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Section 1 The fluids

Chapter 1

The essentials

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Fluid requirement

Minimum 1 ml/kg per hour, i.e. 2.4 liters daily for a person with a body weight of 100 kg and 1.2 liters for a person with body weight of 50 kg. In children add 50%.

Most common to provide 1.3–1.5 ml/kg per hour to those who can excrete fluid well.

Maintenance therapy

Provide fluid and nutrition intravenously for those who cannot eat and drink.

- Glucose 5% per 4–6 hours with electrolytes up to the daily fluid requirement. This provides a minimum of calories and can be used only for a few days.
- Electrolytes should be 1 mmol/kg each of sodium and potassium per 24 hours.
- Potassium should not be infused faster than 10 mmol/hour.

Preoperative fasting

Patients may drink clear fluids up to 2 hours before surgery.

Solid food up to 6 hours before surgery.

Contraindications may apply.

Induction of anesthesia

Common practice is to provide 500 ml of balanced crystalloid fluid during the induction to compensate for vasodilatation and as a safeguard against undetected hypovolemia. The fluid has no effect on the concomitant drop in arterial pressure.

Intraoperative fluid

Fluid elimination is slow. A restrictive program reduces the complications.

- 3–5 ml/kg per hour of a balanced crystalloid fluid (Ringer's lactate or Ringer's acetate, or Plasma-Lyte). This also covers minimal blood losses.
- Alternatively, 1–2 ml/kg per hour *and* volume optimization guided by stroke volume monitoring or equivalents. This option is of most obvious benefit in the sickest patients.
- Isotonic saline to be given only on special indications. These are vomiting, hyponatremia, trauma, and (especially) neurotrauma.
- Blood loss up to 500 ml is replaced by 3 times the bled volume of balanced fluid.
- Blood losses exceeding approximately 500 ml can be replaced by a colloid fluid before the target hematocrit, which depends on the preoperative blood hemoglobin (Hb) concentration and the patient's health status, is reached.

Postoperative care unit

Fluid elimination is normal or increased.

No evidence of benefit from fluid restriction, which increases the risk of nausea.

- 5–6 ml/kg per hour of a balanced crystalloid fluid.

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Back at the surgical ward

(From 3–4 hours after the surgery)
Normalization stage.

* Drink clear fluids, alone or combined with:
* Glucose 2.5% with electrolytes 1.5 ml/kg per hour (approximately 100 ml/hour in an adult). If necessary, add more electrolytes as guided from blood analysis. Use infusion pump.

Check for dehydration before you induce anesthesia

You must always evaluate the possibility of a preoperative fluid deficit.

* *Inability to drink* leads to **hypertonic dehydration** where serum osmolality >300 mosmol/kg. Slow correction with glucose solution is the cure. If you are in a hurry, restore extracellular volume with balanced Ringer's and then turn to glucose.
* *Vomiting* and *diarrhea* lead to **hypotonic dehydration**. Restore with isotonic saline.
* *Enteric lavage* should replaced 1:1 with balanced electrolyte solution.
* *Ileus* may result in very large fluid deficits (4–6 liters) resulting both from inability to drink and from vomiting. Estimate is 3 liters of loss for each day of complete ileus. Replace at least half the missing volume before inducing anesthesia under cardiovascular monitoring.

Two general guidelines for the use of fluid therapy in hospital patients have been published by British authors and can be downloaded free of charge from the Internet:

GIFTASUP (2007) – British Consensus Guidelines on Intravenous Fluid Therapy for Adult Surgical Patients; http://www.bapen_pubs/giftasup.pdf (last visited on 18 March 2016)

NICE (2013) – Intravenous fluid therapy in adults in hospital; http://www.nice.org.uk/guidance/cg174

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Chapter 2

Crystalloid fluids

Robert G. Hahn

Summary

Crystalloid electrolyte solutions include isotonic saline, Ringer's lactate, Ringer's acetate, and Plasma-Lyte. In the perioperative period these fluids are used to compensate for anesthesia-induced vasodilatation, small to moderate blood losses, and urinary excretion. Although evaporation consists of electrolyte-free water, such fluid losses are relatively small during short-term surgery and may also be compensated by a crystalloid electrolyte solution.

