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Resuscitation from Burn Shock: Back to the Future

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Abstract

Numerous and, at times, widely different burn resuscitation formulae have been proposed over the past 70 years. This brief historical review of those formulae provides an understanding of how they were arrived at and how each was used as a foundation for the subsequent formulae. A glimpse into the future ends the article by concluding that fluids alone do not cure burn shock and cites early publications with a call to "shift the focus of burn resuscitation away from fluid intake to adequate endpoint monitoring, edema control and adjuvant therapies".

Keywords: Resuscitation formula; Historical review; Fluids

Introduction

"The local treatment of burns is a subject on which many books have been written and perhaps more numerous remedies recommended than in any branch of surgery. The success which is said to have attended very different, and even opposite modes of treatment, shows that the authors must either be misrepresenting the facts or speaking about different matters" [1].

Those words apply as well today as when they were written in 1881. Perhaps no area of burn treatment illustrates this better than the various formulae that have been proposed for burn shock resuscitation.

The fluid shift characteristic of all burn injuries was the focus of one of the first papers published on the subject, The Significance of Anhydremia in Extensive Superficial Burns [2] by Frank P. Underhill, Ph. D. Doctor Underhill was the Chairman of Pharmacology and Toxicology at the Yale School of Medicine from 1921 to 1932. The paper, based on Dr. Underhill's observations of patients following the Rialto Theater fire in 1921, recommended the early treatment of burned patients to consist of 1) control of pain by morphine and atropine, 2) treatment of shock through the application of heat and putting the patient to bed without removing the clothing, 3) intravenous infusion of saline at 25cc per minute supplemented by the drinking of water, hypodermoclysis and proctoclysis, and 4) cleansing and dressing the burned surface with trinitrophenol, tannic acid, open air exposure or radiant and ultraviolet light therapy. He cautioned that "the systemic treatment in the early stage is of much greater significance than the treatment of the injured surface."

Further interest in burn shock resuscitation was piqued following the disastrous fire at the Cocoanut Grove nightclub in Boston on November 28, 1942. Earlier that same year at the meeting of the National Research Council, Dr. Henry N. Harkins proposed, for the first time, that burn resuscitation be based on the amount of body surface area burned [3]. His formula that administered plasma and saline (Table 1) appeared in the U.S. Military Surgical Manuals the following year [4].

Guides to determining body surface area had been published, first by Weidenfeld in 1902, next by Berkow in 1924, again by Seeger in 1937 and by Wallace in 1941 [5-8]. But it was not until the work of Lund and Browder that the body's surface was divided into clearly demarcated areas [9]. That important contribution, published in 1944, is memorialized in the Lund-Browder chart, some form of which is used in all of the nation's burn centers today (Figure 1).

In 1947, Drs. Oliver Cope and Francis D. Moore, working at The Massachusetts General Hospital, published one of the landmark articles in burn therapy, *The Redistribution of Body Water and the Fluid Therapy of the Burned Patient* [10]. In it, they reported their clinical observations of 19 patients along with measurements of several fluid spaces. Based on those observations and measurements, Cope and Moore proposed the "Surface Area Formula for Fluid Therapy" in which the patient was to receive 75cc of plasma and 75cc of isotonic electrolyte solution per total body surface area burned. The electrolyte solution was 1/3 sodium bicarbonate and 2/3 sodium chloride and was given by mouth. In addition to this, 2000cc of fresh fruit juice was given by mouth or 2000cc of glucose in water was given intravenously. One-half of the total amount was administered in the first 8 hours following the burn and the second half was administered in the subsequent 16 hours. For the second 24 hour period post-burn, one-half of the total volume was given.

