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A Review: Intravenous Fluid Therapy

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ABSTRACT

Fifty years after the publication of a prescription for maintenance fluid therapy, concerns have been raised about the use of hypotonic fluids in hospitalized persons. Pharmacists often challenge doctors on prescribing drugs, but fewer pharmacists challenge the prescribing of IV fluids. . Recent advances in critical care have underlined the importance of tailoring fluid input to physiological needs and hemodynamic performance. We discuss what maintenance fluid therapy is or what it is not; Types intravenous fluid devices. This article outlines key concepts about the therapy and situations in which it is used. It also describes how pharmacists can conduct treatment reviews and offers case examples showing what problems might occur.

Key words: *Intravenous Therapy, fluid maintenance, IV devices, Pharmacokinetics.*

INTRODUCTION

Formulating a fluid therapy plan for the critical small animal patient requires careful determination of the current volume status. Once a need for fluids has been established, it must be determined which fluid compartment (s) are involved in the pathology (intravascular, interstitial, or intracellular) and what components need to be supplemented or reduced in the fluids administered. The volume and rate of administration will be guided by pathologic conditions such as cardiac disease, systemic inflammatory response syndrome diseases, and fluid loss into the third body fluid space, blood pressure, and pulmonary and cerebral edema. The volume of fluid and rate of administration must be more accurate in the critically ill than in the usual hospital patient. The kidneys and cardiovascular system, which can correct most fluid therapy miscalculations, may be compromised in the critically ill animal. Fluid therapy is used to replace intravascular volume (perfusion), to replace interstitial fluid volume (dehydration), or to correct electrolyte abnormalities (hypocalcaemia, hypokalemia, hyper- or hyponatremia). It is important to understand the dynamics that occur between the fluid compartments and the specific components of each fluid to select the best fluid for the individual situation [4].

New methods and devices for administration of intravenous medications are entering the market. Providers are forced to re-evaluate current methods of delivering services to patients. This decision-making process must include an evaluation of the costs associated with each system as well as an evaluation of system characteristics.

Basic fluid physiology:

Fluid electrolyte levels in the body are kept relatively constant by several homeostatic mechanisms. Normally, fluid is gained from a person's food and drink intake (including a small amount from carbohydrate metabolism). It is lost via the urine, sweat and faeces, as well as through insensible losses via the lungs and skin. Within the body water is distributed into intracellular and extracellular compartments. The extracellular compartment comprises both interstitial and plasma compartments

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Indications of Intravenous Therapy:

1. Establish or maintain a fluid or electrolyte balance
2. Administer continuous or intermittent medication
3. Administer intravenous anaesthetics
4. Administer fluid to keep vein open (KVO)
5. Administer blood or blood components
6. Administer bolus medication
7. Maintain or correct a patient's nutritional state
8. Administer diagnostic reagents
9. Monitor hemodynamic functions

Table No. 1: Major components of body fluid

Constituent	Plasma conc. (mmol/L)	Interstitial fluid conc. (mmol/L)	Intracellular conc. (mmol/L)
Sodium	142	145	12
Potassium	4	4.1	150
Chloride	103	113	4
Bicarbonate	25	27	12

Review of normal electrolyte distribution: [9]

Sodium

- The major component of ECF
- Osmotic concentration is regulated by maintaining sodium balance and provides osmotic forces to maintain water balance in interstitial fluid compartment
- Generally, water and sodium disturbances occur simultaneously
- Sodium levels indicate overall fluid balance
- Sodium levels are regulated by the kidney, through aldosterone and other related factors

Potassium

- The major component of ICF
- 98% of total body potassium is located intracellularly
- Provides osmotic forces to maintain water balance in intracellular fluid compartment
- Plasma potassium levels may not reflect total body potassium levels! Because it is indirect measure of intracellular K^+
- Potassium imbalances result in altered function of excitable membranes (e.g., heart, CNS)
- Normal renal function is required to prevent hyperkalemia
- Hypokalemia should be treated slowly: do not exceed 0.5- 1 mEq K^+/kg/hr, also maximum concentration 40 mEq/L.

