**Albumin in the Emergency Department**

**A Clinical Scenario**

A 70-year-old woman presents to the Emergency Department (ED) with an episode of collapse at the supermarket. A bystander calls an ambulance and by the arrival of paramedics a few minutes later the patient is lucid and responsive. She is found to be Hypotensive (91/50), Febrile (38.9 degrees), Tachycardic (105) and has an increased Respiratory Rate (>25).

On arrival in the ED she is seen quickly by the medical team and started on the local “Sepsis Pathway” after receiving an ATS triage category 2.

She states that she has recently been diagnosed with Liver Cirrhosis and Atrial Fibrillation. On a recent admission her Albumin Level was low and associated with deranged Liver Function Tests (LFTs). On examination she is found to have bilateral swelling of both lower limbs with associated asymmetrical cellulitis (worse in the left leg).

Having been diagnosed with Sepsis associated with the cellulitis she is started on appropriate broad spectrum antibiotics. The Albumin level today is 17 (Reference Range 35-50 g/L) and the patient remains hypotensive after a 20ml/kg crystalloid bolus. The patient was given 4 units of Albumin over a 3 hours with some evidence of improvement in their haemodynamics.

**This case scenario raises a number of questions regarding fluid resuscitation and hypoalbuminaemia which we will discuss:**

**What exactly is albumin?**

- **Albumin** = Is a water-soluble, globular protein of molecular weight 65,000
- **Albumin** = Is a ‘Colloid’
  - A Colloid fluid refers to substances of large molecular weight (e.g. >30,000) in a solution.
  - In humans plasma proteins are the main colloid
- In normal physiological conditions the liver produces around 200 mg/kg per day of albumin
- **Albumin** = 80% of normal plasma colloid oncotic pressure
- **Albumin** = 50% of protein content in serum
- **Albumin** = a weak acid
  - **Albumin** = is a major unmeasured anion and contributes much of the value of the anion gap. Every ’10’ decrease in albumin the anion gap (AIG) will go down by about 2.5. For every 10 below the Normal Albumin add 2.5 to the Anion Gap
  - *Normal Albumin is 40g/L so for an Albumin of 30 add 2.5 to AIG
• **Albumin** = has a ½ life in plasma of 20 days (infusions are redistributed after 1 week)

**Albumin** = Has multiple important physiological functions:

<table>
<thead>
<tr>
<th>Vascular</th>
<th>Transport</th>
<th>Metabolic</th>
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<tr>
<td>• Maintenance of oncotic pressure&lt;br&gt;• Microvascular integrity&lt;br&gt;• Hormones (steroids, thyroxine)&lt;br&gt;• Fatty acids&lt;br&gt;• Bile salts&lt;br&gt;• Bilirubin&lt;br&gt;• Ca²⁺, Mg²⁺, and other metals (copper, zinc)&lt;br&gt;• Drugs: - warfarin&lt;br&gt; - diazepam&lt;br&gt;• Acid–base balance&lt;br&gt;• Antioxidant&lt;br&gt;• Anticoagulant</td>
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**What is the association with a low serum albumin and Mortality?**


*Mortality prediction at admission to intensive care: a comparison of microalbuminuria with acute physiology scores after 24 hours.*

Goaling P, Brudney S, McGrath L, Ribeiro S, Manji M.

• Albumin is associated with an increased mortality in many prospective cohort studies and has been shown to be as good as the traditional APACHE II and SAP II mortality scores in predicting outcome in Surgical, Burns and Trauma patients.

• Low albumin may be an independent predictor of poor outcomes when taken in the Emergency Department for Trauma patients

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**What are the causes of a low albumin (Hypoalbuminaemia)?**

(1) **Reduced Synthesis of Albumin**

• Liver Disease
• Acute Phase Response (increased vascular permeability due to sepsis, trauma or surgery)
• Malnutrition or Malabsorption
• Malignancy
(2) Increased Loss of Albumin
- Nephrotic Syndrome
- Enteropathy (protein-losing)
- Burns

(3) Haemodilution
- Pregnancy
- Postural
- Pseudohypoalbuminaemia (drip arm)

Should we replace albumin in Emergency Department patients?

The patient described above would seem a reasonable patient to replace albumin for in the first instance. She has significant liver disease and now presents with septic shock. However, she has no ascites and spontaneous bacterial peritonitis (SBP) seems less likely. We discuss the overall paucity of evidence for albumin in Critical Care below. Given its cost, many have concluded that it should be restricted to highly specific indications. In the Emergency Department these may include the following:

