Additional information - General considerations

Денис Овечкін
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General considerations

PERIOPERATIVE MANAGEMENT

Compared with adults, infants and small children have a higher resting metabolic rate and oxygen consumption. Respiratory exchange and cardiac output are therefore increased also. Furthermore, the pulmonary oxygen reserve is reduced, and consequently failure to oxygenate results in rapid hypoxia. The airway is narrowest at the cricoid ring and may be damaged permanently by a tracheal tube that is too large. Minor tracheal damage or laryngeal oedema may cause stridor or obstruction [3, 8].

Hepatic and renal function may be immature and extracellular fluid is increased so that pharmacokinetics and dynamics are altered. Relative blood volume is highest in infants (95-100 mL/kg). Vasoconstriction is slower but is effective so that blood pressure can be preserved in hypovolemic shock (absent peripheral pulses and cool skin). Blood loss must be assessed and managed carefully. Body surface area in proportion to mass is increased, causing vulnerability to hypothermia. All of the problems above are greatest in infancy especially in neonates and preterm (or ex-preterm) infants [5, 6, 21].

Coincident fever and upper respiratory infections

Upper respiratory infections are common and are associated with increased respiratory complications (laryngospasm and hypoxia), particularly if the trachea has been intubated. Postponement of elective surgery should be considered for 4 weeks if the child has a high fever (>38 C), purulent secretions, or signs of collapse or consolidation. Fever of any cause may justify postponement. Vaccination is neither a contraindication to nor a reason for a delaying anaesthesia [3, 21].
Screening blood tests are rarely required for routine non-major surgery in normal children. Investigations should be appropriate to the disease.

**Fasting**

The following guidelines are recommended to avoid aspiration of gastric contents related to anaesthesia:

- 6 h for solids and non-breast milk
- 4 h for breast milk
- 2-3 h for water or any clear fluid.

Most oral medications should be taken as usual with a small volume of water. Small infants should be first on routine operating lists to avoid distress from hunger [21, 43].

**Recovery and postoperative care**

Agitation in children due to pain or delirium is a common problem that usually resolves within 10 minutes after awakening. Airway obstruction is common. Parents may help to calm their children. Extra or 'rescue' analgesia should be administered promptly before discharge to the ward. Postoperative nausea and vomiting (PONV) is common over the age of three years, and is associated with opioids, certain types of surgery (e.g. ENT, dental, gastrointestinal, and squint). The best anti-emetic drug combination may be ondansetron (100 microgram/kg 2-12 years, 4 mg >12 years), and dexamethasone [21, 36].

Neonates and ex-preterm infants <60 weeks post-conceptional age are at risk of apnoeas for the first 12 h after anaesthesia.

**FLUIDS AND ELECTROLYTES**

**Fluids**

Fluid loss is composed of sensible water (urine, feces, sweat) and insensible water loss (respiratory and transepidermal). Sensible water loss can be measured and replaced. The exact losses can be determined, if necessary, through analysis of a specimen. The insensible water loss is harder to quantitate, must be determined sometimes indirectly and is replaced through knowledge of the constituent parts of the fluid loss [14, 21].

<table>
<thead>
<tr>
<th>Estimated maintenance fluid requirements for premature to term infants (mL/kg/d):</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Day</strong></td>
</tr>
<tr>
<td>&lt;1250g</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
</tbody>
</table>

**NB:** The above table is only an estimate of fluid requirements. Careful monitoring of fluid status is essential. Some Very Low Birth Weight (VLBW) infants (which are less than 1500 g) require very large amounts (e.g., 250-300 mL/kg/d) of fluid. Patients under warmers or receiving phototherapy may require an additional 15-25 mL/kg/d.

