Recent developments in the perioperative fluid management for the paediatric patient
Olivier Paut and Frédéric Lacroix

Purpose of review
Maintenance fluid therapy represents the volume of fluids and amount of electrolytes and glucose needed to replace anticipated physiological losses from breath, sweat and urine and to prevent hypoglycaemia. For 50 years, this therapy was based on Holliday and Segar’s formula, which proposed to match children’s water and electrolyte requirements on a weight-based calculation using hypotonic solutions. Recent publications highlight the risk of hyponatraemia in the postoperative period and the facilitating role of a hypotonic infusion, leading some people to recommend replacing hypotonic with isotonic solutions.

Recent findings
The postoperative period is at risk for nonosmotic secretion of antidiuretic hormone, which reduces the ability of the kidneys to excrete free water. In the context of antidiuretic hormone release, the associated low urine output makes maintenance volume requirement decrease to 50% of the calculated hourly rate. While isotonic fluids are recommended during anaesthesia, controversies still exist on the nature of fluid for maintenance therapy in the postoperative period. The proof for a benefit of isotonic fluids in this context is weak; further investigations are needed to make a decision. Whatever the choice, an individualized maintenance infusion protocol for each patient is necessary.

Summary
As free water excretion is altered for all children in the postoperative period, it is necessary to reduce the volume of maintenance fluid therapy to half the previously recommended volume. The choice of an isotonic solution should be more pertinent to that of a hypotonic solution, but evidence is lacking for a definitive answer.

Keywords
anaesthesia, hyponatraemia, paediatrics, postoperative fluids

Abbreviations
ADH antidiuretic hormone
ECF extracellular fluid
ICF intracellular fluid
SIADH syndrome of inappropriate antidiuretic hormone secretion

Introduction
Fluid therapy in the surgical patient is designed to provide for different fluid requirements: fluid deficits, maintenance fluid requirements, and volume of fluid needed to maintain an adequate tissue perfusion (and to counteract the effects of anaesthetics). Fluid deficits consist of preoperative deficits (fasting, gastrointestinal, renal or cutaneous losses), haemorrhage and third space losses. These third space losses consist mainly of extracellular fluids (ECFs) that result from trauma and surgery. This review will focus on perioperative maintenance fluid therapy.

Maintenance fluid therapy in children has been based for half a century on Holliday and Segar’s recommendation [1], which was related to studies of metabolism in paediatrics. This recommendation, best known as the ‘4/2/1’ rule, has been largely used in paediatric practice and particularly in paediatric anaesthesia, and still figures among the most widespread quoted in paediatric anaesthesia textbooks [2]. While a consensus has existed for a long time on this rule for fluid management in children, several papers on severe complications of perioperative infusions have been published in the recent years, raising some concerns on this topic [3–7].

The historical basis of fluid management
Maintenance therapy represents the fluids and electrolyte requirements needed by the average individual with a normal intracellular fluid (ICF) and ECF volumes over a 24 h period [8]. Thereby, maintenance therapy is the provision of fluid and electrolytes to replace anticipated physiological losses from breathing, sweating and urine output. In 1957, Holliday and Segar published an important paper [1] entitled The maintenance need for water in parenteral fluid therapy. They calculated the metabolic rate of healthy children at rest and during activity. As the maintenance needs for water paralleled energy metabolism, then the estimated caloric...

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.
expenditure was used to determine the maintenance fluid therapy (1 ml of water is required for each calorie consumed). They elaborated recommendations, known as the Holliday and Segar's formula. In the absence of sweating, insensible water losses and urine are the sole significant components of water requirements Using Holliday and Segar's methodology, the insensible water losses for a 10 kg child are 50 ml/kg/day, with 16 ml/kg/day subtracted for endogenous water production, equating to a net insensible loss of 34 ml/kg/day. As the obligatory urinary losses for excreting the solute load of cow’s milk is 66 ml/kg/day, the total of the maintenance fluid requirements in this child would be 100 ml/kg/day (34 + 66) [1]. The classic Holliday and Segar's formula is reported in Table 1 [9,10]. In the same study, the maintenance electrolyte needs were calculated from the amount of electrolyte delivered by the same volume of human milk. The daily needs were 3 mmol/kg/day sodium and 2 mmol/kg/day potassium.

The impact of Holliday and Segar’s paper was considerable. Electrolyte and water requirements, hypotonic solutions (0.2% saline equivalent), have had widespread use for decades and are still popular in paediatrics despite recent controversies [7,11–16]. In another study, indirect calorimetry was used for the calculation of metabolic rate, fluid volume and electrolyte requirements in anaesthetized infants and children [17]. Lindahl [17] found that energy expenditure during anaesthesia was 50% lower than that calculated by Holliday and Segar for hospitalized children, and was close to the basal metabolic rate. There was a good agreement in fluid requirements within the two studies. The principal formulae for maintenance fluid therapy in children are reported in Table 1.

The need for glucose during maintenance fluid therapy

After this brief historical review, two aspects of fluid management are important to consider for a safe fluid therapy in children: the need for glucose and the sodium content of the infusion solution.

