Chapter

13

Perioperative Fluid Management in Children

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Introduction

Intravenous fluids are given to children when the enteral route is not sufficient or is not an option, such as during surgery and anaesthesia. In the past, a lack of appreciation of the physiology of intravenous fluid management, particularly in the unwell child, has led to reports of serious morbidity and mortality, mainly due to acute hyponatraemia. Recent evidence has shown that giving children isotonic crystalloid fluids with a sodium concentration similar to plasma reduces the risk of hyponatraemia without increasing adverse effects. This has led to a change in intravenous fluid guidelines to now recommend that only isotonic fluids are used, with regular monitoring of fluid balance and electrolytes. This chapter considers the rationale for current recommendations for intravenous fluids in children, and fluid management and blood transfusion in the perioperative period and other special circumstances. The treatment of hyponatraemia is also considered.

The Holliday and Segar Formula and the Choice of Fluid in Intravenous Fluid Management

In the 1950s, paediatricians were looking for a simple formula that could be used at the bedside to calculate fluid and electrolyte requirements in children rather than using calculations based on body surface area. Holliday and Segar linked water requirements and expenditure of calories to body weight, and electrolyte requirements to the concentration of sodium and potassium in human and cow's milk. They devised a simple formula for daily maintenance fluid requirements, which has been adapted to an hourly calculation (the '4-2-1 formula') (Table 13.1). The Holliday and Segar formula is still used as a guide to calculations for the volume of maintenance fluids required by children today.

The tonicity of intravenous (IV) fluids is mainly affected by the concentration of sodium and potassium. 'Hypotonic' crystalloids such as 0.45% sodium chloride with 2.5% or 5% glucose have lower sodium concentration than plasma. 'Isotonic' fluid contains sodium and potassium concentrations similar to plasma with a sodium concentration in the range 131–154 mmol l^{-1}. Examples include Hartmann's, Ringer's lactate, 0.9% saline and Plasmalyte (Table 13.2). Glucose in IV fluid does not contribute to tonicity because it is rapidly metabolised after entering the bloodstream.

Holiday and Segar suggested that hypotonic crystalloids should be used for intravenous maintenance in children, as there were concerns that excessive sodium intake in isotonic fluids would lead to hypernatraemia (if considering this as being equivalent to dietary sodium intake). However, following worldwide reports of hospital acquired hyponatraemia in children receiving hypotonic intravenous fluids, and high-quality randomised clinical trials, it has been recognised that the routine use of hypotonic fluids in children is not appropriate, particularly in the presence of raised antidiuretic hormone (ADH), such as in the postoperative period or in sick, hospitalised children. It has also been recognised that the '4-2-1 formula' may overestimate fluid requirements in certain situations. The updated UK National Institute for Health and Care Excellence (NICE) guidelines recommend isotonic crystalloids containing sodium in the range

Table 13.1 The '4-2-1 formula' for calculating hourly fluid requirements in children

Weight	Hourly fluid requirement (ml h^{-1})
First 10 kg	4 ml kg^{-1}
10–20 kg	40 ml + 2 ml kg^{-1} for each kg > 10 kg
>20 kg	60 ml + 1 ml kg^{-1} for each kg > 20 kg (max 100 ml h^{-1})

Table 13.2 Composition of intravenous fluids

Solution	Sodium (mmol/L)	Potassium (mmol/L)	Chloride (mmol/L)	Glucose (g/L)	Buffer	Tonicity (after glucose metabolism)
5% glucose	0	0	0	**50**	–	**Hypotonic**
10% glucose	0	0	0	**100**	–	**Hypotonic**
0.18% sodium chloride with 4% glucose	31	0	30	**40**	–	**Hypotonic**
0.45% sodium chloride with 2.5% glucose	77	0	77	**25**	–	**Hypotonic**
0.45% sodium chloride with 5% glucose	77	0	77	**50**	–	**Hypotonic**
Lactated Ringer's	130	4	109	**0**	Lactate	**Isotonic**
Hartmann's	131	5	111	**0**	Lactate	**Isotonic**
Plasmalyte 148	140	5	98	**0**	Acetate gluconate	**Isotonic**
Plasmalyte 148 with 5% glucose	140	5	98	**55**	Acetate gluconate	**Isotonic**
Sterofundin® ISO	145	4	127	**0**	Acetate malate	**Isotonic**
0.9% sodium chloride with 5% glucose	150	0	154	**50**	–	**Isotonic**
Sodium chloride 0.9%	154	0	154	**0**	–	**Isotonic**
4.5% albumin	100–160	0	0	**0**	–	**Isotonic**
Succinylated gelatin (gelofusine)	154	0	120	**0**	–	**Isotonic**

131–154 mmol l^{-1} as first choice for routine IV maintenance in children.

Choice of Isotonic Crystalloid

There are a number of isotonic crystalloids with a sodium concentration of 131–154 mmol l^{-1} used in clinical practice (Table 13.2). Normal saline (0.9% saline) is widely available and inexpensive. It contains 154 mmol l^{-1} of sodium and chloride. 'Balanced' isotonic solutions have been formulated to more closely mimic the electrolyte composition and pH of normal plasma. They have lower concentrations of sodium and chloride; additional cations such as calcium, potassium or magnesium; and anions such as lactate, acetate or gluconate that are metabolised to bicarbonate to exert an additional buffering effect. The most common balanced isotonic solutions currently in use are Hartmann's, Ringer's Lactate and Plasmalyte 148.

