Intravenous fluid therapy restores the normal circulating blood volume and helps to maintain the perfusion of organs. Total body water in normal adults is around 60% of body weight in male and about 55% of body weight in females. In children slightly higher proportion of body weight is represented as water (in infants about 80% of body weight is water).

Total body water is about 42 L in an average adult of 70 kg. This is distributed between two compartments, extra-cellular and intracellular fluid compartments.

**Basic Concepts**

**Mole:** It is the molecular weight of a substance in grams. e.g. 1 mole of NaCl is (23+35.5) 58.5 gm. 1mmol = 58.5 mg

**Normality (N):** The number of gram equivalents in 1 litre.

1 Normal solution of NaCl should contain 1 gm of NaCl in 1 litre.
0.9% Normal solution of NaCl should contain 0.9gm in 100ml or 9 gm in 1000ml.
58.5 gm of NaCl =1mol =1000mmols, Hence 0.9% of NaCl solution contains 154 mmol of Na⁺ per litre.

**Osmolarity:** Number of osmoles of solute in a litre of water
**Osmolality:** Number of osmoles per kg of water or other solvent.

**Tonicity:** Solutions which have same effective osmotic pressure as plasma are isotonic. e.g: 0.9% NaCl.
Table 5.1 Composition of body fluid compartments

<table>
<thead>
<tr>
<th>Ion</th>
<th>Intravascular (plasma) (mmol/l)</th>
<th>Intracellular (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺</td>
<td>142</td>
<td>10</td>
</tr>
<tr>
<td>K⁺</td>
<td>5</td>
<td>150</td>
</tr>
<tr>
<td>Mg²⁺</td>
<td>0.9</td>
<td>25</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>105</td>
<td>5</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>25</td>
<td>10</td>
</tr>
<tr>
<td>HPO₄²⁻</td>
<td>0.4</td>
<td>30</td>
</tr>
<tr>
<td>Protein</td>
<td>15</td>
<td>60</td>
</tr>
</tbody>
</table>

Sodium is the major cation present in the extra cellular fluid (ECF) and potassium is the principle cation in ICF. Sodium and its associated anions account for about 85% of ECF osmolality and for about 90% of the ECF tonicity. Under usual physiological conditions, the distribution of total body water between the ECF and intracellular fluid (ICF) is effectively determined by the sodium concentration in the ECF. Cell membranes are permeable to water and there is continual flux of fluid among different body compartments at different rates of exchange. Osmotic pressure and hydrostatic pressure are the two main mechanisms that control the fluid movement.

Clinical assessment of fluid loss

The clinical assessment includes heart rate, skin turgor, hydration of mucous membrane, core-peripheral temperature gradient, pulse rate and volume, BP and urine output. Loss of skin turgor indicates an intravascular deficit of about 10%. Supine hypotension implies a blood volume deficit exceeding 30% and orthostatic hypotension implies a 20% blood loss. Blood pressure is not a reliable sign as compensatory mechanisms produce vasoconstriction and tend to maintain blood pressure until severe hypovolaemia has occurred. Hourly urine output of less than 0.5ml/kg is observed in severe hypovolaemia.

In addition to above clinical assessment patient’s fluid balance chart and drug therapy should carefully reviewed. Role of invasive measurements such as CVP and pulmonary artery capillary wedge pressure in fluid resuscitation is discussed in chapter 7, management of shock.

Biochemical assessment of fluid loss

Fluid loss also accompanied by a various degree of electrolyte imbalance that can be assessed by biochemical tests.

Full blood count: Haemoglobin and haematocrit values are increased in patients with dehydration due to extracellular fluid loss.
Hyponatraemia: Hypovolaemia associated with hyponatraemia can be produced by use of diuretics and salt losing renal disease. Urinary sodium concentration > 20 mmol/L suggests renal loss or mineralocorticoid deficiency. Urinary sodium concentration < 20 mmol/L suggests hypovolaemia due to extrarenal fluid loss such as vomiting, peritonitis, trauma and burns.

