American Burn Association Practice Guidelines Burn Shock Resuscitation

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RECOMMENDATIONS

Standards

There are insufficient data to support a treatment standard treatment at this time.

Guidelines

- Adults and children with burns greater than 20% TBSA should undergo formal fluid resuscitation using estimates based on body size and surface area burned.
- Common formulas used to initiate of resuscitation estimate a crystalloid need for 2 to 4 ml/kg body weight/%TBSA during the first 24 hours.
- Fluid resuscitation, regardless of solution type or estimated need, should be titrated to maintain a urine output of approximately 0.5–1.0 ml/kg/hr in adults and 1.0–1.5 ml/kg/hr in children.
- Maintenance fluids should be administered to children in addition to their calculated fluid requirements caused by injury.
- Increased volume requirements can be anticipated in patients with full-thickness injuries, inhalation injury, and a delay in resuscitation.

Options

- The addition of colloid-containing fluid following burn injury, especially after the first 12 to 24 hours postburn, may decrease overall fluid requirements.
- Oral resuscitation should be considered in awake alert patients with moderately sized burns and is worthy of further study.
- Hypertonic saline should be reserved to providers experienced in this approach. Plasma sodium concentrations should be closely monitored to avoid excessive hypernatremia.
- Administration of high-dose ascorbic acid may decrease overall fluid requirements, and is worthy of further study.

OVERVIEW

Purpose

The purpose of this guideline is to review the principles of resuscitation after burn injury, including type and rate of fluid administration, and the use of adjunct measures. It presents a rational approach for the initial treatment of burn patients.

Users

This guideline is designed to aid those physicians who are responsible for the triage and initial management of burn patients.

Clinical Problem

Burns greater than 20 to 25% TBSA are associated with increased capillary permeability and intravascular volume deficits that are most severe in the first 24 hours following injury. Optimal fluid resuscitation aims to support organ perfusion with the least amount of fluid necessary, at the least physiological cost. Under-resuscitation leads to decreased perfusion, acute renal failure, and death. Since the adoption of weight and injury-size based formulas for resuscitation, multiple organ dysfunction caused by inadequate resuscitation has become uncommon in modern American burn care. Instead, administration of fluid volumes well in excess of 4 ml/kg/%burn has been reported by multiple centers. This phenomenon has been termed "fluid creep."[1–3] Just as under-resuscitation is associated with poor outcome, in-

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The opinions or assertions contained herein are the private views of the authors, and are not to be construed as official or as reflecting the views of the Department of the Army or Department of Defense.

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1559-047X/2008

DOI: 10.1097/BCR.0b013e31815f3876

creased fluid administration is associated with adverse outcomes, such as worsening edema formation, elevated compartment pressures, Acute Respiratory Distress Syndrome (ARDS), and multiple organ dysfunction.[4–6] Hence, what constitutes "optimal" fluid resuscitation remains a matter of debate. There unfortunately is a lack of sufficient class I evidence to make strong recommendations on this clinical problem. However, given the success of various approaches to resuscitate severely burned patients, one may postulate that the composition of the fluid, the initial rate of administration and the addition of colloid are relatively unimportant—provided that the clinician diligently tailors fluid therapy to the individual patient and monitors hemodynamic endpoints associated with adequate tissue perfusion.

PROCESS

A Medline search of the English-language literature was conducted for the years 1966 to 2007 for all publications involving the key words "burns," "thermal injury," "burn shock," and "resuscitation." Additional publications were retrieved by searching through references from the available articles. They were collectively reviewed and summary recommendations were made using the following grading scale (Table 1)[7]: grade A-supported by at least one well-designed prospective trial with clear-cut results, grade B-supported by several small prospective trials with a similar conclusion, grade C-supported by a single small prospective trial, retrospective analyses, cases studies, and expert opinions based on investigators' practices.

Table 1. Grading of scientific evidence*

Level of Evidence	Recommendation Grade Level
Class I: large prospective clinical trial	Grade A: supported by at least one large prospective clinical trial with clear-cut results
Class II: small prospective clinical trial (low power)	Grade B: supported by several small prospective clinical trials supporting a similar conclusion
Class III: retrospective analytical study, contemporaneous controls	Grade C: supported by a single small prospective trial, retrospective studies and consensus expert opinions
Class IV: retrospective analytical study, historical controls	
Class V: case series, expert opinions	

* Adapted with permission from Sackett DL. Rules of evidence and clinical recommendations on the use of antithrombotic agents. Chest 1989;95: 2S–4S.