Large volumes of 0.9% saline may lead to hyperchloraemia and subsequent metabolic acidosis. In vitro and animal studies have shown several adverse effects of hyperchloraemia on renal physiology, inflammation and haemolysis. In clinical use 0.9% saline may be associated with worse biochemical outcomes and higher incidence of acute kidney injury when compared to balanced isotonic solutions, although a difference in mortality has not been demonstrated.

In children with dehydration and hypovolaemia, the use of a balanced isotonic solution is thought to produce more physiological volume replacement and a faster improvement of metabolic acidosis than 0.9% saline. The Resuscitation Council UK 2021 Paediatric Advanced Life Support Guidelines recommend the use of balanced isotonic crystalloids as the first choice of fluid in volume resuscitation, with 0.9% saline as an acceptable alternative.

The Need for Glucose in Intravenous Fluids

Restriction of glucose intake during fasting may lead to breakdown of fats in the liver to provide ketones as an alternative energy supply. Some children are at special risk of hypoglycaemia (see Table 13.3). Under normal circumstances, children under six years require glucose of at least 50 mg ml^{-1} in maintenance fluids to prevent lipolysis. It is recommended that balanced isotonic crystalloids such as Hartmann's and Plasmalyte 148 (or 0.9% saline) with 5% glucose should be used as standard for maintenance therapy in children under six years to prevent hyponatraemia, maintain normoglycaemia and prevent ketosis. Children at special risk of hypoglycaemia should receive a balanced isotonic solution containing 5–10% glucose with regular glucose monitoring.

During surgery, most children are able maintain their blood glucose as a result of the stress response, and routine inclusion of 5% glucose in intravenous fluids has been shown to result in hyperglycaemia.

Table 13.3 Children at risk of hypoglycaemia

Children at risk of hypoglycaemia
Neonates in the first 48 hours of life
Infants undergoing prolonged/major surgery
Prolonged fasting
Children with sepsis
Children receiving parenteral nutrition
Children receiving glucose infusions
Low body weight (<3rd centile)
Extensive regional anaesthesia
Children with metabolic syndromes

The 2011 European consensus statement for intraoperative fluid therapy in children recommended that intraoperative maintenance fluids in children should consist of balanced isotonic crystalloid with a lower concentration of glucose (1–2.5%) in order to both prevent hypoglycaemia and lipolysis and to avoid potential hyperglycaemia. However, solutions with 1–2.5% glucose are not yet commercially available in many countries.

Currently, for short minor procedures, children at low risk of hypoglycaemia usually receive glucose-free balanced isotonic crystalloids. For major or longer procedures in younger children especially, a second infusion of isotonic crystalloid with glucose should be considered for maintenance requirements, taking care to only give glucose-free isotonic solutions as boluses to replace intraoperative fluid losses. Blood glucose should be monitored.

Colloids

Synthetic colloids include starches, dextrans, albumin and gelatins. They contain macromolecules from either plant or animal sources suspended in an electrolyte solution. Such colloids are used for volume expansion and fluid resuscitation. It was traditionally believed that colloids remain in the intravascular space longer than crystalloids due to their larger molecules which could not pass through the endothelium. However, emerging evidence considering new models of endothelial permeability in the presence of a damaged endothelial glycocalyx have demonstrated that crystalloids and colloids have similar volume-expanding and interstitial oedema-forming properties in critically ill patients.

Colloids are more expensive than crystalloids, and synthetic colloids carry a risk of anaphylaxis and have a dose-dependent effect on coagulation. Starches are associated with itching, the long-term side effects of which are not known. Albumin is the most commonly used non-synthetic colloid in children. It is often used in neonates, sepsis and in cardiac surgery, but there is no evidence for its use in children with traumatic brain injury, burns or in the postoperative period.

A 2018 Cochrane systematic review comparing colloids versus crystalloids for fluid resuscitation in critically ill people (including children) concluded that the choice of fluid probably makes no difference to mortality and that starches probably

Figure 13.1 Volumes of clear fluids based on age that children can be offered on arrival to hospital to ensure they drink up to one hour before elective surgery.

slightly increase the need for blood transfusion and renal replacement therapy. Synthetic colloids in children have now largely fallen out of use due to lack of evidence of benefit.

Fluid Management in the Perioperative Period

Ideally, children should be allowed to control their own fluid balance by taking oral fluids for as long as possible before surgery and recommencing oral intake as soon as possible following surgery. When intravenous fluids are required, they should be prescribed with the same care as any drug.

Preoperative Fasting and Clear Fluids

Children are fasted before surgery to minimise the risk of aspiration. Preoperative fasting in children has traditionally followed the rule of six hours nil by mouth for solids and formula milk, four hours for breast milk and two hours for clear fluids. However, in practice, children tend to be fasted for much longer than necessary, particularly those presenting to hospital on the day of surgery. Prolonged fasting has detrimental behavioural, metabolic and haemodynamic effects in children; it can make cannulation more difficult, and could potentially affect outcomes such as wound healing.

Recent evidence shows that after ingestion of 3–5 ml kg^{-1} of clear fluid, residual gastric volume assessed by serial magnetic resonance or ultrasound imaging is back to baseline within one hour. A large prospective study involving over 10,000 children from birth to 16 years showed that liberal clear fluid intake preoperatively did not increase the risk of aspiration or related serious complications. In 2018, several European paediatric anaesthesia societies published a consensus statement affirming that, in the absence of increased risk of aspiration, it is safe for all children to be encouraged to have clear fluids up to one hour before elective surgery. One practical approach to save time for day-case units is to offer children a clear sugary drink when they arrive in hospital, with the volume based on the age of the child rather than the weight (Figure 13.1).