Calcium

- Vital ion in normal neuromuscular activity, cardiac rhythm and contractility, cell membrane function, and coagulation

- Highly protein bound: total plasma calcium levels vary with plasma albumin levels, however ionized calcium levels may remain constant

Chloride

- The major component of ECF
- Renal regulation of electroneutrality usually results in an inverse relationship between Cl^- and HCO_3^-
- Tends to follow Na^+, so chloride deranges, in general, do not need to be directly corrected

Bicarbonate

- Part of the major buffer system in the body
- Discussed previously (see Acid Base Physiology and Anaesthesia lecture)

Other Anions

- Plasma proteins, organic acids, sulphates
- Not routinely measured
- Constitute the "anion gap"

General Principles of Fluid Administration: [10]

Maintenance vs. replacement therapy

- Maintenance fluid therapy (plasmalyte 56, 0.45 NaCl with dextrose etc) is designed to meet the patient's ongoing sensible and insensible fluid losses with normal fluid volume over 1 – 2 days; in the normal animal this is primarily water loss, with a lesser degree of electrolyte loss.
- Replacement fluid therapy (LRS, Plasmalyte A, Normosol, 0.9 NaCl, etc) is designed to replace existing fluid deficits; this usually requires replacement of both water and electrolytes
- The optimal fluid type for each of the above settings depends upon serum electrolytes, acid-base status, and concurrent administration of drugs and blood products.

Precautions for rapid fluid administration

- In dogs, maximum fluid administration rate is 90 ml/kg/hr (1 blood volume/hour)
- In cats, maximum fluid administration rate is 60 ml/kg/hr (1 blood volume/hour)
- Monitor cardiopulmonary status carefully.
- Monitor packed cell volume and total plasma protein levels: maintain PCV > 20% and TPP > 4 g/dl

Normal fluid administration rates during anaesthesia

- Dogs, cats: 10 - 20 ml/kg/hr
- Horses, cattle: 5 - 10 ml/kg/hr

What pharmacists need to monitor in IV fluid therapy:

Pharmacists review prescribed medicines critically, but their reviewing and monitoring of IV fluids is less consistent. This is the area where the pharmaceutical expertise should systematically apply their skills. IV fluids are often administered with little regard for actual fluid and electrolyte needs, but both over and under dosing can cause serious adverse effects. Studies shows that junior doctors are responsible for prescribing of IV fluid therapy with unknown of sodium, potassium contents. Pharmacists should validate intravenous fluid prescription as thoroughly as drug prescriptions. They are required to review drug therapy for patients, but if this review is undertaken without assess through all clinical information related to patient, it is simply a prescription review.

A comprehensive treatment review should undertake with the knowledge of patients diagnosis and pathophysiological status. Reviewing one prescribed atom or section of prescription (parentral or non-parentral) in isolation does not provide clear picture of patient's treatment.

The problems undertaken by pharmacists are

- How the drugs are to be administered (i.e.; what type of pump will be used)
- Whether drugs are to be administered through center or peripheral line
- Whether more than one drug is intended to be administered at the same time

Intravenous access devices:

Needle and syringe:

The simplest form of intravenous access is a syringe with an attached hypodermic needle. The needle is inserted through the skin into a vein, and the contents of the syringe are injected through the needle into the bloodstream. This is most easily done with an arm vein, especially one of the metacarpal veins. Usually it is necessary to use a tourniquet first to make the vein bulge; once the needle is in place, it is common to draw back slightly on the syringe to aspirate blood, thus verifying that the needle is really in a vein; then the tourniquet is removed before injecting

Peripheral IV lines:

This is the most common intravenous access method in both hospitals and pre-hospital services. A **peripheral IV line** consists of a short catheter (a few centimeters long) inserted through the skin into a peripheral vein, any vein that is not in the chest or abdomen. There are times; however, when underlying physiological factors (obesity, peripheral vascular disease and IV drug abuse, to name a few) make insertion into any available vein a medical necessity particularly if the patient is exsanguinations. The adage "time is tissue" should be paramount during times like these or if the patient is at risk for a cardiac event. Arm and hand veins are typically used although leg and foot veins are occasionally used. Veins in the arm are the common site in emergency settings, commonly performed by paramedics and emergency physicians. On infants the scalp veins are sometimes used. The part of the catheter that remains outside the skin is called the connecting hub; it can be connected to a syringe or an intravenous infusion line, or capped with a bung between treatments. Ported cannulae have an injection port on the top that is often used to administer medicine. The caliber of cannula is commonly indicated in gauge, with 14 being a very large cannula (used in resuscitation settings) and 24-26 the smallest. The most common sizes are 16-gauge (midsize line used for blood donation and transfusion), 18- and 20-gauge (all-purpose line for infusions and blood draws), and 22-gauge (all-purpose pediatric line). 12- and 14-gauge peripheral lines actually deliver equivalent volumes of fluid faster than central lines, accounting for their popularity in emergency medicine; these lines are frequently called "large bores" or "trauma lines".