Maintenance fluid requirements for term infants and older children [14]:

<table>
<thead>
<tr>
<th>Weight</th>
<th>Daily Fluid Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10 kg</td>
<td>100 mL/kg/d or 4 mL/kg/h</td>
</tr>
<tr>
<td>10-20 kg</td>
<td>1000 mL + 50 mL/kg/d &gt;10 kg or 40 mL + 2 mL/kg/h &gt;10 kg</td>
</tr>
<tr>
<td>&gt;20 kg</td>
<td>1500 mL + 20 mL/kg/d &gt;20 kg</td>
</tr>
</tbody>
</table>
**Electrolytes**

**Maintenance Electrolytes for Premature Infants**

**Sodium (Na)**
- Maintenance: 2-4 mEq/kg/d for infants >30 weeks gestation; 3-5 mEq/kg/d for infants <30 weeks gestation
- Generally not given in the first 24 hours
- In VLBW infants and infants born with gastroschisis and omphalocele, check baseline sodium (electrolytes) at birth
- Remember bicarbonate is a sodium salt: 1 mEq NaHCO₃ = 1 mEq Na

**Potassium (K)**
- Maintenance: 2 mEq/kg/d
- Generally not in first 24 hours of age, or until infant has urinated
- Decrease need with renal compromise or extensive tissue breakdown (e.g., NEC, burns)
- Increase need with diuretics and certain drugs (e.g., Amphotericin B)

**Maintenance Electrolytes for Term Infants and Children Up to 20 kg**

<table>
<thead>
<tr>
<th>Supplied As</th>
<th>Amount Required</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Na</strong></td>
<td>2-4 mEq/kg/d</td>
<td>The acetate salt should be used in hyperchloremic patients. When used as a phosphate source, each millimole of Na phosphate provides approximately 1.3 mEq Na.</td>
</tr>
<tr>
<td><strong>K</strong></td>
<td>2-4 mEq/kg/d</td>
<td>Each millimole of K phosphate provides approximately 1.5 mEq potassium.</td>
</tr>
<tr>
<td><strong>Ca</strong></td>
<td>0.5-3.0 mEq/kg/d</td>
<td>Premature infants require more calcium than full-term infants or children. An initial dose of 1 mEq/kg/d should be adjusted on basis of serum calcium and PO₄ measurements. Precipitation factor should be calculated and should not exceed a factor of 3:</td>
</tr>
<tr>
<td><strong>PO₄</strong></td>
<td>0.5-1.5 mM/kg/d</td>
<td>Order only to provide maintenance phosphorus, the major anion of intracellular fluids, important in the formation of ATP, ADP and creatine phosphate. Due to valence change with pH, PO₄ is ordered in millimoles rather than millequiva-</td>
</tr>
</tbody>
</table>

**Calcium-Phosphate Precipitation Factor**

\[
\text{Calcium-Phosphate Precipitation Factor} = \frac{[(\text{Calcium mEq/kg}) + (\text{Phosphate mM/kg})] \times \text{Wt(kg)} \times 100}{\text{Total Infusion Volume per Bottle}}
\]

Adjust calcium or phosphate to maintain Precipitation Factor ≤ 3 (per 100 mL).
Phosphate levels. The normal serum level for term newborns is 3.5 to 8.6 mg/dL; for premature newborns during the first week only it is 5.4-10.9 mg/dL and declines toward term newborns in 3-4 weeks.

| Mg  | MgSO₄  | 0.5-1.0 mEq/kg/d | A major cation in the body acting as a catalyst for many intracellular enzymatic reactions. |

Electrolyte Ranges are for Patients Up to 20 kg.

Heavier (and older) patients should be given electrolytes based on standard replacement solutions (0.5 NS or NS) supplemented according to serum electrolyte measurements.

**Dehydration**

Add to maintenance fluids any losses from dehydration.

<table>
<thead>
<tr>
<th>% Weight</th>
<th>H₂O</th>
<th>Na</th>
<th>Cl</th>
<th>K</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss</td>
<td>mL/kg</td>
<td>mEq/kg</td>
<td>mEq/kg</td>
<td>mEq/kg</td>
</tr>
<tr>
<td>5</td>
<td>50</td>
<td>4</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>10</td>
<td>100</td>
<td>8</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>15</td>
<td>150</td>
<td>12</td>
<td>9</td>
<td>9</td>
</tr>
</tbody>
</table>

For practical purposes, mild to moderate dehydration should be corrected with IV D₅ 1/2NS (5% dextrose in half amount of normal saline) + 20 mEq KC/L; and severe dehydration should be corrected with Ringers Lactate or normal saline (NS) + 20 mEq KC/L [14].