Hyponatraemia can result from water loss in excess of sodium loss as in diabetes insipidus, diabetes mellitus and use of diuretics.

Hypokalaemia usually results from potassium loss via lower gastrointestinal tract or renal loss (diuretics, renal tubular disease).

Hyperkalaemia can result due to associated renal failure, hypoadrenalism, drugs such as angiotensin converting enzyme inhibitors and potassium sparing diuretics.

Rational approach to fluid therapy

Intravenous fluids can be administered for following three main reasons.

- Maintenance: includes basic requirement. Maintenance fluids are designed to replace water normally lost through GIT, kidneys and normal evaporative losses from respiratory tract.
- Replacement: includes replacing on going losses. Electrolyte composition of these fluids is equivalent to that of extracellular fluid.
- Resuscitation: includes restoration of already lost fluid or blood.

Fluid therapy is the most controversial topic in perioperative management. There is ongoing debate about the type and amount of fluid to be used in resuscitation. In a patient undergoing major surgery, metabolic response to surgical stress causes sodium and water retention. Following factors should be considered during fluid resuscitation.

1. Consider fluid and electrolyte requirements: An average adult requires 30-35 ml/kg/day of fluid with sodium 2 mmol/kg and potassium1 mmol/kg. This amount will replace GI water losses of 100-200 ml, insensible water losses (respiratory and cutaneous) of 1000 ml and urinary losses. Basic fluid requirement for children is given in table 5.2.

Table 5.2 Basic fluid requirement

<table>
<thead>
<tr>
<th>Increments in kg (wt)</th>
<th>Per hour (ml/kg)</th>
<th>Per day (ml/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First 10 kg (1-10 Kg)</td>
<td>4</td>
<td>100</td>
</tr>
<tr>
<td>Second 10 kg (11-20 Kg)</td>
<td>2</td>
<td>50</td>
</tr>
<tr>
<td>Above 21 kg</td>
<td>1</td>
<td>20</td>
</tr>
</tbody>
</table>
2. Consider previous fluid and electrolyte status: The factors leading to fluid depletion include such as starvation, vomiting, diarrhoea, bowel preparation, burns, pyrexia, haemorrhage and drugs (diuretics) should be considered.

Fluid deficits owing to fasting should be replaced during surgery. Total deficit is calculated by hourly deficit times the number of hours without intake. One half of this amount is given in the first hour, one-quarter in second half and final quarter in 3rd hour.

3. Anticipate ongoing excess losses: Surgical losses include external losses from surgical field and fluid sequestration, colloquially called “third space loss” which is found in wound or burns, oedema, ascitis and in the gastrointestinal tract.

Third space loss, frequently described as expansion of interstitial fluid space into which salt and water distribute from intravascular space. There is also fluid loss from evaporation from the exposed surgical site. Table 5.3 is an approximate guide for fluid replacement during intra-operative period. In addition any blood loss from the surgical field should be replaced with intravenous fluids or blood.

Table 5.3 Approximate guide for intra-operative fluid replacement

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Rate (ml/kg/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal trauma</td>
<td>4</td>
</tr>
<tr>
<td>Moderate trauma</td>
<td>6-8</td>
</tr>
<tr>
<td>Severe trauma</td>
<td>10-15</td>
</tr>
</tbody>
</table>

Consider Repeated reassessment: Fluid balance should be frequently reassessed during peri-operative period.

Excessive intravenous fluids during peri-operative period, in patients undergoing major surgery can lead to increased morbidity and prolonged stay in intensive care. Following are the recognized consequences of excessive intravascular volume.

- It increases demand on cardiac function and may result in myocardial dysfunction
- It increases extravascular lung water and can predispose to pneumonia and respiratory failure.
- Excessive intravascular volume increases the workload of kidneys.
• It can lead to oedema of the gut which can result in gastrointestinal dysfunction.

