and oncotic pressure gradients across the capillary walls as the determinant of the fluid – i.e. volume fusion. This effect is possibly also relevant in certain cases of acute liver failure with rapidly increasing amino acid mixture are the methods of choice for the treatment of protein malnutrition as such, though with a given amino acid mixture. For infants, the amino acid content does not exceed 200 mg/100 mL. The solution is stabilized with 0.08 m mole of sodium acetylglucosamine plus 0.08 m mole of sodium caprylate per gram of albumin. The solution contains no preservative.

CLINICAL PHARMACOLOGY (13, 17)

Albumin (Human) 25% solution, AlbuRx™ 25 should not be used as an intravenous nutrient because of the slow breakdown and relatively unfavorable composition of the albumin molecule with respect to its content of essential amino acids. Oral provision of proteins or an intravenous regimen providing adequate calories and a suitable amino acid mixture are the methods of choice for the treatment of protein malnutrition as such, though they may not prevent the rapid correction of hypoproteinemia.

The binding properties of albumin may provide an indication for its use in severe hemolytic disease of the newborn, where it may lower the plasma concentration of free bilirubin pending an exchange transfusion. This effect is possibly also relevant in certain cases of acute liver failure with rapidly increasing serum bilirubin.

The colloid oncotic or oncoprotein properties of albumin at this moment constitute the predominant reason for its clinical use. The rationale for this is the Starling concept of the capillary balance of hydrostatic and oncotic gradients across the capillary walls as the determinant of the fluid – i.e. volume distribution – between the interstitial and the intravascular compartment (16). The two main indications for the use of AlbuRx™ 25 are therefore a plasma or blood volume deficit and the oncotic deficit resulting from hypoproteinemia. The 25% concentration is oncotically equivalent to approximately five times its volume of normal human plasma. The effective colloid osmotic pressure of the serum proteins depends very largely on the relative size and numerous albumin molecules, which therefore play a decisive role in the maintenance of the circulating plasma volume.

INDICATIONS AND USAGE

General Principles (17)

Volume Deficit
Since the oncotic pressure of AlbuRx™ 25 is about four times higher than that of normal human serum, it will correct an acute volume deficit if interstitial water enters into the capillary walls. However, many patients suffering from an acute volume deficit also have some degree of interstitial dehydration. In the absence of hyperfusion, the treatment of an acute volume deficit with AlbuRx™ 25 should include isotonic electrolyte solutions in an albumin electrolyte ratio of 1:3 or 1:4. By contrast, chronic volume deficits have usually been at least partially compensated for by the renal retention of sodium and water with some degree of tissue edema, and in these circumstances a trial with AlbuRx™ 25 is only indicated. In any case, an anemia of clinically relevant magnitude requires specific treatment, and the metabolic needs of the patient with respect to fluid and electrolytes must be considered.

Oncotic Deficit
The common causes of hypoproteinemia are protein-calorie malnutrition, defective absorption in gastrentestinal disorders, faulty albumin synthesis in chronic hepatic failure, increased protein catabolism postoperatively or with sepsis, and other causes. Albumin with chronic kidney disease. In all these settings, the circulating albumin mass is initially maintained by a gradual transfer of extravascular albumin to the circulation, and hypoproteinemia ensues only when this compensatory potential has been exhausted. This process usually requires an extravascular albumin deficit of equal magnitude as the measurable intravascular deficit, which must be allowed for if AlbuRx™ 25 is infused because of the capillary permeability of that tissue.

The primary sequel of the oncotic deficit resulting from hypoproteinemia is a loss of plasma and oncotic pressure which may be returned almost to normal when the interstitial hydrostatic pressure increases sufficiently to compensate for the decrease of the serum oncotic pressure. This chain of events is accelerated by the infusion of crystalloid fluids. The plasma volume is maintained at the price of interstitial edema (2).

With restoration of normal capillary function, a close relationship exists once again between infused Albumin (Human) and resultant increase in plasma oncotic pressure. A goal should be sought of maintaining a plasma albumin concentration of about 2.5 g/dL or 50 mL% and a plasma oncotic pressure of 20 mmHg (equal to a TSP concentration of 5.2 g/100 mL) (17). In the presence of extensive granulating wounds, a daily loss of up to 30 g of albumin may continue into the late post-burn period (13). Protein-rich oral feedings, or adequate parenteral nutrition should be included in the overall regimen to the fullest possible extent, though such treatment does not permit the rapid correction of an oncotic deficit.

Acute Circumstances in whichAlbumin (Human) 25% solution, AlbuRx™ 25 may use be appropriate.

Acute Respiratory Distress Syndrome
Several factors are usually involved in the development of the state now commonly called the adult respiratorystress distress syndrome, one of these being a hypoproteinemic fluid overload. If present, this may be correct by the use of AlbuRx™ 25 and a diuretic (14, 17).