More fluid is required for insensible and/or third space losses. On the second day after birth, sodium and potassium may be added in accordance with fluid status, renal function and electrolyte determination. On the third day after birth, IV fluids are gradually increased, dependent on clinical status.

Sodium and potassium may be required within the first day after birth if fluid losses after surgery are high. Sodium should not be added to the IV fluid until serum sodium is <135 mMol/l and there is no evidence of edema or other overhydration. The acetate forms of sodium and potassium are given to small for gestational age (SGA) neonates. Usually sodium and potassium chloride can be given to surgical patients if the base excess is >0 and urine pH is greater than 7.

If the patient is unable to take oral nutrition by the third day of age, parenteral nutrition should be started at that time, once fluid and electrolyte balance has been attained [14, 21].

**SHOCK**

Shock can be defined in a variety of ways. In general, shock exists when there is evidence of multisystem organ hypoperfusion [14, 35].

This evidence is gathered during the initial clinical assessment and supported by laboratory tests, monitoring and systemic acid-base balance. On a cellular level, shock is characterized as an imbalance between oxygen delivery and oxygen consumption. This imbalance leads to failure of tissue perfusion and to failure to meet the metabolic demands of the cell and results in anaerobic metabolism, metabolic acidosis, the release of inflammatory mediators and eventually multisystem organ failure. Implicit in this definition is that inadequate perfusion can be caused by decreased oxygen supply, increased oxygen demand, or a combination of both of these factors.

Children manifest a shock state differently than adults. Perhaps the most striking difference between adults and children is the degree to which cardiac output can fall without exhibiting systemic hypotension. The intrinsic compensatory mechanisms (primarily tachycardia) allow a loss of 40-45% of the...
intravascular volume before systemic blood pressure can no longer be maintained. However, at the point where compensatory mechanisms fail, children often decompensate with a precipitous drop in blood pressure.

**Types of Shock**

_Anaphylactic shock_ occurs when an allergen triggers degranulation of mast cells, releasing large amounts of inflammatory mediators that lead to systemic vasodilatation and hypotension, sometimes accompanied by laryngeal edema and bronchoconstriction. A typical presentation in the emergency department is the patient with a bee sting, while in the operating room anaphylaxis is seen as a reaction to latex, drugs, or intravenous contrast material.

_Neurogenic shock_ is encountered when a patient suffers a traumatic spinal cord injury above the T6 level. The hallmark of this type of shock is hypotension accompanied by bradycardia, caused by loss of sympathetic innervation and subsequent unopposed vagal innervation of the heart.

_Cardiogenic shock_ can result from a variety of causes: failure after open heart surgery, myocardial contusion secondary to trauma, viral myocarditis, pericardial tamponade, congenital rhythm disturbances, and tension pneumothorax. Drug intoxication with tricyclic depressants or calcium- or sodium-channel blockers are also significant causes of cardiogenic shock. In neonates, patent ductus arteriosus-dependent cardiac lesions and inborn errors of metabolism can also produce cardiogenic shock.

_Sepctic shock_ occurs in the setting of bacteremia and the initiation of a systemic inflammatory response. In the strictest sense, a positive blood culture is required to confirm the diagnosis, however there are many situations in which blood cultures remain negative. In surgical patients, septic shock might occur due to perforated viscus with peritonitis, wound infection, meningococcemia, necrotizing fasciitis, community- or hospital-acquired methicillin resistant Staphylococcus aureus (MRSA) infection, catheter-associated blood-stream infection, ventilator-associated pneumonia, or necrotizing enterocolitis.

_Hypovolemic shock_ in the pediatric patient is usually due to either excessive fluid loss from the gastrointestinal tract or from hemorrhage. Examples of excessive fluid loss from the GI tract include the patient with pyloric stenosis, sequestration of fluid due to bowel obstruction, bacterial or viral gastroenteritis, or malabsorption syndromes. Hemorrhage can be due to resection of an intra-thoracic or intra-abdominal tumor, gastrointestinal bleeding, or trauma.