Table 1 Calculation of the volume of fluid needed for maintenance therapy

<table>
<thead>
<tr>
<th>Author, year, Reference</th>
<th>Daily water requirement</th>
<th>Hourly water requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holliday and Segar, 1957 [1]</td>
<td>3–10 kg: 100 ml/kg 10–20 kg: 1000 ml plus 50 ml/kg for each kg from 11 to 20 &gt;20 kg: 1500 ml plus 20 ml/kg for each kg from &gt;20</td>
<td>4 ml/kg/h 40 ml/h plus 2 ml/kg/h for each kg from 11 to 20 60 ml/h plus 1 ml/kg/h* for each kg from 20</td>
</tr>
<tr>
<td>Oh, 1980 [9]</td>
<td>3–10 kg: 4 ml/kg 10–20 kg: 20 ml plus weight (kg) × 2 ml &gt;20 kg: 40 ml plus weight (kg)</td>
<td></td>
</tr>
<tr>
<td>Adelman and Solhaugh, 2000 [10]</td>
<td>1500 ml/m²*</td>
<td></td>
</tr>
</tbody>
</table>

*Body surface calculation: [weight (kg) × height (cm)]/3600.

The risk of cerebral damage by blood glucose concentrations abnormalities

The glucose requirements in paediatric patients have been reassessed recently with consideration of the hazards of hyperglycaemia and hypoglycaemia and the changes in blood glucose levels during surgery.

Hyperglycaemia

Hyperglycaemia can be detrimental for the brain. In experimental studies, the effects of brain ischemia and/or anoxia are worsened if glucose is given before the insult, the result of structural alterations [18]. Among the mechanisms involved in the production of this damage are both glucose aerobic metabolism and the production of an intracellular acidosis with the associated hydrogen ions, it is proposed that this is injurious to glia and neurons [18]. It is important to make a distinction between adults and children and particularly the youngest ones. A recent article reviewed the differences between neonates and adults for glucose [19]. There is a fivefold increase in concentration of some glucose transporter proteins (GluT3) and phosphorylation enzymes (hexokinase I) in the brain from the neonatal period to adults, as the metabolic rate increases [19]. The cerebral metabolic rate for glucose increases from the neonatal period to reach a maximum at 6 years (6.8 mg glucose/min/100 g) and then decreases to the adult value (5.5 mg glucose/min/100 g). Unlike the adult brain, the neonatal brain is able to metabolize ketone bodies and free fatty acids to generate adenosine triphosphate (ATP). The brain is also able to metabolize lactate to produce ATP. Thereby it is possible that hyperglycaemia may be less deleterious in neonates than in adults for several reasons: hyperglycaemia is responsible for an increase in high-energy reserves and glycogen stores, glucose uptake and lactate accumulation are slower during hyperglycaemia and lactate clearance is greater [19].

In a recent paper, De Ferranti et al. [20] performed an electroencephalographic study and a long-term neurodevelopmental evaluation in a prospective cohort of
171 neonates operated on for a transposition of the great arteries at a single centre. The neonates received an infusion of lactated Ringer’s solution during surgery (10–20 ml/kg/h) with supplemental glucose if blood glucose was low (less than 2.8 mmol/l, 50 mg/dl). They found that there were large variations in blood glucose during surgery, with hypoglycaemia more frequent during early time points and higher glucose more frequent at the later times. The most interesting findings of this article were first that, at the end of surgery, children who presented the lowest blood glucose levels had a higher probability of electroencephalographic seizures and second, that high glucose levels did not correlate with a worse neurological outcome [20].

The risk of hyperglycaemia is not limited to the brain. Elevated blood glucose concentration can lead to osmotic diuresis. The proximal tubule of the kidney reabsorbs all the filtered glucose until threshold limit of the blood glucose level, normally 10–11 mmol/l, is reached. The hazards of osmotic diuresis lead to the possible accompanying hypovolaemia.

Hypoglycaemia

Glucose, like oxygen, is essential for the normal brain to function. Depending on its severity, hypoglycaemia has three important effects on central nervous system. First, it may provoke a counter-regulatory stress response (increase in plasma cortisol, epinephrine, glucagon and growth hormone). Second, regional blood flow may increase to a maximal 300% change with a loss of cerebral vascular autoregulation in the case of severe hypoglycaemia. Third, it alters cerebral metabolism leading to a shift from glycolytic precursors to Krebs’ cycle intermediates, alteration of ion homeostasis and acid–base abnormalities [21]. All these changes can lead to clinical symptoms and permanent neuronal damage. In a recent paper, cerebral imaging performed in neonates sustaining isolated hypoglycaemia showed evidence of abnormality in 39% of cases, that is, four times more often than in control neonates. Most often, these lesions tended to recover 2 months later [22].