These fluids expand the plasma volume to a lesser degree than colloid fluids as they hydrate both the plasma and the interstitial fluid space. However, the distribution to the interstitial fluid space takes 25–30 min to be completed, which is probably due to the restriction of fluid movement by the finer filaments in the interstitial gel. The slow distribution gives crystalloid electrolyte solutions a fairly good plasma volume-expanding effect as long as the infusion continues and shortly thereafter.

Isotonic saline is widely used, but has an electrolyte composition that deviates from that of the extracellular fluid ("unbalanced"). This fluid is best reserved for special indications, such as hyponatremia, hypochloremic metabolic alkalosis, and disease states associated with vomiting. Isotonic saline may also be considered in trauma and in children undergoing surgery. Hypertonic saline might be considered in neurosurgery and, possibly, in preoperative emergency care.

Ringer's lactate, Ringer's acetate, and Plasma-Lyte have been formulated to be more similar to the composition of the ECF ("balanced fluids"). They are the mainstay of fluid administration in the perioperative period and should be used in all situations where isotonic saline is not indicated.

The term *crystalloid fluid* refers to sterile water solutions that contain small molecules, such as salt and glucose, which are able to crystallize. These solutes easily pass through the capillary membrane, which is the thin fenestrated endothelium that divides the plasma volume from the interstitial fluid volume. This process of solute distribution brings water along with it. Hence, the volume of a crystalloid fluid is spread throughout the extracellular fluid (ECF) space.

Osmolality is the number of particles dissolved in the water solution. The osmolality of the body fluids is approximately 295 milliosmoles (mosmol) per kg and is a powerful driving force for water distribution. However, it is both the type of dissolved particles and the osmolality of the solution that determine the tonicity, i.e. to what degree the infusion fluid hydrates or dehydrates the intracellular fluid (ICF) space.[1]

If the solutes in the infusion fluid remain outside the cells, as is the case for sodium and chloride, the osmolality and the tonicity agree. An iso-osmotic infusion fluid (295 mosmol/kg) is then isotonic. In contrast, osmolality and tonicity are not equivalent in the case where the solutes easily penetrate the cell membrane, which separates the ECF from the ICF. An example is ethanol, which markedly raises the body osmolality but without redistributing water. Therefore, ethanol is said to have low tonicity.

The cell membrane regulates the distribution of many other solutes across the cell membrane in a finely graded manner via energy-consuming pump mechanisms, which then also modify the water distribution.

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Table 2.1 Composition of plasma and the most common crystalloid solutions

	Osmolality (mosmol/kg)	pH	Na^+ (mmol/l)	K^+ (mmol/l)	HCO_3^- (mmol/l) equivalent	Cl^- (mmol/l)	Glucose (mmol/l)
Plasma	295	7.4	140	3.6–5.1	30	100	5
0.9% saline	308	5.0	154	0	0	154	0
7.5% saline	2400	3.5–7.0	1250	0	0	1250	0
Lactated Ringer's	274	6.5	130	4	30	110	0
Acetated Ringer's	270	6.0	130	4	30	110	0
Plasma-Lyte[a]	295	7.4	140	5	27	98	0
Glucose (5%)	278	5.0	0	0	0	0	278
Glucose (2.5%) + electrolytes	280	6.0	70	0	25	45	139

[a] Plasma-Lyte A also contains 23 mmol/l of gluconate.
The infusion fluids may contain small amounts of electrolytes such as magnesium and calcium.

These pumping mechanisms operate slowly (minutes to hours) whereas changes in osmolality redistribute water within seconds.