Current European Society of Anaesthesiology guidance on preoperative fasting in children recommends a six-hour nil by mouth time for solids and formula milk, three hours for breast milk and one hour for clear fluids. This guidance is practised in the fasting policy at this author's institution.

Intraoperative Fluid Management

Intravenous fluids may be required during surgery for replacement of deficits/resuscitation, routine maintenance and to replace ongoing losses. Balanced isotonic solutions should be given, with blood given when necessary. Most children do not need glucose in their IV fluids during surgery (as indicated previously in the section 'The Need for Glucose in Intravenous Fluids').

The 'third space' for body fluids was traditionally used to describe a hypothetical transcellular space where fluid was sequestered intraoperatively. Third space losses were replaced at a variable rate depending on the magnitude of the surgical procedure, with high volumes of fluid sometimes being given. This concept has now been questioned, with tracer studies in adults showing that fluid is either in the intravascular, extracellular or intracellular space. There is also evidence that evaporative insensible losses during surgery are

lower than previously thought. More restrictive intraoperative fluid regimens are now used, which have been associated with better outcomes.

Minor surgery: For healthy children who are undergoing minor procedures and will resume oral intake soon after surgery, 10–20 ml kg^{-1} kg IV bolus during the procedure is acceptable and will reduce the need to drink immediately postoperatively and the risk of postoperative nausea and vomiting.

Major surgery: For children undergoing major surgery an initial fluid bolus of 10–20 ml kg^{-1} is given, with subsequent fluid boluses of 10–20 ml kg^{-1} balanced isotonic crystalloid or blood determined by clinical assessment (heart rate, capillary refill, blood pressure, core–peripheral temperature difference, base excess, urine output and haematocrit) and estimation of fluid losses (observation of the surgical field, weighing of swabs). Urine output may decrease due to raised ADH as part of the stress response and is an unreliable sign of volume status. It is important to avoid excessive volume loading as this will cause fluid retention and generalised oedema after surgery. Cardiac output monitoring should be considered for major surgery involving large volume losses, or for children with limited cardiac or renal reserve. A variety of cardiac output monitors have been validated for use in children (e.g., oesophageal Doppler, Lidco®). Monitors used to assess end organ perfusion such as near-infrared spectroscopy (NIRS) or central venous oxygen saturation monitoring (target $S_{CV}O_2$ >70%) may also be useful.

Emergency Surgery

Children presenting for emergency surgery may be significantly dehydrated or hypovolaemic and require careful clinical assessment and replacement of fluid deficits before surgery. A similar approach of giving an isotonic crystalloid bolus of 10–20 ml kg^{-1} may be used, with careful monitoring of electrolytes and haemoglobin and assessment of response before further fluid boluses are administered.

Neurosurgery: Neurosurgical patients are susceptible to a variety of conditions that affect sodium balance and in which fluid management requires special consideration, including diabetes insipidus, cerebral salt wasting and syndrome of inappropriate ADH (see Table 13.4).

Postoperative Fluid Management

Children should resume oral intake of fluids as soon as possible in the postoperative period. Isotonic crystalloids containing glucose are recommended for postoperative maintenance if children are unable to resume full oral intake. The volume is calculated using the '4-2-1 formula' as a guide, restricted to 50–80% of full maintenance in children at risk of significant ADH secretion (e.g. those recovering from major surgery or who are critically unwell). Ongoing enteral losses should be replaced with 0.9% saline with added potassium ml for ml. Other losses (such as 'water' loss from sweating or inappropriate urinary losses with variable sodium and potassium content) should be considered on a case-by-case basis. Use of body surface area to calculate fluid requirements should be considered if the child is obese (over the 91st centile).

Hypovolaemia is treated with a bolus of 20 ml kg^{-1} glucose-free isotonic crystalloid (e.g. Hartmann's, 0.9% saline) over less than 10 minutes, or blood products if required. Fluid balance, electrolytes and glucose should be monitored every 24 hours (or more frequently if abnormal) in all children receiving IV fluids, with daily weight if possible. Hypernatraemia during maintenance therapy is most likely due to inadequate volume and dehydration (see below). Fluids should be liberalised, and a hypotonic solution considered. Plasma sodium should be corrected slowly with frequent assessments of electrolytes. Correction should not exceed 12 mmol l^{-1} in a 24-hour period.

Enhanced Recovery after Surgery (ERAS)

The concept of enhanced recovery after surgery (ERAS) is that multiple small, evidence-based interventions combined in the perioperative period improve patient outcomes, reduce length of stay and increase patient satisfaction. The success of adult ERAS protocols has led to the development of paediatric ERAS pathways. Perioperative fluid management is a major component of ERAS and includes reducing fasting times for clear fluids, preoperative fluid and carbohydrate loading and judicious use of intravenous fluids during surgery, all of which are supported by existing good practice. Evidence of improved outcomes is starting to emerge from ERAS programmes in children.

Table 13.4 Disorders of sodium and water balance

	Diabetes insipidus	SIADH	Salt wasting
Description	Low ADH due to e.g. - Craniopharyngioma - Head injury - Hypoxic brain injury	High ADH after e.g. - Neurosurgery - Head injury - Meningitis	Natriuretic peptides release after e.g. - Neurosurgery - Head injury - Meningitis
Plasma sodium	↑	↓	↓
Urine sodium	↑ / normal	↑ / normal	↑↑
Plasma osmolality	↑	↓	↓
Plasma glucose	Normal	Normal	Normal
Urine glucose	No	No	No
Urine output	↑↑ Dilute polyuria	↓ Concentrated oliguria	↑↑ Concentrated polyuria
Urine SG	↓	↑	↑ / normal
Fluid volume	Depleted	Overloaded	Depleted
Management	Fluids +/– DDAVP	Fluid restriction 3% saline if seizures/coma	Replace sodium & water with a bolus of isotonic fluid

Notes: SIADH: Syndrome of inappropriate secretion of antidiuretic hormone; SG: specific gravity; DDAVP: desmopressin.