The incidence of blood glucose abnormalities during anaesthesia

The risk of hypoglycaemia at induction of anaesthesia has been evaluated in several studies. It varies between 0 and 10% among the studies, depending on the blood plasma level threshold for hypoglycaemia (range 1.7–2.7 mmol/l) [23–30]. The most recent studies on this topic are presented in Table 2. When defined as a blood glucose level less than 2.6 or 2.8 mmol/l, the incidence of hypoglycaemia at induction of anaesthesia is low, between 0 and 2.5%. Most of the children who presented with hypoglycaemia sustained prolonged true fast durations, from 8 to 19 h (median 10 h) [23,24,27,30]. Two papers fulfilled the more recent recommendations for preoperative fast duration [28,30]. Hypoglycaemia was not found in those two studies in the children who drank clear fluids 2–3 h before surgery. Furthermore, in the study by Welborn et al. [30], the children who were allowed to drink clear fluids 2–3 h before anaesthesia presented with the same normal blood glucose level at induction of anaesthesia than the children allowed to drink clear fluids up to 6 h before surgery. The two children who sustained hypoglycaemia were in the prolonged fast group. Intraoperative glucose homeostasis was not modified by apple juice consumed 2–3 h prior to surgery [30].

The use of glucose in the perioperative period: from 5% dextrose solutions to 1% or less

While the incidence of hypoglycaemia is not as common an occurrence as previously thought, most of anaesthesiologists continue to administer glucose in the paediatric population (see below). The amount of glucose administered has dramatically decreased since the 1990s, however. The infusion of 5 to 10% dextrose in the paediatric population leads invariably to hyperglycaemia [23,25,26,28,29,31]. Nishina and colleagues [28] found that up to 30% of children receiving a 5% dextrose (D5) lactated Ringer’s solution presented hyperglycaemia (more than 11 mmol/l). In another study [23], the mean blood glucose concentrations in children receiving preoperative D5 lactated Ringer’s solution was 13.4 mmol/l, with a maximum at 17 mmol/l. As 5% dextrose solutions are associated with an unacceptably high blood glucose level, solutions with a lower glucose concentration have been assessed in paediatric anaesthesia. It was shown, in three prospective randomized studies [26,28,29], that using 2 or 2.5% dextrose solutions raised blood glucose levels during surgery to a lesser extent than 5% solutions, while they were in the normal range (less than 8.3 mmol/l). Assuming that 2 or 2.5% solutions were associated with an elevation in blood glucose concentration, some investigators [24,27,32] examined the use of low dextrose (1 or 0.9%) lactated Ringer’s solutions in paediatric patients. All these prospective studies were randomized and are reported in Table 3 [33]. These groups showed that low dextrose concentration solutions prevented hypoglycaemia and are associated with blood glucose concentrations in the normal range [24,27,32].

The case of children receiving a total parenteral nutrition

These children are at increased risk for intraoperative blood glucose derangements. It is recommended that patients have frequent intraoperative blood glucose monitoring to adapt the glucose input [34].
Dubois et al. noted that the blood glucose levels and incidence of hypoglycaemia at induction varied with duration of fast. There was a large variation in glucose use reported using intraoperative glucose-containing solutions.

### Table 2: Blood glucose levels and incidence of hypoglycaemia at induction of anaesthesia in the literature

<table>
<thead>
<tr>
<th>Author, year, Reference</th>
<th>Number of patients</th>
<th>Age (range, or mean)</th>
<th>Fast duration (protocol) h</th>
<th>Blood glucose at induction (mmol/l)*</th>
<th>Hypoglycaemia, N (%)</th>
<th>Details</th>
<th>Hypoglycaemia (age, fast duration)</th>
<th>Type of surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Welborn et al. 1986 [23]</td>
<td>446</td>
<td>1 month to 6 years</td>
<td>Solid: midnight; Clear fluids 4 h: 6 h: 1–6 years</td>
<td>6.1–12.7</td>
<td>4.6–4.7</td>
<td>2 (0.4%) (–2.8)</td>
<td>6 years, 10 h; 15 months, 19 h</td>
<td>Minor</td>
</tr>
<tr>
<td>Welborn et al. 1987 [24]</td>
<td>162</td>
<td>2.5–2.9 years</td>
<td>Solid: midnight; Clear fluids 4 h: 6 h: 1–6 years</td>
<td>11–12</td>
<td>4.3–4.6</td>
<td>2 (1.2%) (–2.8)</td>
<td>13 months, 10 h; 3.5 years, 8 h</td>
<td>Minor</td>
</tr>
<tr>
<td>Hongnat et al. 1991 [26]</td>
<td>68</td>
<td>3 months to 10 years</td>
<td>Solid and fluids: midnight; Clear fluids 4 h if 6 months</td>
<td>10.8–12.3</td>
<td>4.3 ± 0.8 to 4.6 ± 0.7</td>
<td>5 (7.4%) (–3.5)</td>
<td>Not available</td>
<td>Minor</td>
</tr>
<tr>
<td>Mikawa et al. 1991 [29]</td>
<td>45</td>
<td>18 months to 9 years</td>
<td>Solid: midnight; Clear fluids 4 to 6 h</td>
<td>6.1</td>
<td>5.5 ± 0.5</td>
<td>0 (–2.8)</td>
<td>–</td>
<td>Long duration surgery</td>
</tr>
<tr>
<td>Dubois et al. 1992 [27]</td>
<td>79</td>
<td>3 months to 10 years</td>
<td>Solid: midnight; Clear fluids 4 h if 1 year</td>
<td>Not available</td>
<td>4.3 ± 0.7 to 4.9 ± 0.8</td>
<td>2 (2.5%) (–2.6)</td>
<td>5.4 months, 10 h; 102 months, 10 h</td>
<td>Minor</td>
</tr>
<tr>
<td>Welborn et al. 1993 [30]</td>
<td>200</td>
<td>1–10 years</td>
<td>Solid: midnight; Clear fluids 6 h (Gr A) or 2 to 3 h (Gr B)</td>
<td>2.9–13.1</td>
<td>4.4–4.3</td>
<td>2 (1.8%) Group A, 0 (–2.8) Group B**</td>
<td>Not available</td>
<td>Minor</td>
</tr>
<tr>
<td>Sandström et al. 1994 [25]</td>
<td>40</td>
<td>6 months to 2 years</td>
<td>Solid and fluids 6 h if 6–12 months; 6–8 h &gt;1 year</td>
<td>Not available</td>
<td>3.8–4.4</td>
<td>0 (–2.6)</td>
<td>–</td>
<td>Minor</td>
</tr>
<tr>
<td>Nishina et al. 1995 [28]</td>
<td>60</td>
<td>1–11 months</td>
<td>Solid: midnight; Clear fluids 6 h; &gt;5 months midnight</td>
<td>Not available</td>
<td>5.5 ± 2.5</td>
<td>0 (–2.7)</td>
<td>–</td>
<td>Minor</td>
</tr>
</tbody>
</table>