The marketed crystalloid infusion fluids are usually isotonic or nearly isotonic. Hence, they expand the ECF volume but not the ICF volume. Their main use in the perioperative period is to compensate for anesthesia-induced vasodilatation, small to moderate blood losses, and urinary excretion. Although evaporation consists of electrolyte-free water, such fluid losses are relatively small and can also be compensated by crystalloid electrolyte solutions.

Isotonic saline

A 0.9% solution of saline is isotonic and is therefore called physiological or "normal." However, the fluid can also be called "unbalanced" because no attempt has been made to mimic the electrolyte composition of the ECF. The fluid still contains a marked surplus of chloride ions and no buffer (Table 2.1) and, hence, infusion of >2 liters of the fluid causes hyperchloremic metabolic acidosis.[2]

Isotonic saline is the most widely used infusion fluid in Europe and probably worldwide, although the indications are limited. In adults, normal saline should be reserved for patients with hyponatremia and hypochloremic metabolic alkalosis, as in disease states associated with vomiting. The fluid has a more accepted role for perioperative fluid therapy in children where the risk of subacute postoperative hyponatremia is a more serious concern than in adults.

When infused in healthy volunteers, 2 liters of normal saline caused abdominal pain, which was not the case for lactated Ringer's.[3] The use of approximately 4 liters of isotonic saline during surgery caused more postoperative complications than the use of the same amount of Ringer's lactate.[4]

Normal saline is excreted more slowly than both lactated and acetated Ringer's solutions,[5] increasing the volume effect ("efficiency") of the fluid to be about 10% greater than for the Ringer's solutions (Figure 2.1). The reason for the slow elimination is probably that the surplus of chloride ions has a vasoconstrictive effect on the renal blood vessels.[6]

Small prospective [4] and large retrospective [7] studies have shown that surgical complications are more common after open abdominal operations where isotonic saline has been infused than for similar operations with Ringer's lactate. However, a difference in complication rate is unlikely if the infused volume is <2 liters. A more detailed comparison between isotonic saline and the buffered Ringer's solutions is given in Chapter 12, "Monitoring of the microcirculation."

Isotonic saline is devoid of calcium. This means that the fluid can be infused together with packed erythrocytes where citrate has been used as preservative without causing coagulation in the infusion line. Large volumes of saline dilute the plasma concentration of ionized calcium, which might be an untoward effect because hypocalcemia decreases myocardial contractility. Therefore, calcium needs to be substituted if large volumes of isotonic saline are provided. No

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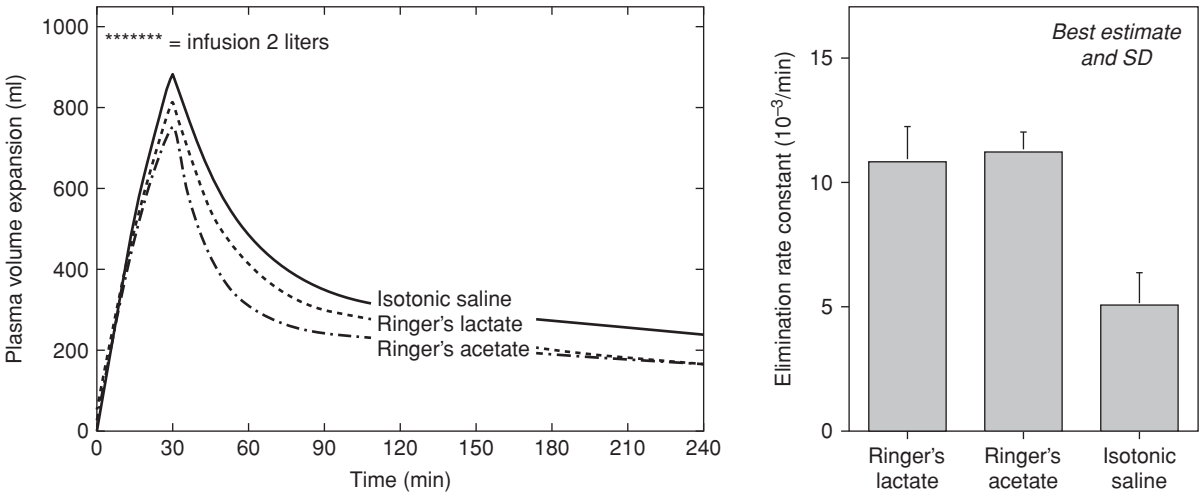