Blood can be drawn from a peripheral IV if necessary, but only if it is in a relatively large vein and only if the IV is newly inserted. Blood draws are typically taken with specialized IV access sets known as phlebotomy kits, and once the draw is complete, the needle is removed and the site is not used again. If a patient needs frequent venous access, the veins may scar and narrow, making any future access extremely difficult or impossible; this situation is known as a "blown vein," and the person attempting to obtain the access must find a new access site proximal to the "blown" area.

Central IV lines:

Central IV lines flow through a catheter with its tip within a large vein, usually the superior vena cava or inferior vena cava, or within the right atrium of the heart. This has several advantages over a peripheral IV:

- It can deliver fluids and medications that would be overly irritating to peripheral veins because of their concentration or chemical composition. These include some chemotherapy drugs and total parenteral nutrition.
- Medications reach the heart immediately, and are quickly distributed to the rest of the body.
- There is room for multiple parallel compartments (lumen) within the catheter, so that multiple medications can be delivered at once even if they would not be chemically compatible within a single tube.
- Caregivers can measure central venous pressure and other physiological variables through the line.

Central IV lines carry risks of bleeding; infection, gangrene, and gas embolism (see Risks below). Gangrene is likely if the injection accidentally hits an artery. There are several types of central IVs, depending on the route that the catheter takes from the outside of the body to the vein.

Peripherally inserted central catheter:

PICC lines are used when intravenous access is required over a prolonged period of time, as in the case of long chemotherapy regimens, extended antibiotic therapy, or total parenteral nutrition.

The PICC line is inserted into a peripheral vein using the Seldinger technique under ultrasound guidance, usually in the arm, and then carefully advanced upward until the catheter is in the superior vena cava or the right atrium. This is usually done by feel and estimation; an X-ray then verifies that the tip is in the right place. A PICC may have two parallel compartments, each with its own external connector (double-lumen), or a single tube and connector (single-lumen). Triple connectors (triple-lumen) catheters and power-inject able PICCs are now available as well. From the outside, a single-lumen PICC resembles a peripheral IV, except that the tubing is slightly wider.

The insertion site must be covered by a larger sterile dressing than would be required for a peripheral IV, due to the higher risk of infection if bacteria travel up the catheter. However, a PICC poses less of a systemic infection risk than other central IVs, because bacteria would have to travel up the entire length of the narrow catheter before spreading through the bloodstream.

The chief advantage of a PICC over other types of central lines is that it is easy to insert, poses a relatively low risk of bleeding, is externally unobtrusive, and can be left in place for months to years for patients who require extended treatment. The chief disadvantage is that it must travel through a relatively small peripheral vein and is therefore limited in diameter, and also somewhat vulnerable to occlusion or damage from movement or squeezing of the arm.

Central venous lines:

There are several types of catheters that take a more direct route into central veins. These are collectively called *lines. In* the simplest type of central venous access, a catheter is inserted into a subclavian, internal jugular, or (less commonly) a femoral vein and advanced toward the heart until it reaches the superior vena cava or right atrium. Because all of these veins are larger than peripheral veins, central lines can deliver a higher volume of fluid and can have multiple lumens.

Another type of central line, called a Hickman line or Broviac catheter, is inserted into the target vein and then "tunneled" under the skin to emerge a short distance away. This reduces the risk of infection, since bacteria from the skin surface are not able to travel directly into the vein; these catheters are also made of materials that resist infection and clotting.

