The Phenomenon of "Fluid Creep" in Acute Burn Resuscitation

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Several reports have documented that modern burn patients receive far more resuscitation fluid than predicted by the Parkland formula—a phenomenon termed "fluid creep." This article reviews the incidence, consequences, and possible etiologies of fluid creep in modern practice and uses this information to propose some therapeutic strategies to reduce or eliminate excessive fluid resuscitation in burn care. A literature review was performed of historical references that form the foundation of modern fluid resuscitation, as well as reports of fluid creep and its consequences. The original Parkland formula required a 24-hour volume of 4 ml/kg/%TBSA lactated Ringer's solution followed by an infusion of 0.3–0.5 ml/kg/%TBSA plasma. Modern iterations of this formula have omitted the colloid bolus. Numerous exceptions to the formula have been noted, most consistently patients with inhalation injuries. In contrast, recent reports document greatly increased fluid requirements in unselected patients, which seems to consist largely of progressive edema formation in unburned areas, increasing after the first 8 hours post-burn. This has been linked to occurrence of the abdominal compartment syndrome and other serious complications. Strategies to reduce fluid creep include the avoidance of early overresuscitation, use of colloid as a routine component of resuscitation or for "rescue," and adherence to protocols for fluid resuscitation. Fluid creep is a significant problem in modern burn care. Review of original investigations of burn shock, coupled with modern reports of fluid creep, suggests several mechanisms by which this problem can be controlled. Prospective trials of these therapies are needed to confirm their effectiveness. (J Burn Care Res 2007;28:382–395)

The development of effective fluid resuscitation regimens is one of the cornerstones of modern burn treatment and perhaps the advance which has most directly improved patient survival. At the beginning of World War II, patients with even moderate burns often died within a few days, of progressive shock and renal failure. In 1921, Underhill's study of victims of the Rialto Theater fire led him to conclude that loss of intravascular volume led to a life-threatening "shock-like" syndrome that should be treated with infusions of normal saline.[1] In 1942, Cope and Moore designed the first formal resuscitation regimen to treat victims of the Cocoanut Grove nightclub fire, with demonstrated reduction in mortality.[2–4] With continued refinements in resuscitation, almost all patients can now be resuscitated successfully, and renal failure complicating acute burn injury has become rare.

A host of formulas have been used for burn resuscitation, almost all based on body weight and burn size, and using various combinations of fluids. The archetype for such regimens and unquestionably the most widely used is the Parkland formula, described by Charles Baxter.[5] During the interval—now almost 40 years—since publication of this formula, its accuracy has become universally accepted in the burn care community. It has been very surprising, therefore, that recent reviews have repeatedly demonstrated that patients with major burns now often require resuscitation volumes which significantly exceed Parkland predictions.[6–11] The explanation for this experience is unclear, but its occurrence has been linked to increased recognition of the complications of edema, including the abdominal compartment syndrome (ACS), and been viewed with alarm by clinicians. Pruitt coined the term "fluid creep" to describe this insidious trend, and called for clinicians to "push the

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pendulum back" in the direction of more conservative resuscitation.[12]

Is "fluid creep" really a new phenomenon, or has the intimidating stature of the Parkland formula kept clinicians from speaking up to challenge one of the most cherished icons of burn treatment until recently? Has the nature of burn injury changed, as Engrav et al have suggested,[11] or have clinicians been influenced by attitudes in other areas of medicine to practice fluid therapy differently? Most important, is "fluid creep" harmful to patients and can it be prevented or controlled? This review addresses these questions.

EVOLUTION OF THE PARKLAND FORMULA

The period from 1965 to 1980 was a time of unprecedented progress in burn treatment: effective topical antibiotics were introduced, successful nutritional support was pioneered, early excision was popularized, and resuscitation regimens were perfected.[13] Many now-legendary physicians contributed to our understanding of the pathophysiology of burn shock, including Evans,[14] Moncrief,[15] Moyer,[16] Arturson,[17] Pruitt,[18] Monafo,[19] Shires, and others.

In 1968, Baxter reported that resuscitation of dogs with 50% TBSA burns with a volume of lactated Ringer's solution (LR) equal to 24% to 32% body weight returned cardiac output and extracellular fluid (ECF) and plasma volumes to near normal, restored transcellular membrane potentials, and corrected metabolic and lactic acidosis by the end of 24 hours.[20] Optimal results were achieved when most of this fluid was given in the first 8 hours after injury. A trial group of 11 patients with burns of 30% to 85% TBSA were similarly resuscitated and required a volume of 3.5 to 4.5 ml of LR per kilogram body weight, per percent TBSA burned (ml/kg/%TBSA) over the first 24 hours. Baxter noted that crystalloid alone, however, would not completely replete ECF volume; some colloid replacement was also needed to accomplish this.