Figure 2.1 Left panel: Plasma volume expansion from infusion of 2 liters of isotonic saline, Ringer's lactate and Ringer's acetate over 30 min (asterisks) in 10 healthy volunteers. Each curve is based on the modeled average plasma dilution from experiments performed in 10 male volunteers multiplied by the plasma volume at baseline as estimated by anthropometry. Right panel: The rate of elimination of the three fluids. The half-life is the inverse of the shown elimination rate constant times 0.693. Hence, the half-life is about 60 min for the Ringer's solutions and 130 min for isotonic saline. Recalculations of data from Ref. [5] using a mixed-models analytical program (Phoenix NLME).

precise limit is given but it should be in the range of 4 liters in an adult.

Saline may also be marketed as hypertonic solutions at strengths of 3% and 7.5% solution. The first is mainly intended as a means of raising the serum sodium concentration in hospital in-patients and of reducing the intracranial pressure in neurotrauma patients. The latter is used for plasma volume expansion in emergency care, although the benefits have been questioned. In volunteers, 7.5% saline is four times as effective a plasma volume expander as normal saline.[5]

The Ringer's solutions

Ringer's solution is a composition created by Sydney Ringer in the 1880s to be as similar as possible to the ECF. Alexis Hartmann later added a lactate buffer to the fluid and made it Hartmann's solution, or "lactated" Ringer's solution.

Lactate and acetate

Today, Ringer's solution is used with the addition of buffer in the form of *lactate* or *acetate*, of which the former is more common. Both ions are metabolized to bicarbonate in the body, albeit with certain differences. Lactate is metabolized in the liver and the kidneys with the aid of oxygen and under production of bicarbonate and carbon dioxide. Acetate is metabolized faster and in most tissues, and it consumes only half as much oxygen per mole of produced bicarbonate compared with lactate. Hence, lactate slightly increases the oxygen consumption [8] and might also raise plasma glucose, particularly in diabetic patients.[8,9] Large amounts of lactated Ringer's confuse assays used to monitor lactic acidosis.

Both lactate and acetate are vasodilatators. Rapid administration aggravates the reduction of the systemic vascular resistance that normally occurs in response to volume loading. Both lactate and acetate are also fuels, although the calorific content in 1 liter of any Ringer's solution is quite low (approximately 5 kcal).

Although the differences between lactate and acetate are usually negligible, several factors suggest that acetate is the better buffer in the presence of a compromised circulation and in shock. Lactate is metabolized in the liver and, therefore, Ringer's acetate is to be preferred in patients with impaired liver function. A more detailed comparison between lactate and acetate as buffers is given in Chapter 25, "Transplantations."

Pharmacokinetics

During intravenous infusion the Ringer's solutions distribute from the plasma to the interstitial fluid space

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in a process that requires 25–30 min for completion. The distribution half-life is approximately 8 min.[5,10]

Distribution. There is a difference in the pattern of distribution for small and large volumes of the Ringer's solutions. Infusing 300–400 ml at a rate of 10–20 ml/min will distribute fluid almost exclusively over the plasma volume.[11,12] This is rather due to the high compliance for volume expansion of the interstitial matrix than to a limiting effect of the capillary membrane. A three times higher rate of infusion overcomes the low compliance of the interstitial gel, but the fine filaments in the meshwork still retard the rate of the distribution, which explains why this process still requires 25–30 min to be completed. When the rate of infusion is further raised (50 ml/min and higher) the return of fluid from the interstitium to the plasma becomes progressively retarded, which is due to loss of stiffness in the matrix. Free fluid can even accumulate in the interstitium if an infusion is provided fast enough to overcome the normally negative interstitial fluid pressure.[1] This causes *pitting edema*, by which we can expect that the ratio of 1:2 for the fluid distribution between the plasma and interstitial fluid space has been abruptly reduced.