Doctor Everett Evans and co-workers from the Medical College of Virginia, citing the "increased hazards of thermal injury" from atomic warfare sought to answer "how much salt does the extensively burned patient need?" [11]. The unsatisfactory results they encountered following the application of the Cope and Moore guidelines prompted their development of the surface area-weight formula, better known as the Evans formula. In this 1952 report, 68 patients received both colloid and normal saline at 1cc per kilogram body weight per total body surface area burned and 2000cc of glucose in water during the first 24 hours. During the second 24 hour period the patients received one-half of the saline and colloid given in the first 24 hours and 2000cc of glucose in water. Interestingly, the decision to administer half the dose of fluids during the second 24 hour period was, in the authors' own words, "arbitrary." Outcome was judged to be dependent upon the age of the patient, extent of the burn, presence of an inhalation injury and the general state of the patient. The so-called "Rule of 50" was also proposed urging great caution in managing those patients over age 50 or with burns more extensive than 50% total body surface area.

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Table 1: Comparison of various burn resuscitation formulae.

Investigator (Formula)	Year of publication	1st 24 hour period	2nd 24 hour period
Harkins	1942	Plasma @ 1000cc x TBSA + Saline @ ≤ plasma volume administered	
Cope & Moore (Surface Area Formula)	1947	Plasma 75cc x TBSA (IV) + Electrolyte sol. 75cc x TBSA (po) + 2000cc fruit juice (po) or 2000cc glucose in water (IV) Electrolyte sol. = 1/3 $NaHCO_3$ + 2/3 NaCl. Half of the total to be given in first 8 hrs, second half given in subsequent 16 hrs.	One half the total volume given in the first 24 hrs.
Evans (Surface Area-Weight Formula)	1952	Colloid @ 1cc x kg x TBSA + Saline @ 1cc x kg x TBSA + 2000cc glucose in water	Colloid @ (1cc/kg x TBSA)/2 + Saline @ (1cc/kg xTBSA)/2 + 2000cc glucose in water
Brooke Army Hospital	1953	Colloid 0.5cc x kg x TBSA + Electrolyte sol. 1.5cc x kg x TBSA + 2000cc glucose in water	50% to 75% of previous colloid and electrolyte vol. + 2000cc glucose in water
Muir & Barclay	1962	Plasma @ (kg x TBSA)/2 given over 4 hrs x 3, 6 hrs x 2 and 12 hrs x 1 + 60cc to 100cc water po	
Baxter & Shires (Parkland)	1968	RL @ 4cc x kg x TBSA. Half of the total to be given over first 8 hrs, second half given in subsequent 16 hrs	Plasma @ 0.3 to 0.5 cc x kg x TBSA to be given over 8 hrs. + RL and glucose in water titrated to urine output of 50cc/hr
Griffiths & Laing	1981	Plasma @ kg x 7.5%, 1/3 to be given over first 8hrs, 1/3 over next 12 hrs, final 1/3 over the next 20-36 hrs.	
Slater & Goldfarb (West Penn)	1991, 2005	FFP @ 75cc x kg over 36 hrs + RL @ 83cc/hr. FFP titrated to urine output of 0.5 to 1.0 cc/kg.	FFP and RL continued x 48hrs.
Matsuda & Tanaka (Vitamin C)	1992, 1995, 1997	Ascorbic acid @ 66mg x kg in RL titrated to urine output of 0.5 to 1.0 cc/kg for a minimum of 8 hrs	

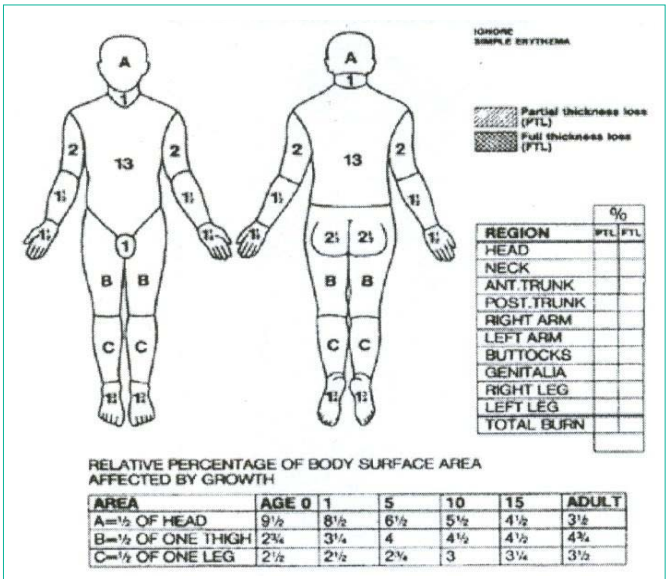

Figure 1: Lund-Browder chart.

