Shock is an acute, complex state of circulatory dysfunction resulting in insufficient oxygen and nutrient delivery to the tissues relative to their metabolic demand leading to cellular dysfunction that may eventually cause cell death.

Tissue perfusion and shock:
Maintenance of tissue perfusion is dependent upon three Factors:

1. Cardiac output
2. Local auto regulation
3. Normal blood characteristics

Cardiac output is the product of heart rate (HR) and stroke volume (SV): CO (L/min) = SV (L) × HR/min

Stroke volume is dependent on
(a) Preload: the amount of filling of the ventricle at end diastole
(b) Afterload: the force against which the ventricle must work to eject blood during systole
(c) Contractility: the force generated by the ventricle during systole
(d) Lusitropy: the degree of myocardial relaxation during diastole

Heart rate variability relies on an intact autonomic nervous system and a healthy cardiac conduction system. Arterial oxygen content also dictates oxygen delivery and is determined by hemoglobin (Hgb), oxygen saturation (SaO2), and the partial pressure of oxygen (PaO2). In a neonate, the resting heart rate is high (140-160) and hence improvement in cardiac output by increasing heart rate is usually limited. Thus interventions for inadequate perfusion are usually limited to fluids and inotropes.

Local autoregulation
Blood flow through the local arterial, capillary and venous bed to the tissues is maintained by a local autoregulatory mechanisms. If this autoregulation is lost, blood flow becomes pressure dependant and results in ischemic and hemorrhagic manifestations. Modulation of systemic vascular resistance (SVR) in different vascular beds is one of the body's primary compensatory mechanisms to shunt blood preferentially to vital organs such as the heart and brain. In this way, an increase in SVR may maintain a normal blood pressure even in the face of inadequate oxygen delivery. In other words, hypotension need not be present for a child to be in shock.

Blood characteristics
The third factor controlling tissue perfusion includes normal characteristics of blood component. Fetal haemoglobin binds oxygen more tightly as compared to adult haemoglobin and supplies less oxygen to tissues. Presence of anemia and methaemoglobinemia would interfere with oxygen carrying capacity of blood. Maintaining haemoglobin within a normal range, nursing in a thermoneutral zone and prompt treatment of hypocarbia and acidosis would helping oxygen delivery to tissues.

ETIOLOGY.
A. Hypovolemic shock= inadequate blood volume. It is the most common form of shock occurring in children around the world. Some other causes include the following:

1. Diarrheal illnesses
2. Bleeding
3. Thermal injury
4. Inappropriate diuretic use.
5. Common scenarios of fluid loss in the neonatal period: Placental hemorrhage, as in abruptio placentae or placenta previa, Fetal-to-maternal hemorrhage (diagnosed by the Kleihauer-Betke test of the mother’s blood for fetal erythrocytes), Twin-to-twin transfusion, Intracranial hemorrhage, Disseminated intravascular coagulation (DIC) or other severe coagulopathies

B. Cardiogenic shock = defects of the pump due to myocardial dysfunction.

1. Congenital heart disease
2. Cardiomyopathies: infectious or acquired, dilated or restrictive
3. Ischemia
4. Arrhythmias

C. Distributive shock =abnormalities within the vascular beds secondary to:

1. Anaphylaxis
2. Neurologic: loss of sympathetic vascular tone secondary to spinal cord or brainstem injury
3. Drugs

D. Obstructive shock. Decreased cardiac output secondary to direct impediment to right or left heart outflow or restriction of all cardiac chambers.

Causes are:
1. Tension pneumothorax
2. Pericardial tamponade
3. Pulmonary embolism
4. Anterior mediastinal masses
5. Critical coarctation of the aorta
E. Septic Shock: Encompasses multiple forms of shock.

Hypovolemic: third spacing of fluids into the extracellular, interstitial space
Distributive: early shock with decreased afterload
Cardiogenic: depression of myocardial function by endotoxins

1. Bacterial
2. Viral
3. Fungal (immunocompromised patients are at increased risk)

Stages of shock

Early/compensated stage
Characterised by: Normal blood pressure and normal perfusion of vital organs including heart, brain and adrenal glands. Compensatory mechanisms are secondary to sympathetic reflexes and redistribution of fluid from skin and GIT to vital organs.