* The two numbers represent the mean values of blood glucose levels among different group of children. **In this article, the incidence of hypoglycaemia at induction varied with duration of fast (group A long-lasting fast, group B short-lasting fast).

### Table 3: Available clinical trials assessing the use of lactated Ringer’s solution with 0.9 or 1% dextrose in paediatric anaesthesia

<table>
<thead>
<tr>
<th>Author, year, Reference</th>
<th>Number of patients</th>
<th>Type of surgery</th>
<th>Age (range, or mean)</th>
<th>Fast duration (protocol) h</th>
<th>Solution assignment</th>
<th>Blood glucose at induction (mmol/l)</th>
<th>Blood glucose at the end of surgery (mmol/l)</th>
<th>Blood glucose change (range) at the end of surgery (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Welborn et al. 1987 [24]</td>
<td>162</td>
<td>Minor</td>
<td>2.5–2.9 years</td>
<td>Solid: midnight; Clear fluids 4 h if 1 year, 6 h 1–6 years</td>
<td>LR</td>
<td>4.3 ± 0.5</td>
<td>Not available</td>
<td>+1.7 (–0.1, +4.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>D₁ LR; D₂ LR</td>
<td></td>
<td>4.6 ± 0.6</td>
<td>Not available</td>
<td>+2.2 (–0.6, +5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.5 ± 0.7</td>
<td>Not available</td>
<td>+3.2 (+1.2, +6.9)</td>
</tr>
<tr>
<td>Dubois et al. 1992 [27]</td>
<td>79</td>
<td>Minor</td>
<td>3 months to 10 years</td>
<td>Solid: midnight; Clear fluids 4 h if 1 year, 6 h 1–6 years</td>
<td>LR</td>
<td>4.4 ± 0.8</td>
<td>Normal range*</td>
<td>Not available</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>D₁ LR; D₂ LR LR₀</td>
<td></td>
<td>4.3 ± 0.7</td>
<td>6.5 ± 2.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.9 ± 0.8</td>
<td>8.1 ± 1.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>D₁ LR</td>
<td></td>
<td>4.4 ± 0.6</td>
<td>5.2</td>
<td></td>
</tr>
<tr>
<td>Geib et al. 1993 [32]</td>
<td>41</td>
<td>Minor</td>
<td>6 months to 11 years</td>
<td>Solid: midnight; Clear fluids 4 h if 1 year, 6 h 1–6 years</td>
<td>LR</td>
<td>B66**</td>
<td>4.2 ± 0.9</td>
<td>6.8</td>
</tr>
</tbody>
</table>

LR: lactated Ringer’s solution; D₁ LR: 1% glucose in lactated Ringer’s solution; D₂ LR: 2.5% glucose in lactated Ringer’s solution; D₂ LR₀: 2.5% glucose in half lactated Ringer’s solution (sodium content 65 mmol/l). *Data are not available in the article. **B66 is a solution manufactured by the Pharmacie centrale des hôpitaux de Paris. It consists in 0.9% dextrose in 120 mmol/l sodium with 4 mmol/l potassium. ~ values are grossly calculated from the histograms in the article.

