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SASA MAIN CONFERENCE

# Which colloid to choose for neonates, infants and children

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## Abstract

This paper considers how the physiology, as it alters with age, may affect the choice of colloid given to a child. The evidence surrounding the use of natural protein and synthetic colloids available for use in children is examined and personal recommendations regarding paediatric colloid use are given.

**Keywords:** colloid, neonate, infants, children

## Introduction

This is not the crystalloids versus colloids debate. The question is: Having decided that you need to give a colloid, which one do you give? Colloids are given to restore or increase intravascular volume, and in theatre, this is frequently in the context of ongoing loss in the form of bleeding. A detailed discussion of transfusion triggers is beyond the scope of this paper. However, in every context, strong consideration should be given to whether a blood or a blood product may be the most appropriate colloid as oxygen-carrying capacity is an important consideration in the developing brain. An informal survey of anaesthetic colleagues abroad indicates that most would reach for blood or a blood product once they had determined that sufficient crystalloid had been given, and would only possibly consider the use of a synthetic colloid in an older child.

Research in this area in paediatric age groups is fraught with ethical and practical problems, and as a result, there is a paucity of high-quality comparative trials. Thus, we are forced to base our practice on a few, limited paediatric studies, extrapolation from adult studies, expert opinion and our understanding of the physiology of each age group.

## Physiology

Neonates have relatively high haemoglobin levels, but this is predominantly haemoglobin F, which has a limited capacity to release oxygen at tissue level. Additionally, particularly in the first week of life, clotting factor levels may be inadequate.[1] For these reasons, blood and blood products are frequently required when large fluid infusions are being given.

Although the full number of adult nephrons is present at birth, the tubular length takes approximately six months to reach adult levels.[2] Therefore, diluting and concentrating abilities are limited. Renal function is not completely developed, and sodium clearance, in particular, is limited, which may reflect in the impaired ability to handle a sodium load. Limited trials in premature infants comparing albumin (Na+ 145mmol/ℓ) with 0.9% NaCl (Na+ 154mmol/ℓ) infusion have, however, not shown this to be significant.[3]

Physiological anaemia is experienced at around 8-12 weeks in an infant. The haemoglobin dips to approximately 9-11 g/dl. This may happen as early as three weeks in the premature infant and can be more profound, dipping to 7-9 g/dl.[4] While this is a physiological adaptation to postnatal life, it may leave the infant vulnerable to inadequate oxygen delivery in a situation of an acute, substantial increase in oxygen demand (surgical stress and infection). Renal function in this age group is approaching adult capacity, and the handling of sodium loads does not appear to be a problem.

With respect to haemoglobin levels, clotting capacity and renal function, children over the age of two years are not vastly different from adults. Their increased metabolic rates and propensity to vasodilation, owing partly to increased parasympathetic tone, may make their oxygen requirements and fluid responsiveness somewhat different to that of adults. This should be assessed clinically and using point-of-care monitoring, such as near-infrared spectroscopy and responded to as appropriate, to maintain adequate tissue oxygen delivery.

## Available colloids

Available colloids for paediatric use in the South African context are classified as those manufactured from natural proteins (albumin, stabilised human serum and freeze-dried plasma) or as synthetic colloids (starches and gelatins). No trials comparing all these agents have been done and, in the paediatric age group, trials using colloids are largely limited to the colloid vs crystalloid variety.

## Natural protein colloids

Although it is one of the most expensive colloids, albumin remains popular with paediatricians throughout the world,

and is also widely used by anaesthetic communities in North America, Australia and New Zealand. It is prepared in concentrations of 5-20%, with 5% being osmotically equivalent to plasma, and concentrations greater than this are possibly indicated in situations of albumin deficit (nephrotic syndrome and cirrhosis). It is the least allergenic of the colloids, but also the most susceptible to migration into the extravascular space, with an increase in vascular permeability.[5] The only clear contraindication to its use, extrapolated from the adult literature, would appear to be traumatic brain injury.[6]

A comparison of albumin versus starch in children aged three years and younger undergoing cardiopulmonary bypass showed an improved urine output with albumin.[7] Priming a paediatric bypass circuit with crystalloid versus crystalloid plus albumin led to better fluid balances and less weight gain, but more transfusion in the albumin group.[8]

Fresh frozen plasma (FFP) is used by some practitioners as a colloid. It should be remembered that this is a blood product, and although the overall risks of blood transfusion remain low, FFP is among the least safe blood components to transfuse. Haemolysis due to anti-A or anti-B antibodies if transfused across blood types; immunological reactions, such as allergy and anaphylaxis; and transfusion-related acute lung injury are among the most concerning adverse reactions that may be precipitated. Viruses are not inactivated in the preparation process and may be transmitted.[9] In addition, FFP is hypertonic, with a sodium concentration of 165 mmol/l[10] and may cause hypernatraemia with injudicious use.

Stabilised human serum (SHS) is a 5% protein product, prepared by filtering and inactivating plasma. The albumin content is approximately 3.6%. The remaining proteins are largely immunoglobulins which have a higher molecular weight than albumin, thus potentially resulting in increased intravascular longevity. Viral inactivation is achieved by ultraviolet irradiation and heat. The electrolyte profile renders it slightly hypo-osmotic at 260 mOsm/kg. Its processing results in a cost substantially more than that of the synthetic colloids.