Intravenous Fluid Management in the Newborn

Fluid requirements in the newborn period merit special consideration. Compared to older children, newborn infants have a greater percentage of total body water, with an expanded extracellular fluid compartment. During the first 24–96 hours of life, ADH levels are high, and urine output is low. This represents an appropriate evolutionary response to a period of low fluid intake whilst lactation is established. After the first few days of life, pressure changes in the heart results in increased secretion of atrial natriuretic peptide, stimulating a brisk diuresis of sodium and water and a period of postnatal weight loss.

Renal function is immature, and neonates cannot excrete a large water or sodium load. Conversely, neonates do not tolerate dehydration well as urine can only be concentrated to half its adult capacity. Excessive sodium intake in the first few days of life may result in hypernatraemia. Premature neonates have limited capacity for sodium re-absorption in the kidneys, so they may require sodium supplements in the first weeks of life to avoid hyponatraemia.

The premature or sick neonate is particularly vulnerable to hypoglycaemia due to low glycogen stores, reduced liver gluconeogenesis and limited glucose re-absorption causing glycosuria. Hypoglycaemia is defined as a blood glucose level <2.6 mmol l^{-1} in a neonate and can lead to profound neurodevelopmental impairment. Neonates require frequent measurements of blood glucose and should receive routine maintenance containing 10% glucose in isotonic crystalloid if required (see the section 'Maintenance Fluids in Neonates' for the first few days of life). Acute hypoglycaemia should be treated with 2 ml kg^{-1} of 10% glucose.

Replacement of Fluid Deficit/ Resuscitation in Neonates

A bolus of 10–20 ml kg^{-1} of glucose-free isotonic crystalloid should be given over less than 10 minutes. Reassess and repeat if necessary. The 2020 International Consensus for Neonatal Resuscitation recommends early volume replacement with isotonic crystalloid or red cells for newborn infants with blood loss who are not responding to resuscitation.

Maintenance Fluids in Neonates

In the first few days of life, maintenance fluids should contain 10% glucose with minimal or no added sodium to ensure basal requirements are

Table 13.5 Maintenance fluids rates in term neonates (based on NICE guidance NG29); commonly given as 10% glucose with sodium and potassium added from day 1

Age	Total fluid required (ml $kg^{-1}day^{-1}$)
Day 0–1	60 ml $kg^{-1}day^{-1}$
Day 2	70–80 ml $kg^{-1}day^{-1}$
Day 3	80–100 ml $kg^{-1}day^{-1}$
Day 4	100–120 ml $kg^{-1}day^{-1}$
Day 5	120–150 ml $kg^{-1}day^{-1}$

met and to avoid hypoglycaemia (see Table 13.5). Sodium and potassium are usually added from day 1 after the postnatal diuresis, but this should be reviewed on an individual basis. Intravenous fluids are normally started at 60 ml kg^{-1} day^{-1} on the first day of life unless the baby is critically unwell, in which case 40 ml kg^{-1} day^{-1} should be considered. Fluid volumes should be reviewed daily and can be increased until full enteral requirements have been met, and unless there are any contraindications this should be up to a maximum of 150 ml kg^{-1} day^{-1}. Enteral losses should be replaced with 0.9% saline with added potassium.

Perioperative Fluids in Neonates

Neonates receiving intermittent feeds do not need IV fluids routinely preoperatively, but IV fluids should be given if fasting is prolonged. Intraoperatively, an infusion of 10% glucose in isotonic crystalloid at 50–100% of maintenance rate should be considered, with regular glucose monitoring. The use of infusion pumps is recommended to prevent inadvertent boluses of glucose. A balanced isotonic crystalloid solution without glucose (or blood/blood products) should be used as boluses of 10–20 ml kg^{-1} to replace losses during surgery. Large volumes of fluid should be avoided as this may cause fluid retention and generalised oedema after surgery.

Fluid Management in Special Situations

Dehydration

Dehydration occurs when fluid is lost from all fluid compartments, often over a prolonged period of time, most commonly due to gastrointestinal causes. The mainstay of treatment is fluid replacement, ideally via the oral route if possible. The most accurate assessment of the degree of dehydration is based on the difference between the previous (last two weeks) and current body weight:

Water deficit (ml) = [Previous weight (kg) – current weight (kg)] × 1,000

If a previous weight is not available:

Water deficit (ml) = weight (kg) × % dehydration × 10

Signs and symptoms of dehydration and shock in children are shown in Table 13.6. Individual signs are unreliable; the higher the number and the greater the severity of signs, especially in the presence of red flags, indicate a greater degree of dehydration. Hypotension is a late sign in dehydration.

- For children with mild or moderate dehydration, enteral (oral or nasogastric) rehydration is preferable.
- Children with severe dehydration or shock may require a bolus of 20 ml kg^{-1} glucose-free isotonic crystalloid (i.e. Hartmann's, 0.9% sodium chloride). Further boluses may be given if signs of shock persist. After initial treatment of shock, the remaining deficit is replaced slowly over 24–48 hours. Replace half the calculated requirement (not including losses) over 24 hours and then reassess and consider replacing the rest in the following 24 hours.