SCIENTIFIC FOUNDATION

Burn Shock Pathophysiology

Seminal contributions by Baxter and Shires, Arturson and Jonsson, Moyer et al, and others have established that burn shock begins at the cellular level.[8–11] In their experimental studies, major burn injuries cause a decrease in cellular transmembrane potential in both injured and noninjured tissue. Disruption of the transmembrane sodium-ATPase activity presumably accounts for a rise in intracellular sodium, an effect that gradually normalizes during the next several days. Intracellular sodium shift contributes to hypovolemia and cellular edema. Heat injury activates the release of inflammatory and vasoactive mediators responsible for local vasoconstriction and systemic vasodilation, as well as increased transcapillary permeability. Endothelial cells and sensory nerves within the burn wound contribute to the local and systemic inflammatory response. Released mediators include complement proteins, kinins, histamine, serotonin, prostaglandins and oxygen-derived free-radicals, and neuropeptides.[12,13] Disrupted capillary integrity allows for rapid equilibration of water, inorganic solutes, and plasma proteins (but not cellular elements) between the intravascular and interstitial spaces. This sequence of events leads to intravascular hypovolemia and hemoconcentration that are maximal at about 12 hours postburn.[14,15] Thermal injury-induced hypovolemia consists of a steady loss of intravascular volume that requires sustained replacement to avoid end-organ hypoperfusion and ischemia. In other words, the goal of proper fluid resuscitation aims to prevent rather than to treat burn shock.

Reduced cardiac output is a hallmark of the early postinjury phase. Although its precise mechanism remains unclear, studies on isolated heart preparations after cutaneous burn suggest that impaired intrinsic myocardial contractility is likely caused by circulating mediators.[16] From a clinical standpoint, reduced cardiac output is the combined result of decreased plasma volume, increased afterload, and decreased contractility. A recent clinical trial aimed at maximizing preload was able to restore neither preload nor normal cardiac output until 24 hours after injury.[17] Interestingly, these results mirror earlier observations made by Baxter and Shires in their canine model of burn injury.[8]

Optimal Route and Necessity of Formal Resuscitation

The advent of widely available intravenous cannulas has helped popularize current strategies of intravenous resuscitation. An intact gastrointestinal tract can tolerate a large amount of fluid replenishment as evidenced by successful oral resuscitation of patients with infectious diarrheal illnesses throughout the world.[18,19] In burn patients, oral salt solutions were frequently used either alone or in combination with intravenous infusion in early studies of burn resuscitation.[20–22] Although oral resuscitation has been attempted for even massive burn injuries, a significant number of patients experienced vomiting during this process. This aspect makes enteral resuscitation somewhat unreliable and impractical, except perhaps when resources are severely limited. In instances where access to medical care is limited, and provided that the gastrointestinal tract is uninjured, oral resuscitation can be effectively initiated with balanced salt solutions. The actual volume each burn patient can tolerate will depend on the magnitude of injury, the presence of gastric ileus, and the timing of enteral administration. Early provision of enteral calories may also decrease the incidence of adynamic ileus, and is an effective method to supplement volume resuscitation. Oral resuscitation is also appropriate for burns <20% since these burns are not associated with severe systemic inflammation, rapid formation of edema, and vasodilation in nonburned tissues.[23,24] Current recommendations are to initiate formal fluid resuscitation when burns >20% TBSA, preferably through the intravenous route. *Recommendation grade: C.*

Crystalloid Resuscitation

There are no available level I or level II publications to guide the choice of isotonic crystalloid resuscitation. The 1978 National Institutes of Health workshop on fluid resuscitation did not reach a consensus on the specific formula nor the type of fluid to be administered to burn patients. The participants nevertheless agreed on two important guidelines: a) that the least amount of fluid necessary to maintain adequate organ perfusion should be given, and b) that the volume infused should be continually titrated to avoid both under- and over-resuscitation.[25] Titration of fluids to maintain renal perfusion to obtain a urinary output of 0.5 ml/kg/hr is considered adequate for adults, whereas a urinary output of 1 ml/kg/hr is an appropriate target for young pediatric patients. Thus, resuscitation formulas are useful as starting guidelines, rather than rigid goals for volume resuscitation. *Recommendation grade: C.*