These observations formed the basis of the original Parkland formula. It called for LR at a volume of 4.0 ml/kg/%TBSA for the first 24 hours. Half was given in the first 8 hours after injury and the rest was given over the next 16 hours and adjusted to maintain urine output. Importantly, Baxter's formula also included a fourth 8-hour period during which plasma, at a volume of 0.3 to 0.5 ml/kg/%TBSA, was given to complete resuscitation. During the remainder of the second 24-hour period, dextrose and water were given as needed to maintain urine output.[21]

In 1979, Baxter reported results of this formula in the resuscitation of 954 patients treated from 1973 to 1977.[22] He found that 70% of 438 adults and 98% of 516 children were resuscitated successfully, with 24-hour volumes ranging from 3.7 to 4.3 ml/kg/%TBSA. Only 12% of adults required more than this volume, whereas 18% required less. He emphasized the importance of restoring cardiac output with the use of plasma, noting that output tended to level off at a low-normal level and that "further increases are unusual until plasma is administered in the 4th 8-hour period." In experiments in which patients were given boluses of plasma at various times post-injury, plasma was found to be most effective in restoring ECF volume if given after 24 hours post-burn.[23]

These principles and their results were reiterated repeatedly in the next few years and were combined with recommendations from other burn centers. The formula represented an improvement over the earlier Brooke[15] and Evans[14] formulas. As reviewed by Moncrief,[24] all three formulas were designed to continue resuscitation though an initial *48-hour* period; all resulted in administration of roughly equivalent amounts of sodium; and all relied on colloid administration as an important adjunct to replete plasma volume.

Also in 1979, an NIH-sponsored conference on burn care was summarized with a statement that burn patients should be resuscitated with as little fluid as possible to maintain organ perfusion. Initial fluid therapy should consist of isotonic crystalloid at a volume between 2 and 4 ml/kg/%TBSA for the first 24 hours and titrated to maintain urine output of 30 to 50 ml/hr.[25] The use of colloid in the second 24-hour period was not included. This recommendation has stood as the accepted "consensus" for burn resuscitation for over 25 years[25,26] and has resulted in the concurrent definition of the Parkland formula as a method to predict fluid requirements in the first 24 hours only, and without the use of supplementary colloid.[27,28] This departure from the original Parkland formula may help explain the occurrence of fluid creep.

OBSERVATIONS OF FLUID CREEP

Even before the Parkland formula was published, exceptions began to be identified. Baxter found that the formula would successfully resuscitate most burn patients but noted that response was variable and that adjustment in infusion rates on the basis of response was essential. He identified some patient groups who routinely required additional fluid. These included patients with inhalation injuries, patients with electrical burns, and those in whom resuscitation was delayed.[5,29]

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Inhalation Injuries

In a subsequent NIH consensus conference in 1981, both Baxter and Pruitt identified this group as requiring increased resuscitation.[30,31] This observation has been confirmed repeatedly, as reviewed in Table 1.[32–36] The absolute quantity of fluid required has varied substantially between studies, possibly depending on other variables, such as the use of colloid. For example, Navar et al used only crystalloid for acute resuscitation, and their patients required more fluid than did the patients reviewed by Herndon's group, which has historically used a combination of colloid and LR for initial resuscitation.[37] Hughes et al resuscitated their patients entirely with plasma protein fraction but still found a roughly equivalent increase in relative fluid requirements.[38] Thus, every review has confirmed that patients with inhalation injury require an increase in fluid requirements, from 35% to 65% above those of patients without inhalation injury, regardless of the regimen used.

Other Patient Groups

Subsequently, a number of other patients have been identified who are acknowledged to require fluid resuscitation that can significantly exceed Parkland predictions. In addition to inhalation injury, the list includes patients with secondary injuries, including multiple trauma and electrical burns; patients in whom the onset of resuscitation is substantially delayed[39]; and patients with alcohol or drug addiction.[40,41] In addition, inexperienced clinicians often make substantial errors in estimating burn extent and depth, which can result in significant under- or overcalculation of fluid requirements.[42] However, although these exceptions have been widely recognized, the accuracy of Parkland-based resuscitation for the majority of patients has not been impugned by these reports. Rather, these experiences have been used to emphasize the necessity of monitoring patients carefully and adjusting fluid infusions on the basis of patients' response.

Table 1. Comparison of fluid requirements in adult patients with and without inhalation injury

