ABSTRACT
Appropriate fluid management is vital for adequate tissue perfusion and balancing the internal milieu especially in perioperative settings and critically ill children. Pediatric population is heterogeneous so one formula may not suffice and hence both the quantitative and qualitative perspective of fluid management should be based on physiology and pathology of the child along with their perioperative needs. In perioperative setup, the fluid is administered to meet fluid deficits (fasting, and other daily based losses), blood losses and third space losses. Anesthetists have always followed pediatric maintenance fluid calculations based on Holiday and Segar formula; based on studies conducted on healthy children more than 70 years ago. Recently, there has been a lot of debate about this concept, especially as there are serious concerns regarding the development of complications like hyponatremia and hyperglycemia, both of which can result in neurological damage or even mortality in a sick child. This review is an attempt to provide a historical perspective and current evidence-based approach to peri-operative pediatric fluid management. We performed a PUBMED search for articles using keywords including ‘children’, ‘intravenous fluid therapy’, ‘crystalloids’, ‘colloids’, ‘fluid homeostasis’, ‘blood loss’, ‘estimation of blood loss’, ‘blood loss management’, ‘perioperative fluid’ to get our source articles.

Key words: Cerebral edema; colloids; crystalloids; fasting; fluid isotonic; intraoperative; management; pediatrics; perioperative; postoperative

Introduction
The main aim of the perioperative fluid strategy is to maintain “homeostasis” by re-establishing normal physiology through central euwolemia and providing adequate electrolytes based on the child’s need due to various deficits like preoperative fasting, losses due to renal, cutaneous, gastrointestinal, and third space losses. Children have a higher metabolic rate, larger surface area to weight ratio and faster respiration resulting in extensive fluid losses which translates to higher fluid requirement. Fluid deficit in children may vary preoperatively from no deficit to severe deficit based on the etiology for which the child is coming into theatre. Fluid Management can be broadly covered in three main parts: (1) resuscitation fluid, (2) maintenance fluid and (3) replacement for the losses.

Physiological considerations
Around 50 to 80% of the body is composed of water, and the percentage is inversely proportional to the age. For clinical explanation, there are two fluid compartments intracellular (ICF) and extracellular (ECF) as shown.
ECF is further divided into 3 compartments – plasma, interstitial, and transcellular fluid. Figure 1 describes the compartmentalization of fluids along with emphasis on the higher proportion of extracellular fluid in a 30 kg child. In preterm infants the ECF it is around 80% and reduces to around 60% by 6 months of age. The loss of fluid, as the child ages, is predominantly from the extracellular fluid (ECF). The ECF accounts for one-third of body water and is usually larger in children compared to adults.

The Intracellular fluid accounts for two-thirds of body water and around 24 weeks gestation, close 80% of total body weight of the fetus is made up of water, which reduces to around 60% at the age of one year of age and in adults it is between 50% and 60%.[3]

Sodium (Na⁺) is the primary cation and chloride (Cl⁻) the major anion in plasma which is part of extracellular compartment. Intracellular compartment predominantly consists of potassium (K), magnesium (Mg), proteins, and phosphates. Interstitial fluid has lower proteins but otherwise has a composition equivalent to ICF.[3]

The distribution of content (fluid and ions) in ECF and ICF compartment is controlled by the Donnan effect and Starling forces. By definition Donnan effect states that when a semipermeable membrane separates a solution of non-diffusible ions from another solution of diffusible ions, equilibrium is attained with unequal distribution of diffusible ions across the semipermeable membrane due to presence of proteins. At equilibrium the product of molar concentration of diffusible ions on either side of membrane will equal, maintaining the electrical neutrality.

The Starling hypothesis says that the fluid movement due to filtration across the capillary wall is dependent on the balance between the hydrostatic and the oncotic pressure gradient across the capillary wall. Physiologically the amount of fluid filtering outward from the arterial ends of the capillaries equals almost exactly the fluid returned to the circulation by absorption.[4]

Glomerular filtration rate (GFR) in a term neonate reaches adult levels only by two years of age. The low GFR is because of decreased capillary surface area for filtration, low systemic arterial pressure, high renal vascular resistance resulting in low ultrafiltration pressure. The concentrating ability is low at birth and with further water deprivation, urine concentrates to only 600–700 mOsm/kg because of hypotonicity of renal medulla.[4]

**Historical perspective**

Fluid therapy is as important as any other medication that a child receives in the perioperative period. The type and volume of fluid that a child receives perioperatively has been widely studied over the last 75 years. Holiday and Segar published their paper “The maintenance need for water in parenteral fluid therapy” and came up with the widely used 4/2/1 principle of fluid (Table 1) and calorie management in 1957.[6] Their calculation considered the daily requirement of electrolytes like sodium requirement of 3 mmol/kg and a potassium requirement of 2 mmol/kg which had led physicians to give hypotonic fluids with 5% dextrose. In the 1990s there were reports of hyponatremia induced encephalopathy secondary to hypotonic fluids infused perioperatively and stress induced ADH levels being elevated leading to cerebral edema and respiratory insufficiency.[2] This has created a paradigm shift in the perioperative fluid management both for type and volume of fluid infused perioperatively for children.