Currently, the most popular resuscitation formulas employ lactated Ringer's (LR) solution, which contains 130 mEq/L of sodium. Although this solution is slightly hypotonic compared with plasma, it effectively treats both hypovolemia and extracellular sodium deficits caused by thermal injury. A number of formulas estimate volume requirements in the first 24 hours (summarized in Table 2). All predict fluid volume resuscitation based on body weight and surface area burned. The Baxter formula was developed at Parkland Hospital in the 1960s and is by far the most commonly used formula at U.S. burn centers.[26] It recommends administering 4 ml/kg/%burn of LR solution in the first 24 hours, with half given in the first 8 hours. The modified Brooke formula, developed at the U.S. Army Burn Center, represents an alternative fluid prediction model which estimates 2 ml/kg/%burn/24hr as a starting point.[27]

In 1978, Baxter retrospectively reviewed 954 adult and pediatric resuscitations and documented that most patients' total fluid requirements ranged from 3.7 to 4.3 ml/kg/%burn. Only specific subgroups of patients required increased volume requirements,

Table 2. Common estimates of volume resuscitation in the first 24 hours

	Formula Name	Solution	Volume in First 24 hr	Rate of Administration
Adult	Parkland	Lactated Ringer's	4 ml/kg/%burn	Over 8 hr, over 16 hr
	Modified Brooke	Lactated Ringer's	2 ml/kg/%burn	over 8 hr, Over 16 hr
Children	Shriners-Cincinnati	Lactated Ringer's	4 ml/kg/%burn + 1500 ml/m^2 BSA	Over 8 hr, over 16 hr
	Shriners-Cincinnati (for young pediatric patients)	Lactated Ringer's + 50 meQ $NaHCO_3$	4 ml/kg/%burn + 1500 ml/m^2 BSA	1st 8 hr
		Lactated Ringer's		2nd 8 hr
		5% Albumin in Lactated Ringer's		3rd 8 hr
	Galveston	Lactated Ringer's	5000 ml/m^2burn + 2000 ml/m^2 BSA	over 8 hr, Over 16 hr

namely patients with 1) deeper burns, 2) a delay in resuscitation, or 3) inhalation injury.[23,28] These observations have been confirmed by other groups.[29,30] Recent studies, however, have found that average volumes administered to contemporary burn patients far exceed formula predictions, often exceeding 5 to 7 ml/kg/%burn.[1,2,31] Unless the nature of burns has drastically changed, one may postulate that most of this "fluid creep" is attributable to changes in clinicians' behavior. These may include: a) a tendency to maximize preload using invasive monitors over targeting urine output, b) a reluctance to decrease infusion rates when urine output exceeds target goals, c) an increased use of opioids and sedatives that may antagonize the stress response or increase vasodilation, and d) a higher likelihood to resuscitate more severely injured patients (>80% TBSA) who typically exceed formula calculations.[4,32] Whereas acute renal failure has become a rare complication of burn resuscitation, increased volume administration has been associated with a different set of complications. Intra-abdominal hypertension with abdominal compartment syndrome is one dramatic example, but extremity compartment syndrome and recently reported ocular compartment syndrome are also potential complications.[4–6] In October 2006, the American Burn Association sponsored a "State of the Science in Burn Care" meeting to construct a research agenda for the next decade. In this meeting, participants highlighted over-resuscitation as a common, but potentially avoidable phenomenon in today's burn units. Defining better endpoints of resuscitation to avoid excessive volume administration represents a high priority for future investigations.[33]

Hypertonic Saline Resuscitation

Hypertonic saline has appealed to burn clinicians ever since it was recognized that extracellular sodium deficit was an important component of burn shock.[9] Studies by Monafo and others demonstrated that smaller fluid volumes were required to maintain urine output with hypertonic saline resuscitation.[34–36] Hyperosmolarity effectively helps expand plasma volume as it favors water shift into the intravascular space, at the price of intracellular water depletion; whether intracellular water depletion is harmful to patients has not been determined. The proposed benefits of decreased volume administration to burn patients include reduced extremity edema and improved respiratory function in the days following resuscitation.[34,37] A hyperosmolar load may also improve early urine output through osmotic diuresis, perhaps enabling clinicians to avoid over-resuscitation. Whereas prospective clinical trials using hypertonic saline, for the most part, have confirmed earlier findings of Monafo and colleagues, small numbers of enrolled patients precluded meaningful analyses of hospital outcomes (Table 3). These studies also highlight wide variations with respect to the sodium concentration used.