• Excessive crystalloids and some of the colloids can also cause coagulation abnormality.

**Choice of fluid therapy**

**Crystalloids:** are fluids that contain a crystalline solid dissolved in water (combination of water and electrolytes). They are divided into "balanced" salt solutions (e.g. Ringer's lactate) and hypotonic solutions. Either their electrolyte composition approximates that of plasma, or they have a total calculated osmolality that is similar to that of plasma.

Advantages: Cheap, replaces extravascular loss.

Disadvantages: Only 1/3 of the volume is distributed to intravascular space, hence larger volume is needed for replacing the losses. When used in large quantities can result in peripheral and pulmonary oedema

**Colloids:** contains suspension of particles of sufficiently large molecular weight that they normally do not cross capillary membranes in significant numbers. Most of an administered colloid remains intravascular unless an altered permeability is present.

Advantages: Smaller volumes needed, stays in the vascular compartment for longer time, reduced peripheral oedema and higher systemic O\(_2\) delivery.

Disadvantages: Risk of anaphylaxis, relatively expensive, can interfere with coagulation system.

**Table 5.4 Composition of commonly used fluids**

<table>
<thead>
<tr>
<th>Fluids</th>
<th>Na(^+)</th>
<th>K(^+)</th>
<th>Ca(^{2+})</th>
<th>Cl(^-)</th>
<th>pH</th>
<th>Osmolarity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal saline (0.9% NaCl)</td>
<td>154</td>
<td>154</td>
<td>5</td>
<td>308</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 g of NaCl per L of water</td>
<td>30</td>
<td>30</td>
<td>4</td>
<td>284</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4% Dextrose with 0.18% saline</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dextrose 40 g per L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Warwick Medical School- Handbook of Anaesthesia 2006
Dextrose 5%
Dextrose 50 g per L
Bicarbonate 8.4%
HCO₃⁻ 1000 mmol /L
Hartmann’s
Lactate 29 mmol/L

<table>
<thead>
<tr>
<th>Colloids</th>
<th>Haemaccel</th>
<th>145</th>
<th>5</th>
<th>6.25</th>
<th>145</th>
<th>7.3</th>
<th>301</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gelatin 35 g /L</td>
<td>154</td>
<td>0.4</td>
<td>0.4</td>
<td>125</td>
<td>7.4</td>
<td>274</td>
<td></td>
</tr>
<tr>
<td>Gelatin 40g /L</td>
<td>154</td>
<td>154</td>
<td>5.5</td>
<td>310</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hespan 6%</td>
<td>Starch 60g /L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Albumin 4.5% | 100- | 100- | 7.4 | 270-300 |
| Albumin 45 g / L | 160 | 160 |

**Commonly used crystalloids**

**Normal saline (0.9% NaCl solution):** It is isotonic and isoosmotic solution and distributes throughout the ECF compartment. ECF is made up of ¾ interstitial volume and ¼ intravascular volume. Therefore about ¼ of the administered normal saline will eventually remain in the circulation. Potential problem of normal saline is hyperchloraemic metabolic acidosis which is more likely in patients with renal insufficiency. Therefore, a balanced salt solution (eg: Hartmann’s solution) with a sodium concentration of 130 mmol/l or more is normally chosen when major operative procedures are performed and when excessive blood loss is anticipated. Potential problem of Hartmann’s solution is that potassium may accumulate. More hypotonic solutions and 5% dextrose should be restricted to minor procedures and for some paediatric operations.

**5% Dextrose:** It is an electrolyte-free solution and less than 10% stays in the intravascular space. The glucose component is metabolized and only water remains. This equally distributes into the total body water (TBW). ECF being ¼ of TBW, only about 333 ml of the administered 1000ml remains in ECF. Of this 333 ml only ¼ remain in intravascular compartment, which is about 84 ml. Intravascular resuscitation is minimal and cellular swelling occurs.