Pyloric Stenosis

If long-standing, pyloric stenosis results in a characteristic pattern of dehydration with hypochloraemic hypokalemic metabolic alkalosis. There may not be any electrolyte changes if diagnosed early (first few weeks of life). The plasma sodium may be normal, high or low. If the baby is shocked, they should receive a bolus of 20 ml kg^{-1} isotonic crystalloid. Mild dehydration may be corrected with intravenous fluid given over 6–12 hours, but severe dehydration should be corrected over 36–72 hours. The fluid deficit should be estimated (a record of body weight may be available) and given in addition to maintenance. The choice of fluid depends on plasma sodium and should be given as isotonic crystalloid with 5% glucose in the first instance. Potassium should be added once the baby is passing urine, and fluid balance and electrolytes must be monitored. Ongoing metabolic alkalosis is associated with postoperative apnoeas, so surgery should only be undertaken when the metabolic alkalosis is

Table 13.6 Signs and symptoms of dehydration and shock in children

Degree of dehydration	Mild (not clinically detectable)	Moderate clinical dehydration	Hypovolaemic shock
Weight loss	5%	10%	15%
Volume deficit	50 ml kg^{-1}	100 ml kg^{-1}	150 ml kg^{-1}
Clinical state	Appears well	Unwell or deteriorating*	Shocked
Mental state	Alert and responsive	Altered: irritable, lethargic*	Decreased consciousness
Heart rate	Normal	Tachycardia*	Tachycardia
Breathing pattern	Normal	Tachypnoea*	Tachypnoea
Eyes	Normal	Sunken*	Deeply sunken
Skin turgor	Normal	Reduced*	Doughy
Peripheral pulses	Normal	Normal	Weak
Capillary refill time	<2 s	2–4 s	>4 s
Anterior fontanelle	Normal	Normal	Sunken
Tears	Present	Decreased	Absent
Mucous membranes	Moist	Dry	Parched
Blood pressure	Normal	Normal	Hypotension (decompensated shock)
Urine output	Normal	Decreased	Oliguric/anuric
Skin colour	Normal	Normal	Pale or mottled skin
Extremities	Warm	Warm	Cold

* These signs of dehydration are 'red flags' to help to identify children at increased risk of progression to shock. (Based on the NICE guidance NG29.)

corrected (bicarbonate <26 mmol l^{-1} and chloride >90 mmol l^{-1}).

Diabetic Ketoacidosis

Dehydration due to the osmotic diuresis in diabetic ketoacidosis (DKA) has developed over a period of many weeks and must not be corrected rapidly. Water moves from the intracellular to the extracellular fluid compartment as part of the physiological adaptation, and rapid rehydration, especially when plasma sodium is allowed to fall, will result in cerebral oedema, the leading cause of death in children with DKA. Shock is rare, but if it occurs, a fluid bolus will be required, but should be limited to 7.5–10 ml kg^{-1}. The fluid deficit should be replaced over a minimum of 48 hours with isotonic fluid only. The blood sugar should be reduced slowly using an infusion of insulin with glucose introduced as it falls. Children with severe DKA should be monitored closely in an intensive care unit.

Hyponatraemia

Hyponatremia is defined as a plasma sodium concentration <135 mmol l^{-1}. Hyponatraemia produces osmotic movement of free water across the cell membranes from the extracellular to the intracellular compartments and cell swelling. Symptomatic cerebral oedema develops relatively rapidly in children with hyponatraemia. The brain is relatively large compared to the skull, and cellular physiology is immature, so there is limited ability to adapt to excess free water. A low index of suspicion and lack of timely treatment may have contributed to poor outcomes in children in the past.

Symptoms of Acute Hyponatraemic Encephalopathy in Children

- Headache
- Nausea and vomiting
- Confusion and disorientation

- Irritability
- Lethargy
- Reduced consciousness
- Convulsions
- Coma
- Apnoea

Antidiuretic Hormone

Plasma sodium concentration depends on the balance between sodium and water content. In a healthy child, plasma osmolality is around 300 mOsmol l^{-1} and water intake (determined by thirst) is matched by water loss (insensible losses and urinary losses determined by the action of ADH). ADH is released in response to a rise in plasma osmolality and activates water retention in the kidneys. ADH is also released in response to a variety of 'non-osmotic' stimuli that are common in hospitalised children such as:

- Postoperative pain, stress and nausea
- Drugs: opioids, non-steroidal anti-inflammatory drugs (NSAIDs), carbamazepine, vincristine
- Respiratory disorders: pneumonia, bronchiolitis, intermittent positive pressure ventilation (IPPV)
- Neurological disorders: tumours, trauma, meningitis, haemorrhage
- Endocrine and metabolic disorders

The non-osmotic release of ADH overrides osmotic control; if hypotonic IV fluids are administered to patients in the presence of non-osmotic release of ADH, concentrated urine will be excreted, and the extra free water load will be retained. Major surgery is frequently associated with increased ADH secretion and water retention. Hypotonic fluids and inappropriately high volumes of fluids should be avoided (Table 13.7).

The management of hyponatremia depends on the sodium concentration and the severity of the symptoms and is based on NICE guidance NG29.