<table>
<thead>
<tr>
<th>Types of shock</th>
<th>Etiology</th>
<th>Pathophysiology</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypovolemic</td>
<td>Hemorrhage - Dehydration</td>
<td>Lack of preload - Secondary vasoconstriction</td>
<td>Fluid resuscitation - Blood transfusion</td>
</tr>
<tr>
<td>Septic</td>
<td>Bacteremia</td>
<td>Peripheral vasodilation - Afterload reduction</td>
<td>Fluid resuscitation - Pressors - Antibiotics</td>
</tr>
<tr>
<td>Anaphylactic</td>
<td>Allergen - Histamine release</td>
<td>Peripheral vasodilation - Afterload reduction</td>
<td>Fluid resuscitation - Pressors - Histamine blockade</td>
</tr>
<tr>
<td>Cardiogenic</td>
<td>Multiple - Cardiomyopathy - Valve dysfunction</td>
<td>Low cardiac output - Decreased stroke volume</td>
<td>Fluid resuscitation - Pressors - Cardiac assist</td>
</tr>
<tr>
<td>Neurogenic</td>
<td>Spinal cord injury</td>
<td>Peripheral vasodilation - Collapse of venous tone - Bradycardia</td>
<td>Fluid resuscitation - Pressors</td>
</tr>
</tbody>
</table>
Clinical Indicators of Inadequate Tissue Perfusion:

**Tachycardia**
Tachycardia is the earliest sign of shock in children, but it is not specific. An increased heart rate is also caused by other factors such as fear, anxiety and pain. The response of the heart rate to a fluid challenge provides insight as to ongoing fluid losses or the degree of volume deficit.

**Altered Mental Status**
Mental status changes are observed when cerebral perfusion is compromised as a result of hypovolemia. Unfortunately, children with head injuries present in a similar fashion. An example of altered mental status is a child who exhibits a minimal response to blood draws or placement of an intravenous catheter. Another example is a child who initially appears combative or somnolent after losing blood from a femur fracture or deep laceration. Such a child undergoes a significant improvement in mental status after 20-40 mL/kg fluid challenge.

**Decreased Diastolic Pressure**
The diastolic pressure should normally be two-thirds of the systolic pressure. A decrease in diastolic pressure of 20 mm Hg or greater indicates significant intravascular volume loss. This finding can be subtle but is also one of the early indicators of inadequate tissue perfusion.

**Mottled Cool Extremities**
One of the body's compensatory mechanisms to counter the effects of hypovolemia is to shunt blood away from the less critical areas in the periphery to the essential internal organs. The result is a mottled appearance of the skin beginning in the extremities and, in severe shock states, extending onto the torso. Peripheral perfusion is frequently measured by evaluation of capillary refill at the nail bed, which is normally less than 2 seconds.

In hypovolemic and cardiogenic shock, pulses are usually diminished, the extremities are mottled and cool, and capillary refill is increased to greater than 2 seconds. This is due to a compensatory vasoconstriction that diverts blood flow from the skin and extremities to help preserve flow to vital organs such as the brain, heart, and kidneys. This constellation of signs is often referred to as "cold shock." In contrast, patients with "warm shock" have full and bounding pulses, warm extremities, and brisk capillary refill. This is due to peripheral vasodilatation from a loss of vasomotor tone and is typical of septic and anaphylactic shock. Aberrations in pulse pressure are also found in these shock states: narrow pulse pressure in "cold shock" and wide in "warm shock."

Children in shock frequently have measurable delays in capillary refill. A more subjective measure of the central shunting of blood is in the assessment of the quality of peripheral versus central arterial pulses. Children in shock frequently exhibit thready distal pluses compared to a femoral or carotid arterial pulse. In severe shock states distal pulses may not be palpable. Distal pulses return after appropriate fluid resuscitation, and the peripheral pulses will subjectively feel as strong as the central pulsations.