Physical signs seen are: tachycardia to maintain cardiac output; increased systemic vascular resistance (SVR) presenting as cold, pale skin (A difference of >2°C Between core and peripheral temperature is suggestive of hypotension) delayed capillary refill and weak peripheral pulses with narrow pulse pressure (raised diastolic BP); and increased splanchic vascular resistance manifesting as oliguria and ileus.

The physiologic response of increased SVR is altered in septic shock with release of inf ammatory mediators causing vasodilation and increased capillary permeability. In such cases, hypotension and wide pulse pressure are early indicators of shock.

Uncompensated stage
Diagnosed by onset of hypotension. It heralds the failure of compensatory mechanisms and is characterised by hypoperfusion of vital organs.

Characterised by hypotension, mottled or pale skin, weak and thready peripheral pulses, CRT>5sec, oliguria and cerebral hypoperfusion results in irritability, altered sensorium and seizures.

Irreversible Stage
When shock has progressed to cause irreversible functional loss to vital organs. This stage is characterised by MODS (MULTIORGAN DYSFUNCTION SYNDROME) and eventually results in death.

INVESTIGATIONS

- Measurement of central venous pressure (CVP)
- CVP is measured using a catheter with its tip in the right atrium or in the intrathoracic superior vena cava. The catheter can be placed through the umbilical vein or percutaneously through the external or internal jugular or subclavian vein.
- Septic screen including hematocrit and blood counts
- CRP, proclacitonin
- Sr. Electrolytes
- Blood gas analysis
- Renal and liver function tests
- Various cultures
- Blood glucose, serum lactate and pyruvate levels
- Skigram of chest for Pneumonia and aspiration and abdomen for paralytic ileus or NEC
- EKG and 2D colour Doppler echocardiography for diagnosis of cardiac defects
- Ultrasonography of head and abdomen for diagnosis of periventricular-intraventricular haemorrhage, leukomalacia, adrenal haemorrhage and rupture of liver and spleen

- Near-infrared spectroscopy (NIRS) can be used to assess the peripheral perfusion and cerebral oxygenation.

TREATMENT

Fluids, supportive therapy, inotropes, vasopressors, and hydrocortisone replacement are used to treat shock in the neonate.

Airway
Initial resuscitation must be guided by the ABCs (airway, breathing, circulation). Supplemental oxygen should be administered immediately. For the patient whose mental status is altered, who is unable to protect his or her airway, or who has impending respiratory failure, intubation is indicated. Early intubation should be considered to decrease metabolic demands, help regulate ventilation and temperature, and if needed, allow for the administration of sedation and analgesia for invasive procedures. Positive-pressure ventilation also is a powerful tool to decrease afterload to the left heart of the patient presenting in cardiogenic shock.

Fluid therapy.

The initial approach is usually to administer crystalloids such as normal saline. An infusion of 10 to 20 mL/kg isoslitotic saline solution over 30-60 minutes is used to treat hypovolemic and septic shock. In case of inadequate response a repeat bolus of the same amount should be given. Any further bolus should be given under CVP monitoring. In cases of cardiogenic shock, a bolus of 10-20ml/kg may be tried in absence of signs of pulmonary edema.

In preterm neonates, smaller volumes of 10 ml/kg should be used as they have higher circulating intravascular volume. Similarly shock secondary to myocardial dysfunction in perinatal asphyxia may be treated with 1-2 boluses of not more than 10ml/kg. Blood cell transfusions or fresh frozen plasma is recommended in cases of blood loss or DIC.

Monitoring during Fluid therapy

Heart rate, blood pressure, peripheral perfusion, sensorium and urine output should be strictly monitored.

The infant should be monitored for signs of fluid overload including hepatomegaly, periorbital puffiness, third and fourth heart sounds. Ideally, a central venous line should be placed to monitor CVP and to assist in adjusting therapy.

IF CVP< 10cm H2O and signs of fluid overload are absent: further fluid boluses should be given.