Table 13.7 Factors contributing to hyponatraemia in children

Factors contributing to hyponatraemia in children
• Hypotonic IV fluids
• High volume of IV fluids
• Non-osmotic ADH secretion
• Non-specific symptoms of hyponatraemia
• Higher risk of cerebral oedema due to:
○ Higher brain-to-skull ratio
○ Lower levels of Na/K ATPase
○ 10% less CSF
• Failure to monitor electrolytes and fluid balance
• Failure to act appropriately to abnormal results
• Lack of training and education in IV fluid therapy in children

Notes: IV: intravenous; ADH: antidiuretic hormone; Na: sodium; K: potassium; CSF: cerebrospinal fluid

Management of Asymptomatic Hyponatraemia

- If a child has been prescribed a hypotonic fluid, change to an isotonic fluid.
- Restrict IV fluids to 50–80% of routine maintenance in children who are hypervolaemic or at risk of hypervolaemia (for example, if there is a risk of increased ADH secretion).

Management of Acute Symptomatic Hyponatraemic Encephalopathy

- Seek immediate expert advice (for instance, from the paediatric intensive care team).
- Give a bolus of 2 ml kg^{-1} 2.7% saline (hypertonic saline) over 10–15 minutes (maximum 100 ml).
- Give a further bolus of 2 ml kg^{-1} 2.7% saline over the next 10–15 minutes (maximum 100 ml) if symptoms are still present after the initial bolus.
- If symptoms are still present after the second bolus, check the plasma sodium level and consider a third bolus of 2 ml kg^{-1} 2.7% saline over 10–15 minutes (maximum 100 ml).
- Measure the plasma sodium concentration at least hourly.
- As symptoms resolve, decrease the frequency of plasma sodium measurements based on the response to treatment.
- Do not manage acute hyponatraemic encephalopathy using fluid restriction alone.
- After the acute symptoms of hyponatraemia have resolved, ensure that the rate of increase

of plasma sodium does not exceed 12 mmol l^{-1} in a 24-hour period. Faster correction may result in osmotic demyelination syndrome (quadriplegia and locked-in state).
- One ml kg^{-1} of 2.7% sodium chloride will normally raise the serum sodium by 1 mmol l^{-1}.
- The sodium correction required can be calculated using the formula:

$$\text{mmol of sodium required} = (130 - \text{current serum sodium}) \times 0.6 \times \text{weight (kg)}.$$

Prevention of Hyponatraemia

- Use isotonic maintenance fluids.
- Give 50–80% restriction of maintenance fluids in children at risk of ADH secretion.
- Monitor fluid balance and electrolytes at least every 24 hours whilst the child is receiving IV fluids.

Table 13.8 Transfusion triggers in children

	Haemoglobin g l^{-1}
First 24h of life	120
Neonates in intensive care	100–120
Neonates not requiring oxygen	75–85
Acutely ill child	70
Cyanotic congenital heart disease	100–120

Table 13.9 Estimated blood volume (EBV) at different ages

Age	EBV ml kg^{-1}
Preterm neonate	90–100
Term neonate	80–90
Infant and children	70–80
Adult	70

Transfusion of Blood and Blood Components

Children may need a blood transfusion to replace blood loss during surgery, following trauma or to treat certain blood disorders. Compared to adults, blood transfusion is associated with a higher rate of adverse events in children, especially in the first year of life.

Transfusion should be minimised in all patients if possible, in line with NHS Blood and Transplant 'Better Blood Transfusion' initiatives. Strategies include optimising cardiovascular or respiratory disease, correction of preoperative anaemia (iron therapy, erythropoietin), nutritional advice, stopping NSAIDs prior to surgery, a perioperative plan for children who are anticoagulated, meticulous surgical technique, acute normovolaemic haemodilution and cell salvage. Treating iron deficiency anaemia with supplemental oral iron can increase haemoglobin by 10 g l^{-1} per week.

Haemoglobin concentration of 70 g l^{-1} should be used as a threshold for transfusion in stable patients without a major comorbidity or active bleeding. Healthy children can usually compensate for acute anaemia better than adults because they have normal cardiorespiratory physiology and effective oxygen delivery. A haemoglobin concentration of 70 g l^{-1} is well tolerated outside the immediate neonatal period. A higher trigger for transfusion is used in neonates or children with cyanotic heart disease. The decision to transfuse should not be based solely on the haemoglobin level; it should also take into account the clinical situation, coexisting pathology, likelihood of continued bleeding, patient age and physiological parameters. Suggested triggers for transfusion in different circumstances are shown in Table 13.8.

In the surgical setting, it is useful to estimate the maximum allowable blood loss (MABL) as a guide to when blood is likely to be needed:

$$\text{MABL} = \frac{\text{initial haemoglobin} - \text{final haemoglobin}}{\text{initial haemoglobin}} \times \text{EBV}$$

The estimated blood volume (EBV) is calculated using the body weight and age (Table 13.9).

Transfusion volumes for children should be calculated carefully and prescribed in millilitres, not component units, to minimise dosing errors and reduce the risk of circulatory overload. In the absence of ongoing losses, 4 ml kg^{-1} of packed red cells will raise the haemoglobin level by approximately 10 g l^{-1}.

If arterial or central venous access is available, regular haemoglobin estimation ensures that the smallest volume of blood necessary is transfused. However, in smaller infants, donor exposure can

Table 13.10 Blood component therapy in children

Component	Volume
Packed red blood cells	4 ml kg^{-1} raises haemoglobin by 10 g l^{-1}
Platelets	10–15 ml kg^{-1}
Fresh frozen plasma	15–20 ml kg^{-1}
Cryoprecipitate	5–10 ml kg^{-1}

be minimised by using as much blood as possible from one unit, although the posttransfusion haemoglobin should not exceed 200 g l^{-1}. Recommended transfusion volumes of blood components are shown in Table 13.10.