For the infusion rates normally used during surgery, the ratio of the plasma to the expandable parts of the interstitial fluid space is 1:2, which means that 33% of the infused fluid is retained in the plasma (if we disregard elimination).[13] However, slow distribution results in a stronger plasma volume expansion than offered by this relationship as long as the infusion continues (Figure 2.1).

Elimination. The elimination (by voiding) in volunteers is so rapid that the fluid may exhibit one-compartment kinetics, which has been interpreted to imply that the fluid is distributed only to the plasma and to areas of the interstitial fluid space with the highest compliance for volume expansion (half-life 20 min). In contrast, elimination is greatly retarded during surgery, where Ringer's always exhibits two-compartment kinetics.[10] Infusion of 2 liters of Ringer's in volunteers is followed by elimination of 50–80% of the fluid within 2 hours, whereas the corresponding figure in anesthetized patients is only 10–20%. This corresponds to a half-life of 200–400 min. Lowered blood pressure, vasodilatation and activation of the renin–aldosterone axis are factors thought to be responsible for the slow turnover of Ringer's during anesthesia and surgery.[14] The retarded elimination facilitates the development of edema as the retained fluid distributes both in the plasma and the interstitial fluid space.

Clinical use

The pharmacodynamics of the Ringer's solutions is strongly related to their capacity to expand the ECF volume.

These fluids may be used to replace preoperative losses of fluid due to diarrhea or bowel preparation. In contrast, vomiting should be replaced by normal saline.

The Ringer's solutions are commonly used (in a volume of approximately 500 ml) to compensate the blood volume for the expansion of the vascular tree that occurs from induction of both regional and general anesthesia.

The Ringer's solutions reverse the compensatory changes in blood pressure and sympathetic tone resulting from hypovolemia. There are numerous reports confirming that rapid infusion of Ringer's is a life-saving treatment in excessive hemorrhage, owing to the resulting expansion of the plasma volume.

In contrast, crystalloid fluid cannot reverse drug-induced hypotension.[14] If a crystalloid bolus has no effect in reversing hypotension during surgery, the anesthetist should change strategy and lighten the anesthesia, or else institute treatment with an adrenergic drug, rather than providing several liters of crystalloid fluid.

As crystalloids are inexpensive and carry no risk of allergic reactions, a Ringer's solution is often used to replace smaller blood losses while colloids are withheld until 10–15% of the blood volume has been lost. The commonly recommended dosage is to infuse three times as much Ringer's as the amount of blood lost (3:1 principle). If the patient's legs are placed in stirrups, a 2:1 replacement scheme can be used, with the last third given as a bolus infusion when the legs are lowered from the stirrups.[15]

There are concerns about the use of Ringer's in brain injury, because the fluid is slightly hypotonic (270 mosmol/kg) and increases brain cell mass when the central nervous system is traumatized. Normal saline is likely to be a better choice during neurosurgery and also in acute trauma. In volunteers, however, acetated Ringer's did not increase the ICF volume, as shown by the fact that the urinary sodium concentration was only half as high as that of the plasma.[16]

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All Ringer's should be infused cautiously in patients with renal insufficiency, since these patients may not be able to excrete an excess amount of crystalloid fluid.

The buffered Ringer's solutions contain 2 mmol/l of calcium and therefore cause coagulation in the infusion line if given together with erythrocytes preserved with citrate. This agent operates as an anticoagulant by binding calcium, which is a co-factor in the coagulation process.