IF CVP>10cm H2O: Inotropes should be started
IF CVP>15 cm H2O: fiuorosamide (1mg/kg) and dobutamine should be given.

The 2007 ACCC/clinical practice guidelines for treatment of neonatal and pediatric septic shock recommend further that volume resuscitation beyond the first hour be titrated not only to signs of improved perfusion and normal blood pressure, but to an age-appropriate perfusion pressure (approximately 55 to 65 mm Hg), a mixed venous saturation greater than 70%, and a cardiac index greater than 3.3 L/min/m² and less than 6.0 L/min/m². The Figure 1. provides an algorithm for goal-directed management of hemodynamic support in septic shock based on these guidelines.

Supportive treatment

Correction of negative inotropic factors such as hypoxia, acidosis, hypoglycemia, and other metabolic derangements will improve cardiac output. In addition, hypocalcemia frequently occurs in infants with circulatory failure, especially if they have received large amounts of volume resuscitation. In this setting, calcium frequently produces a positive inotropic response. Calcium gluconate 10% (100 mg/kg) can be infused slowly if ionized calcium levels are low.
Broad-spectrum antibiotics based on age should be administered within the first hour of presentation when sepsis is suspected.

**Inotropes**

a. Sympathomimetic amines are commonly used in infants. The advantages include rapidity of onset, ability to control dosage, and ultrashort half-life.

## I. Dopamine

Dopamine activates receptors in a dose-dependent manner.

At low doses (0.5–2 mcg/kg/minute), dopamine stimulates peripheral dopamine receptors and increases renal, mesenteric, and coronary blood flow with little effect on cardiac output. In intermediate doses (5–9 mcg/kg/minute), dopamine has positive inotropic and chronotropic effects. The increase in myocardial contractility depends in part on myocardial norepinephrine stores.

It is the inotrope of choice if Shock is associated with hypotension. The dose varies from 5–20 mcg/kg/minute.

ii. Dobutamine is a synthetic catecholamine with relatively cardiosselective inotropic effects. In doses of 5 to 15 mcg/kg per minute, dobutamine increases cardiac output with little effect on heart rate.

Dobutamine can decrease SVR and is often used with dopamine to improve cardiac output in cases of decreased myocardial function as its inotropic effects, unlike those of dopamine, which are independent of norepinephrine stores.

It is inotrope of choice in shock without Hypotension, cardiogenic shock, shock with CVP>10 cm H2O and shock with congestive cardiac failure. The dose varies from 5–20 mcg/kg/minute.

iii. Epinephrine

It has potent inotropic and chronotropic effects in the 0.05 to 0.3 mcg/kg/minute doses and leads to fall in SVR.

It is not a first-line drug in newborns; however, it may be effective in patients who do not respond to dopamine because cardiac norepinephrine stores are readily depleted with prolonged and high rate dopamine infusions.

It is inotrope of choice in Anaphylactic shock, post cardiac arrest ad septic shock with severe hypotension.

iv. Norepinephrine

It is almost exclusively reserved for sepsis with severe refractory hypotension unresponsive to dopamine and dobutamine.

b. Milrinone and inamrinone are phosphodiesterase-III inhibitor that enhances intracellular cyclic adenosine monophosphate (cAMP) content preferentially in the myocardium leading to increase in cardiac contractility and also reduce afterload by virtue of their vasodilator effect.

c. Isoproterenol is a pure beta-adrenergic stimulator with marked inotropic and chronotropic effect. In infants with cardiogenic shock isoproterenol and digoxin are beneficial.

**Protocols For Starting Inotropes**

Dopamine is inotrope of choice in shock associated with hypotension and in septic shock. It may started in dose of 5mcg/kg/min and increased to 10mcg/kg/min under BP monitoring.

- dopamine-refractory hypovolemic or septic shock (persistent hypotension despite at least
- 60 mL/kg volume and dopamine infusing at 10 mcg/kg) : Epinephrine should be added.