**Preoperative management**

Preoperative fasting is essential to reduce the risk of aspiration. However, it is advised to continue enteral feeding till the recommended fasting guidelines for reasons like reducing the incidence of dehydration, postoperative nausea and vomiting, the need for early drinking postoperatively. Children can be allowed to drink clear fluids until 1 hr before the surgery safely.[8] Shortened fasting times for clear fluids have shown to improve perioperative experience for children and parents without increasing the incidence of pulmonary aspiration.[9] Studies have shown that the stomach empties itself within 1 hr of clear fluids without increased risk of pulmonary aspiration. The recommendation for other fluids and solids are mentioned in Table 2.[10]

Holiday and Segar formula is still recommended widely to calculate the deficit and maintenance fluid requirements including the APA and NICE guidelines.[11] Subsequently Berry
et al. suggested that children younger than 3 years should receive 25 mL/kg, whereas children 4 years and older should receive 15 mL/kg of balanced salt solution over the first h of surgery.\[4\] Both these were done on the presumption that the child was NPO for 6‑8 hrs. With the liberalization of fasting guidelines these corrections might not be required.

If preoperative and postoperative fasting times are as per fasting guidelines,[9,10] perioperative IV fluid therapy is not required in children beyond neonatal age who undergo short procedures (<1 hr) with an intravenous access in place. If the child is fasting for >6 hrs appropriate volume of fluid can be administered based on the degree of dehydration (1% dehydration = 10 ml/kg fluid loss). For preoperative fluid resuscitation it is recommended that a crystalloid without glucose-containing sodium (range of 131–154 mmol/L) is administered as a bolus of 20 ml/kg over 10 min in children for a maximum of 40–60 ml/kg provided there is no pre-existing cardiac and renal disease.\[11\] Use of Transthoracic Echo for preoperative fluid assessment is a becoming a common tool in combination with clinical parameters.\[12\]

Clinical assessment of dehydration guides us towards the fluid management and can be easily done at the bedside. [Table 3].

### Table 1: Hly 4/2/1 rule and fluid requirement\[9\]

| Weight    | Fluid requirement per hr | Daily fluid requirement |
|-----------|--------------------------|-------------------------|
| <10 kg    | 4 ml/kg                  | 100 ml/kg               |
| 10-20 kg  | 40 ml + 2 ml/kg for each kg above 10 kgs | 1000 ml + 50 ml/kg for each kg above 10 kgs |
| >20 kg    | 60 ml + 1 ml/kg for each kg above 20 kgs | 1500 ml + 25 ml/kg for each kg above 20 kgs |

### Table 2: Recommendations on preoperative fasting guidelines\[9,10\]

| Type of food | Hours of fasting | Recommendation |
|--------------|------------------|----------------|
| Heavy Solids | 8 hrs            | A              |
| Light meals (solids)/Formula milk/juice with pulp | 6 hrs | A |
| Breast Milk  | 4 hrs            | A              |
| Clear fluids (water, fruit juices without pulp, clear tea, and black coffee excluding alcohol) | 1 h | A |

**Intraoperative fluid management**

All the guidelines (APA, NICE) still follow the Holiday Segar Formula for maintenance therapy\[1\] and they recommend infusion of isotonic solutions. NICE guidelines recommend restriction of fluids by 50 to 80% because of non-osmotic ADH secretion. The current guidelines recommend giving balanced solutions with 1-2.5% Dextrose to start with and then adjust the infusion according to clinical parameters.\[11\]

**Should we give Glucose containing fluids for maintenance?**

In pediatric patients, both hypoglycaemia and hyperglycemia can cause neuronal injury which goes unidentified resulting in permanent damage. So, administering by default 5% glucose in children also can be harmful.

Presently it is well accepted that to balance between hypoglycemia and hyperglycemia is to use isotonic fluids with lower glucose concentration (1-2.5%) for children less than 2 years.\[13\] There are also certain situations where in glucose supplementation is recommended. These are children with high risk of developing hypoglycemia as in preterm neonates, children receiving hyperalimentation, children with liver failure patients with mitochondrial diseases and those with endocrinopathies.\[14\]

Other than these special situations, routine dextrose administration is now no longer advised for healthy children receiving anesthesia even in neonatal period.