Dosing

The rate and volume of infused Ringer's solutions vary considerably during surgery. Overall, the volumes used in clinical practice today are lower than they were in the 1980s and 1990s. The most widely used basic rate of infusion to provide is 3–4 ml/kg per hour, i.e. about 300 ml per hour in an adult male. In major surgery, a widely advocated concept is to provide a basic rate of 2 ml/kg per hour of one of the buffered Ringer's solutions and then to increase the fluid administration whenever stroke volume decreases by >10% (goal-directed fluid therapy). To provide a Ringer's solution only at a rate of 2 ml/kg per hour or less with no additional infusions increases the risk of postoperative nausea.[17]

In healthy adult females, very rapid infusions of Ringer's (2 liters over 15 min) caused swelling sensations, dyspnea, and headache.[18] This rate (133 ml/min) should not be exceeded in the absence of severe hypovolemia. No symptoms were observed after infusing the same volume more slowly.

In elderly and debilitated patients, the rate of infusion of crystalloid fluid should be further reduced and adjusted according to the patient's cardiovascular status.

Too rapid volume loading might be complicated by instant pulmonary edema. Both the dilution of the plasma proteins and the increased cardiac pressures promote such edema, which should be treated with acute vasodilatation, administration of loop diuretics, and application of continuous positive airway pressure (or positive end-expiratory pressure if the patient is mechanically ventilated).

There is also a risk of pulmonary edema developing in the postoperative period if the total volume infused during the day of surgery amounts to 7 liters or more. Arieff [19] reported development of pulmonary edema in 7.6% of 8,195 patients who underwent major surgery. The mortality in this group was 11.9%.

Volume loading with 3 liters of lactated Ringer's in volunteers (mean age 63 years) reduced the forced expiratory capacity and the peak flow rate.[20]

Outcome studies using prospective registration of postoperative adverse events have demonstrated that crystalloid fluid administration during colonic surgery should be closer to 4 ml/kg per hour than 12 ml/kg per hour.[21] One of the earliest problems is that >2 liters prolongs the gastrointestinal recovery time after surgery, which has not been described after administration of hydroxyethyl starch.[22] Larger volumes of crystalloid electrolyte fluid promote a large number of postoperative complications, such as impaired wound healing and pneumonia.[23] Many similar outcome studies will be discussed later in this book that advise the anesthetist about the optimal infusion rates during various surgeries.

The restrictive protocol is best studied, and of undisputable value, in open abdominal surgery. Patients undergoing laparoscopic cholecystectomy and bariatric surgery seem to fare better with a more liberal program (7 ml/kg per hour or higher). There is little evidence that a restrictive fluid program is of value in the postoperative care unit, where the fluid turnover is normal, or rather slightly accelerated, owing to the surgical inflammatory response.

Plasma-Lyte

The infusion fluid Plasma-Lyte is constructed to further refine the "balanced" composition of acetated Ringer's solution. Here, the sodium and chloride concentrations are virtually identical to those of human plasma, and the osmolality is the same as that of the plasma (Table 2.1).

To make up for the increase in cation and decrease of anion concentration the solution also contains the negatively charged ion gluconate, which is also metabolized to carbon dioxide and water but still has only a weak alkalinizing effect. Gluconate has been used as a taste improver in the food industry during the past 150 years and is non-toxic. Gluconate is also a part of our intermediary metabolism, and an amount corresponding to the content of 4 liters of Plasma-Lyte is produced each day in the human body.

The Plasma-Lyte composition has been known for several decades and has only recently been marketed widely. Countries that are used to Ringer's lactate may

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show reluctance to use Plasma-Lyte because of the content of acetate, but the differences between the lactate and acetate buffers are indeed quite small. Clinicians may also hesitate to use the fluid owing to uncertainty caused by the presence of gluconate, which is not used in clinical medicine except perhaps as a chelate in oral calcium tablets.

