

# Fluid balance: all aspects

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This chapter aims to cover the basics of fluid balance. It is loosely divided into four sections. The first outlines fluid physiology. The use of crystalloid maintenance fluids is dealt with in the second. The third section deals with colloids and touches on the crystalloid:colloid debate for volume replacement. The final part covers the use of blood and its components in paediatric anaesthesia.

Body water is conventionally divided into three compartments: intracellular, extracellular and transcellular. In adults 60% of water is intracellular, 10% transcellular and 30% extracellular, of which 7.5% is intravascular. Although it is well recognized that disease states may affect the distribution of water in the body, it is less well known that age will also influence it. Extracellular water decreases from 60% in a 20-week fetus to 45% at term and falls a further 5% in the first 5 days of life.<sup>1</sup> Adult levels are reached by the end of the second year of life.

## FLUID PHYSIOLOGY

### TOTAL BODY WATER AND FLUID BALANCE

Total body water varies with degree of adiposity (90% of muscle weight is water vs 10% of fat), disease state and age. Ninety-four per cent of the body weight of a 12-week fetus is water and this falls to 80% by 32 weeks' gestation and 78% by term. There is a further reduction of about 5% in the first week of life, followed by a gradual fall to adult levels of 50-60% by 18 months of age.<sup>1</sup>

### THE STARLING EQUATION

The extracellular compartment is further subdivided into the interstitial and intravascular spaces, with the interstitial space being three and a half times larger than the intravascular.<sup>2</sup> Fluid flux between the two was first described by Starling, who noted that the rate of fluid movement into or out of a capillary was related to the net hydrostatic pressure minus the net osmotic pressure.<sup>3</sup> The Starling equation:<sup>4</sup>

$$J_v = K_{fc}[(P_c - P_t) - \delta_c(\pi_c - \pi_t)]$$

where  $J_v$  = rate of fluid movement into/out of

capillary:  $K_{fc}$  = capillary filtration coefficient;  $P_c$  = capillary hydrostatic pressure;  $P_t$  = tissue fluid hydrostatic pressure;  $\sigma_c$  = reflection coefficient;  $\pi_c$  = capillary colloid osmotic pressure;  $\pi_t$  = tissue colloid osmotic pressure. has been further modified to incorporate coefficients which represent the permeability of the capillary membrane to small solutes ( $K_{fc}$ ) and the reflection coefficient which describes the membrane's ability to prevent large molecules such as plasma proteins from crossing it: the Starling coefficient (sc).<sup>5</sup> If sc is 1, then a fluid can realize its full osmotic pressure: if sc for a membrane is 0 then fluids will pass freely across it and no pressure will be exerted. The coefficients vary between different organs of the body and are altered by disease. Burns, sepsis and cardiopulmonary bypass, in particular, reduce sc, resulting in capillaries which are increasingly 'leaky'. This has two effects: it allows water to leak out causing tissue oedema and it allows osmotically active particles to escape into the interstitial space. If sc then increases again, these particles will remain in the interstitial space, increasing its osmotic pressure and altering the balance of the Starling equation until they can be removed by the lymphatic system.

Most of the components of the Starling equation can be measured only with difficulty in the laboratory but the intravascular osmotic pressure and the capillary hydrostatic pressure can be measured clinically.<sup>6,7</sup> Guyton *et al.* describe certain 'oedema protection factors', such as increased lymphatic flow, which prevent the accumulation of oedema until the capillary hydrostatic pressure has increased by more than 15 mmHg.<sup>8</sup> This is supported clinically by the observation that in the absence of pulmonary capillary damage, the left atrial pressure (equivalent to hydrostatic pressure) must be increased to 15–20 mmHg before pulmonary oedema is seen.

One of the main differences between the fluid balance of adults and infants is the relatively large water turnover in the infant. The water contained within the extracellular space of a 70 kg man is about 14 l. Just under 3 l day<sup>-1</sup> is lost in urine, faeces, sweat and during respiration (20%). In a 7 kg infant, the extracellular space contains about 1.6 l and obligatory losses are around 0.7 l day<sup>-1</sup> (44%).<sup>2</sup> Any relatively

small increase in losses will therefore have a much greater effect on a small child and this explains why diarrhoea remains such an important cause of infant mortality world-wide.

## MAINTENANCE CRYSTALLOID REQUIREMENTS

### MAINTENANCE WATER REQUIREMENTS

Although there are numerous formulae for calculating maintenance fluid requirements, it is important to stress that these are all guidelines only. They may be used as a starting point but the individual child's response to the fluid given must be monitored and appropriate adjustments made to the regimen.

The formulae available for calculating fluid requirement have as their basis body surface area (BSA), calorie requirement and the weight of the child.