**Replacement fluids**

Replacement of intraoperative blood losses with isotonic solution or blood will depend upon the hematocrit of the patient.\[15\] The 3rd space loss (its existence is a matter of debate) because of leaking of fluid from vascular space into tissues around the surgical site is difficult to account for and is roughly estimated as 2 ml/kg/h for superficial surgery, 4–7 ml/kg/h for thoracotomy and 5–10 ml/kg/h for abdominal surgery. The NICE guidelines only mention replacement of ongoing losses with isotonic saline without mentioning the rate of fluid administration. Sumplemann et al. recommend that in patients with circulatory instability balanced isotonic electrolyte solutions without glucose can be given as repeat-dose infusions of 10–20 ml/kg until the desired effect is obtained\[11\]

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**Key points**

- Preoperative deficit to be calculated on a case-to-case basis
- ESA/ASA Guidelines for preoperative fasting – Clear fluids may be given up till 1 h
- Holiday and Segar – 4/2/1 rule to give a general direction
- Clinical Assessment of dehydration and its correction

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Saudi Journal of Anesthesia / Volume 15 / Issue 4 / October-December 2021 437
Table 3: Assessment of dehydration in Pediatrics

| Severity of Dehydration | % Dehydration Infant | % Dehydration Child | Symptoms |
|-------------------------|----------------------|---------------------|----------|
| Mild                    | 5                    | 3-4                 | Thirst, mucus membranes moist, EJV visible in supine, CRT > 2 sec, Urine sp gr > 1.020 |
| Moderate                | 10                   | 6-8                 | Dry mucus membranes, ↑ HR, ↓ tears, Sunken fontanelle, Decreased skin turgor, CRT 2-4 sec, ↓ Urine Output |
| Severe                  | 15                   | 10                  | Eye sunken, cool peripheries, apathy, somnolence, orthostatic to shock |
| Shock                   | >15                  | >10                 | Decompensation, Poor O₂ delivery, ↓ BP |

Table 4: On blood volume in children[28]

| Age of the child | Blood volume (ml/kg) |
|------------------|----------------------|
| Neonates         | 85-90                |
| Infants          | 75-80                |
| Children         | 70-75                |
| Adults           | 65-70                |

Recent studies predominantly in adults indicate that third space loss does not exist; however, more studies need to be done in pediatrics for the same. Studies done in adults indicate that in abdominal surgery outcomes are improved after a conservative fluid strategy than liberal fluid management as calculated by a different formula. Ideally individualized goal-directed therapy (GDT) using appropriate amount of colloid and crystalloid in order to optimize variables like pulse pressure and stroke volume is required and may reduce postoperative complications.

**Which isotonic fluid is most preferred?**

The most commonly available isotonic fluids include 0.9% normal saline, ringer lactate, and plasmalyte. 0.9% saline is the most commonly available and the cheapest fluid available, but it has excess of chloride and absence of bicarbonate precursor. Infusion of large volumes results in suppression of RAS, renal blood flow and in effect leads hyperchloremic acidosis. It has been not that in children undergoing major pediatric and neurosurgeries have shown better acid-base status with balanced crystalloids like plasmalyte and ringer lactate.\[15\] By definition balanced crystalloids should ideally mimic the electrolyte pattern of that of plasma. As compared with lactate, metabolization of acetate (Plasmalyte) is significantly faster, more independent of hepatic function, with a lower increase in oxygen consumption and no interference with the diagnostic use of lactate as a marker of low tissue perfusion.\[16\] Most of the anesthetic drugs are compatible with acetate except phenytoin and diazepam.\[17\]

**Colloids and its use in pediatrics**

After administration of a total of 30–50 ml/kg⁻¹ of crystalloid solution, the administration of a colloid solution (albumin or synthetic colloid) to maintain intravascular osmotic pressure is indicated\[18\]

This is an area that needs more studies and so is still debatable. There is scope for high-quality RCTs in this area to come to a safe conclusion regarding the use of colloids. A meta-analysis done did not show any alteration of renal parameters, blood transfusion, or blood loss with infusion of low molecular weight 6% HES.\[19\]

There is no role for non-emergent use for volume replacement with colloids and no advantage of one colloid over the other in preventing shift of fluids to interstitial space.\[20\]

Albumin remains the main colloid used in the neonatal period and early infancy for volume expansion. However, its use is restricted in view of high cost and possibility of it carrying other sources of infection. In hypotensive premature infants, 5% albumin was shown to be more effective than 20% albumin. This suggests that the volume of albumin administered is more important that its concentration to maintain or restore cardiovascular stability. Thus 5% albumin remains the preferred colloid in young infants as it is iso-oncotic to plasma and very effective to maintain blood pressure and plasma colloid perfusion pressure.\[21,22\]

**Blood and blood product transfusion intraoperatively**

The need of blood transfusion depends on factors like age, amount of blood loss, the baseline hemoglobin. Neonates and infants have higher blood volume per weight but are less tolerant of the blood loss and to add to that the metabolic rate and baseline oxygen demands are greater than adults [Table 4].