Plasma-Lyte has no acidifying effect and is therefore more effective than isotonic saline to combat metabolic acidosis in diabetic ketosis [24] and trauma.[25] In kidney transplantation patients, infusion of Plasma-Lyte caused less aberration of the electrolyte balance than both isotonic saline and Ringer's lactate.[26] These differences are expected since the composition of Plasma-Lyte is more similar to the ECF than any of the other crystalloid electrolyte solutions are. Although Plasma-Lyte is intuitively the best of these fluids, a benefit with respect to clinical outcome might be difficult to demonstrate relative to the balanced Ringer's solutions as the composition-related problems associated with their use are few.

Plasma-Lyte is used on the same indications as the buffered Ringer's solutions. This fluid might also be considered in trauma patients and in children, given that it is iso-osmotic.

Similar to isotonic saline, Plasma-Lyte is devoid of calcium, which makes it possible to infuse the fluid in the same intravenous line as erythrocytes preserved with citrate. Calcium might need to be substituted when more than 4 liters of the fluid has been administered, owing to dilution of the plasma calcium concentration.

The SPLIT clinical trial did not disclose any difference in the incidence of acute kidney injury and mortality when isotonic saline or Plasma-Lyte was given in a mean volume of 2 liters on the first day of admission to intensive care.[27]

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Chapter 3

Colloid fluids

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Summary

Colloid fluids are crystalloid electrolyte solutions with a macromolecule added that binds water by its colloid osmotic pressure. As macromolecules escape the plasma only with difficulty, the resulting plasma volume expansion is strong and has a duration of many hours. Clinically used colloid fluids include albumin, hydroxyethyl starch, gelatin, and dextran.

The plasma volume expansion shows one-compartment kinetics, which means that colloids, in contrast to crystalloids, have no detectable distribution phase. Marketed fluids are usually composed so that the infused volume expands the plasma volume by the infused amount. Exceptions include rarely used hyperoncotic variants and mixtures with hypertonic saline.

The main indication for colloid fluids is as second-line treatment of hemorrhage. Because of inherent allergenic properties, crystalloid electrolyte fluids should be used when the hemorrhage is small. A changeover to a colloid should be performed only when the crystalloid volume is so large that adverse effects may ensue (mild effects at 3 liters, severe at 6 liters). The only other clinical indication is that dextran can be prescribed to improve microcirculatory flow.

There has been lively debate about clinical use of colloid fluids after studies in septic patients have shown that hydroxyethyl starch increases the need for renal replacement therapy. This problem has not been found in the perioperative setting but the use of starch has still been restricted.

The colloids have defined maximum amounts that can be infused before adverse effects, usually arising from the coagulation system, become a problem.

The term *colloid fluid* refers to a sterile water solution with added macromolecules that pass through the capillary wall only with great difficulty. The osmotic strength of macromolecules is not great, so a colloid fluid must also contain electrolytes to be non-hemolytic. As long as macromolecules reside within the capillary walls their contribution to the total osmolality (the *colloid osmotic pressure*) is still sufficient to maintain a large proportion (or all) of the infused fluid volume inside the bloodstream.

Colloid fluids are used as plasma volume expanders and have a longer-lasting effect than crystalloid fluids. They carry a risk of allergic reactions not shared by crystalloid fluids. Therefore, one usually replaces smaller blood losses by crystalloid fluid, while colloids are withheld until 10–15% of the blood volume has been lost. The recommended use of colloid fluids in more specific clinical situations is further explained in many chapters in this book.

The colloids should be mixed in balanced electrolyte solutions instead of in normal saline. The reason for this is the metabolic acidosis induced by normal saline, but the changeover is important only if 2–3 liters of the colloid is administered. However, even minor acidosis from the saline in a colloid fluid adds to acidosis caused for other reasons.

Overall, the use of colloid solutions has declined in recent years. The change is due to the disclosure of

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