#### Body surface area

Various nomograms are published which calculate BSA from height and weight. In older children the calculation of BSA is relatively easy and accurate because it is possible to obtain an accurate height. Measurements of the length of a neonate or small infant are not as reliable and errors of up to 20% in BSA are well recognized in babies less than 3 kg.<sup>9</sup> Because the height-length measurement is inaccurate, most centres now use a formula based on weight alone to calculate fluid requirement and the use of BSA has fallen from favour.<sup>10</sup>

#### Calorie requirements

The metabolism of 1 calorie requires 1 ml of water because, although 0.2 ml of water is produced, a further 1.2 ml is consumed. Therefore, 100 calories will require 100 ml of water for metabolism and knowing the calorie requirement of a child will also reveal the water requirement.<sup>11</sup> In 1911 Howland calculated the calorie requirement of an infant from 3–10 kg

to be  $100 \text{ cal kg}^{-1}$ , with older children needing 75 and adults  $35 \text{ cal kg}^{-1}$ . The extra calories metabolized by the younger children are attributed to proportionally larger surface area and growth.<sup>12</sup> In infants of less than 10 kg body weight,  $50 \text{ cal kg}^{-1}$  will be needed for basal metabolic requirements and the rest for growth. Children of less than 20 kg body weight need 1000 calories for the first 10 kg but only  $50 \text{ cal kg}^{-1}$  for the next 10 kg because of slower growth rate, and larger children and adults need only three times the calories of a neonate (1500 calories for the first 20 kg and  $20 \text{ cal kg}^{-1}$  thereafter).<sup>11</sup>

### Normal maintenance fluid requirements calculated by weight

Whatever mechanism is used to calculate fluid requirements, it must be simple and foolproof because small miscalculations can result in significant errors in fluids administered. It has already been said that 100 calories requires 100 ml of water. A 25 kg child, therefore, requires  $100 \text{ ml kg}^{-1}$  for the first 10 kg (1000 ml),  $50 \text{ ml kg}^{-1}$  for the next 10 kg (500 ml) and  $20 \text{ ml kg}^{-1}$  thereafter (100 ml), making a total of 1600 ml per day or  $66 \text{ ml h}^{-1}$ . This can be simplified by assuming that there are 25 h in a day. The child then needs  $4 \text{ ml kg}^{-1} \text{ h}^{-1}$  for the first 10 kg (40 ml),  $2 \text{ ml kg}^{-1} \text{ h}^{-1}$  for the next 10 kg (20 ml) and  $1 \text{ ml kg}^{-1} \text{ h}^{-1}$  thereafter (5 ml), giving an hourly total of 65 ml, which can be computed at the bedside without a calculator.

Neonates have greater fluid requirements than infants. As a general rule, most neonatal units allow  $60 \text{ ml kg}^{-1}$  for the first day, increasing by  $30 \text{ ml kg}^{-1} \text{ day}^{-1}$  to  $150 \text{ ml kg}^{-1}$  for a term neonate and  $180 \text{ ml kg}^{-1} \text{ day}^{-1}$  for preterm. This requirement will be affected by

environment (overhead heaters increase water loss compared with incubators), by whether the baby is ventilated (when there will be a humidifier in the circuit) and by the general state of the neonate. A premature baby with a patent ductus arteriosus may close the duct in response to fluid restriction and this may avoid the need for more aggressive management.

### Dextrose requirements

In the UK, intravenous dextrose infusions are usually supplied as 4%, 5%, 10% and 20% strengths. In addition, 50% dextrose is available for management of hypoglycaemia. Most infants and children require 4% or 5% dextrose. A recent study from Germany, however, suggests that when these infusions are given preoperatively, children may become hyperglycaemic with dextrose concentrations as low as 2.5% although these were administered at large volumes equivalent to  $200 \text{ ml kg}^{-1} \text{ day}^{-1}$ .<sup>13</sup> Neonates have poor glycogen stores and require higher glucose infusions to maintain their blood glucose levels. The majority of neonates, therefore, are traditionally managed using infusions of 10% dextrose which can be given through a peripheral cannula. Sick neonates on the intensive care unit, particularly in the presence of sepsis, may require higher infusions than this. Such patients may also need fluid restriction and it is not uncommon for small septic babies to need 20% infusions of dextrose. A neonate who cannot be fed enterally for more than a couple of days will require parenteral hyperalimentation rather than simple dextrose saline solutions. Hyperglycaemia can develop in response to stress. Both hypoglycaemia and hyperglycaemia can occur and blood sugar levels should be regularly monitored.

### Electrolyte requirements

Electrolyte requirements vary with prematurity, losses and disease states. There is some debate as to whether a neonate needs sodium on the first day of life. Some units use a dextrose solution without added electrolytes, whilst others add sodium, potassium and calcium, particularly for premature infants. Preterm breast milk contains higher concentrations of sodium, calcium and phosphorus for the first 2-

Table 8.1 Normal maintenance fluid requirements

Weight (kg)	Maintenance fluid requirement (cumulative values) ( $\text{ml kg}^{-1} \text{ day}^{-1}$ )
< 10	100
11-20	50
> 20	20

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4 weeks of lactation, and meets the preterm infant's increased requirements for these elements. Preterm formulae with similar electrolyte composition are also available. As a guide for prescribing, most children require 2-3 mmol kg<sup>-1</sup> of sodium and 2 mmol kg<sup>-1</sup> of potassium. This means that a 10 kg infant who needs 1000 ml of fluid per day will also need around 30 mmol of sodium. In the UK, fluids are available as dextrose (4% or 10%) and 0.18% saline (i.e. containing 30 mmol l<sup>-1</sup>). For most patients, a ready-made bag of fluid will provide their electrolyte needs. In some instances, additional sodium will be required. This can be added to a standard bag using a strong sodium (30%: 5000 mmol l<sup>-1</sup>) solution, or Normal saline (0.9%: 150 mmol l<sup>-1</sup>) or half Normal saline (0.45%: 75 mmol l<sup>-1</sup>) can be used in its place.