The following year, the Surgical Research Unit at Brooke Army Hospital published *Fluid and Electrolyte Balance in Burns* [12]. What came to be known as the Brooke Formula was proposed in which 1.5cc of electrolyte solution and 0.5cc of colloid per body weight in kilograms per total body surface area burned along with 2000cc of glucose in water were given in the first 24 hours post-burn. During the second 24 hours the patient was to receive 50-75% of the electrolyte and colloid amount administered during the first 24 hours and 2000cc of glucose in water. The colloid was in the form of gelatin, dextran or polyvinylpyrrolidone because of the risk of hepatitis with the use of plasma. This formula would be modified a few years later by Pruitt to infusion of lactated Ringer's solution at 2cc/% body burn in the first 24 hours followed in the second 24 hours with colloid in the form of plasma at a rate of 0.3-0.5 cc/% burn/kg body weight plus glucose [13].

What all of the resuscitation formulae proposed up to this point had in common was a reliance on colloid administration as the foundation of burn shock therapy. Soon, significant questions were being asked regarding the role and amount of sodium ion required for adequate burn resuscitation. The landmark work of Drs. Charles Baxter and G. Tom Shires seemed to answer those questions. Published in 1968, *Physiological Response to Crystalloid Resuscitation of Severe Burns* described what has become known as the Parkland Formula (Baxter Formula) [14]. This most widely used of resuscitation guidelines directed fluid administration to be Ringer's lactate at 4cc per body weight in kilograms per total body surface area burned, one-half of the total being administered in the first 8 hours post-burn and the second half over the subsequent 16 hours. During the second 24 hour period the electrolyte solution was titrated to maintain urine output at 50cc/hour. An often overlooked part of the Parkland Formula is that during the 4th 8 hour period post-burn, plasma is administered at 0.3 to 0.5cc per weight in kilograms per total body surface area burned. Additionally, Baxter and Shires placed the maximum size of the burn for calculation purposes at 50%.

Recently, the adequacy of resuscitation observed with application of the Parkland Formula has come under scrutiny [15-18]. The concept of "fluid creep", a term introduced by Dr. Basil Pruitt to describe the additional fluid often needed for proper resuscitation of the patient, has prompted interest in other forms and formulae for burn shock therapy [19]. A 1979 NIH conference concluded that burned patients should be resuscitated with isotonic crystalloid at a rate of 2-4cc per kilogram body weight per total body surface area burned [20]. Surprisingly, the addition of colloid during the second 24 hour post-burn period, as included in the original formula of Baxter and Shires, was not included in this "Consensus Formula." As pointed out by Saffle, this omission of colloid in the resuscitation fluid regimen may explain "fluid creep" [21].

A few years before the publication of the Parkland Formula, Muir and Barclay introduced their recipe for burn resuscitation [22]. Their formula, which receives wide-spread use in Great Britain, uses plasma as the primary resuscitation fluid in an amount determined by percent total body surface area burned multiplied by the patient's weight in kilograms then divided by half [23,24]. That calculated

