Disorders of Albumin Metabolism in Liver Diseases

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in collaboration with
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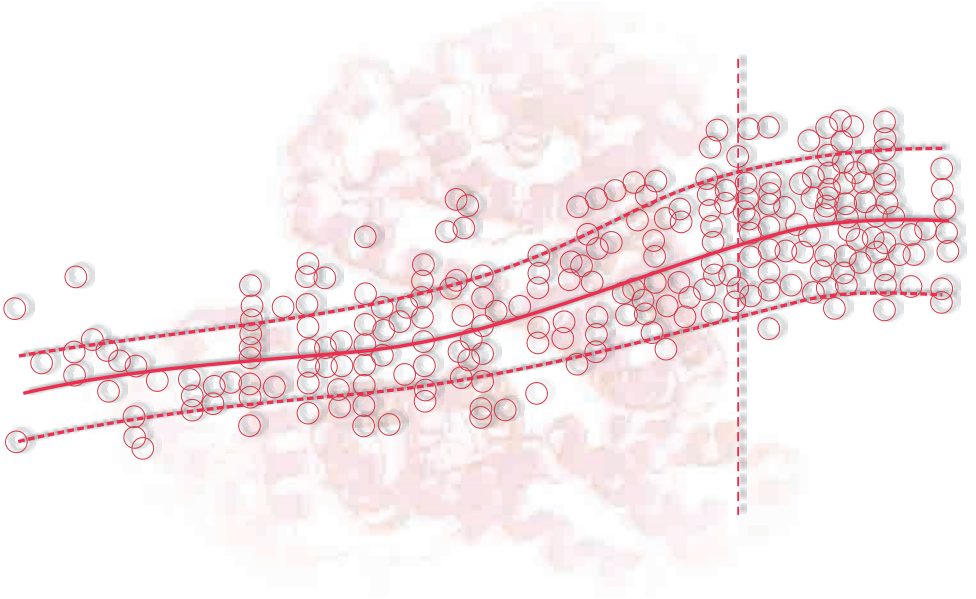

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MEDICINE - STATE OF THE ART

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Editorial

The editors are confident they are meeting a current demand with this reference book, which is devoted exclusively to the current therapeutic aspects of albumin in clinical medicine.

Human albumin solution (HAS) has been increasingly used as volume replacement starting in the late 1940s. At that time, it was generally uncommon to perform randomised trials on long-term outcomes of most medical interventions, and albumin therapy was no exception. The first batches of industrially-produced HAS frequently contained vasodilators and contaminants, causing hypotension and anaphylaxis. Current albumin production, however, has reached a high standard of technical perfection and modern quality control. Commercial HAS preparations are extremely safe with regard to transmission of viral or bacterial agents, in particular when compared to other plasma products, as reviewed in the opening chapter of this volume by Rentsch et al.

Albumin plasma levels are independently related to prognosis of several chronic diseases and are routinely used for calculation of the Child Pugh Score, quantifying disease severity in cirrhosis. In her chapter on albumin measurement, Dr Seimiya from Japan demonstrates that the modified bromocresol purple (BCP) method provides more accurate albumin measurements compared to bromocresol green (BCG) or traditional BCP methods. In particular, an increased ratio of oxidised albumin in serum may give rise to a falsely high Child Pugh Score, compared to the traditional BCP method. Given that these scores are currently used for deciding liver transplantation, this information is potentially clinically relevant.

Drs Oettl and Stauber from Austria have devoted a chapter to the detection of dysfunctional and oxidised albumin in patients with cirrhosis and acute-on-chronic liver failure, who are characterised by an extremely grave prognosis. Ongoing research by this group indicates that the oxidative forms of albumin non-mercaptalbumin 1 and 2 are progressively increased in parallel with the severity of liver failure, with the irreversibly oxidised HNA2 fraction comprising up to 30% of total albumin. They also demonstrate that an HNA2 value >12% indicates a markedly increased short-term mortality.

The highest level of evidence for therapeutic use of HSA is in the area of advanced cirrhosis. This might be due to the fact, that in this setting albumin is damaged and not fully functioning. The unique role of albumin in the management and – equally important – prevention of renal and/or circulatory dysfunction and spontaneous bacterial peritonitis is masterfully reviewed by Dr Bernardi and co-workers from Bologna, Italy, who also speculate on future perspectives of albumin treatment.

A different use of albumin in patients with decompensated liver failure has been the advent of albumin dialysis (mainly by the molecular adsorbents recycling system, MARS®). Despite its use in ICUs setting, two recently published studies were unable to show a reduction in mortality of MARS® treatment in patients with both acute and acute-on-chronic liver failure [1, 2].

The use of albumin compared to synthetic colloids for volume replacement in critically ill patients has been subject of fierce debate, as reviewed in the exciting chapter by Drs Wiedermann and Joannidis. The first 1998 Cochrane analysis on albumin suggested significantly increased mortality in critically ill patients, boosting a massive and sustained use of synthetic colloids. Later analyses and the large Australian SAFE study, however, found either no detrimental effects of HAS [3] oder even survival benefits in subgroups of critically ill patients [4-6]. The recent "6S study" even reports a significantly increased mortality risk of HES compared to Ringer's acetate [7]. Even worse, HES infusion increased the need for renal replacement therapy and the number of blood transfusions significantly. Another large study by the CHEST investigators reports a 21% increased rate of renal failure in patients receiving HES versus saline. Results of several important European studies comparing the use of HAS versus crystalloids in sepsis, septic shock and cirrhosis are currently awaited (NCT00707122, 01932151, 01337934).

The short-lived euphoria on synthetic colloids has finally been challenged, not only by the high-quality data mentioned above, but also by the fact that part of the "evidence" in favour of synthetic colloids was

finally retracted for clear evidence of procedural irregularities and research misconduct [8]. Several meta-analyses on synthetic colloids still stand to be cleared from scientific misconduct.

A special indication is the use of albumin in critically ill neonates, as reviewed in the chapter by Dr Repa. Due to the imminent lack of randomised trials in paediatric populations, valid clinical experience is still required and also guides decisions on treatment in this vulnerable population.

Most recently, recombinant albumin identical to plasma-derived HAS has been produced from transgenic rice seeds, completely eliminating the more theoretical risk of human-to-human infection [9, 10]. It remains to be shown whether this will be a safe and cost-effective production method for the future. For the time being, the editors hope this issue will assist clinicians in selecting evidence-based indications for HAS therapy.

The editors would like to thank all who have contributed to the successful creation of the book, authors and co-authors, as well the publishers for supporting editorial work.

We expect the reader to gain new insights in available levels of evidence of albumin function and disease-related changes in albumin function, as well as more information about appropriate treatment with albumin in critically ill patients, especially those with advanced liver disease.

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