**Decreased Systolic Blood Pressure**
In children with hypovolemic shock, decreased systolic blood pressure is a late finding and indicates severe intravascular volume loss of over 40% of circulating blood volume. A normal systolic blood pressure is approximately 80 mm Hg plus two times the age in years [43]. For example, a 4-year-old child should have a systolic blood pressure of $80 + (4 \times 2) = 88$ mm Hg. A decreased systolic blood pressure indicates all of the body's intrinsic compensatory mechanisms are unable to maintain adequate perfusion to the vital organs. This situation is referred to as uncompensated shock and requires immediate attention to prevent cardiorespiratory arrest and death.

**Urine Output**
A decrease in urine output represents diminished organ perfusion and is a late finding in children with intravascular volume loss. Oliguria usually indicates a deficit of 25-40% of blood volume. Accurate hourly assessment of urine output requires a bladder catheter. Another frequently used urine measurement is the specific gravity. Children with a high specific gravity (1.010-1.030) have concentrated urine which is suggestive of a volume deficit. It must be emphasized that both of these indicators are late findings and only confirm the other signs of inadequate tissue perfusion and volume deficit.

Besides clinical parameters such as heart rate and blood pressure, sensitive measures of tissue perfusion include: capillary refill, urine output, mixed venous oxygen saturation, and lactic acid levels.

**Treatment**
In children with shock, priorities are quite close to the priorities of trauma and ATLS (Advanced Trauma...
Life Support) guidelines. First, insure a secure airway with protection of the cervical spine if there is any concern about neck instability or injury. Second, insure adequate ventilation and oxygenation. Third, assess for signs of inadequate tissue perfusion. Once these tasks have been accomplished, direct attention to evaluation of shock and restoration of adequate circulating volume.

**Fluid Resuscitation**

After demonstrating signs of inadequate perfusion and securing intravenous access, it is appropriate to administer a 20 mL/kg crystalloid fluid bolus. A careful reassessment following the bolus provides information as to the need for further fluid challenges. If the heart rate decreases significantly, the mental status clears, or other signs of poor perfusion subside, no additional fluid boluses are needed. If the child's status is either unchanged or only slightly improved, a second challenge of 20 mL/kg is required. Reassessment after the second bolus using the same evaluation criteria usually reveals a restoration of adequate circulating intravascular volume. Evidence of persistent hypovolemia requires the clinician to conduct a careful search for sources of ongoing or unrecognized hemorrhage. A third crystalloid bolus is initiated and 10 mL/kg of crossmatched packed red blood cells (PRBCs) is delivered via a rapid fluid warmer [14, 36, 41].

If hemorrhage is occurring, resuscitation with packed red cells, fresh frozen plasma, and platelets in a 1:1:1 ration should be considered since recent literature on military casualty victims demonstrated improved mortality using this approach [14].

If there is insufficient time for a full crossmatch, unmatched type specific cells or O-negative PRBCs are given. Male recipients should receive O-positive PRBCs, allowing O-negative blood to be reserved for female patients of child bearing age (Rh incompatibility in future pregnancies is a potential problem for females).

**Thermoregulation**

The maintenance of the body's core temperature is an essential component in restoring homeostasis to an injured child or a child in shock. Hypothermia, defined as a core temperature less than 36°C, causes coagulopathy and acidosis. All fluids are warmed to as near body temperature as possible via in-line warming devices. This is especially true for blood and blood products, which are normally stored at 4°C. The temperature in the resuscitation area is kept high and the child kept covered unless exposure is necessary for examination or intervention. It is much easier to keep an injured child warm than it is to rewarm a child who has become hypothermic [14, 16, 45].

**SEPSIS**

Sepsis remains a leading cause of morbidity and mortality in children.

Sepsis is a reaction to severe infection. It can involve many different parts of the body. When infection invades the bloodstream it is called *septicaemia*. The germs causing the infection can be bacteria, viruses or fungi. When bacteria spread into the blood, the condition is known as *bacteraemia*.