A large volume of hypertonic saline may raise plasma sodium to 160 mEq/L, corresponding to an osmolarity of 340 mosm/kg. Shimazaki et al found that this threshold level was associated with a decrease in urine output below 50 ml/hr, and cautioned against this level of hypernatremia.[45] Frequent monitoring of sodium concentration is essential since severe hypernatremia is associated with acute renal failure, whereas its rapid correction induces excessive cerebral edema.[46] Huang et al have published the largest outcome study to date of burn patients resuscitated with hypertonic saline (65 patients) vs Parkland formula (148 patients).[47] In this retrospective historical control study, patients who received hypertonic saline had a 4-fold increase in acute renal failure (40 vs 10.1%, $P < .001$) and twice the mortality rate (53.8 vs 26.6%, $P < .001$). Furthermore, patients with acute renal failure had significantly elevated plasma sodium after the first postburn day compared with the nonrenal failure group. Hypertonic saline resuscitation should be reserved for experienced burn physicians, with close monitoring of plasma sodium concentration. *Recommendation grade: B.*

Colloid Resuscitation

Considerable controversy persists as to the role (and type) of colloid in burn resuscitation. Whereas many burn centers report that they never use colloids in their initial resuscitation schemes, others have reported successful resuscitation with plasma, albumin, and high molecular weight glucose polymers such as dextran and hydroxyethylstarch.[26,48–51] Plasma proteins serve an important role in maintaining oncotic pressure to balance the outward hydrostatic pressure. Administration of large volumes of crystalloid during burn resuscitation decreases plasma protein concentration and further promotes extravascular egress of fluid and edema formation. Replenishment of plasma protein using colloids (either with albumin or plasma) would theoretically mitigate this effect. As a result, early formulas developed by Evans and by surgeons at the US Army Burn Center contained significant amounts of colloid in their calculations.[52] More recently, Slater and coworkers have championed a fixed crystalloid volume (2 liters of LR), coupled with fresh frozen plasma titrated to achieve adequate urinary output. Their protocol has enabled them to significantly reduce the total volume infused during the

Table 3. Evidentiary table: prospective clinical studies of hypertonic saline resuscitation

Author, Year	Study Design, Allocation	Patients and Characteristics	Main Findings	Study Conclusions	Data Class
Caldwell and Bowser, 1979[38]	Alternate assignment to LR or HLS	37 children with burns ≥30%	HLS received 26% more Na load, but 38% less water load	HLS is safe in children, with reduced free water requirements	II
Jelenko etal, 1979[39]	Random assignment to LR, hypertonic lactate solution*, or hypertonic lactate + albumin	19 adults with burns ≥20% (7 LR, 5 hypertonic, 7 hypertonic/albumin)	Total fluid in first 76 hr, LR group: 5.7 ml/kg. Hypertonic group: 3 ml/kg, hypertonic/albumin group: 1 ml/kg	Hypertonic saline permits a reduction in volume requirement. Addition of albumin further reduces this volume requirement	II
Bowser-Wallace and Caldwell, 1986[40]	Alternate assignment to LR/colloid and HLS	38 patients aged 5 months to 21 years, with burns ≥30%	Patients in the LR/colloid group gained more weight at 48 hr	HLS reduces fluid volume requirements in pediatric patients	II
Gunn et al, 1989[41]	Random assignment to LR or HSL	51 adults with burns ≥20%	No difference in total fluids, weight gain, total sodium load, or mortality	No advantage of HSL over LR resuscitation	I
Shimazaki et al, 1991[37]	Alternate assignment to LR or hypertonic saline "ladder"†	46 adults with burns >30%, without inhalation injury	Hypertonic saline more effectively maintained interstitial fluid volume, and fewer patients required mechanical ventilation	Hypertonic saline resuscitation may lead to improved respiratory function	II
Bortolani et al, 1996[42]	Random assignment to LR or HLS	40 adults with burns >30%	HLS was associated with smaller infusion volume, but higher mortality (this latter group had larger burns)	HLS resuscitation is feasible	I
Murphy et al, 1999[43]	LR resuscitation, with 8 nonrandomized patients receiving a supplemental bolus of HSD‖ (4 ml/kg over 30 min)	18 adults with burns >35%, without inhalation injury	Patients who received a supplemental HSD bolus had equivalent total fluid volume requirements to the control group, (both in excess of 6 ml/kg/%burn)	A single HSD bolus is ineffective at reducing fluid volume requirements	II
Oda et al, 2006[44]	Nonrandom assignment to LR or hypertonic saline "ladder"†	36 adults with burns 40%, without inhalation injury	Hypertonic group averaged 3.1 compared 5.2 ml/kg/%burn in controls by 24 hr with fewer patients >30 cm H_2O intrabladder pressure	Hypertonic saline reduces fluid requirements and decreases the incidence of intra-abdominal hypertension	II