The amount of sodium administered to neonates in the immediate postoperative period needs to be monitored. Krummel *et al.* studied 20 surgical newborns and found that hypernatraemia occurred in 64% of term babies and 67% of preterms. In all cases this appeared to be due predominantly to an administered sodium load of more than 400% of the estimated maintenance requirements. This was compounded by a slightly reduced ability to excrete sodium and a short period of post-operative sodium retention.<sup>14</sup>

## SPECIAL REQUIREMENTS

### Gastrointestinal losses

Gastrointestinal surgery is relatively common in small infants. Ileus may also occur in a sick child; therefore, gastrointestinal losses are of importance. Nasogastric aspirates should be replaced volume for volume with normal saline containing 10 mmol potassium chloride per 500 ml. This sodium load allows the patient's kidneys to correct the hydrogen deficit incurred by the loss of gastric secretions. Stoma losses may also need to be replaced. High stomas in particular may be associated with significant sodium losses leading to as much a 6-fold increase in sodium requirements. Losses of more than 40 ml kg<sup>-1</sup> day<sup>-1</sup> are likely to require parenteral replacement using the same solution of normal saline with 10 mmol potas-

ium per 500 ml. Usually, 0.5 ml is replaced for every 1 ml lost but, depending on the volume of losses and the site of the stoma, anything from one-third to three-quarter replacement may be required. Children who have ileus, either from gastrointestinal surgery and pathology or secondary to another cause, can secrete large amounts of fluid within the gut and peritoneal cavity. Babies with abdominal distension due to Hirschsprung's disease (colonic aganglionosis) may be intravascularly depleted in the presence of steady weight or even weight gain and such patients may need intravascular volume replacement despite normal indices.

### Pyloric stenosis

Hypertrophic pyloric stenosis is a common condition with an incidence of about 1:200. All babies with this condition vomit and will require preoperative intravenous fluids. About 50% of patients will have a significant derangement of their electrolytes and acid: base status as a result of vomiting. The most useful electrolyte to gauge the seriousness of the metabolic upset is chloride, which can be used to calculate the chloride deficit and this must often be specifically requested as it is no longer performed routinely in most hospitals. While the serum chloride remains low, the infant will be alkalotic.<sup>15</sup> The vomiting of HCl, together with the kidney's attempts to conserve sodium, results in a metabolic alkalosis and a depletion of total body potassium. Because potassium is an intracellular ion, the serum potassium is a poor guide to potassium requirements and will usually be within the normal range.

To correct the metabolic alkalosis, the infant must be given sufficient sodium and potassium so that the kidneys can conserve hydrogen ions and correct the acid: base status. Chloride is also given as the anion to both sodium and potassium. Most babies with mild derangement (sodium bicarbonate < 35 mmol) will be corrected within 24 h using a solution of 5% dextrose plus 0.45% saline with 15 mmol of potassium chloride per 500 ml bag at 150-180 ml kg<sup>-1</sup> day<sup>-1</sup>. In extreme cases, normal saline (or 4.5% albumin which contains 150 mmol NaCl l<sup>-1</sup>) may be required and 2-3 days of parenteral fluids may be needed preoperatively. It is also important to remember

that any gastric distension results in more gastric juices being secreted and lost. A wide-bore nasogastric tube should be left on free drainage with regular aspirations and any nasogastric losses should be replaced millilitre for millilitre with normal saline with added potassium (10 mmol in 500 ml).

### Posterior urethral valves

Posterior urethral valves cause a congenital obstruction of the male posterior urethra and affected infants may also have a degree of renal dysplasia. Nowadays, the condition is increasingly diagnosed antenatally and most other children present within the first month of life. The initial management of a neonate with valves is to catheterize the patient and then confirm the diagnosis by cystogram and/or cystoscopy. Surgery consists of valve ablation via the cystoscope. A significant number of these children will have renal impairment which may be long-term, and almost all have a diuresis in response to catheterization and relief of the obstruction. Urine output must be closely monitored in these patients and their fluid intake will be based on their creatinine and their output. Most of these babies are well enough to receive oral feeds but will also require parenteral supplementary fluids to keep up with urinary losses. This diuretic phase can last for between 24 h and a couple of weeks, again emphasizing that strict criteria cannot be laid down for neonatal fluid infusions.