Bacterial sepsis refers to *symptomatic bacteremia*, with or without organ dysfunction. Sepsis is commonly defined as the presence of infection in conjunction with the systemic inflammatory response syndrome (SIRS); *severe sepsis*, as sepsis complicated by organ dysfunction; and *septic shock*, as sepsis-induced acute circulatory failure characterized by persistent arterial hypotension despite adequate volume resuscitation and not explained by other causes.

**Definitions (according M.Davenport, 2009 [21])**

- Sepsis = inflammation + evidence or suspicion of microbial invasion
- Severe sepsis = sepsis + organ dysfunction
- Septic shock = sepsis + hypotension despite adequate fluid resuscitation.

In severe sepsis, organ dysfunction includes sepsis plus one of the following:
- Cardiovascular organ dysfunction
- Acute respiratory distress syndrome (ARDS)
- Or two or more organ dysfunctions (respiratory, renal, neurological, haematological, or hepatic)

In septic shock, infection is associated with hypotension in spite of an adequate fluid administration ($\geq 40$ mL/kg in 1h).
SIRS must have two of the following four criteria, one of which must be abnormal temperature or leucocyte count.

- Core temperature >38.5°C or <36°C
- Tachycardia (HR > 2 SD for age)
- Tachypnoea (mean respiratory rate > 2 SD for age)
- Leucocyte count elevated or depressed for age or >10% immature cells

Septic shock can also be described as fluid refractory or inotrope refractory [21].

Clinical features
Sepsis is a clinical diagnosis characterized by the classical triad of fever, tachycardia, and vasodilatation. Signs are highly variable and depend upon host resistance, the inoculum dose, and the subsequent response. Shock occurs before hypertension in children, and the following are clinical signs of septic shock:

- tachycardia and decreased peripheral pulses
- altered alertness
- flash capillary refill or capillary refill > 2 sec
- mottled cool extremities
- decreased urine output.

The classical triad of septic shock includes:
- hypothermia or hyperthermia
- altered mental status
- peripheral vasodilatation (warm shock) / cool extremities (cold shock).

Pathophysiology
In children, septic shock is associated with severe hypotension (in adults it is associated with myocardial dysfunction and vasomotor paralysis) and children respond well to aggressive volume resuscitation (e.g. 60 mL/kg in the first hour). Oxygen delivery (not oxygen extraction) is a major determinant of prognosis.

Treatment

Antibiotics
The crucial element in effective treatment is prompt and appropriate empiric antimicrobial therapy guided by clinical diagnosis, susceptibility of patient (if any), and knowledge of local bacterial sensitivities. Early administration (< 4 h from admission) reduces mortality and length of stay [19].

Intravenous fluids
The colloid versus crystalloid controversy is unresolved in children. Fluid is given in boluses of 20 mL/kg titrated against cardiac output (heart rate, urine output, capillary refill, level of consciousness), in an attempt to optimize perfusion pressure (mean arterial pressure – central venous pressure) [14, 19].

Oxygen delivery
Oxygen delivery = Cardiac output (CO) x Blood oxygen content where,

\[
\text{Blood oxygen content} = (Hb \text{ bound} + \text{dissolved in plasma}) \\
(1.36 \times Hb \text{ (in g/dl)} \times O_2 \text{ saturation (as decimal)}) + (PaO_2 \times 0.0003)
\]

NB: PaO₂ is relatively unimportant compared to O₂ saturation

Monitoring

- Oximetry and ECG
- Blood pressure and temperature
- Urine output
- Plasma glucose and calcium
- CVP and intra-arterial monitoring should be used in fluid refractory shock.
- SVC oxygen saturation >70% is associated with good outcome. Pulmonary artery catheter placement is restricted to fluid refractory and dopamine refractory shock.
**Vasopressor therapy**
- Dopamine remains the first-line vasopressor
  - 2-5 microgram/kg/min ('renal dose', dopaminergic receptors)
  - 10-15 microgram/kg/min (+ve inotropic, β agonist)
- Dobutamine, selective β₁ agonist
  - 5-20 microgram/kg/min
- Adrenaline (epinephrine) acts on α and β₁ adrenergic receptors
  - 2 microgram/kg/min (starting), reducing to 0.1-1 microgram/kg/min
- Noradrenaline (norepinephrine) acts on α (especially) and β receptors, and increases peripheral resistance, thereby countering vasodilatation seen in sepsis
  - 0.05-1 microgram/kg/min

Some authors recommend low-dose adrenaline as the first-line choice for cold hypodynamic shock (10 microgram/kg/min) and noradrenaline for warm shock [14].