- If myocardial dysfunction appears dobutamine should be added.
- If hypotension persists, higher doses of dopamine and dobutamine till 15-20 mcg/kg/min may be used.
- Shock resistant to high doses of dopamine and dobutamine should be treated with infusions of epinephrine and norepinephrine for cold shock and warm shock respectively.

**Vasopressin**

Vasopressin is not routinely used to treat shock in the children but may be a therapeutic option to consider in the setting of abnormal peripheral vasoregulation.

**Hydrocortisone replacement**

The 2008 Surviving Sepsis Campaign guidelines recommend consideration of stress-dose corticosteroids (hydrocortisone 50 mg/m2 per 24 hours) for hypotension refractory to volume expansion and vasopressors (catecholamine resistant) and suspected or proven adrenal insufficiency.

Corticosteroids also should be administered to patients who have distributive shock caused by anaphylaxis or spinal trauma.

Fig 1: Recommendations for stepwise management of hemodynamic support in infants and children with septic shock.

**OTHER DRUGS USED IN SHOCK**

**Activated Protein C**

Severe sepsis and septic shock often are accompanied by a significant disruption of the delicate balance between pro- and anticoagulants, leading to life-threatening disseminated intravascular coagulation. Activated protein C is an anticoagulant that helps regulate coagulation and inflammation, and it has been found to be deficient in patients experiencing septic shock.

**Extracorporeal Life Support**

Although ECMO has a definitive role in the treatment of cardiogenic shock refractory to maximum pharmacologic support, its role in the treatment of refractory septic shock has been less clear.

**TYPICAL CLINICAL SCENARIOS OF SHOCK IN THE NEONATE AND THEIR MANAGEMENT**
A. Very low birth weight (VLBW) neonate in the immediate postnatal period
Recommended therapy is dopamine and judicious use of volume if hypovolemia is suspected. It is important not to give large volume infusions due to their association with increased risk of bronchopulmonary dysplasia and intraventricular hemorrhage.

B. Perinatal depression in preterm or full-term neonate
Recommended therapy is dopamine with or without dobutamine up to 10 mcg/kg/minute. Milrinone can be considered to provide afterload reduction and inotropy effects.
In cases with associated pulmonary hypertension, the use of inhaled NO is warranted for infants >34 weeks’ gestation.

C. Preterm neonate with PDA
Avoiding high-dose dopamine (>10 mcg/kg/minute) as its use will further increase left-to-right shunting and reduce vital organ perfusion.
Use dobutamine to enhance cardiac inotropy.
Target ventilation management to increase PVR by increasing positive end-expiratory pressure (PEEP), maintaining permissive hypercarbia, and avoiding hyperoxygenation.

D. Septic shock
Therapy includes volume resuscitation with crystalloid (10–30 mL/kg), which should be repeated as needed, and administration of dopamine 5 to 20 mcg/kg/minute, with or without epinephrine 0.05 to 0.3 mcg/kg/minute.
Consider extracorporeal membrane oxygenation (ECMO) in infants >34 weeks’ gestation if they do not respond to these interventions.

E. Preterm neonates with “pressor-resistant” hypotension
Consider low-dose hydrocortisone (3 mg/kg/day for 2–5 days in three divided doses) after drawing serum cortisol level.

Management of complications:
Acidosis
Severe metabolic acidosis (pH<7.5) should be treated with sodium bicarbonate, 1-2 meq/kg (diluted in 1:1 NS) and IV slowly.

Hematological support
Vitamin K, platelet transfusion or fresh frozen plasma is recommended in cases of blood loss or DIC. Hematocrit should be maintained above 40 with use of packed cell transfusion.

Renal support
Dopamine help in renal failure by supporting the blood pressure and improving the renal blood flow.

Adult Respiratory Distress Syndrome (ARDS)
Positive pressure ventilation with High PEEP should be used in the treatment in ARDS.

Nutritional Support
Total parenteral nutrition should be started if enteral nutrition not possible for more than 72 hours.

REFERENCES
2. Principles of Pediatric and Neonatal Emergencies. A Publication of Indian Pediatrics
5. American Heart Association (AHA) guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiovascular care (ECC) of pediatric and neonatal patients: PALS. Pediatrics. 2006;117; e1005–e1028