Blood products should be warmed to 37°C to prevent hypothermia, as this may worsen coagulopathy or cardiac arrhythmias. Large-volume transfusion in neonates and small infants and rapid transfusions into a central catheter in older children may cause metabolic derangements, in particular hyperkalaemia and hypocalcaemia.

Cell salvage for neonates and children with large-volume blood loss is technically feasible and should be used to reduce allogeneic transfusion. Contraindications include sickle cell disease and other conditions characterised by red cell fragility. As in adults, careful risk assessment is essential in malignancy and abdominal injury when the salvaged blood may contain a high concentration of malignant cells or bacteria.

Blood Components and Specifications

Blood components provided for the foetal, neonatal and infant age group in the United Kingdom have additional safety features and are suitable for all recipients under one year of age:

- All blood components (except granulocytes) in the United Kingdom are leucodepleted to reduce transfusion reactions and reduce the risk of variant Creutzfeldt–Jacob disease (vCJD). Fresh frozen plasma (FFP) and cryoprecipitate are currently sourced in the United Kingdom as the risk of vCJD has reduced.
- Cytomegalovirus (CMV) negative red cells and platelets should be provided for neonates.
- Irradiated blood is required in children with known or suspected T-cell immunodeficiency, such as DiGeorge syndrome, or those at risk of transfusion-associated graft-versus-host disease.

Consent for Transfusion

Consent for blood transfusion should be obtained to include a description of risks, benefits and alternatives to blood transfusion.

A clear management plan and a full and timely discussion with the family are crucial where children or their parents refuse to consent to transfusion (e.g. Jehovah's Witnesses). The principles of 'patient blood management' should be used to optimise preoperative haemoglobin levels, minimise blood sampling, correct any coagulopathy and minimise blood loss to reduce the chance of a blood transfusion being required for all patients, and a 'best interest' approach for the child taken (see Chapter 4). Blood and blood components can be given in an emergency to save a child's life, despite parental refusal or refusal of the child. However, a plan needs to be agreed in advance of elective surgery that may require blood transfusion such as cardiac surgery or cardiopulmonary bypass; this may require court approval for surgery and any related transfusions in the case of parental refusal. It is not acceptable to wait until it is an emergency and then to use that as a reason for giving the blood without consent. Individual cases involving parental refusal should always be discussed with the Trust/Health Board legal department to obtain clarity prior to surgery. The Jehovah's Witness Hospital Liaison Committee can be a useful source of advice where relevant.

Blood Transfusion in Neonates

Normal haemoglobin values are significantly higher at birth (160–200 g l^{-1}) and decrease gradually over the first few months of life to reach their lowest values (90–110 g l^{-1}) at around two to three months of age ('physiological anaemia'). At birth, the prevalent haemoglobin is foetal haemoglobin, which has a higher affinity for oxygen than adult haemoglobin, essential for oxygen uptake from the placenta in utero, but which results in decreased extraction of oxygen by the tissues after birth. Delayed cord clamping of at least one minute is recommended for the term and preterm neonate not requiring resuscitation and has been shown to result in a significantly increased haemoglobin after birth and

decreased iron deficiency at two to six months of age. Fetal haemoglobin falls rapidly during the first few months of life with only trace amounts present at six months. Transfusion thresholds in neonates vary according to the cardiorespiratory status and postnatal age of the infant (Table 13.11). Neonatal transfusions are usually given as small volume 'top-up' transfusions to maintain the haemoglobin above a particular threshold or in the presence of surrogate markers of anaemia, such as poor growth, lethargy or increased episodes of apnoea. In preterm infants, low haemoglobin levels are a risk factor for postoperative apnoea. Potential benefits of transfusion in this group include improved tissue oxygenation and a lower cardiac output to maintain the same level of oxygenation.

Normal neonates have different age-related values for common coagulation screening tests compared to older children and adults. At birth, vitamin K–dependent clotting factors are 40–50% of adult levels and are lowest in preterm infants. The prothrombin time (PT), thrombin time (TT) and activated partial thromboplastin time (APTT) may be longer, although overall haemostatic function may be normal. Vitamin K is recommended for every newborn infant. Disseminated intravascular coagulation (DIC) is common in sick neonates, and haemorrhagic disease of the newborn due to vitamin K deficiency can cause major bleeding in babies who have not received appropriate vitamin K prophylaxis at birth. Major vitamin K deficiency bleeding requires urgent treatment. Four factor prothrombin complex concentrate (PCC) is preferable to FFP. Platelets are present in normal numbers at birth and reach adult reactivity at two weeks of age. For neonates where there are no bleeding concerns, platelet transfusion should not be administered if platelet count is $\geq 25 \times 10^9\ l^{-1}$.

Major Haemorrhage

Major haemorrhage may be defined as the loss of either a single circulating blood volume (approximately 80 ml kg^{-1}) in 24 hours, 40 ml kg^{-1} in three hours or 2–3 ml kg^{-1} min^{-1}. In practice, the usual triggers for activation of major haemorrhage protocols are rapid blood loss with shock or with no likelihood of control or anticipated/actual administration of 40 ml kg^{-1} of blood.

Major haemorrhage related to trauma is uncommon in children (see Chapter 39). In paediatric surgery, massive blood loss mostly occurs in craniofacial, neurosurgery, tumour resection, spinal, liver and cardiac surgery.