**Vasodilator therapy**
May be indicated in hypovolemic shock with high systemic vascular resistance. Newer agents (e.g. the phosphodiesterase inhibitors, amrinone and milrinone) are probably better than older agents (e.g. sodium nitroprusside). Inhaled nitric oxide may also be used in septic shock.

**Steroid treatment**
1-2 mg/kg or 50 mg IV hydrocortisone (controversial) [19, 35]
This has been suggested in children with adrenal insufficiency, catecholamine-resistant shock, history of steroid use, and purpura fulminans (widespread skin lesions associated with disseminated intravascular coagulation associated with meningococcal or streptococcal infection).

**Other agents and modalities**
Use of recombinant activated protein C (Xigris®), anti-TNFα and anti-lipopolysaccharide monoclonal antibodies have been reported, but there is a lack real evidence of efficacy in children. High-volume haemofiltration may also have a role [14, 35].

**HEMOSTASIS**
Hemostasis or haemostasis is a process which causes bleeding to stop, meaning to keep blood within a damaged blood vessel.

It is the first stage of wound healing. This involves blood changing from a liquid to a gel. The endothelial cells of intact vessels prevent blood clotting with a heparin-like molecule and thrombomodulin and prevent platelet aggregation with nitric oxide and prostacyclin. When endothelial injury occurs, the endothelial cells stop secretion of coagulation and aggregation inhibitors and instead secrete von Willebrand factor which initiate the maintenance of hemostasis after injury.

_Hemostasis has three major steps:_
1) Vasoconstriction
2) Temporary blockage of a break by a platelet plug
3) Blood coagulation, or formation of a fibrin clot

Hemostasis can be achieved in various other ways if the body cannot do it naturally (or needs help) during surgery or medical treatment. When the body is under shock and stress, hemostasis is harder to achieve. Though natural hemostasis is most desired, having other means of achieving this is vital for survival in many emergency settings. Without the ability to stimulate hemostasis the risk of hemorrhaging is great.

During surgical procedures the types of hemostasis listed below can be used to control bleeding while avoiding and reducing the risk of tissue destruction. Hemostasis can be achieved by chemical (hemostatic) agent as well as mechanical or physical agents. Which hemostasis type used is determined based on the situation.

_Hemostatic (antihemorrhagic) agents have various mechanisms of action:_
- Systemic drugs work by inhibiting fibrinolysis or promoting coagulation. These include antifibrinolytics (such as aminocaproic acid and tranexamic acid), blood coagulation factors, fibrinogen, and vitamin K.
Locally-acting hemostatic agents (topical hemostatic agents) work by causing vasoconstriction or promoting platelet aggregation. They are available in two forms - as a granular powder poured on wounds, or embedded in a dressing.

BLOOD COMPONENT THERAPY

Blood component therapy has revolutionized the ability to care for patients with both acute and chronic medical conditions. However, as with the administration of any medication, inherent risks exist. These risks include immunologic, infectious or metabolic derangements. So the medical practitioner must weigh the benefits and risks of administering any blood product or component.

Indications for Transfusion

Rarely is whole blood indicated. Furthermore, few institutions maintain an active stock of whole blood. It is reserved for acute blood loss >15-30% of total blood volume. For cases less than this, similar results can be obtained with crystalloid/colloid and packed red cell therapy [14].

Packed red cell therapy is reserved for patients with symptomatic anemia and a hemoglobin value <6 g/dL. With autologous transfusion, the criteria may be more liberal. One unit of packed red blood cells (PRBCs) contains 250 mL to 300 mL and in adults raises the hemoglobin by 1 g/dl or the hematocrit by 3%. In neonates 10 mL/kg is the usual initial transfusion amount which raises the hematocrit about 10% [14, 43].