The administered free water causes a decrease in the serum and interstitial electrolyte concentrations (dilutional effect) and may lead to symptomatic hyponatraemia.

**Commonly used colloids**

**Gelatins**

- Gelofusin is 4% solution of succinated gelatin in saline. It has a colloid oncotic pressure of 35 mmHg and half life of 2-4 hours.
  - Haemacel is a 3.5 % solution of polygelin mixed salt solution. It is cross linked with urea to form larger polymers. It has a colloid oncotic pressure of 28 mmHg and half life 4-6 hours.
Dextrans are glucose polymers and available as solutions with either NaCl 0.9% or dextrose 5%.

**Starches:** Composed of amylopectin that is linked with hydroxyethyl group in glucose moiety making the resultant polymer similar to glycogen.

- Hespan is 6% hetastarch in sodium chloride with colloid oncotic pressure of 20 mmHg. 60% remains in the intravascular space for 24 hours.

- Voluven is similar to Hespan but of smaller molecular weight. Tissue storage are 75% less than Hespan and allergic reactions less likely

**Blood Transfusion**

The primary purpose of transfusing blood is to increase $O_2$ carrying capacity. The decision to transfuse should take into account several factors.

- Acute or Chronic blood loss
- The expected amount of further blood loss
- The current intravascular volume
- The presence of coexisting cardiovascular diseases.

Anaemia and the transfusion trigger: In the past it was routine practice to transfuse to all patients with haemoglobin less than 10g/ dl. A more specific transfusion thresholds (Hb level at which to consider transfusion) should be considered depending on the clinical situation.

- A minimum hemoglobin of 10g/dl is acceptable for patients who are unable to increase the cardiac output or regional blood flow enough to offset hemodilution (ischaemic heart disease, valvular heart disease, new born and patients with significant respiratory disease)
- A minimum hemoglobin of 8g/dl is accepted as a threshold for surgery in which more than 500 ml of blood is anticipated, during and after operation,
- A minimum Hb of 6-7 g/dl as a threshold is acceptable for well-compensated chronically anaemic patients before acute blood loss, healthy patients who are undergoing intentional intraoperative hemodilution and in patients undergoing hypothermic cardiopulmonary bypass.

The various clinical situations that might lead to requiring blood and blood products are enlisted in tabular form

**Blood Components**

All blood components supplied by the UK transfusion services are leucodepleted in an attempt to decrease the risk of potential transfusion transmitted variant Creutzfeldt-Jakob (vCJD) disease. Other benefits of leucosepletion include reduced incidence of nonhaemolytic febrile transfusion reaction, reduced transmission of other leukocyte associated viruses such as cytomegalovirus.
**Packed red cells:** In an emergency and extreme situation it may be necessary to use uncross matched group O blood. In pre-menopausal females if blood group is not known, O Rh negative blood should be given to reduce the risk of haemolytic disease of the newborn in subsequent pregnancy.

**Platelets:** platelets are collected from the pooled buffy coats of the whole blood or by individual donor apheresis. They may be stored up to 5 days on an agitator at 22°C. During surgery and invasive procedure platelets should be transfused if the platelet count is less than 50 x 10⁹/L. In a stable patient, in the absence of bleeding a platelet count > 10 x 10⁹/L may be accepted.

**Fresh Frozen Plasma:** It is produced by centrifugation of whole blood and frozen to -30°C to achieve factor VIII concentration > 0.7iu/ml. It should be thawed before transfusion and thawed FFP is best used immediately, may be stored at 4°C and transfused within 24 hrs. FFP is used to treat acquired coagulopathy with prolonged INR, PT or APTT to 1.5 times the normal.

**Cryoprecipitate:** It is the cryoglobulin fraction of the plasma obtained by thawing a single donation of FFP at 4°C. It is rich in factor VIII, von Willebrand factor, factor XIII and fibrinogen. It is used if the fibrinogen level is less than 1 g/dl in acquired coagulopathy related to haemorrhage, sepsis and trauma.