### Current clinical practice among paediatric anaesthesiologists

In a recent survey most of the members of two European societies of paediatric anaesthesiologists reported using intraoperative glucose-containing solutions [35]. There was a large variation in glucose use within age groups, with most of the premature infants, neonates and infants receiving glucose, while two-thirds of children aged 6–12 years receiving glucose-free solutions [35]. In another study, a questionnaire was sent to survey British paediatric anaesthesiologists.
regarding their perioperative management of blood glucose and total parenteral nutrition in children [34]. The large variation in responses showed that there is no consensus on this subject. A majority of the youngest patients, however, had their blood glucose concentrations monitored and received an intraoperative glucose-containing solution (glucose concentration at 2.5 or 5% in 76% of cases) [34]. In the patients receiving total parenteral nutrition, most respondents routinely administered glucose-containing solutions and/or monitored blood glucose levels, with a wide variety of infusion handling [34].

Sodium content of the infusion solution: still under debate?

For more than half a century children have been infused with hypotonic fluids, mainly dextrose 5 or 10% in 0.2–0.25% saline [1]. The relevance of this principle has been questioned recently, as a significant number of articles have reported severe hyponatraemic encephalopathies related, totally or partly, to the use of hypotonic solutions [3–6].

The hazards of acute hyponatraemia: the hyponatraemic encephalopathy

Hyponatraemic encephalopathy is the most severe complication of hyponatraemia and can lead to death or permanent neurological damage [36**]. Over 50% of children with a serum sodium less than 125 mmol/l will develop hyponatraemic encephalopathy [36**]. Sodium is the main cation of extracellular fluid (ECF). Changes in the blood sodium concentration mirrors ECF volume changes. As water moves freely across the cell wall, water movement across membranes will follow the variations of the effective osmolality (tonicity) in the ICF and the ECF [37]. In the brain, the endothelial tight junctions prevent sodium moving across the blood–brain barrier. Normally, there is equilibrium between the tonicity of the brain intracellular content and that of the extracellular space. When there is an acute decrease in serum osmolality, in the case of hyponatraemia, there is a shift in water from the extracellular space to the brain interstitium and the brain cells, in order to lower the brain osmolality and to match that of hypotonic plasma [5]. If there is an acute drop in plasma tonicity, the brain water accumulation can lead to cerebral edema. If the increase in brain volume exceeds 5–7% of its initial volume, there is a risk of brain herniation and death. For a complete review of hyponatraemic encephalopathy see reference [38]. Children are a group at risk of hyponatraemic encephalopathy. This is because the number of brain cells decreases with age and children have a larger brain to intracranial volume ratio compared with that of adults. Otherwise, animal studies, reviewed elsewhere [5], have shown that there was a limited cerebral Na⁺–K⁺–ATPase system in prepubertal rats and newborn dogs, reflecting a limited ability to extrude sodium from the brain and, as a consequence, a greater vulnerability to hyponatraemia. This finding explains why the clinical symptoms of hyponatraemic encephalopathy occur at lower sodium concentrations in children [5]. The average sodium concentration in children with hyponatraemic encephalopathy is 120 mmol/l, while the concentration in adults is 111 mmol/l [36**].

The conditions for creating a hyponatraemia

Hyponatraemia (sodium concentration less than 136 mmol/l) can result from a deficit of sodium or an excess of water, the later condition being more frequent. Independent of whether hyponatraemia is caused by a positive balance for water or a negative balance for sodium, ICF will rise equally, because the intracellular tonicity (number of particles restricted to the ICF compartment) does not change appreciably and Na⁺ ions are restricted to the ECF compartment. To create a positive water balance, input of water must exceed output. A low water output is usually caused by the release of antidiuretic hormone (ADH) either appropriately (hypovolaemia or hypertonicity) or for nonsomotic stimuli.

Dilution hyponatraemia and hypotonic parenteral fluids

In a retrospective study, Halberthal et al. [3] reviewed casual cases of acute in-hospital-acquired hyponatraemia. They found that all cases received a hypotonic solution, while the majority (13/23) developed hyponatraemia postoperatively. Some of these children showed an aptitude to excrete free water, the remainder of the patients had a larger variation in their sodium concentration than predicted by the volume of free water infused. This later point could be explained either by a supplemental unknown input of water or the excretion of a large volume of hypertonic urine (known as a desalination phenomenon, see below) (Fig. 1). In another retrospective study, seven cases of hyponatraemic encephalopathies were reported after minor surgery. All the children received a preoperative and postoperative infusion of hypotonic solution, most of them to a greater rate than recommended [6]. While dangerous, the infusion of hypotonic solution in the perioperative period is still performed. A survey in one British hospital showed that almost 25% of children received hypotonic solution during anaesthesia, while another 10% received a variable mixture of isotonic and hypotonic solutions [39]. In Table 4, the effects of the infusion of different solutions on sodium concentration are reported. It is important to note that the number of patients is low in these papers. In scoliosis children,
the use of hypotonic solutions during and postoperatively led to a decrease in sodium concentration [40–42], while the use of isotonic solutions was associated with stable [41] or a minimal decrease in sodium concentration [40]. In one study, all adolescents receiving a hypotonic solution (0.18% normal saline or 0.3% normal saline) showed hyponatraemia, and most of them a severe hyponatraemia [41]. Among the studies dealing with the intraoperative and short-term postoperative infusates, and reported in Table 4, it is interesting to note that the infusion of isotonic fluids was associated with a stable sodium concentration, while the infusion of hypotonic fluids led to a significant decrease in sodium concentration [26,27,32].