LR, Lactated Ringer's solution; *HLS*, Hypertonic Lactated Saline solution (Na: 250 mEq/L, osm: 500 mosm/kg); *HSL*, Hypertonic Saline (Na: 250 mEq/L, osm: 514 mosm/kg); *HSD,* Hypertonic saline dextran: 7.5% sodium chloride in 6% dextran-70.

* Hypertonic lactate solution: Na: 240 mEq/L, osm: 480 mosm/kg.

† Hypertonic saline ladder: Initial solution with Na: 300 mEq/L, 600 mosm/kg × 2 liters, progressively decreasing to final solution with Na: 150 mEq/L, 300 mosm/kg.

first 24 hours.[53,54] Allogeneic plasma, however, carries a risk of blood-borne infectious transmission, and is a known risk factor for development of acute lung injury.[55] Thus, the routine use of this limited blood bank resource to treat hypovolemia without active bleeding or coagulopathy may be inadvisable outside a clinical trial when other choices are available.[56,57]

The opposite school of thought is to not administer any colloid in the first 24 hours. Radioisotope experiments by Baxter and Pruitt et al have demon-

strated that plasma expansion during this phase was independent of the type of fluid given, whether crystalloid or colloid.[8,27] At 24 hours however, capillary integrity may be sufficiently restored to allow manipulation of intravascular oncotic pressure.[23] Several class I studies indicate that colloids provide little clinical benefit to burn patients (especially when given in the first 12 hours postburn), and may increase lung water content after the resuscitation phase (Table 4). In nonburn patients, the use of albumin for resuscitation has not shown to be beneficial in a number of prospective randomized trials.[60] The recently com-

Table 4. Evidentiary table: prospective clinical studies of colloid resuscitation

Author, Year	Study Design, Allocation	Patients and Characteristics	Main Findings	Study Conclusions	Data Class
Bocanegra et al, 1966[58]	Alternate assignment to: 1) isotonic saline or plasma + dextrose water (Phase 1), and 2) isotonic saline or plasma + saline (Phase 2)	308 patients, age 11 to 73, with burns ≥10%, no inhalation injury Isotonic saline: 152 Plasma + Dextrose: 74 Plasma + Saline: 82	Shock developed in 4% in saline group, 5% in saline + plasma, and 12% in dextrose + plasma	Addition of plasma offers no advantage of isotonic saline. Sodium replacement is essential	I
Jelenko et al, 1979[39]	Random assignment to LR, hypertonic lactate solution*, or hypertonic lactate + albumin	19 adults with burns ≥20% (7 LR, 5 hypertonic, 7 hypertonic/albumin)	Total fluid in first 76 hr, LR group: 5.7 ml/kg, hypertonic group: 3 ml/kg, hypertonic/albumin group: 1 ml/kg	Hypertonic saline permits a reduction in volume requirement. Addition of albumin further reduces this volume requirement	II
Goodwin et al, 1983[59]	Random assignment to LR or LR + 2.5% albumin solution	79 adult patients with burns ≥35%, no inhalation injury	Colloid resuscitation decreases fluid requirement by 0.9 ml/kg/%burn, but was associated with increased lung water after resuscitation	Addition of colloid provides no long lasting benefit and may promote pulmonary edema	I
Waxman et al, 1989[50]	Random assignment to 500 ml of 5% albumin or pentastarch, cross-over study at mean of 23.6 hr after injury	12 adults with burns ≥25%	Both pentastarch and albumin boluses increase stroke volume, cardiac index, CVP, PAOP, and slightly prolonged coagulation parameters	Pentastarch and albumin are both effective plasma expanders at the end of the first 24 hr	II
Du et al, 1991[53]	Nonrandom assignment to LR, and HPT formula†, or 2L LR + 75 ml/kg FFP‡	30 patients, age 16 and older with burns ≥30%, equally divided into the 3 groups	The FFP group had the least volume infused (2.7 ml/kg/%burn) and the least weight gain	Plasma resuscitation decreases volume resuscitation need and minimizes edema formation	II
O'Mara et al, 2005[54]	Random assignment to LR (Parkland formula) or 2L LR + 75 ml/kg FFP‡	31 adult patients with burns ≥25%	Mean volume infused in crystalloid group: 22.1 L, compared to 12.3 L in colloid group. Peak intra-abdominal pressures and airway pressures lower in colloid group	Colloid resuscitation reduces volume requirements and mitigates increases in intra-abdominal pressures during resuscitation	II

