spells*)
Vasopressin[1,2,5]	0.0003-0.002 units/kg/min (0.018-0.12 units/kg/h)	Vasopressor (*via* V_1) without inotrope activity; may be indicated in refractory shock
Nitroglycerin[1,4,6]	0.5-3 µg/kg/min	Dos dependent venodilator and vasodilator (cGMP mediated)
Nitroprusside[1,7]	0.5-3 µg/kg/min	Systemic arterial vasodilator (c GMP mediated)
Inamrinone[1,8]	0.75 mg/kg I.V. bolus over 2-3 minutes followed by maintenance infusion 5-10 µg/kg/minute	Inodilator (Type III phosphodiesterase inhibitor); increases cardiac output *via* increased contractility and afterload reduction
Milrinone[1,9]	50 µg/kg administered over 15 minutes followed by a continuous infusion of 0.5-0.75 µg/kg/minute	Inodilator (Type III phosphodiesterase inhibitor); increases cardiac output *via* increased contractility and afterload reduction
Prostaglandin E_1 (PGE$_1$)[10]	0.3-0.1 µg/kg/min	Maintains patent ductus arteriosus (cAMP effect)

[1] Correct volume depletion prior to starting infusion.

[2] Extravasation may produce tissue necrosis (as a general recommendation, should be administered *via* central venous access). Treatment with subcutaneous administration of phentolamine as follows:
Neonates: Infiltrate area with a small amount (e.g., 1 mL) of solution (made by diluting 2.5-5 mg in 10 mL of preservative free NS) within 12 hours of extravasation; do not exceed 0.1 mg/kg or 2.5 mg total.
Infants, Children, and Adults: Infiltrate area with a small amount (eg, 1 mL) of solution (made by diluting 5-10 mg in 10 mL of NS) within 12 hours of extravasation; do not exceed 0.1-0.2 mg/kg or 5 mg total.

[3] Dopamine has exhibited nonlinear kinetics in children (dose changes may not achieve steady-state for approximately 1 hour, compared to 20 minutes in adults).

[4] Exhibits rapid tachyphylaxis (dose may need to be increased with time to achieve same clinical effect).

[5] Dose not well established in children or adults; Abrupt discontinuation of infusion may result in hypotension (gradually taper dose to discontinue the infusion); May be associated with profound peripheral vasoconstriction (leading to tissue ischemia).

[6] May cause profound hypotension in volume-depleted patients; Nitroglycerin adsorbs to plastics; I.V. must be prepared in glass bottles and special administration sets intended for nitroglycerin (nonpolyvinyl chloride) must be used.

[7] Converted to cyanide by erythrocyte and tissue sulfhydryl group interactions; cyanide is converted in the liver by the enzyme rhodanase to thiocyanate (thiocyanate levels should be monitored).

[8] Metabolized in the liver; Causes thrombocytopenia (may be dose-related); Milrinone is now preferred agent

[9] Metabolized in the kidney; Relatively long half-life (use with caution in children with hemodynamic instability)

[10] Dose may be decreased once the ductusarteriosus has opened with very little change in therapeutic effects; may cause hypotension, apnea, cutaneous flushing

appropriate management. In the remainder of this review, we will provide a general overview on the management of shock in children. However, the subtle nuances in clinical presentation, pathophysiology, and management of each of these categories of shock will be discussed in greater detail in subsequent reviews in this supplement.

MANAGEMENT OF SHOCK – GENERAL CONSIDERATIONS

General initial shock management can be divided into three epochs: resuscitation, stabilization, and ongoing management/treatment of multiple organ injury. The initial resuscitation and stabilization phases will be discussed below. Ongoing management and treatment of multiple organ injury occurs in the pediatric intensive care unit (PICU) setting and will not be discussed further here.

Initial Resuscitation Phase

Initial resuscitation of shock depends on early recognition and the "golden hour" of treatment. The first hour of resuscitation of a child in shock should be directed towards the goals of maintaining an airway, oxygenation, ventilation, and adequate circulation (the ABCs). Specifically, following recognition of shock, vascular access

should be secured as rapidly as possible, followed by volume resuscitation with isotonic saline or colloid fluid boluses of 20 mL/kg every 5 minutes to a total of 60 mL/kg [29, 30]. Antibiotics should be administered to children with suspected sepsis within the first 15 minutes of shock management. In addition, any electrolyte abnormalities (hypoglycemia, hypocalcemia) should be corrected [30]. Additionally, stress-dose hydrocortisone should be administered to children at risk for adrenal insufficiency (e.g., chronic steroid use or history of adrenal suppression).

Critically ill children with shock require close monitoring with continuous pulse oximetry, continuous electrocardio-graphy (ECG) (usually lead II), and either non-invasive (but frequent) or invasive (e.g., arterial catheter) blood pressure monitoring. Urine output and mental status should also be monitored closely. Several clinical signs can be used as therapeutic endpoints of resuscitation, including heart rate (generally < 90 or > 160 beats per minutes in infants and <70 or >150 beats per minute in young children), capillary refill of less than 2 seconds, normal pulses without a differential between central and peripheral pulses, and warm extremities. Appropriate targets for blood pressure are age-dependent to maintain adequate end-organ perfusion pressure (Mean blood pressure – central venous pressure) between 55 mm Hg (neonates and infants) and 65 mm Hg (older children) [30-32].

If the child's clinical state has not significantly improved after 60 mL/kg volume resuscitation, central vascular access should be obtained, if possible. If necessary (though not ideal), inotropes (dopamine and epinephrine) may be administered peripherally until central vascular access can be obtained – as a dilute solution and with a fast flow rate to ensure delivery to target organs [33]. Care must be taken to ensure there is no peripheral infiltration or ischemia when running a central acting agent through a peripheral IV [34, 35].

Stabilization Phase

During stabilization, more advanced interventional skills and monitoring capability is often required. A stable airway should be secured, if necessary, and adequate ventilation should be maintained. In shock, children may progress rapidly from respiratory alkalosis (mediated from central hyperventilation from the etiology of shock) to a respiratory acidosis (as patients decompensate and metabolic acidosis complicates hemodynamic stability). Assuming control of a patient's airway and breathing can shift the 40% of the cardiac output dedicated to the respiratory system towards the other vital organs such as the brain and kidneys. Central vascular access should be obtained, if it was not already done so during the initial resuscitation phase. Restoration of a more normal hemodynamic state at this stage will often require administration of vasoactive medications (Table **5**). There have not been any randomized, controlled trials to determine which vasoactive medication is best in pediatric shock. However, expert consensus [30] suggests that dopamine is the first-line vasoactive agent for the management of pediatric shock. Epinephrine is frequently used to further augment cardiac contractility (and thus cardiac output) and increase systemic vascular resistance. In the presence of catecholamine-refractory shock (e.g, poor

hemodynamics despite escalating inotropic and vasopressor support, with appropriate correction of electrolytes and fluid resuscitation), more advanced monitoring techniques for titration of therapies to specific hemodynamic variablesare required. Additional therapies at this stage may include extracorporeal support (e.g., ECMO – extracorporeal membrane oxygenation).

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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