- Liver disease (associated with renal dysfunction)
- Drainage of Ascites (with significant volume)
- SBP
- Sepsis (in specific circumstances)
- The use of albumin in burns patients, trauma, surgical and other medical patients may be best limited to judicious use in the Intensive Care Unit or Ward setting.
**Suggested Possible Indications for an Albumin Infusion** (Liumbruno et al)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Notes</th>
<th>GoR</th>
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<tbody>
<tr>
<td><strong>Appropriate indications (for which there is widespread consensus)</strong></td>
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<td>Paracentesis</td>
<td>5 g of albumin/L ascitic fluid removed, after paracentesis of volumes &gt; 5 L.</td>
<td>1C+</td>
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<td>Therapeutic plasmapheresis</td>
<td>For exchanges of &gt; 20 mL/kg in one session or &gt; 20 mL/kg/week in more than one session.</td>
<td>2C+</td>
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<td>Spontaneous bacterial peritonitis</td>
<td>In association with antibiotics.</td>
<td>1C+</td>
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<td><strong>Occasionally appropriate indications (when other criteria are fulfilled)</strong></td>
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<td>Heart surgery</td>
<td>Last-choice treatment after crystalloids and non-protein colloids.</td>
<td>2C+</td>
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<tr>
<td>Major surgery</td>
<td>Albumin should not be used in the immediate post-operative period.</td>
<td>2C+</td>
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<tr>
<td>Cirrhosis of the liver with refractory ascites</td>
<td>Generally ineffective, except in patients with serum albumin &lt; 2 g/dL.</td>
<td>2C</td>
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<tr>
<td>Contraindications to the use of non-protein colloids</td>
<td>- pregnancy and breastfeeding;</td>
<td>2C</td>
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<td></td>
<td>- perinatal period and early infancy;</td>
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<td>- acute liver failure;</td>
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<td>- moderate-severe renal failure (particularly when anuria/oliguria);</td>
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<td>- dialysis treatment in the presence of severe abnormalities of haemostasis and baseline albumin &lt; 2 –2.5 g/dL;</td>
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<td>- intracranial haemorrhage;</td>
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<td>- hypersensitivity.</td>
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<td>Haemorrhagic shock</td>
<td>Only in the case of:</td>
<td>1A</td>
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<td>- lack of response to crystalloids or colloids;</td>
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<td></td>
<td>- contraindication to the use of non-protein colloids.</td>
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<td>Hepatorenal syndrome</td>
<td>In association with vasoconstricting drugs.</td>
<td>2B</td>
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<td>Nephrotic syndrome</td>
<td>Only in patients with albumin &lt; 2 g/dL with hypovolaemia and/or pulmonary oedema.</td>
<td>2C</td>
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<tr>
<td>Organ transplantation</td>
<td>In the post-operative period after liver transplantation to control ascites and peripheral oedema, to replace the loss of ascitic fluid from the drainage tubes, if albumin &lt; 2.5 g/dL, with a haematocrit &gt; 30%.</td>
<td>1C</td>
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<tr>
<td>Burns</td>
<td>In the case of burns of &gt; 30% body surface area, after the first 24 hours.</td>
<td>2C+</td>
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**Dose**

The dose needed to obtain a serum albumin ≥ 2.5 g/dL is calculated using the following formula:

\[
\text{Dose (g)} = [\text{desired albumin concentration (2.5 g/dL)} - \text{actual albumin concentration (g/dL)}] \times \text{plasma volume (0.8 x kg)}
\]

**GoR: Grade of Recommendation**

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**What albumin is available for administration to patients?**

- Preparations of Human Albumin are widely available in heat-treated form
- In Australia they are manufactured by CSL and made from pooled human plasma
- They undergo alcoholic precipitation and pasteurisation for at least 10 hours at >60°C

- Various Concentrations are available diluted in normal saline
  - 4%, 4.5%, or 5% solution (50 g/L) (‘salt rich’)
  - 20% solution (200 g/L) (‘salt poor’) - given in small volumes (20% is slightly hypopsmotic and very hyperoncotic)

- 20% albumin solution has a very high Colloid Osmotic Pressure and can expand the plasma volume by 4 times the volume infused. Plasma volume expansion occurs at the expense of the interstitial fluid volume.
A basic schematic illustration of this process is outlined below:

**An Infusion of 4.5% Albumin** (Simplified Fluid Compartment Model)

Green = Intracellular Fluid (30L)  
Yellow/Pink = Extracellular Fluid (12L)

 Effects of an Albumin Infusion = Expansion of Plasma Volume

What is the evidence of the administration of Human Albumin?

**SAFE Study (Finfer et al)**


*A comparison of albumin and saline for fluid resuscitation in the intensive care unit.*


- No overall benefit in the primary outcome of ‘28 day mortality’
  - The study used 4% albumin in ICU patients.
  - Included almost 7000 patients
- Patients with Head Inj. did worse in later analysis. This may be as the fluid is ‘hypo-osmolar’
Cochrane Review (Roberts et al)

Human albumin solution for resuscitation and volume expansion in critically ill patients (Review)

Roberts I, Blackhall K, Alderson P, Bunn F, Schierhout G

Looked at the effect of giving albumin compared with saline in critically ill or injured people and concluded that there was very limited evidence and that cost should significantly limit its use.

Study Conclusion: “For patients with hypovolaemia, there is no evidence that albumin reduces mortality when compared with cheaper alternatives such as saline. There is no evidence that albumin reduces mortality in critically ill patients with burns and hypoalbuminaemia.”

Recent Review (Myburgh et al)

Study Conclusion – “Although the SAFE study confirmed the safety of using albumin compared with saline in a heterogeneous population of critically ill patients, and many ICU clinicians continue to favour colloid resuscitation, there is no definitive evidence that colloid solutions offer benefits over crystalloid solutions such as saline. Crystalloid solutions appear equally effective and are substantially cheaper; use of saline is associated with significantly improved outcomes in patients with traumatic brain injury. The use of colloids in patients with severe sepsis requires further study to determine firstly whether starch is safe, and secondly whether the use of any colloid improves outcomes compared with crystalloid.”

So what is the ‘Take Home’ Message?

The take home is that while Albumin has many ‘theoretical’ benefits in critically unwell patients there is a lack of evidence to support its use in clinical studies. While there are specific indications which are considered routine such as administering albumin following an ascitic tap, the everyday use of albumin ‘to correct a number’ is not recommended for clinical practice.