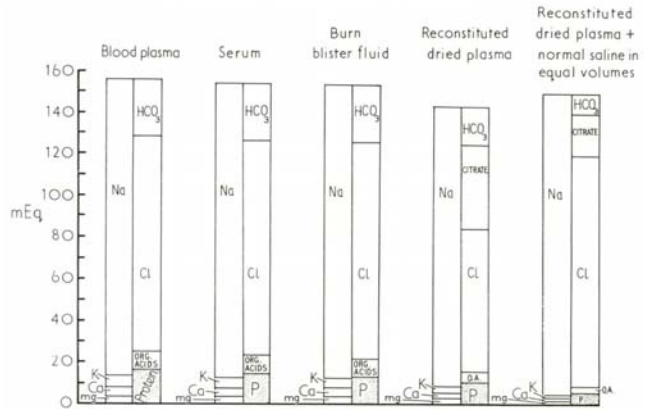

Figure 2: Composition of various body fluids (from Muir and Barclay) [22].

amount is then administered over 6 time periods; 3 of 4 hours, 2 of 6 hours and a final 12 hour period. In addition, 60 to 100cc of water are given per hour by mouth.

The Muir and Barclay Formula was modified in a publication by Griffiths and Laing that prescribed resuscitation for burns of only greater than 20% total body surface area (Figure 2) [25]. This suggestion can also be found in the original report by Evans, et al. [11]. Griffiths and Laing calculated the patient's circulating blood volume to be 7.5% of their admission weight. They then administered 1/3 of this amount in the first 8 hours post-burn, 1/3 over the next 12 hours and the final 1/3 over the next 20-36 hours. The fluid used is plasma and the patient's response is measured by pulse rate, cerebral orientation, restlessness, good skin temperature and color. Urine output and central venous pressure measurements are not used, but urine osmolality and serum sodium determinations are sometimes used to supplement clinical observations.

While these various resuscitation formulae differ slightly in the role and amount of crystalloid infused, the one ingredient they have in common is colloid. That commonality was the basis for *Influences of Different Resuscitation Regimens on Acute Early Weight Gain in Extensively Burned Patients* published by Drs. Harvey Slater and I. William Goldfarb in 1991 [26]. In what has become known as the West Penn Formula, named for The Western Pennsylvania Hospital Burn Center in Pittsburgh where this work was carried out, patients receive fresh frozen plasma (FFP) at a rate of 75cc per kilogram body weight over a 36 hour period along with Ringer's lactate at 83cc per hour. The FFP is titrated to a rate that produces 0.5 to 1.0cc per kilogram body weight per hour of urine and is continued for 48 hours post-burn. At the end of that time, the patient receives crystalloids at a maintenance rate. In a follow-up report, these investigators were able to avoid intra-abdominal hypertension and the subsequent occurrence of abdominal compartment syndrome in burned patients resuscitated with the West Penn Formula [27]. This formula has received renewed interest in the past few years and has become the resuscitation protocol at The Wexner Medical Center at The Ohio State University for burns of greater than 40% total body surface area or 30% total body surface area with associated inhalation injury. There, investigators compared patients who received fresh frozen plasma (27 patients) with historical controls who had been resuscitated with the Parkland Formula (31 patients). They found a statistically significant reduction in fluid requirements in the FFP group with no increase in morbidity or mortality [28].

During the 1970's and early 1980's, Monafo advocated resuscitation with hypertonic saline solutions [29,30]. His initial and somewhat encouraging results could not be reproduced, however, by other investigators. Hypertonic saline resuscitation lost favor with published reports that its use resulted in severe renal failure and death [31].

The movement away from colloid as the crucial ingredient in burn resuscitation, as illustrated by Monafo's work, along with recognition of the role anti-oxidants play in human health led several reports from Japanese investigators advocating the use of ascorbic acid as part of the resuscitation fluid [32-34]. Matsuda, Tanaka et al. reported resuscitating laboratory animals with ascorbic acid in a dose of 66mg per kilogram body weight per hour in Ringer's lactate solution and titrated to produce urine output of 0.5 to 1.0 cc per kilogram body weight per hour. They concluded "High dose vitamin C infusion maintains hemodynamic stability in the presence of a reduced resuscitation fluid volume provided vitamin C is administered for a minimum of 8 hours post-burn" [33]. In a confirmatory report in humans consisting of 17 study patients matched with 16 patient controls, Kahn et al. concluded that high-dose vitamin C resuscitation decreased fluid requirements and increased urine output without an increased risk of renal failure [35]. In an unpublished report presented at the American Burn Association 43rd Annual Meeting, Ziembicki and colleagues from the University of Pittsburgh Medical Center's Burn Center at Mercy Hospital reported on 15 patients with burns greater than 25% total body surface area [36]. Thirteen survived with an average of 22.8% less fluid than predicted by the Parkland Formula.