### Congenital diaphragmatic hernia

The fluid handling of a neonate with congenital diaphragmatic hernia merits special mention. There appears to be only a narrow path between hypovolaemia and fluid overload, either of which may have catastrophic effects resulting in a worsening spiral of acidosis and hypoxia. Rowe *et al.* studied the urine output and osmolarity of both urine and serum in 22 infants with diaphragmatic hernia vs 12 control infants undergoing laparotomy for some other reason. They found that although all controls responded appropriately, 64% of the diaphragmatic hernia group inappropriately retained fluid in the first 16 h after surgery and one-third still had an inappropriate urine output

24 h after surgery.<sup>15</sup> Fluid management of these children involves strict crystalloid restrictions (30 ml kg<sup>-1</sup> day<sup>-1</sup> for the first 24 h) and colloid boluses to maintain normovolaemia. Close monitoring of urine output and serum and urine osmolarity will help in the management.

### Phototherapy

Neonatal 'physiological' jaundice is relatively common and is worsened by dehydration. Some neonates with a rising unconjugated hyperbilirubinaemia can be managed simply by liberalizing their fluids. This may need to be via a nasogastric tube or parenterally as the jaundice tends to make the baby sleepy and therefore less able to feed, which compounds the problem. If phototherapy is required, environmental water loss is increased significantly and an extra 25 ml kg<sup>-1</sup> day<sup>-1</sup> should be added to the fluids to compensate.

### Effects of surgery

In 1968 Reid showed in adult patients that fluid accumulation occurred in the early postoperative phase and that this occurred entirely within the extravascular space. There was no change in the intravascular volume even when large fluid increases were seen extravascularly.<sup>17</sup> Seven years earlier, Shires *et al.* had studied fluid shifts preoperatively and noted an acute contraction of the functional extracellular fluid which, in the absence of blood loss, they presumed to be due to internal redistribution. They noted that the magnitude of the internal redistribution was related to the degree of surgical trauma and particularly to the duration and degree of retraction. They concluded that this was a major stimulus to the fluid and sodium retention seen postoperatively.<sup>18</sup> Certainly, after major abdominal surgery there is a fall in the serum sodium and evidence of fluid retention with periorbital and dependent oedema, which can be reduced by restricting fluids for the first 24-48 h following surgery. Following minor procedures patients are allowed their full maintenance fluids, but after any major surgery their intake is reduced to 50% of requirements for the first postoperative day, and if additional fluid is required it may be better to be given as colloid.

### Sepsis

Hyponatraemia in sepsis is well recognized and is associated with a worse prognosis. Hannon and Boston looked at fluid and ion redistribution in an animal model of sepsis and found significant shifts of sodium, chloride and water into cells compared with sham controls.<sup>19</sup> They found this trend to be exacerbated by infusing 5% dextrose compared with normal saline with fluid shifts occurring when the volume infused was less than the estimated fluid requirement. They suggested that the hyponatraemia and plasma hypo-osmolality were caused by a combination of intracellular shift of sodium and water, and a dilution of the extracellular space, probably caused by physiological anti-diuretic hormone (ADH) secretion. Their conclusion was that, in the presence of sepsis, 4% dextrose + 0.18% sodium chloride is inappropriate, potentially dangerous and should be avoided.

### Burns (see also Chapter 15)

Significant burns cause large fluid losses and burns patients require large volumes of fluid resuscitation. In addition to normal maintenance fluids, such patients need resuscitation fluids, such as Normal saline, Ringer's solution or Gelofusine<sup>®</sup> given over at least the first 36 h after injury. The 36 h are divided into six periods: three of 4 h, two of 6 h and one of 12 h. The timing starts from the moment of injury so that the first infusion is inevitably delayed. During each period the child needs an average of 0.5 ml kg<sup>-1</sup> per % burn. The precise volume given is adjusted on the basis of urine output, urine and plasma osmolality, perfusion and the calculated plasma deficit. This can be calculated from the formula:

$$\text{plasma deficit} = \text{blood volume} - \left( \text{blood volume} \times \frac{\text{normal haematocrit}}{\text{observed haematocrit}} \right)$$

Deep burns result in red cell destruction and the usual blood requirement is of 1% of normal blood volume per 1% burn for deep burns of more than 10% surface area. Because the

haematocrit is a useful guide to the plasma deficit, blood is usually best administered during the last 12 h of fluid resuscitation.<sup>20</sup>

### Clinical assessment of dehydration

Although thirst appears with the loss of approximately 2% of total body water, the state of the peripheral circulation is the most sensitive guide to more serious levels of clinical dehydration in children. Core-peripheral temperature difference becomes clinically detectable and mucous membranes dry at around 5% loss of total body water. With 10% dehydration the peripheries are cold and capillary refill, normally complete within 2 s, is delayed. Pulse and respiratory rates increase, consciousness may be clouded, and in the neonate the fontanelle is sunken. Blood pressure may fall, although because of the increased cardiac output caused by the tachycardia this is not an early or reliable sign. Urine output is decreased. At 15% dehydration capillary refill may be incomplete even after 10 s, the mouth is parched and the eyes are sunken. The pulse is rapid and thready and blood pressure low. The child is stuporose and oliguric, and may show signs of respiratory distress. Losses in excess of 20% may be fatal.