CVP, central venous pressure; *PAOP*, pulmonary artery occlusion pressure, obtained from pulmonary artery catheter; *FFP*, fresh-frozen plasma; *LR*, Lactated Ringer's solution.

* Hypertonic lactate solution: Na: 240 mEq/L, osm: 480 mosm/kg.

† HPT formula: 154 mEq/L NaCl + 100 mEq/L Na-acetate.

‡ FPP titrated to keep hourly urine output between 0.5 ml/kg/hr and 1.0 ml/kg/hr.

pleted "Saline versus Albumin Fluid Evaluation" Study enrolled nearly 7000 patients to evaluate the usefulness of 4% albumin for resuscitation.[61] Although the albumin group was successfully resuscitated with less volume, there was no difference in organ failure rates, days on the ventilator, length of stay or mortality. It is important to note that burn patients were excluded from enrollment in this study.

Demling and others demonstrated experimentally that the rate of edema formation was maximal at 8 to 12 hours after injury.[62,63] Except for a transient loss of capillary integrity, nonburn tissues soon regain the ability to sieve plasma proteins. Virtually all studies using large macromolecules to augment oncotic pressure have documented reduced edema formation in nonburn tissue, but not in the burn wound itself.[48,64] This physiologic argument has prompted some clinicians to adopt a "middle-of-the-road" approach, whereby colloids are administered later in the second half of the first 24 hours. Warden and associates report routinely added 5% albumin to LR 17 to 24 hours postinjury for patients with burn size >40%.[52] This compromise is perhaps the most popular method of colloid implementation in U.S. burn centers according to the survey results by Fakhry et al.[26] Although the Parkland formula is applied in the majority of centers (78%), most responders reported using colloids in the first 24 hours some of the time. The evidence reviewed indicates that the addition of colloids to resuscitation can decrease total volume requirements, but randomized controlled trials would be needed to document other benefits. *Recommendation grade: A.*

Pediatric Resuscitation

Limited physiological reserves in children mandate increased vigilance and precision during resuscitation from burn injuries. Mortality in the young pediatric patient (age <2 years) is higher than in other age groups.[65,66] Children require more fluid than adults with a similar injury size. Several groups have estimated their fluid requirements at approximately 6 ml/kg/%burn.[67,68] One explanation may be that children's body surface area to weight ratio is higher than adults. Bowser-Wallace reported that when body surface area was substituted for weight to calculate fluid needs, children less than 3 years of age had comparable volume requirements to older children.[69] Thus, weight-based formulas alone are probably insufficient for pediatric resuscitation. In centers experienced with pediatric burns, formulas have been developed that include maintenance fluid based on body surface area in addition to estimated needs based on burn size (Table 2).[52] Glucose homeostasis is an important parameter in children. Hepatic glycogen stores in young children are depleted after 12 to 14 hours of fasting,[70] after which amino acids, glycerol, and lactate are used to generate new glucose molecules. It is therefore important to provide sufficient glucose substrates during first 24 hours of resuscitation. This can either be achieved by adding dextrose to the maintenance fluid, or by provision of early enteral nutrition. *Recommendation grade: C.*

Monitoring of Resuscitation

Reliance on hourly urine output as the primary index of optimum resuscitation sharply contrasts with ever more sophisticated monitoring devices available in modern burn centers. Intensivists now have at their disposition many monitoring tools to assess the moment-to-moment physiological state of the patient. For instance, abnormal admission arterial lactate and base excess values correlate with the magnitude of injury and their failure to correct over time predicts mortality.[71–73] There are, however, no prospective studies to support the use of these parameters to guide fluid resuscitation. Because the pathophysiology of burn shock creates a persistent hypovolemic state that gradually subsides, attempts at rapidly clearing anaerobic by-products with aggressive volume replacement may be unsuccessful and exacerbate edema formation.