## Hydroxyethyl starches

Hydroxyethyl starches (HES) are modified polysaccharides suspended in 0.9% NaCl, or more recently, a more iso-osmotic solution. Hydroxyethyl groups are substituted for hydroxyl groups to improve the stability of the molecule. The molecular weight, degree of molar substitution and the position of substitution (usually C2 or C6) affects the time that the molecule remains active intravascularly, as well as the side-effects experienced.

The high molecular weight/molar subsistution HES solutions particularly tend to be associated with hypocoagulability owing to as yet poorly understood effects on factor VIII, the von Willebrand factor and platelets.[11,12] This effect is reduced, but not eliminated, in the medium- and low-molecular-weight starches.[13,14] Renal effects, also maximal in the higher-molecular-weight solutions, include tubular swelling and hyperviscosity of the urine, and may be linked to the amount of time that the molecule is active intravascularly.[15] The higher the C2:C6 substitution ratio, the slower the breakdown of the product, resulting in a prolonged intravascular effect. The newer starches are low to medium molecular weight, with a high C2:C6 substitution ratio, which may account for their observed renal effects, particularly in critically ill patients. Tissue accumulation, leading to pruritus, is a prominent side-effect with high-molecular-weight/molar substitution starches, which, while seldom causing significant clinical impact, can be very troubling to the patient.[16]

It has been suggested in several studies on adult and paediatric patients that there is a possible increase in blood loss post-cardiopulmonary bypass (CPB) when HES solutions are used, although this is not always accompanied by an increase in transfusion requirements.[11,17-20] These findings in children are supported by an in vitro study on infant thromboelastograms that compared albumin, gelatin and HES fluid boluses. The study demonstrated a reduced maximum amplitude and α-angle with a 15 ml/kg HES bolus.[19] It must be borne in mind that not all HES studies are equal, and the older studies were conducted using high- or medium-molecular-weight solutions known to have a greater effect on coagulation. That said, the evidence seems to point to the rationale that HES may not be the ideal colloid in neonates, infants and children after a CPB.

Studies on the use of starches in paediatric patients, particularly those who are critically ill and/or have renal dysfunction are lacking, but extrapolation from adult evidence[21-23] suggests that it is prudent to avoid starches in these patients. In other patients particular attention must be paid to recommended maximum daily doses.

## Gelatins

Gelatins are polypeptides manufactured from the degradation of bovine collagen. Its molecular weight (30-35 kDa) is the lowest of all commercially available colloids, and results in its relatively reduced plasma oncotic effect. In fact, due to rapid glomerular filtration, enzymatic cleavage and transient passage into the interstitial space, the increase in blood volume seen with the infusion of gelatins is actually less than the volume infused.[15] As a result, repeated infusions are required to maintain the effect. There is no prescribed limit to the amount of gelatin that may be infused.

Although not as marked as that with the starches, there is some effect on coagulation,[19,24,25] and caution is advised when considering the use of gelatins in patients with underlying bleeding tendencies, such as von Willebrand's disease. Gelatin is the most allergenic of all the commercially available colloid solutions.[26]

Paediatric gelatin studies are limited. It was noted in a Cochrane review of early volume expansion in preterm infants that there was an increased likelihood of necrotising enterocolitis developing with the use of gelatin or no treatment, compared with the use of FFP.[27] Adult studies have suggested a possible implication for the worsening of a capillary leak with the use of gelatins, which may have implications for septic neonates.[28,29]

Gelatins remain the least expensive commercially available colloid, are effective plasma volume replacers and aside from the increased hypersensitivity reactions, are not associated with clinically significant adverse effects.

## What I do

I seldom use colloids in the neonate and infant, and tend to give blood and blood products once I have determined that I have given sufficient crystalloid. Barring the contraindications mentioned, if I choose to give a colloid, a naturally occurring protein colloid, such as SHS, is my choice for a neonate, and 130/0.4 HES for an infant. 130/0.4 HES is my first choice in children requiring colloid fluids.

## Conclusion

It should be remembered that fluids are only one aspect of a resuscitation strategy which should aim to correct deficits in circulating volumes and constituents. Intrinsic cardiac and microvascular function, as well as neurohumeral changes, should also be considered. Adjunctive therapies, such as catecholamines which augment cardiac contraction and venous return, should not be forgotten. There is a tendency by clinicians to view catecholamines as a last resort, forgetting that many of our anaesthetic agents cause vasodilation and myocardial depression which will be reversed at the end of anaesthesia. Clinicians should rather consider starting with a low-dose infusion and to resist the urge to give more fluid. It may be given peripherally for a short while, if necessary, and weaned at the end of the case.

In the absence of an ideal colloid or conclusive evidence to support one or other available option, the clinician is forced to rely on personal and institutional experience, extrapolation from adult studies, the consideration of evidence from limited paediatric studies, and expert opinion, when deciding which colloid to administer. Cost may also influence clinical decision-making. What is clear is that this choice may have significant clinical implications, and should be undertaken with the same degree of consideration as that given to a drug prescription.

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