Cardiopulmonary Bypass
An adequate blood volume during cardiopulmonary bypass can be maintained with crystalloids as the only pump priming fluid, but only at the price of interstitial edema. A commonly employed program is an AlbuRx™ 25 and crystalloid pump prime adjusted so as to achieve a hematocrit of 20% and a plasma oncotic pressure level of 2.5 g/dL in the patient, but the level to which either may be lowered safely has not yet been defined (17).

Anaphylactic Shock
Patients undergoing major surgery may lose more than half of their circulating albumin mass (6, 9, 15), and complications attributable to an oncotic deficit may occur in such cases, as well as in septic and intensive care patients. Oncotic therapy with AlbuRx™ 25 may therefore be indicated in such patients, according to the principles outlined in 3.1.2. Temporary redistribution of protein is usually not an indication for Albumin (Human).

Third Space Problems of Infectious Origin
An oncotic deficit of protein-rich fluid during acute peritonitis, pancreatitis, mediastinitis or extensive cellulitis may be of sufficient magnitude to require the treatment of a volume or an oncotic deficit with AlbuRx™ 25 (3), although this occurrence is relatively rare.

Acute Liver Failure
In acute liver failure, AlbuRx™ 25 may serve the triple purpose of stabilizing the circulation, correcting an oncotic deficit and binding excessive serum bilirubin. The therapeutic approach is guided by the individual circumstances (17).

Acute Nephrosis
Patients with acute nephrosis may prove refractory to cyclophosphamide or steroid therapy and their edema may even be aggravated initially by steroids. In such cases, a response may be elicited by combining 20-25% Albumin (Human) with standard electrolyte solutions, though this combination should be repeated daily for about one week, after which the patient may react satisfactorily to drug therapy (17).

Acutes
The use of AlbuRx™ 25 for blood volume support may be indicated if circulatory instability follows the withdrawal of acut fluid.

Red Cell Resuspension Media
The use of Albumin (Human) for resuspending red cells can be dispensed with. In exceptional circumstances such as certain types of exchange transfusions and the use of very large volumes of erythrocyte concentrates and frozen or washed red cells, the addition of AlbuRx™ 25 to the red cell resuspension medium may be indicated to provide sufficient oncotic pressure for protein transport during the subsequent transfusion. If necessary, 20-25% or more of Albumin (Human) per liter of red cell suspension should be added as a concentrated solution to the isotonic, electrolyte solution used as the resuspension of erythrocytes immediately before transfusion, the individual dosage depending on the TSP level of the recipient.

Renal Dialysis
Patients undergoing long-term hemodialysis may need AlbuRx™ 25 for the treatment of a volume or an oncotic deficit. As a rule, the initial dose should not exceed 100 mL of a 20-25% solution, and the patient should be carefully observed for signs of a circulatory overload, to which they are particularly sensitive.

Hemolytic Disease of the Newborn
AlbuRx™ 25 may be indicated in order to bind and thereby detoxify free bilirubin in severely affected infants pending an exchange transfusion.

Circumstances in which AlbuRx™ 25 use is not justified
For the reasons set forth in sections 2. and 3.1, there is no valid reason for the use of AlbuRx™ 25 as an intravenous nutrient or for treating the stabilized hypoproteinemia accompanying chronic cirrhosis, chronic nephrosis, protein-losing enteropathy, malnutrition and pancreatic insufficiency.

However, if a patient in this category has to cope with a superimposed acute stress, e.g. anesthesia, surgery with extensive hemorraghes, the patient’s hemodynamic state, oncotic deficit and fluid balance should be carefully assessed and the appropriate steps taken as indicated by the individual circumstances.

CONTRAINDICATIONS
The only specific contraindication to the use of AlbuRx™ 25 is a history of an incompatibility reaction to Albumin (Human) in the individual recipient (see ADVERSE REACTIONS).

WARNINGS
AlbuRx™ 25 is MADE FROM HUMAN PLASMA. PRODUCTS MADE FROM HUMAN PLASMA MAY CONTAIN INFECTIONOUS AGENTS, SUCH AS VIRUSES, THAT CAN CAUSE DISEASE. THE RISK THAT SUCH PRODUCTS WILL TRANSMIT AN INFECTIOUS AGENT HAS BEEN EXTREMELY REDUCED BY SCREENING Plasma donors for prior exposure to certain viruses, by testing for the presence of specific virus infection antibodies, and by fractionation and inactivation of viruses. ALBUMIN (HUMAN) IS TREATED THROUGH ALCOHOL FRACTIONATION AND THROUGH HEAT TREATMENT OF THE PRODUCT IN THE FINAL CONTAINER FOR 10 HOURS AT 60°C. DESPITE THESE MEASURES, SUCH PRODUCTS CAN STILL POTENTIALLY TRANSMIT DISEASE. A THEORETICAL RISK FOR TRANSMISSION OF CREUTZFELDT-JAKOB DISEASE (CJD) IS CONSIDERED EXTREMELY REMOTE. NO CASES OF TRANSMISSION OF VIRAL DISEASES OR CID HAVE EVER BEEN IDENTIFIED FOR ALBUMIN (HUMAN). THERE IS ALSO THE POSSIBILTY THAT UNKNOWN INFECTIOUS AGENTS MAY BE PRESENT IN SUCH PRODUCTS. ALL INFEC TIONS THOUGHT BY A PHYSICIAN POSSIBLY TO HAVE BEEN TRANSMITTED BY THIS PRODUCT SHOULD BE REPORTED BY THE PHYSICIAN OR OTHER HEALTHCARE PROVIDER TO ZLB BEHRING AT 800-504-5434. THE PHYSICIAN SHOULD DISCUSS THE RISKS AND BENEFITS OF THIS PRODUCT WITH THE PATIENT.