The syndrome of inappropriate antidiuretic hormone secretion

The syndrome of inappropriate antidiuretic hormone secretion (SIADH) is caused by an elevated ADH secretion in the absence of a hypovolaemia or hypertonic state, or to a normal ADH secretion associated with an abnormal high sensitivity of the distal renal tubule and collecting ducts to ADH. It is characterized by hyponatraemia and oliguria, while the haemodynamic status is normal. Postoperative SIADH is often associated with cardiac surgery, spine surgery [41–43] and neurosurgery [44]. The incidence of SIADH after scoliosis surgery has been evaluated as between 21 and 33% [40,43]. Figure 2 reports the postoperative course of urine concentrations after spine surgery in children. This figure shows clearly that there is a limited kidney ability to excrete dilute urine in the postoperative period and that a return to a normal dilution aptitude takes 2 or 3 days [42]. SIADH can be encountered after minor surgery [6,36**,45].

### Table 4 Some examples of the effects of perioperative infusion of isotonic or hypotonic fluids in surgical patients. The first three rows represents perioperative fluid administration during spine surgery and the three other rows represent preoperative fluid administration during minor surgery

<table>
<thead>
<tr>
<th>Author, year, reference</th>
<th>Surgery</th>
<th>N</th>
<th>Infusion solute</th>
<th>Sodium concentration preoperatively mmol/l</th>
<th>Sodium concentration postoperatively (nadir) or sodium concentration variations mmol/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burrows, 1983 [40]</td>
<td>Spine</td>
<td>4</td>
<td>LR</td>
<td>138 ± 2.7</td>
<td>−3 ± 0.8 (135 ± 1.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>0.22 or 0.45% NaCl</td>
<td>138 ± 1.7</td>
<td>−6.2 ± 2.9 (131 ± 2.8)</td>
</tr>
<tr>
<td>Cowley, 1988 [42]</td>
<td>Spine</td>
<td>8</td>
<td>0.45% NaCl</td>
<td>140.6 ± 1.1</td>
<td>134.1 ± 1.3</td>
</tr>
<tr>
<td>Brazel, 1996 [41]</td>
<td>Spine</td>
<td>5</td>
<td>Hartmann’s solution</td>
<td>141 ± 2.8</td>
<td>138 ± 1.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7</td>
<td>0.18 or 0.3% NaCl</td>
<td>142.5</td>
<td>129.5*</td>
</tr>
<tr>
<td>Hongnat, 1991 [26]</td>
<td>Minor</td>
<td>35</td>
<td>0.33% or 0.43% NaCl, D_{0.5}</td>
<td>Normal range</td>
<td>&lt;4 years: − 2.2*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>33</td>
<td>0.33% or 0.43% NaCl, D_{6}</td>
<td>Normal range</td>
<td>&lt;4 years: − 2.7*</td>
</tr>
<tr>
<td>Dubois, 1992 [27]</td>
<td>Minor</td>
<td>27</td>
<td>LR</td>
<td>139 ± 1.5</td>
<td>138.6 ± 1.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25</td>
<td>D_{1} LR</td>
<td>139.6 ± 1.5</td>
<td>139 ± 1.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>27</td>
<td>D_{2.5}LR_{0.6}</td>
<td>139.5 ± 1.5</td>
<td>136.3 ± 2.5</td>
</tr>
<tr>
<td>Geib, 1993 [32]</td>
<td>Minor</td>
<td>19</td>
<td>D_{1} LR</td>
<td>139 ± 0.8</td>
<td>138 ± 1.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>22</td>
<td>D_{0.9}, LR *</td>
<td>139 ± 1.3</td>
<td>138 ± 1.3</td>
</tr>
</tbody>
</table>

* Plasma sodium variation (mmol/l) = sodium concentration preoperatively – sodium concentration postoperatively. Some of the values featuring in this table are extrapolated from histograms. LR: lactated Ringer’s solution; D_{0.6} LR: 0.9% glucose in lactated Ringer’s solution; D_{1} LR: 1% glucose in lactated Ringer’s solution; D_{2.5} LR_{0.6}: 2.5% glucose in half lactated Ringer’s solution (sodium content 65 mmol/l).
The perioperative period is at risk for the development of a hyponatraemia

In this period, the ADH secretion is unpredictable [10]. It may be considered as potentially elevated in all children whether this secretion is appropriate or not. Many factors in these settings can contribute to a nonosmotic ADH secretion. A prolonged preoperative fast duration can lead to hypovolaemia, which in turn stimulates ADH secretion. Minor surgery has been associated with a hormonal stress response. In 42 infants and children operated on for scheduled surgery, ADH blood levels were increased in 84% of patients [46]. After tonsillectomy, ADH blood concentrations were significantly increased in children who presented with clinical signs of hypovolaemia [47]. Pain, stress, anxiety, nausea and vomiting, and morphine represent some nonosmotic stimuli for ADH release that are routinely encountered in the postoperative patient [3,36]. In a recent review of the literature, Moritz and Ayus [15] reported more than 50 cases of published hospital-acquired hyponatraemic encephalopathy. Mortality was as high as 50% and more than half of the cases occurred in the postoperative setting in previously healthy children undergoing minor surgery [15].