## COLLOIDS

### THE CRYSTALLOID VERSUS COLLOID DEBATE

The superiority of colloid over crystalloid for volume replacement remains controversial.<sup>21,22</sup> Whilst crystalloids are generally more popular in the USA, colloids are preferred in Europe.<sup>23</sup> The debate centres on which fluid space needs replenishing and the importance or otherwise of colloid osmotic pressure.

Colloids theoretically remain within the intravascular space, therefore expanding the intravascular volume more efficiently, producing the same increase in cardiac output for a smaller volume of fluid. The proponents of crystalloid argue that the whole extracellular fluid space is reduced in hypovolaemia because of fluid movement from the interstitial compart-

undergone a circulating volume transfusion of red cells. In babies and infants, a transfusion of 5–10 ml kg<sup>-1</sup> is usually sufficient, whilst unit transfusions are appropriate in older patients.

### FRESH-FROZEN PLASMA AND CRYOPRECIPITATE

FFP contains 1 unit of factor activity per millilitre of plasma. A decision to use FFP or cryoprecipitate should be based on a combination of clinical and laboratory findings. An INT of less than 1.4 or a partial thromboplastin time of less than 60 s is unlikely to cause significant bleeding problems and correction is not required. Laboratory values greater than these levels or significant bleeding will require correction. An empiric dose of 5–10 ml kg<sup>-1</sup> is usually adequate or the dose can be calculated by body weight, plasma volume and desired increment of clotting factors.

Cryoprecipitate is a poor source of factors II, V, IX, X, XI and XII but contains factors VIII : C, VIII-WF, XIII, fibrinogen and fibronectin. Indications for its use include haemophilia A, von Willebrand disease, fibrinogen deficiency, massive transfusion and uraemic platelet dysfunction. Its advantage over FFP is that it is concentrated and one bag (of 15–20 ml) is the dose per 10 kg body weight.

### SPECIAL SITUATIONS

#### Jehovah's witnesses

The Royal College of Surgeons of England have produced a code of practice for the surgical management of Jehovah's Witnesses. This acknowledges that the children of Jehovah's Witnesses requiring blood transfusion present a most difficult management problem.<sup>84</sup> There are some mitigating factors, however. Either parent may sign a consent form permitting a transfusion. Most operations on children do not require or involve blood transfusion, but it is unethical to let a child die for want of a blood transfusion. The surgeon and anaesthetist must, however, respect the beliefs of the family and should make every effort to avoid the perioperative use of blood or blood products. For

children under 13 years of age who require or may require a transfusion but whose parents refuse to give consent, legal advice should be sought. Such children will normally be made a temporary ward of court. This subject is covered more fully in Chapter 2.

#### Sickle cell disease

Traditionally, patients with sickle cell disease have been routinely transfused before elective surgery. There has, however, been little consensus as to whether simple correction of the anaemia is sufficient or whether the level of HbS should be reduced to less than 30%. Vichinsky *et al.* compared a conservative regimen (transfusing to a haemoglobin level of around 10 g dl<sup>-1</sup>) with an aggressive regimen (haemoglobin of around 10 g dl<sup>-1</sup> and an HbS level of less than 30%). They found the conservative regimen to be as effective in preventing perioperative complications and this group had half as many transfusion-associated complications.<sup>85</sup> Similarly, immediately preoperative transfusion to a haematocrit of more than 36% was as efficacious as two-volume exchanges beginning 2 weeks prior to surgery, with less disruption to the family.<sup>86</sup> Patients with HbSS disease should receive transfusions to correct their anaemia. They should be given adequate perioperative hydration with crystalloid. Postoperatively, they should receive adequate analgesia in addition to oxygen and physiotherapy to prevent atelectasis. For more information, see Chapter 1.

### CONCLUSION

Fluid management in paediatrics is an art as well as a science: clinicians need to monitor the response to therapy and change the regimen appropriately. This chapter contains guidelines and suggestions for safe fluid administration but cannot replace clinical experience.