Implantable ports:

A *port* (often referred to by brand names such as *Port-a-Cath* or *MediPort*) is a central venous line that does not have an external connector; instead, it has a small reservoir that is covered with silicone rubber and is implanted under the skin. Medication is administered intermittently by placing a small needle through the skin, piercing the silicone, into the reservoir. When the needle is withdrawn the reservoir cover reseals itself. The cover can accept hundreds of needle sticks during its lifetime. It is possible to leave the ports in the patient's body for years; if this is done however, the port must be accessed monthly and flushed with an anti-coagulant, or the patient risks it getting plugged up. If it is plugged it becomes a hazard as a thrombus will eventually form with an accompanying risk of embolisation. Removal of a port is usually a simple outpatient procedure; however, installation is more complex and a good implant is fairly dependent on the skill of the radiologist. Ports cause less inconvenience and have a lower risk of infection than PICCs, and are therefore commonly used for patients on long-term intermittent treatment.

Types of Fluids Available & General Indications for their use: [11]

I. Crystalloid: a solution of crystalline solid dissolved in water

II. Colloids: a suspension of particles in a liquid ie, does not cross a semi permeable membrane, so exerts a colloid osmotic (oncotic) pressure

Crystalloids: Replacement fluids

- Generally are polyionic isotonic fluids
- Ringer's, Lactated Ringer's (LRS), PlasmaLyte 148, PlasmaLyte A are all polyionic isotonic crystalloid fluids that *closely mimic plasma electrolyte concentrations* (with or without bicarbonate precursors)
- 0.9% NaCl (normal saline) is an isotonic solution of Na, Cl, and water
- 5% dextrose is an isotonic solution of dextrose in water; the dextrose is rapidly metabolized, thus this essentially *results in the administration of free water*
- Commonly administered during general anesthesia to diminish the cardiovascular effects of anesthetic drugs and replace ongoing fluid losses
- Usually administered at 10-20 ml/kg/hr in small animal
- Usually administered at 5-10 ml/kg/hr in large animals
- May need to infuse 40 – 90 ml/kg/hr during shock using multiple catheters or fluid pumps
- Replace acute blood loss by administering 3 volumes of crystalloid solution for each 1 volume of blood lost

Crystalloids: Maintenance fluids

- Are hypotonic crystalloids that are low in sodium, chloride, and osmolality, but high in potassium compared to normal plasma compositions?
- May or may not contain dextrose
- Generally polyionic isotonic or hypotonic fluids
- Used for *long term fluid therapy*, such as the ICU setting; not generally used during anesthesia
- e.g., 0.45 % sodium chloride, 2.5 % dextrose with 0.45 % saline, 2.5 % dextrose with half strength LRS, Normosol M, Normosol M in 5 % dextrose, PlasmaLyte 56 in 5% dextrose, and Plasmalyte 56 (see Table 2).

Hypertonic fluids

- Hypertonic crystalloid saline (7.5% NaCl) has been indicated in some shock states to maintain cardiovascular function; pulls fluid into intravascular space by osmosis by creating transient hypernatremia. Dose is 4 ml/kg. Must follow with isotonic, polyionic fluids
- Generally used to treat particular deficits (e.g., 10% dextrose given to a hypoglycemic neonatal foal) or to treat edema (e.g., mannitol; colloid)

Table No. 2: Composition of Several Crystalloid Fluids

Solution	Type*	Na	Cl	K	Ca	Mg	Lact	Acet	Gluc	% Dex	pH	Osm
Plasma	-	144	107	5	5	1.5	-	-	-	-	7.5	290
2.5% Dextrose, 0.45% NaCl	M	77	77	-	-	-	-	-	-	2.5	4.0	280
2.5% Dextrose, 1/2 strength LRS	M	65.5	55	2	1.5	-	14	-	-	2.5	5.0	263
5% Dextrose	-	-	-	-	-	-	-	-	-	5	4.0	252
10% Dextrose	-	-	-	-	-	-	-	-	-	10	4.0	505
0.9% NaCl	R	154	154	-	-	-	-	-	-	-	5.0	308
Ringer's Soln	R	148	156	4	4.5	-	-	-	-	-	6.0	309
LRS	R	130	109	4	3	-	28	-	-	-	6.5	273
PlasmaLyte A	R	140	98	5	-	3	-	27	23	-	7.4	294
PlasmaLyte 148	R	140	98	5	-	3	-	27	23	-	5.5	294
PlasmaLyte 56 + 5% Dextrose	M	40	40	16	-	3	-	16	-	5	5.0	362
PlasmaLyte 56	M	40	40	13	-	3	-	16	-	-	5.5	110