Platelet therapy is reserved for patients with postoperative bleeding and platelet counts <50,000/µL, as well as cancer/chemotherapy patients with rapidly falling or low platelet counts <10,000/µL. Of note, platelet transfusions are usually ineffective in patients with thrombocytopenia secondary to destruction or circulating autoimmune disorders, such as immune thrombocytopenic purpura (ITP) or thrombotic thrombocytopenic purpura (TTP). One unit (approximately 50 mL) raises the platelet count between 5-10,000 plts/µL in a 70 kg adult and 20,000 plts/µL in an 18 kg child.

Fresh frozen plasma can be used for rapid reversal when insufficient time is available for vitamin K reversal (approximately six hours). Other indications include [14]:

1. Unidentifiable coagulation factor defects or coagulation factor deficiencies for which specific factor component therapy is unavailable.
2. Prothrombin time >1.5 times normal with microvascular bleeding.
3. Massive transfusion with subsequent coagulopathy and (4) conditions such as TTP.

NB: Fresh frozen plasma is not used for plasma volume expansion.

Cryoprecipitate is used for specific factor deficiencies, i.e., factors VIII, XIII, fibrinogen, fibronectin and von Willebrand's factor. In particular, it is second line therapy for patients with: (1) von Willebrand's disease unresponsive to desmopressin therapy, or (2) Factor VIII: C (hemophilia A) deficiency when specific Factor VIII concentrate is unavailable. Cryoprecipitate may occasionally be indicated when serum fibrinogen levels are below 80-100 mg/dL. The indications for use in patients with fibronectin deficiency are not well defined. Another use of cryoprecipitate is to make "fibrin glue" by mixing it with topical thrombin to enhance hemostasis.

Albumin and plasma protein fractions are reserved purely for volume expansion. There is currently little support for its use as a nutritional supplementation.

Granulocyte transfusions are available for patients with neutropenia and active infection unresponsive to antibiotic therapy. A recombinant granulocyte colony stimulating factor (gCSF) is also currently available.

A variety of other factors are available for specific deficiencies. Viral inactivated Factor VIII exists for treatment of hemophilia A and von Willebrand's disease. Factor IX (prothrombin complex concentrate) may be used for coumadin reversal and specific factor deficiency. Activated prothrombin complex concentrate (composed of Factors II, VII, IX and X) is available for hemophilia A and those with Factor VIII antibody.

Rh immune globulin is available for those receiving Rh positive platelet concentrates, or pregnant/postpartum females to minimize isoimmunization.

Intravenous immune globulin is available to treat patients with immunoglobulin deficiency or thrombotic thrombocytopenic purpura (TTP).
Transfusion Reactions

Immediate and delayed, immunologic and nonimmunologic reactions to blood products are well described.

Immediate immunologic complications include:
  - hemolytic transfusion reactions
  - immune-mediated platelet destruction
  - febrile nonhemolytic reactions
  - allergic reactions

Delayed immunologic reactions include hemolysis, alloimmunization and graft-versus-host disease (GVHD). Delayed hemolysis occurs from 2-14 days after transfusion as a result of previous alloimmunization to red blood cell antigen.

Nonimmunologic complications include infectious disease transmission such as: cytomegalovirus (CMV), hepatitis, HIV and rarely babesia, bartonella, borrelia, brucella, leishmania, parvovirus, plasmodia, toxoplasma and trypanosome. Bacterial contamination occurs secondary to both Gram-positive or -negative organisms.

Metabolic complications of transfusion therapy include: alkalosis or acidosis, citrate toxicity with subsequent hypocalcemia, hyperkalemia from prolonged blood storage, hypokalemia from alkalosis, diminished 2,3-diphosphoglycerate (2,3-DPG) with subsequent leftward shift of the oxygen dissociation curve and hemosiderosis from chronic transfusions [3, 14].

Massive transfusion of cold blood products can produce hypothermic complications that present with cardiac arrhythmia and arrest. These are best prevented by using fluid warming devices <42°C.