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## REFERENCES

- 1 Rowe, M.I. A dynamic approach to fluid and electrolyte management of the newborn. *Zeitschrift für Kinderchirurgie* 1985; 40: 270-7.
- 2 Lippold, O.C.J. and Winton, F.R. The distribution of body fluids. In: Lippold, O.C.J. and Winton, F.R. (eds). *Human Physiology*. Edinburgh: Churchill Livingstone, 1979: 118-21.
- 3 Starling, E.H. On the absorption of fluids from the connective tissue spaces. *Journal of Physiology* 1896; 19: 312-26.
- 4 Bush, G.H. Intravenous fluid therapy in paediatrics. *Annals RCS* 1971; 49: 92-101.
- 5 Bevan, D.R. Colloid osmotic pressure. *Anaesthesia* 1930; 35: 263-70.
- 6 Morissette, M.P. Colloid osmotic pressure: its measurement and clinical value. *Canadian Medical Association Journal* 1977; 116: 897-900.
- 7 Barclay, S.A. Colloid osmotic pressure: its measurement and role in clinical cardiovascular medicine. PhD Thesis, University of London, 1986.
- 8 Guyton, A.C., Granger, H.J. and Taylor, A.E. Interstitial fluid pressure. *Physiology Review* 1971; 51: 527-63.
- 9 Boyd, E. *Growth of Surface Area of the Human Body*. Institute of Child Welfare, Monograph Series 10. Minneapolis, MN: University of Minnesota Press, 1933.
- 10 Oliver, W.L., Graham, B.D. and Wilson, J.L. Lack of scientific validity of body surface as a basis for parenteral fluid dosage. *Journal of the American Medical Association* 1956; 167: 1211-18.
- 11 Siker, D. Pediatric fluids and electrolytes. In: Gregory, G.A. (ed.). *Pediatric Anaesthesia*, 2nd edn. New York: Churchill Livingstone, 1989: 581-617.
- 12 Howland, J. The fundamental requirements of an infant's nutrition. *American Journal of Diseases of Childhood* 1911; 2: 49.
- 13 Fosel, T.H., Uth M., Wilhelm W., Gruness Z. Comparison of two solutions with different glucose concentrations for infusion therapy during laparotomies in infants. *Intensivtherapie und Transfusionsmedizin* 1996; 23: 80-4.
- 14 Krummel, T.M., Lloyd, D.A. and Rowe, M.I. The postoperative response of the term and preterm newborn infant to sodium administration. *Journal of Pediatric Surgery* 1985; 20: 803-9.
- 15 Cori, D.W., Hall, S.K., Gomall, P., Buick, R.G., Green, A. and Corkery, J.J. Plasma chloride and alkalaemia in pyloric stenosis. *British Journal of Surgery* 1990; 77: 922-3.
- 16 Rowe, M.I., Smith, S.D. and Cheu, H. Inappropriate fluid response in congenital diaphragmatic hernia: first report of a frequent occurrence. *Journal of Pediatric Surgery* 1988; 23: 1147-53.
- 17 Reid, D.J. Intracellular and extracellular fluid volume during surgery. *British Journal of Surgery* 1968; 55: 594-6.
- 18 Shires, T., Williams, J. and Brown, F. Acute changes in extracellular fluids associated with major surgical procedures. *Annals of Surgery* 1961; 154: 803-10.
- 19 Hannon, R.J. and Boston, V.E. Hyponatraemia and intracellular water in sepsis: an experimental comparison of the effect of fluid replacement with either 0.9% Normal saline or 5% dextrose. *Journal of Pediatric Surgery* 1990; 25: 422-5.
- 20 Muir, I.F.K. and Barclay, T.L. Treatment of burn shock. In: *Burns and Their Treatment*. London: Lloyd-Luke, 1962.
- 21 Laks, H., O'Connor, N.E., Anderson, W., et al. Crystalloid versus colloid hemodilution in man. *Surgery, Gynecology and Obstetrics* 1970; 142: 506-12.
- 22 Poole, G.V., Meredith, J.W., Pennell, T., et al. Comparisons of colloids and crystalloids in resuscitation from hemorrhagic shock. *Surgery, Gynecology and Obstetrics* 1982; 154: 577-86.
- 23 Shoemaker, W.C. Hemodynamic and oxygen transport effects of crystalloids and colloids in critically ill patients. *Current Studies in Hematology and Blood Transfusion* 1980; 53: 177-70.
- 24 Ross, A.D. and Angaran, D.M. Colloids versus crystalloids - a continuing controversy. *Drug Intelligence and Clinical Pharmacology* 1986; 18: 202-12.
- 25 Hunt, T.E., Kabkin, I. and von Smitten, K. Effects of edema and anemia on wound healing and infection. *Current Studies in Hematology and Blood Transfusion* 1980; 53: 177-11.
- 26 Chan, S.T.F., Kapadia, C.R., Johnson, A.W., et al. Extracellular fluid volume expansion and third space sequestration at the site of small bowel anastomoses. *British Journal of Surgery* 1983; 70: 36-9.
- 27 Falk, J.L., Rackow, E.C., Aziz, M., et al. Fluid resuscitation in shock. *Journal of Cardiothoracic Anesthesia* 1988; 2 (Suppl): 33-6.
- 28 Weil, M.H., Henning, R.J., Morissette, M.P., et al. Relationship between colloid osmotic pressure and pulmonary artery wedge pressure in patients with acute cardiorespiratory failure. *American Journal of Medicine* 1978; 64: 643-50.
- 29 Viriglio, R.W., Rice, C.L., Smith, D.E., et al. Crystalloid versus colloid resuscitation: is one better? A randomized clinical study. *Surgery* 1979; 85: 129-39.
- 30 Velanovich, V. Crystalloid versus colloid fluid resuscitation: a meta-analysis of mortality. *Surgery* 1989; 105: 65-71.
- 31 Huskisson L.J. Intravenous volume replacement - which fluid and why. *Archives of Disease in Childhood* 1992; 67: 649-53.
- 32 Cochran Injuries Group Albumin Reviewers. Human albumin administration in critically ill patients: systemic review of randomised controlled trials. *British Medical Journal* 1998; 317: 235-40.
- 33 APLS. Advanced Life Support Group. London: BMA Publishing 1997.
- 34 Ryan, C.A. and Soder, C.M. Relationship between core peripheral temperature gradient and central hemodynamics in children after open heart surgery. *Critical Care Medicine* 1989; 17: 638-40.
- 35 de Felipe, J., Timoner, J., Velasco, I.T., et al. Treatment of refractory hypovolaemic shock by 7.5% sodium chloride injections. *Lancet* 1980; ii: 1002-4.
- 36 Vincent, J.-L. Fluids for resuscitation. *British Journal of Anaesthesia* 1991; 67: 185-93.
- 37 Wilkins, B.H. Renal function in sick very low birthweight infants: 3. Sodium, potassium and water excretion. *Archives of Disease in Childhood* 1992; 67: 1154-61.