Ions are presented as mEq/L; *M = Maintenance; R = Replacement

Colloids

- Synthetic colloids are polydisperse (various molecular weight) and do not readily cross semipermeable membrane.
- Hypertonicity pulls fluids into the vascular space and increase blood volume which effect is longer lasting compared to crystalloid therapy.
- Smaller volumes of colloids are as effective as larger volumes of crystalloids in maintaining intravascular fluid volume
- Historically have had a number of problems associated with their use, including allergic reactions, impaired coagulation, and renal damage; solutions available now have less problems associated with their use
- Expensive compared to crystalloids

Table No. 3: Composition of Several Colloidal Fluids

Solution	Na	Cl	k	Ca	Colliod	COP (mmHg)	pH	Osm
plasma	144	107	5	5	-	-	7.5	290
Hetastarch 6 % in 0.9 % NaCl	154	154			Hydroxyethylated amylopectic 60 g/L MW 450 KD	31	5.5	310
7.5 % NaCl-6% dextran 70	1283	1283			-	75	4-5	2567
Dextran 70 in 0.9 % NaCl					Dextran 60 g/L MW 70 KD	>100	5.0	309

Table No. 4: Fluid Type and Volume Ratio for Plasma Volume Restoration

Fluid Type	Examples	Volume needed to increase plasma volume by 1 liter	Distribution	Examples of clinical indication
Colloid	Starch Gelatin Dextrans	1 liter	Plasma volume	Hypovolemia, hypotension, normovolemic hemodilution, hypoalbuminemia
Hypertonic crystalloid	7.5 % saline	300 ml	Immediate plasma volume expansion causing ICFV reduction	Hypovolemic shock, cerebral edema
Hypotonic crystalloid	5 % dextrose	14 liters	Total body weight	Free water deficit, hypernatremia
Isotonic crystalloid	0.9 % NaCL, LRS	3 liters	ECFV (plasma volume and ISFV expansion)	Dehydration, hypovolemia, hypotension, normovlemic hemodilution

Blood and blood components:

Whole blood

- Contains it all: colloids (plasma proteins), clotting factors including platelets, red blood cells for oxygen carrying capacity
- Relatively easy to collect and store
- *Indications*: acute blood loss, concurrent anemia, hypoproteinemia and clotting defects
- Stored blood is not quite as useful as fresh blood: reduced oxygen carrying capacity (review 2, 3-DPG), platelets are inactive, clotting factors may be degraded
- A blood filter must be always used to sieve microthrombi from the blood product.
- 5 – 15 ml/kg/hr rate is used to treat acute hypovolemia, and 40-60 ml/kg/hr can be used in life-threatening emergency.
- In massive transfusion, defined as blood volume replacement greater than 1.5 times the recipient volume, abnormal bleeding may occur.
- This homeostatic defects is characterized by oozing from the operative wound, mucous membranes, and intravenous puncture sites.
- Blood types and crossmatching
- Crossmatching between donor and recipient will minimize a fatal outcome.
- There are about 12 types in dogs but DEA 1.1, 1.2, 1.7 are most antigenic.
- Cats have AB blood group system; the most common being type A.
- Always administer slowly in the beginning so as to allow adequate time to detect any adverse reactions, such as rashes, edema, vomiting, fever, DIC, dyspnea, hypotension, unconsciousness and tachycardia

Packed red blood cells

- Red cell fraction of separating plasma from whole blood
- Usually has a PCV of 70%
- Useful in treating *anemia*
- Reduces risk of fluid overload
- Reconstitute with equal volumes of 0.9% saline
- Two types: fresh or frozen
- *Fresh plasma* contains colloids, active platelets, and clotting factors
- Useful in treating coagulation defects
- *Frozen plasma* can be stored for periods up to a year; serve as a source of colloids (plasma proteins); often collected from stored whole blood when the red cell fraction is no longer viable
- Useful in treating hypoproteinemia and maintaining normal colloidal osmotic pressure

Principles of blood and plasma transfusions

- Consider transfusion if PCV < 20% and/or TPP < 4 gm/dl
- Transfuse appropriate blood components
- Administration rate: < 10 ml/kg/hr (unless in crisis)

Complications of blood and plasma transfusions

- Immune response to red cell antigens
- Immune response to white cell antigens
- Coagulation defects
- Citrate intoxication
- Hyperkalemia
- Hypothermia
- Sepsis