Key Principles for the Management of Major Haemorrhage in Children

- Early recognition and activation of the major haemorrhage protocol (including the necessary clinical and transfusion teams)
- Active resuscitation to restore circulating volume
- Control of bleeding
- Rapid provision of Group O Rhesus negative or group-specific red cells
- Anticipation and treatment of coagulopathy and thrombocytopenia with early use of FFP and consideration of platelets and cryoprecipitate in ongoing bleeding
- Prevention/correction of the metabolic consequences of massive blood transfusion (hypothermia, hypocalcaemia, acidosis and hyperkalaemia)

Current major haemorrhage protocols, based on adult trauma research, recommend the early use of FFP and platelets prior to the results of coagulation tests where bleeding is ongoing. Table 13.12

Table 13.11 Suggested transfusion thresholds for surgery in neonates (based on the 2016 Guidelines from the British Committee for Standards in Haematology)

	Haemoglobin g l^{-1}		
Postnatal age	**Ventilated**	**Receiving oxygen/NIPPV**	**Not receiving oxygen**
First 24 hours	<120	<120	<100
≤Week 1	<120	<100	<100
Week 2	<100	<95	<75–85
≥Week 3	<100	<85	<75–85

Note: NIPPV: Non-invasive positive pressure ventilation.

shows suggested aliquots of blood and blood components to treat major haemorrhage in children. These aliquots should be repeated in recommended ratios as necessary until bleeding is controlled. Ratios should be modified accordingly once laboratory parameters are available. The therapeutic aims should be:

- Hb >80 g l^{-1}
- Fibrinogen >1·5 g l^{-1}
- PT ratio <1·5
- Platelet count >75 × 1,09 l^{-1}

Early use of tranexamic acid has been shown to reduce mortality in adult trauma, and this beneficial effect may also apply in children. It should be considered in all neonates and children undergoing surgery where there is risk of significant bleeding. An initial dose of 15 mg kg^{-1} (maximum 1 g) intravenously over 10 minutes should be given as soon as possible, followed by 2 mg $kg^{-1}h^{-1}$ for at least eight hours or until bleeding stops.

Careful monitoring for adequacy of resuscitation and for circulatory overload is essential. Unintended over-transfusion of red cells is common in small infants. Volume replacement should be guided by clinical endpoints and laboratory or point-of-care testing. All large-volume transfusions should be given via a blood warmer to avoid hypothermia, and the core temperature should be monitored.

Potential electrolyte disturbances from massive blood transfusion include:

Table 13.12 Blood, clotting factors and tranexamic acid dosing in major haemorrhage

Component	Volume
Emergency transfusion (1:1 ratio)	
PRBC*	20 ml kg^{-1}
FFP	20 ml kg^{-1}
For ongoing bleeding:	
Continue PRBC: FFP 1:1	
Platelets	15 ml kg^{-1}
Cryoprecipitate	10 ml kg^{-1}
Fibrinogen concentrate	70 mg kg^{-1}
Prothrombin concentrate	25–50 IU kg^{-1}
Factor VII	90 mcg kg^{-1}
Tranexamic acid	Loading dose 15 mg kg^{-1} Infusion 2 mg kg^{-1} h^{-1}

Notes: * Use emergency O D-negative blood until group-compatible blood is available; PRBC: packed red blood cells.

- **Hyperkalaemia**
  There is a risk of hyperkalaemia due to high extracellular potassium in old stored or irradiated blood following large-volume transfusions, particularly if infused rapidly. It is recommended that red cells for large-volume neonatal and infant transfusions be used before the end of day 5 following donation (and within 24 hours of irradiation) in order to reduce this risk.
  Rapid transfusion via a central line may represent a particular risk of cardiac arrest. Emergency treatment of hyperkalaemia with 10% calcium gluconate (0.5 ml kg^{-1}), nebulised salbutamol, glucose-insulin infusion or bicarbonate for metabolic acidosis may be required.
- **Hypocalcaemia**
  Low-ionised calcium (<1 mmol l^{-1}) is due to citrate overload from large blood transfusion and can result in myocardial dysfunction.
  It should be corrected with calcium chloride 5–10 mg kg^{-1} by slow intravenous infusion via a central line.
- **Hypomagnesaemia**
  This is also due to citrate toxicity and may result in ventricular arrhythmias.
  Hypomagnesaemia is treated with intravenous magnesium 25–50 mg kg^{-1} (maximum 2 g).

Key Points

- It's safe and recommended to allow children to drink clear fluids up to one hour before elective surgery.
- Isotonic crystalloids with a sodium concentration similar to plasma reduce the risk of hyponatraemia without increasing adverse effects and are the first choice for fluid replacement and maintenance in children.
- Intraoperative fluid management in children should be individualised and aim for normovolaemia.
- ADH secretion in postoperative or unwell children causes water retention and increases their risk of hyponatraemia. The calculated rate for postoperative maintenance fluids should be reduced to 50–80% for at risk patients.
- Children receiving IV fluids should have electrolytes and fluid balance measured daily.

- Most children do not require glucose-containing fluids intraoperatively unless they are at risk of hypoglycaemia (for instance neonates).
- If the child has signs of severe dehydration (presence of red flags) or shock, 10–20 ml kg^{-1} of a glucose-free isotonic crystalloid should be given immediately. Further boluses may be given if signs of shock persist.
- Acute symptomatic hyponatraemia should be treated with hypertonic saline in a high-dependency unit.
- Strategies to reduce blood transfusion include treatment of preoperative iron deficiency, use of appropriate transfusion thresholds, cell salvage and administration of tranexamic acid.

Further Reading

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