Despite the reflex ileus that accompanies burns of 20% total body surface area, the use of the enteral route for resuscitation, included in many of the early guidelines, is still practiced in many parts of the world. In a 1950 report from the National Institute of Health, enteral resuscitation using saline was recommended as the standard of care for mass casualty situations involving burns [37]. The World Health Organization promotes its Oral Resuscitation Solution (Table 2) as an acceptable alternative when access to intravenous therapy is limited, such as mass casualty situations and/or in underdeveloped countries or extreme rural America [38].

A recent survey of practicing burn experts conducted by the International Society of Burn Injuries and the American Burn Association, and summarized by Greenhalgh in 2010, revealed 70% of respondents used the Parkland Formula to resuscitate their patients [39]. Ringer's lactate was the fluid most often used (91.9%) but albumin was also included by 20.8% and FFP by 13.9%. Fifty-five percent felt the need to give more fluid than determined by the formula

Table 2: Comparison of World Health Organization Oral Resuscitation Solution (ORS) to Ringer's lactate (RL). Glucose in mM, Electrolytes in meq/liter. Buffer =citrate in ORS, lactate in RL [36].

Solution	Glucose	Sodium	Chloride	Potassium	Buffer	mOsm
WHO-ORS	111	90	80	20	30	331
Ringers lactate	0	130	109	4	28	270

used. Nearly half of respondents added colloid to their resuscitation before 24 hours post-burn. One-third used oral resuscitation at times and nearly 82% felt that oral resuscitation was appropriate for burns of less than 15% total body surface area.

At this point, one has to ask, "Why so many formulae?" The answer is that as our knowledge of the pathophysiology of burns and burn shock had evolved, so too have the resuscitation formulae changed. The following three statements, made at different times in the evolution of these resuscitation guidelines, serve as an example of that knowledge to resuscitation formulae evolution.

"There is now general agreement that the principal cause of burn shock is loss of circulating plasma and red cell components" (Everett I. Evans, 1952) [11].

"These and other demonstrations of direct myocardial depression support the experimental findings of several investigators that suggest a circulating factor may be responsible for the failure of any fluid regime" (Baxter and Shires, 1968) [14].

"Release of mediators such as histamine, prostaglandins and leukotrienes, together with complement activation, seems to play an important role in permeability changes causing hypovolemia and shock" (Lucian Fodor, 2006) [40].

A study of the numerous, and at times widely different, burn resuscitation formulae that have been proposed over the past 70 years, along with advancing knowledge of burn pathophysiology, can lead us to only one conclusion. Fluids alone do not cure burn shock. We currently know that the normal response to burn injury is the release of mediators such as those listed by Fodor. It is the release of these mediators that can trigger an uncontrolled inflammatory response, leading directly to the Systemic Inflammatory Response Syndrome (SIRS) with Multiple Organ Dysfunction Syndrome (MODS) following closely behind. In a report by Huang, et al. and a subsequent report by Holm, et al. MODS has been determined to be the cause in at least 1/3 of deaths from burns [41,42]. In a 2004 article, Ahrns instructs us to "shift the focus of burn resuscitation away from fluid intake to adequate endpoint monitoring, edema control and adjuvant therapies" [43]. That shift in focus, based on the work of the past, will fall to future investigators following in the footsteps of Cope and Moore, Evans, Baxter and Shires, Slater and Goldfarb and others.

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