Blood substitutes - **Oxyglobin**

- Purified bovine hemoglobin in lactated ringer's solution
- Does not contain red blood cells - instead contains cross linked haemoglobin molecules
- Plasma half life is 30-40 hours
- Approved for use in dogs but may also be used in other species
- Provides oxygen-carrying capacity and oncotic pressure (consists of large protein molecules) - improves oxygenation and provides volume expansion
- Haemoglobin molecules disperse throughout the plasma and provide oxygen to the tissues, and oxyglobin molecules disperse throughout the small vessels more readily due to smaller size, and therefore provide better oxygenation at the microcirculatory ends (see figure above).
- Advantages over whole blood or packed red cells
- Don't need to maintain donors
- Long shelf life - 2 years
- Doesn't require refrigeration
- Doesn't require blood typing or cross matching
- No risk of bacterial or viral contamination
- Few reported adverse effects
- Immediate availability a major advantage over blood products in crisis situations
- Disadvantages
- doesn't provide other components of whole blood that may be desired in some conditions – e.g. clotting factors
- Analogous product, ***Hemopure*** is undergoing FDA trials for use in human medicine
- Biopure Inc. reduced the manufacturing of Oxyglobin substantially in 2004, so current supply is very limited.

Assessing Requirements: [12]

Patient's medical histories give an indication of their expected fluid status. Causes of dehydration include preoperative fasting, ongoing gastrointestinal illness and self neglect following acute confusion. Knowing a detailed diagnosis is vital to gain information on the likely composition of the fluid lost. Practioners also need to be aware of any concurrent conditions that can alter fluid distribution or make patients more susceptible to adverse effects from fluid therapy.

Identifying dehydration:

- Thirst
- Reduced skin turgor(elasticity)
- Dry mucous membranes
- Increase capillary refill time
- Altered level of consciousness

If a patient is suffering from fluid depletion, then the heart rate will increase to improve cardiac output and raise blood pressure here by maintaining the tissue oxygenation. BP falls after the intravascular volume has dropped to 20-30 percent. Urine becomes concentrated in the case of volume depletion and sometimes it results in the fall in urine output.

Fluid balance:

An accurately monitored fluid balance of overall intake and output is vital to tailor fluid administration. Losses via urine, drains, stoma or nasogastric aspirates should be documented. In addition, insensible losses via the respiratory tract and skin should be estimated and compared with patients normal physiological requirements. It is important to interpret all observations in the context of a patients clinical diagnosis- an oedematous patient may show a positive fluid balance but still be intravascularly depleted, resulting in insufficient tissue perfusion and oxygenation.

Special considerations:

Some pathological conditions require special consideration. Patients with major burns require copious amounts of IV fluids, calculated according to the body weight and percentage of the body surface that is affected. In traumatic brain injury, fluid volume may be adjusted according to mean arterial pressure because this is related to cerebral perfusion pressure. Large amounts of IV fluids are also often required following trauma or septic peritonitis. Fluid administration has to be particularly carefully balanced in individuals with heart failure, renal impairment or apparent respiratory failure.

Conditions That Benefit From Fluid Therapy

- Dehydration
- Hypovolemia / Hypovolemic shock
- Decreased intake
- Increased losses
- Electrolyte disorders

CONCLUSION

As with all medicines that we prescribe, it appears that even common intravenous solutions carry a certain amount of risk that must be assessed against the presumed benefit when choosing among fluids for an individual patient. As more attention has been focused on fluid resuscitation and the consequences thereof, the science of fluid administration has been evolving very rapidly [13]. There are now crystalloid-based intravenous solutions that include ethyl pyruvate as a mediator to alter the inflammatory response, and thus improve survival in preclinical models of sepsis and shock [14, 15]. New biological effects of colloids have been discovered such that albumin may improve antioxidant capacity in critically ill patients [16], and starch solutions may favorably influence the microcirculation. The ultimate clinical benefit of these basic science findings remains to be defined, although preclinical models have suggested that specific colloid administration may adequately modulate the inflammatory response to prevent the development of lung injury after shock. In the meantime, certain colloid solutions, particularly albumin, are growing as products for niche use, with data either confirming or suggesting clinical improvements for conditions, such as spontaneous bacterial peritonitis, ascites, and acute lung injury.

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