Table 5.5 Use of blood components

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>Components to use</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant blood loss</td>
<td>Packed cells</td>
<td></td>
</tr>
<tr>
<td>Massive blood loss</td>
<td>Plasma expanders, Packed cells, FFP &amp; platelets</td>
<td>Request investigations: FBC, PT, APTT and fibrinogen.</td>
</tr>
<tr>
<td>Undefined coagulopathy</td>
<td>FFP</td>
<td>Determine the cause</td>
</tr>
<tr>
<td>Dilutional coagulopathy</td>
<td>Platelets</td>
<td>FFP rarely needed</td>
</tr>
<tr>
<td>DIC</td>
<td>FFP, Platelets, heparin</td>
<td>Treat the underlying cause</td>
</tr>
<tr>
<td>Haemophilia A</td>
<td>Factor VIII</td>
<td>May use cryoprecipitate in mild cases</td>
</tr>
<tr>
<td>Haemophilia B</td>
<td>Factor 1X</td>
<td>May use plasma in mild cases</td>
</tr>
<tr>
<td>Von Willibrands disease</td>
<td>Cryoprecipitate</td>
<td>May use DDAVP in some mild cases</td>
</tr>
</tbody>
</table>
Complications of blood transfusion

Most transfusion reaction are mild and can be treated symptomatically. They can broadly be classified into immunological and non-immunological; immediate and delayed

**Immediate immunological:**
- Haemolytic transfusion reactions (often due to ABO incompatibility)
- Febrile non-haemolytic transfusion reactions (due to recipient anti-leucocyte antibodies)
- Anaphylaxis (related to IgA deficiency in the recipient)
- Urticaria (due to plasma proteins)

**Immediate non-immunological:**
- Metabolic effects: Acid-base changes, hyperkalaemia, reduced ionised calcium
- Citrate toxicity
- Hypothermia
- Dilutional coagulopathy
- Congestive cardiac failure

**Delayed immunological:**
- Delayed haemolytic transfusion reactions
- Delayed febrile reactions
- Transfusion related acute lung injury (TRALI)
- Transfusion associated graft versus host disease (TA-GVHD)

**Delayed non-immunological:**
Infections:
- Viral: HIV, hepatitis C, hepatitis B, hepatitis A
- Bacterial: Contamination of red cells with Yersinia enterocolitica; Contamination of platelets with Staphylococcus epidermidis, Klebsiella pneumonias
- Parasites: Malaria

**Haemolytic transfusion reaction:** It is a rare, potentially serious complication. ABO incompatibility is the most common cause and invariably due to transfusion error resulting wrong blood being administered. The reaction often occurs during the first few ml of transfusion and may be characterised by dyspnoea, chest pain, fever, hypotension and haemoglobinuria.

**Management**
- Stop transfusion
- Summon for help
- Check airway, breathing and circulation
- Promote diuresis
- Maintain circulating blood volume with crystalloids or colloids
- Notify blood bank and request investigations: FBC, Clotting screen, serology
- Treatment of any existing coagulopathy

**Massive Blood Loss:** It is usually defined as the loss of one blood volume within a 24 hour period (blood volume in an adult is 70 ml/kg body weight and in infants 80-85 ml/kg body weight.)
weight). It can also be defined as more than 50% of blood volume loss within 3 hours or blood loss at a rate more than 150 ml/min.

Management of massive blood loss

- Airway, Breathing, Circulation
- Summon for help
- Restore the circulating volume immediately (with crystalloids, colloids) to maintain tissue perfusion and oxygenation.
- Surgical control of bleeding
- Treatment of coagulopathy with blood components. Once stabilized patient will require more intensive monitoring in a controlled environment.

Major blood loss and massive transfusion associated with several complications and increased mortality. Appropriate locally agreed guidelines are useful in early identification and effective management.

References:


