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# AAEM Position Paper

## WHAT IS THE PREFERRED RESUSCITATION FLUID FOR PATIENTS WITH SEVERE SEPSIS AND SEPTIC SHOCK?

Michael E. Winters, MD, FAAEM, FACEP,\* Robert Sherwin, MD,† Gary M. Vilke, MD,‡ and Gabriel Wardi, MD, MPH‡

\*University of Maryland School of Medicine, Baltimore, Maryland, †Wayne State University, Detroit, Michigan, and ‡University of California at San Diego Medical Center, San Diego, California

Reprint Address: Michael E. Winters, MD, FAAEM, FACEP, Departments of Emergency Medicine and Medicine, University of Maryland School of Medicine, Baltimore, MD 21201

**Abstract—Background:** Current guidelines for the management of patients with severe sepsis and septic shock recommend crystalloids as the initial fluid solution of choice in the resuscitation of these patients. In recent years, there have been numerous studies published on the type of fluid used in the resuscitation of patients with sepsis. The primary goal of this article is to determine the preferred intravenous fluid for the resuscitation of patients with severe sepsis and septic shock. **Methods:** A MEDLINE literature review was completed to identify studies that investigated the type of resuscitation fluid in the management of patients with severe sepsis and septic shock. Articles included were those published in English between 2011 and 2016, enrolled human subjects, and limited to the following types: randomized controlled trial, prospective observational trial, retrospective cohort trial, and meta-analyses. All selected articles then underwent a structured review by the authors. **Results:** Nine thousand sixty-two articles were identified in the search. After use of predetermined criteria, 17 articles were selected for review. Eleven of these were original investigations and six were meta-analyses and systemic reviews. **Conclusion:** Crystalloids are the preferred solution for the resuscitation of emergency department patients with severe sepsis and septic shock. Balanced crystalloids may improve patient-centered outcomes and should be considered as an alternative to normal saline, if available. There is strong evidence that suggests semi-synthetic colloids decrease survival and should be avoided. The role of albumin in the resuscitation of patients with severe sepsis and

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### INTRODUCTION

Current management of patients who present to the emergency department (ED) with severe sepsis or septic shock includes early identification, aggressive fluid resuscitation, early and appropriate antibiotic administration, source control, lactate measurement, and the administration of vasopressor medications, if required, to maintain a mean arterial blood pressure of 65 mm Hg (1). Fluid resuscitation is a critical component of the ED resuscitation of patients with severe sepsis and septic shock. Intravenous fluid (IVF) serves to increase intravascular volume, thereby augmenting cardiac output and improving tissue perfusion. In the landmark early goal-directed therapy by Rivers and colleagues, patients randomized to the early goal-directed therapy group received more IVFs within the initial 6 h compared with those randomized to standard care (2). Although IVFs are critical in sepsis resuscitation, there is variation in the choice of which type of

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IVF is used for the resuscitation of these patients. Resuscitation fluids are commonly classified by their composition and whether they are a crystalloid or colloid solution.

Crystalloid solutions are defined by the ability to freely pass semipermeable capillary membranes and are composed of varying amounts of sodium, chloride, and other electrolytes (3).

Crystalloid solutions are generally divided into unbalanced and balanced solutions. The prototypical unbalanced solution is 0.9% normal saline (NS), which contains equivalent amounts of sodium and chloride. Importantly, the amount of chloride contained in 0.9% NS is approximately 40% higher than the plasma chloride concentration. In contrast to 0.9% NS, balanced solutions are designed to better approximate the physiologic composition of plasma. As such, balanced solutions contain inorganic anions (i.e., lactate, gluconate, citrate, acetate) that are rapidly converted to bicarbonate upon administration. In addition to inorganic anions, balanced solutions may also contain cations, such as potassium and calcium. Finally, balanced solutions contain markedly less chloride when compared with 0.9% NS. Common examples of balanced crystalloid solutions include Ringer's lactate, Ringer's acetate, and Plasma-Lyte (Baxter Healthcare Corporation, Deerfield, IL).

Colloid solutions are composed of substances with higher molecular weight than crystalloids, are generally unable to cross the capillary membrane, and are suspended within a carrier solution (3). It is commonly taught that colloid solutions increase intravascular volume by increasing oncotic pressure within the capillary space. Colloid solutions are believed to be beneficial for resuscitation for several reasons, including shorter time to hemodynamic stability, smaller volume of fluid required to achieve stability, and the potential for a longer duration of effect when compared with crystalloid solutions (4,5). The prototypical colloid solution is human albumin. In addition to albumin, a number of semi-synthetic colloids have also been developed and marketed as resuscitation fluids. Examples of these semi-synthetic colloid products include the hydroxyethyl starch (HES), dextran, and gelatin solutions. The most common of these are the HES solutions, which are classified based upon molecular weight and the degree of hydroxyethylation. Semi-synthetic colloid solutions may cause renal failure, impairment of the coagulation system, and anaphylactoid reactions (6).

Over the past several years, numerous articles have discussed the use of crystalloids (i.e., 0.9% NS, balanced solutions) and colloids (i.e., albumin, HES) in sepsis resuscitation. Current international guidelines for the management of patients with sepsis and septic

shock recommend crystalloids as the initial fluid of choice (1). In addition, these guidelines suggest the use of balanced fluid solutions (1). Furthermore, guidelines suggest that albumin be considered in addition to crystalloids for initial resuscitation when patients require a substantial amount of crystalloids (1). Importantly, these latter two recommendations are based on low-quality evidence.

This article is a systematic review of recent evidence regarding the impact of select types of IVF used in the resuscitation of patients with severe sepsis and septic shock. The primary goal of this paper is to determine the preferred IVF for the resuscitation of ED patients with severe sepsis and septic shock.

## METHODS

A structured literature review was performed using MEDLINE to identify articles that investigated the type of resuscitation fluid in the management of patients with severe sepsis and septic shock. The search was limited to studies written in English, involved only human subjects, and were published between January 1, 2011 and December 31, 2016. Articles were also limited to the following design types: randomized controlled trials, meta-analyses, prospective trials, or retrospective cohort trials. Case series, case reports, and review articles were excluded. Abstracts were identified in four separate literature searches, provided in Table 1. Any abstract that met the initial screening criteria then underwent an independent review by two authors (MW, RS) to determine if the article should be included in this review. References in selected articles were also evaluated to identify any other articles of interest. All included articles underwent a "Grade of Evidence" review by two of the study authors (MW, RS). This review was consistent with the established guidelines of the Clinical Practice Committee of the American Academy of Emergency Medicine as listed in Table 2. All included studies were also provided a separate "Quality Ranking Score" based upon methodology and study design (Table 3).

## RESULTS

A total of 9062 articles were identified by the structured literature review. After a thorough review of abstracts and articles, a total of 17 articles were included in the analysis (Table 4) (7–23). Eleven studies were original research investigations and six studies were meta-analyses or systematic reviews. Thirteen studies evaluated the impact of colloid solutions compared with crystalloid solutions, whereas three studies compared

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