TURID SOLUTIONS MUST NOT BE USED. DO NOT BEGIN ADMINISTRATION MORE THAN 4 HOURS AFTER INTRODUCTION OF THE ADMINISTRATION SET. PARTIALLY USED BOTTLES MUST BE DISCARDED. THERE EXISTS A RISK OF POTENTIALLY FATAL HEMOLYSIS AND ACUTE RENAL FAILURE FROM THE INAPPROPRIATE USE OF STERILE WATER FOR INJECTION AS A DILUENT FOR AlbuRx™ 25. ACCEPTABLE DILUENTS INCLUDE 0.9% SODIUM CHLORIDE OR 5% DEXTROSE IN WATER.

PRECAUTIONS
Adequate precautions should be taken against circulatory overload and may include pulmonary auscultation or X-ray as well as monitoring the central venous or pulmonary artery wedge pressure. Special caution is indicated in patients with stabilized chronic anemia, congestive heart failure and renal insufficiency.
Pregnancy Category C. Animal reproduction studies have not been conducted with Albumin (Human) 25% solution, AlbuRx™ 25. It is also not known whether AlbuRx™ 25 can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. AlbuRx™ 25 should be given to a pregnant woman only if clearly needed. There is, however, no evidence for any contraindication to the use of AlbuRx™ 25 specifically associated with reproduction, pregnancy or the fetus. Use an intravenous infusion set suitable for the infusion of blood and blood products.

ADVERSE REACTIONS
Since AlbuRx™ 25 is sterile when coming from the manufacturer, bacterial contamination with the risk of post-infusion septicemia can only occur if the container has been damaged or following puncture of the rubber cap (see WARNINGS). Though very rare, non-septic incompatibility reactions including nausea, chills, fever, urticaria, headache and hypotension following the administration of albumin-containing preparations have been recorded (8, 11, 12, 17). A favorable response was observed to the intravenous administration of 50 to 100 mg of prednisolone (12).

DOSEAGE AND ADMINISTRATION
AlbuRx™ 25 must be administered intravenously. The venipuncture site should not be infected or traumatized, and should be prepared with standard aseptic technique. The solution is compatible with whole blood or packed red cells as well as the usual electrolyte and carbohydrate solutions intended for intravenous use. By contrast, it should not be mixed with protein hydrolysates, amino acid mixtures, or solutions containing alcohol. It is ready for use as contained in the bottle and may be given without regard to the blood group of the recipient.

The dosage of AlbuRx™ 25 is based on the principles outlined in the section on indications but should always be adapted to the individual situation. The quantities required may be underestimated because of hidden extravascular deficits, and the effect of AlbuRx™ 25 infusion on the serum protein level should therefore be checked by laboratory analysis.

Volume Deficit
The appropriate AlbuRx™ 25 dose for the treatment of a volume deficit should be estimated from the recipient’s hemodynamic response (7), supplemented with the established safeguards against a circulatory overload. In the absence of active hemorrhage, the total dose should at any rate not exceed the normal circulating albumin mass, i.e. 2 g per kg body weight.

Oncotic Deficit
The appropriate AlbuRx™ 25 dose in grams of protein for the correction of an oncotic deficit can, as an average, be estimated from the difference between the desired and the actual TSP level x plasma volume (~40 mL/kg) x 2, the latter factor allowing for the hidden extravascular deficit. The individual effect is, however, variable and should be checked by measuring the post-infusion TSP level (10, 17).

Hemolytic Disease of the Newborn
The appropriate AlbuRx™ 25 dose for the binding of free serum bilirubin in severely hemolytic infants is 1 g/kg body weight, to be given about one hour prior to the exchange transfusion, and caution is recommended in hypervolemic infants.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

HOW SUPPLIED
AlbuRx™ 25 is supplied in 50 mL (NDC 44206-251-05) and 100 mL (NDC 44206-251-10) vials, with circular.

STORAGE
AlbuRx™ 25 should be stored at a temperature not exceeding 30°C (86°F). It should not be used after the expiration date printed on the label.

REFERENCES
8. Lowenstein, E.: In: Sgouris and René (Ref. 13), p. 302

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