The infusion of isotonic fluids does not always prevent hyponatraemia: the desalination phenomenon

This is a very interesting new approach for understanding all postoperative hyponatraemia. While more frequent after infusion of hypotonic fluids in the presence of ADH, hyponatraemia may occur when isotonic fluids are used. This finding was demonstrated by Steele and colleagues [48]. In a retrospective analysis of five fatal cases of hyponatraemia, they found that the patients received considerably less free water than expected by sodium concentration and postulated that urinary losses could have played an important role in the production of hyponatraemia. This hypothesis was tested in a prospective study of 22 women who received only isotonic fluids during and postoperatively (average volume 5.3 ± 0.2 l for the first day). Sodium concentration decreased by a mean of 4.2 ± 0.4 mmol/l, with a lowest value at 131 mmol/l for two patients, while their urinary tonicity was high (294 ± 9 mmol/l). Hyponatraemia was caused by the generation hypertonic urine in the presence of ADH, which led to retention of free water, a phenomenon they termed ‘the desalination process’ [48]. Schematically, when 2 l of isotonic fluid (osmolality 150 mmol/l) are infused, there is production of 1 l of hypertonic urine (osmolality 300 mmol/l). The net effect is a gain of 1 l of free water, which explains the decrease in sodium concentration [48]. The causes of desalination are a possible drop of aldosterone concentration, an increase in natriuretic peptide and/or an increase in glomerular filtration. All these conditions occur after overexpansion of the intravascular space [11].

What we have learnt from the recent adult and medical paediatric literature?

Recent studies, in adults and in general paediatrics, showed interesting data on the benefits of fluid regimen limitations and the use of isotonic fluid that could have some implications in the surgical child.

Figure 2 Urinary excretion after spine surgery

The circles represent the total urine output while the squares represent a theoretical isotonic diuresis (urine and plasma tonicities are equivalent). The difference between the two lines represents the aptitude to excrete dilute urine, which is very limited in the immediate postoperative period. Adapted from [42].
Adult studies
In adults, as in children, there are no widely accepted recommendations for the optimal perioperative fluid therapy, and there are wide variations in fluid regimens. While the common practice is to administer relatively large amounts of fluids to prevent hypovolaemia and dehydration, some questions were raised recently on the iniquity of this fluid regimen, which has been associated with cardiac, pulmonary and gastrointestinal complications. The effects of a restrictive fluid management were compared with a ‘standard or liberal’ fluid regimen in recent studies [49,50,51]. The authors found that after colonic resection, a restricted fluid regimen was associated with fewer complications, a more rapid recovery of gastrointestinal function and a reduced length of stay in hospital [49,50,51]. The impact of these experiments needs to be clarified by further studies as it is necessary to evaluate the their clinical relevance in paediatrics.

General paediatrics studies
The question of whether an isotonic solution is safer than a hypotonic solution in the medical paediatric population has been raised, and has led to violent discussions [12–14]. Two papers are interesting to consider. In a recent article, Hoorn and colleagues [52] studied a large cohort of 1586 consecutive paediatric emergency department admissions who had at least one sodium concentration measurement. Using a case–control analysis design, they showed that for 40 of the 131 hyponatraemic children, hyponatraemia was hospital acquired or hospital aggravated. The mean decrease in sodium concentration was 6 mmol in 19 h, caused by free water input. The source of this free water load was predominantly the infusion of hypotonic fluids (two-thirds of patients), whereas in the remainder it could be attributed to an oral intake of free water [52]. Of importance, 73% of the children in the acquired-hyponatraemia group versus 23% of the children in the stable natraemia group had a volume of infusion above the classical recommendations [52].

In a recent prospective, randomized study, Neville and colleagues [53] compared the effects of normal saline in 2.5% dextrose (normal saline–D2.5) to that of 0.45% saline in 2.5% dextrose (half normal saline–D2.5) in 102 children with gastroenteritis. Hypotonic solution exacerbated the tendency to develop dilutional hyponatraemia, while isotonic saline solutions were protective.

Current trends in paediatric fluid therapy and classical point of view: is it possible to find a consensus?
In recent years, after the report of numerous cases of severe hyponatraemia in children infused with hypotonic fluids, conflicting approaches have been discussed to prevent this hyponatraemia [3,5–7,11,13–15].