- 38 National Institute of Health Consensus Conference. Fresh frozen plasma, indications and risks. *Journal of the American Medical Association* 1985; 253: 551-3.
- 39 Messmer, K. Chapter 2. In: Lowe, K.C. (ed.). *Blood Substitutes. Preparation, Physiology and Medical Application*. Hemel Hempstead: Ellis Horwood Series in Biomedicine, 1988.
- 40 Ring, I. Anaphylactoid reactions to plasma substitutes. *International Anesthesiology Clinics* 1985; 23: 67-95.
- 41 Quon, C.Y. Clinical pharmacokinetics and pharmacodynamics of colloidal plasma volume expanders. *Journal of Cardiothoracic Anesthesia* 1988; 2: 13-23.
- 42 McClelland, D.S.L. Human albumin solutions. *British Medical Journal* 1990; 300: 35-7.
- 43 Lewis, R.T. Albumin: role and discriminative use in surgery. *Canadian Journal of Surgery* 1980; 23: 122-8.
- 44 Sædler, J.M. and Horsey, P.I. The new generation gelatins. *Anaesthesia* 1987; 42: 993-1004.
- 45 Webb, A.R., Barclay, S.A. and Bennett, E.D. *In vitro* colloid osmotic pressure of commonly used plasma expanders and substitutes: a study of the diffusibility of colloid molecules. *Intensive Care Medicine* 1989; 13: 116-20.
- 46 Woods, M.P., Clark, D.J., Mark, I.S. *et al.* Compound sodium lactate (Hartmann's solution). Caution: risk of clotting. *Anaesthesia* 1986; 41: 1053-4.
- 47 Jause, J.D. and Yacobi, A. Hetastarch: an overview of the colloid and its metabolism. *Drug Intelligence and Clinical Pharmacology* 1983; 17: 33-41.
- 48 Mishler, I.M. Synthetic plasma volume expanders - their pharmacology, safety and clinical efficacy. *Clinics in Hematology* 1984; 13: 75-92.
- 49 Klotz, U. and Kroemer, H. Clinical pharmacological considerations in the use of plasma expanders. *Clinical Pharmacokinetics* 1987; 12: 123-35.
- 50 Wasman, K., Hodges, R., Flynn, D.J. *et al.* Hemodynamics and oxygen transport during pentastarch in burn resuscitation. *Annals of Surgery* 1989; 209: 741-5.
- 51 Thompson, W., Fukushima, T. and Robertson, R.B. Intravascular persistence, tissue storage, and excretion of hydroxyethyl starch. *Surgery, Gynecology and Obstetrics* 1979; 131: 965-72.
- 52 Lawrence, D.A. and Scheel, R.S. Influence of hydroxyethyl starch on humoral and cell-mediated immune response in mice. *Transfusion* 1987; 25: 223-9.
- 53 Ring, I. and Messmer, K. Incidence and severity of anaphylactoid reactions to colloid volume substitutes. *Lancet* 1977; i: 466-9.
- 54 Mann-Grill, B. and Schoning, B. Lack of evidence for immunological reactions to gelatin. *Developmental Biological Standards* 1981; 48: 237-40.
- 55 Collins, J., Wild, G., Appleyard, T.N. *et al.* Complement activation by polystarch and gelatin volume expanders. *Lancet* 1990; 335: 233.
- 56 Lorenz, W., Durka, D., Dick, W. *et al.* Incidence and clinical importance of perioperative histamine release: an analysis of plasma volume expanders and substitutes after induction of anaesthesia. *Lancet* 1994; 343: 911-20.
- 57 Watkins, I. Allergic and pseudo-allergic reactions to colloid plasma substitutes: which colloid? *Care of the Critically Ill* 1991; 7: 213-17.
- 58 Johnson, S.D., Lucas, C.E., Gerrick, S.J. *et al.* Altered coagulation after albumin supplements for treatment of oligoemic shock. *Archives of Surgery* 1979; 114: 379-83.
- 59 Tullis, J.L. Albumin 1. Background and use. *Journal of the American Medical Association* 1977; 237: 355-9.
- 60 Strauss, R.G. Volume replacement and coagulation: a comparative review. *Journal of Cardiothoracic Anesthesia* 1988; 2: 24-32.
- 61 MacIntyre, E., Mackie, I.L., Ho, D. *et al.* The haemostatic effects of hydroxyethyl starch used as a volume expander. *Intensive Care Medicine* 1985; 11: 300-3.
- 62 Diehl, I.T., Lester, J.L. III and Cosgrove, D.M. Clinical comparison of hetastarch and albumin in postoperative cardiac patients. *Annals of Thoracic Surgery* 1982; 34: 674-9.
- 63 Falk, J.L., Rackow, E.C., Astiz, M. *et al.* Effects of hetastarch and albumin on coagulation in patients with septic shock. *Journal of Clinical Pharmacology* 1988; 28: 412-15.
- 64 Cully, M.C., Larson, C.P. and Silverberg, G.D. Hetastarch coagulopathy in a neurosurgical patient. *Anesthesiology* 1987; 66: 706-7.
- 65 Lockwood, D.N.J., Bullen, C. and Machin, S.J. A severe coagulopathy following volume replacement with hydroxyethyl starch in a Jehovah's Witness. *Anaesthesia* 1988; 43: 391-3.
- 66 Stump, D.C., Strauss, R.G. and Henriksen, R.A. Effects of hydroxyethyl starch on blood coagulation, particularly Factor VIII. *Transfusion* 1985; 25: 349-54.
- 67 Alexander, B., Orlake, K., Lawlor, D. *et al.* Coagulation, hemostasis and plasma expanders: a quarter century enigma. *Federation Proceedings* 1975; 34: 1429-40.
- 68 Fujii, K., Kaneko, S., Iwahori, Y. *et al.* The influence of Gelofusine on the blood coagulating function. *Japanese Gelofusine Symposium* 1967.
- 69 Huskisson, L.J. Evaluation of synthetic colloids in paediatric surgical practice. M.S. Thesis, 1994. University of London.
- 70 Metcalfe, W., Papadopoulos, A., Talaro, R. *et al.* A clinical physiologic study of tetraoxyethyl starch. *Surgery, Gynecology and Obstetrics* 1970; 131: 255-67.
- 71 Killian, I., Spiker, D. and Borst, R. The effect of 6% HES, 4.7% Dextran and 3.3% Oxygel Gel on blood volume and circulation in human volunteers. *Anaesthesist* 1973; 24: 193-7.
- 72 Lamke, L.-O. and Liljedahl, S.-O. Plasma volume changes after infusion of various plasma expanders. *Resuscitation* 1976; 5: 93-102.
- 73 Lazrove, S., Waxman, K., Shippy, C. *et al.* Hemodynamic, blood volume and oxygen transport responses to albumin and HES infusions in critically ill postoperative patients. *Critical Care Medicine* 1980; 8: 302-6.
- 74 Edwards, J.D., Nightingale, P., Wilkins, R.G. *et al.* Hemodynamic and oxygen transport response to modified fluid gelatin in critically ill patients. *Critical Care Medicine* 1989; 17: 996-8.
- 75 Sudhndran, S. Perioperative blood transfusion: a plea for alternatives. *Annals of the Royal College of Surgeons of England* 1997; 79: 299-302.
- 76 Spence, R.A., Carson, J.A., Poles, R. *et al.* Elective surgery without transfusion: influence of preoperative hemoglobin level and blood loss on mortality. *American Journal of Surgery* 1990; 159: 320-4.
- 77 James, L., Greenough, A. and Naik, S. The effect of blood transfusion on oxygenation in premature venti-