The availability of central venous catheters and pulmonary artery catheters[74] has prompted several investigators to challenge Baxter's observations that restoration of preload and cardiac output could not be accomplished before 24 hours.[75–78] Although several preliminary studies documented successful increases in preload and cardiac index with aggressive volume administration, a well-designed prospective randomized trial failed to confirm these benefits (Table 5).[17] In fact, neither restoration of intrathoracic blood volume nor cardiac index could be achieved with the additional 68% of fluid administered in the preload-driven strategy. Based on these results, a preload-driven strategy for burn resuscitation is not advisable. Invasive monitoring with central venous catheters or pulmonary artery catheters may still be occasionally indicated in special circumstances such as burns in older adults,[76] or patients with an inadequate response to standard treatment.[79] *Recommendation grade: A.*

Adjuncts to Fluid Resuscitation

Antioxidant Therapy. Considerable interest exists in antioxidant therapy, because membrane lipid peroxidation and oxygen-derived free radicals are ma-

Table 5. Evidentiary table: prospective studies of invasive monitoring

Author, Year	Study Design, Allocation	Patients and Characteristics	Main Findings	Study Conclusions	Data Class
Barton et al, 1997[75]	Noncomparative study, resuscitation to PAOP = 15, then dobutamine to optimize oxygen delivery	9 adults with burns >25%	Patients averaged 63% more fluid than predicted by Parkland formula, oxygen delivery and consumption had a moderate correlation	Burn patients are responsive to volume loading and inotropic support	V
Holm et al, 2000[77]	Noncomparative study, volume loading to maximize oxygen delivery	16 adults with burns >20%	Survivors (n = 8) were more likely to respond to volume loading (r = .74)	Increased delivery likely beneficial based on survivors' data	V
Holm et al, 2000[78]	Noncomparative study, use of ITBV to guide fluid resuscitation	24 adults, with burns ≥20%	ITBV had good correlation with cardiac index and oxygen delivery	ITBV is a reliable indicator of cardiac preload	V
Holm et al, 2004[17]	Random assignment to Parkland resuscitation or ITBV-driven (preload) therapy	50 adults with burns >20%	Preload-driven therapy group averaged 68% more fluid than controls. No significant rise in intrathoracic blood volume in either group until 24 hr.	No benefit of preload-driven resuscitation	I

PAOP, pulmonary artery occlusion pressure; *ITBV*, intrathoracic blood volume, calculated by transpulmonary dye/temperature dilution technique.

jor components of burn shock pathophysiology.[80] Burn-mediated changes in the liver increase peroxidation and decrease antioxidant capacity.[81,82] Matsuda et al demonstrated in dogs and guinea pigs that treatment with high-dose ascorbic acid reduces edema formation and fluid requirements during resuscitation.[83,84] The same authors have subsequently performed a prospective clinical trial in which the ascorbic acid group had a 45% decrease in fluid administered compared with controls ($P < .01$).[85] Although there did not appear to be significant clinical benefits beyond resuscitation volumes, there was no indication of harm from this strategy either. High-dose ascorbic acid is presently recommended as an option to clinicians. Antioxidant therapy as an adjunct to burn resuscitation mandates large-scale multicenter prospective validation before it should be accepted as a treatment standard. *Recommendation grade: C.*

Plasma Exchange. Although fluid administration prevents vascular collapse, it does not abate the humorally-mediated systemic inflammation. Elegant experiments by Warden et al demonstrated that leukocyte chemotaxis could be restored if extracted leukocytes from burn patients were incubated in noninjured donor serum.[86] Plasma exchange aims to restore the preinjury milieu by removing part of the patient's plasma volume, in return for fresh frozen plasma and albumin. This strategy has been used successfully in immune blood disorders, such as thrombotic thrombocytopenia purpura and autoimmune thrombocytopenia purpura, in which there is suspected accumulation of toxic circulating factors. Warden et al described plasma exchange more than 20 years ago as a rescue maneuver for patients failing fluid resuscitation.[87] A subsequent small prospective randomized trial by the same authors failed to show a decrease in fluid requirements with this intervention.[88] Although still empirically used as a salvage maneuver at some centers, plasma exchange cannot be recommended outside the context of a trial, given the lack of evidence supporting its efficacy. *Recommendation grade: C.*

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