The isotonic fluid defenders’ points of view
For some investigators, the safety of administering maintenance parenteral hypotonic fluids, although in use for 50 years, has never been evaluated prospectively [15]. For Moritz and Ayus [15], isotonic saline in 5% dextrose in water seems to be the safest fluid composition in most hospitalized children. For Halberthal and colleagues [3], in view of the dangers of the routine use of hypotonic solutions in the presence of ADH, sodium concentration should be monitored when starting an intravenous infusion and, if sodium concentration is below 140 mmol/l, an isotonic solution should be administered. A hypotonic solution could be administered if sodium concentration is less than 140 mmol/l under strict sodium concentration monitoring. For Duke and Molyneux [13], if the use of isotonic solution does not rule out the risk of hyponatraemia, it decreases the probability of occurrence. They postulated the use of isotonic saline with 5% dextrose, at a maintenance rate less than the usual recommendations, in children with sodium concentration inferior to 138 mmol/l and at risk for nonosmotic secretion of ADH [13].

Several limitations of the use of isotonic fluids for maintenance therapy must be addressed, however. First, the neonates may differ from the older children and these recommendations do not extent to this group of patients. Second, children with ongoing free-water losses or a free-water deficit will require a more hypotonic fluid. Third, in children with fluid and sodium overload (congestive heart failure, cirrhosis, renal failure), fluid and sodium restriction is of paramount importance to avoid hyponatraemia and the increase of fluid overload [13].

The hypotonic fluid defenders’ point of view
Holliday and Sgar [1] recently changed their recommendations for maintenance fluid therapy. They suggested correcting fluid losses promptly with 20–40 ml/kg normal saline, particularly during surgery [14]. They also suggested giving half of the average maintenance fluid (50 ml/kg/day) for the first day of infusion and monitoring sodium concentration daily should the need for fluid therapy continue [14]. They explained that this important decrease in the daily fluid volume is necessary to match the decrease in urine losses because of nonosmotic ADH secretion [16]. In fact, the traditional volume recommendations are greater than the actual requirements in children at risk for nonosmotic ADH production caused by the volume of urine losses (66 ml/kg/day, corresponding to 2.75 ml/kg/h)
taken into account in the formula of Holliday as Segar [1]. If urine output is less than 1 ml/kg/h, as in presence of ADH secretion, then the daily volume requirement is about 40–50 ml/kg/day. Energy expenditure is more reduced in children hospitalized in Intensive Care Units, and particularly in those children breathing warmed humidified air through a ventilator circuit [11].

In total, while there is still a debate on the ideal solute for maintenance therapy in children, both in general paediatrics or in the postoperative period, all caregivers agree that it is of critical importance to individualize fluid therapy and to monitor sodium concentration in children receiving an infusion. There is also a strong trend to limit the average fluid maintenance volume to half or two-thirds of the classical recommendations given by the Holliday and Segar formula. Prospective, randomized clinical trials, comparing hypertonic and isotonic fluids for postoperative maintenance fluids, are needed.

Conclusion
The postoperative period is at risk for nonsosmotic secretion of ADH, which dramatically reduces the ability of kidney to excrete free water. In this context of ADH release, the infusion of hypertonic fluids to the classical hourly rate represents a risk for development of hyponatraemia. The use of Holliday and Segar’s formula to calculate the maintenance fluid regimen in postoperative children often leads to an overestimation of the volume of fluid needed, as there is a frequent low urine output in this period. The way to resolve the problem of decreasing the amount of free water to be infused, and then to prevent postoperative hyponatraemia, is not consensual and provoked a large and important debate in the paediatric literature. Most investigators, and Holliday and Segar themselves, recognize that it is necessary to reduce the maintenance fluid volume to 50% of the classical recommendations in the postoperative period. Which is the best solution, hypertonic or isotonic? Matching the maintenance requirements to the reduced low hourly infusion rate is not consensual, and both hypertonic and isotonic solutions need to be re-evaluated by means of prospective randomized studies.

References and recommended reading
Papers of particular interest, published within the annual period of review, have been highlighted as:
* of special interest
** of outstanding interest
Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 349).
7 Bohn D. Children are another group at risk of hyponatraemia perioperatively. BMJ 1999; 319:1269.
The use of isotonic fluids in children for maintenance therapy. The authors review the pathophysiology and treatment of hyponatremia, with a focus on its relevance in children with gastrointestinal disorders. They discuss the findings of a randomized controlled trial comparing normal saline vs. half-normal saline for intravenous rehydration in children with gastroenteritis, highlighting the protective effects of normal saline.

In another study, the authors analyze the effects of preoperative fasting on perioperative blood glucose homeostasis in children. They conclude that minimizing preoperative fasting is important in perioperative settings.

The authors also discuss the role of antidiuretic hormone in perioperative fluid management, emphasizing its importance in preventing complications associated with hyponatremia.

Finally, they present a survey of clinical practice among pediatricians regarding fluid regimens in children, highlighting the need for standardized guidelines to improve patient outcomes.