- lated neonates. *European Journal of Pediatrics* 1997; 156: 139-41.
- 78 Welch, H.G., Meehan, K.R. and Greenough L.T. Prudent strategies for elective red blood cell transfusion. *Annals of Internal Medicine* 1992; 116: 393-402.
- 79 Contreras M. and Chapman, C.E. Autologous transfusion and reducing allogenic blood exposure. *Archives of Disease in Childhood* 1994; 71: 105-7.
- 80 Jensen, L.S., Anderson, A.I., Christiansen, P.M., et al. Postoperative infection and natural killer cell function following blood transfusion in patients undergoing elective colorectal surgery. *British Journal of Surgery* 1992; 79: 513-16.
- 81 Nielsen, H.J. Detrimental effects of perioperative blood transfusion. *British Journal of Surgery* 1995; 82: 582-7.
- 82 Blumberg, N., Agarwal, M.M. and Chuang, C. Relation between recurrence of cancer of the colon and blood transfusion. *British Medical Journal* 1985; 290: 1037-9.
- 83 Kaplan I., Sarnaik S., Giriin, I. et al. Diminished helper/suppressor lymphocyte ratios and natural killer activity in recipients of repeated blood transfusions. *Blood* 1984; 64: 308-10.
- 84 The Royal College of Surgeons of England. Code of practice for the surgical management of Jehovah's Witnesses. 1996.
- 85 Vichinsky E.P., Haberkorn, C.M., Neuavt, L., et al. A comparison of conservative and aggressive transfusion regimens in the perioperative management of sickle cell disease. *New England Journal of Medicine* 1995; 333: 206-13.
- 86 Janik, J. and Seeler, R.A. Perioperative management of children with sickle hemoglobinopathy. *Journal of Pediatric Surgery* 1980; 15: 117-20.