The goal is to maintain normovolemia with a close watch on hypervolemia with crystalloids which can cause significant dilutional coagulopathy and peripheral edema. Initially when there is bleeding, 2:1 regimen for volume of colloids to be transfused when compared to crystalloids. After the bleeding has crossed 20% of blood volume preferred ratio of crystalloid to colloid is 1:1.\[24\]

The decision when to transfuse blood to children depends on the maximum allowable blood loss (MABL) calculated as: MABL = EBV × (H₀ – H₁)/H₀ (EBV = estimated blood volume; H₀ = starting Hct; H₁ = lowest acceptable Hct).\[25\]

Transfusion Trigger is usually accepted to be around hemoglobin of 7-8 g/dl in children having intraoperative loss. Hb of 7 g/dl is acceptable if there is no active on-going
loss and stable clinical parameters. The volume of packed cells required is calculated as body weight (kg) × desired increment in hemoglobin (g/dl) × 5.[25]

Low cardiac output and low blood pressure should be treated immediately as it can lead to decreased tissue oxygen delivery. Hence, prompt fluid management and initiating vasopressors is of prime importance.

**Intraoperative targets for fluid management**
Clinical assessment of hydration status preoperatively and postoperatively will help us to guide fluid management during those times. Intraoperative the challenge is to assess the hydration balancing the view on surgical field, hemodynamic parameters on the monitor and losses like renal and evaporative. Urine output is reliable indicator used by a lot of experienced anesthetists. Even till today, perioperative studies using esophageal Doppler, pulse contour analysis, or mixed venous oxygen saturation is lacking, and this is an area that requires further randomized control trials.[26]

### Proposal for perioperative management
The goal preoperatively must be to keep fasting time to the least and whenever possible to give clear fluids up till 1 hr before the surgery. For minor procedures (<1 hr) balanced isotonic fluids without glucose to a maximum of 10 ml/kg/hr. For intermediate procedures to adjust the balanced isotonic infusion according to the requirement during surgery. Glucose in a lower concentration (1-2.5%) can be added if the situation demands. If additional fluids required to give boluses of isotonic fluids (10-20 ml/kg) and if this is not effective colloids can be considered. For major procedures, to follow the same principles as an intermediate procedure. Blood product transfusion to be initiated according to the maximum allowable blood. Postoperatively to allow the child to drink and feed as early as possible provided the child is awake and there is no surgical contraindication.

### Conclusion
Perioperative fluid prescription is very crucial in the management of critically ill children and should be guided by physiology and pathology. The main aim of fluid infusion is establishing euvolemia, adequate tissue perfusion and oxygenation. Minimizing preoperative and postoperative fasting significantly impact comfort and hydration state of children. Holliday and Segar recommendation is a decent guide to the pediatric fluid management provided the surgical catabolic state and stress are kept in mind. Because of such concerns, current recommendations have moved towards the use of total volume infusion to be restricted to 50% of isotonic solutions with a glucose requirement of 1–2.5%.

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### Conflicts of interest
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**Key points**

- Isotonic Fluids the mainstay of maintenance fluids
- 1-2% Dextrose may be added if there is possibility of hypoglycemia
- Routine Dextrose administration no longer advised.

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**Postoperative fluid management**
The recent updates in shortening the preoperative fasting times in children should be extended into the postoperative period too. Children should be encouraged to restart oral fluids as early as possible if there is no surgical contraindication; however, fluid intake need not be insisted before discharge from an ambulatory facility.[29]

Postoperative IV infusions should be with isotonic fluids instead of hypotonic fluids with 5% dextrose as the incidence of hyponatremia was lower.[27,28] Similarly American Academy of Pediatrics (AAP) recommends in a recently published guideline that patients 28 days to 18 years of age requiring maintenance intravenous fluids postoperatively should receive isotonic solutions with appropriate potassium chloride and dextrose as they significantly decrease the risk of developing hyponatremia.[29]
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