Reference	No. of Patients, Group	Resuscitation Required	Difference	Comment
Baxter (1981)[30]	NA, INH	5.37 l/m^2 TBSA		Review of fluid requirements in adult burn injuries.
	NA, Non-INH	3.31 l/m^2 TBSA	62%	
Scheulen and Munster (1982)[34]	48, INH	14.5 l/24 hours (10.6 predicted)	+37%	Review of adults with burns of 10% to 60% TBSA.
	53, Non-INH	9.7 l/24 hours (9.2 predicted)	+5%	
Navar et al (1985)[33]	51, INH	5.76 ± 0.39ml/kg/%burn	45%	Retrospective review of children and adults with burns of ≥25% TBSA. Patients with INH took longer to resuscitate (29.8 ± 1.3 vs 23.8 ± 0.74 hours; $P < .05$). No colloids used.
	120, Non-INH	3.98 ± 0.39ml/kg/%burn		
Herndon et al (1988)[32]	20, INH	3.8 ± 1.5ml/kg/%burn	65%	All adults with major burns. Lactated Ringer's solution alone used during the first 24 hours. Colloids not mentioned.
	14, Non-INH	2.3 ± 1.2 ml/kg/%burn		
Hughes et al (1989)[38]	9, INH	4.38 ± 1.26ml/kg/%burn	29%	Review from Britain. All patients resuscitated entirely with plasma protein fraction. Requirements exceeded predicted value of 3.3 ml/kg/%TBSA.
Darling et al (1996)[36]	100, INH	6.52 ± 0.26ml/kg/%burn		Fluids received increased the odds ratio for death by 1.18 and odds ratio for acute respiratory distress syndrome by 1.06 for every 500 ml, even though central venous/wedge pressures were not elevated; non-INH patients were not evaluated.
Dai et al (1998)[35]	26, INH	3.1 ± 1.0ml/kg/%burn	35%	Review of adults with burns of ≥20% TBSA. All patients received colloid starting at 24 hours.
	36, Non-INH	2.3 ± 0.8 ml/kg/%burn		

NA, data not available; INH, patients with inhalation injuries; Non-INH, patients without inhalation injuries.

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Modern Reports of Fluid Creep

In contrast to reports documenting increased fluid requirements for exceptional patients, recent publications have reported greatly increased requirements for resuscitation of a majority of routine patients with major burn injuries. These reports are reviewed in Table 2.[6–8,10,11] Some of these series document fluid volumes far in excess of those previously reported for patients with inhalation injuries; moreover, they show results from unselected series of patients,

Table 2. Review of modern reports of fluid creep

Reference	No. of Patients Who Exceeded Parkland Requirements	Resuscitation Received, ml/kg/%TBSA	Comments
Kaups et al (1998)[6]	83/83 (100%)	NA	Review of patients treated 1994–1995 to assess the relationship of base deficit to outcomes. All patients exceeded Parkland calculations; the 14 patients with base deficit >6 had larger burns, more inhalation injury, higher mortality, and greater fluid requirements (21 ± 4 vs 12 ± 3 liters, an increase of 75%).
Engrav et al (2000)[11]	29/50 (58%)	5.2 ± 2.3 (no range given)	Review from seven centers. Majority of patient exceeded Parkland requirements; this was more pronounced in patients with inhalation injury.
Ivy et al (2000)[7]	98/109 (90%)	9.36 (2.2–38.6)	Prospective evaluation of the incidence of intra-abdominal hypertension and abdominal compartment syndrome in burn patients; seven developed the former and two developed the latter. Authors recommend routine monitoring of bladder pressure in any patient who receives >250 ml/kg fluid.
Cartotto et al (2002)[10]	26/31 (84%)	6.7 ± 2.8	Retrospective evaluation of patients treated 1998–2000. Two interesting observations: first, patients arrived and began resuscitation a mean of 1.7 hours post-injury but had already received 2.5 ± 1.9 liters of lactated Ringer's solution. Second, Parkland formula was quite accurate for the first 8 hours post-burn but requirements increased after that in 15/31 patients.
Cancio et al (2004)[59]	56/89 (63%)	6.1 ± 0.22 (no range given)	Review of patients resuscitated 1987–1997 with the modified Brooke formula, which included a small amount of albumin. Burn size and body weight were associated with increased fluid requirements.
Friedrich et al (2004)[8], Sullivan et al (2004)[9]	NA	3.6 ± 1.1 (1970s) vs. 8.0 ± 2.5 (2000)	Comparison of 11 patients resuscitated during 1975–1979 with 11 patients matched for age, sex, and burn size treated during 2000. Recent patients received more than double the fluid received by patients in the 1970s despite equal urine output. In second publication, authors suggest that increased opioid use in the first 24 hours may contribute to increased fluid requirements.

NA, data not available.

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most of whom can be presumed not to have inhalation injury, which occurs in only 10% to 20% of burn center admissions.

Though not systematically characterized, enough experience with fluid creep has been obtained to permit some generalization about its presentation.[10] Patients often arrive at burn centers having received substantial amounts of crystalloid, sometimes significantly more than required, because of inaccurate estimations of burn size or overzealous or inattentive treatment. Parkland resuscitation is begun and continues fairly smoothly until 8 to 12 hours post-burn. At that time, instead of decreasing, fluid requirements either remain high or actually begin to escalate and range farther and farther from predictions. As this continues, problems with torso and extremity compartment syndromes, respiratory distress, and facial swelling may develop. Requirements for large quantities of LR often continue unchecked despite efforts to reduce them and taper only very slowly, often requiring much longer than 24 hours to resolve. As an example, Figure 1 charts the course of a 6-year-old boy with burns of 33% TBSA who was recently resuscitated in our burn center with a Parkland-based protocol. Although it could be argued that resuscitation guidelines were a bit too generous (eg, urine output of 0.9–1.8 ml/kg/h), this does not explain the great increase in fluid requirements seen at 10 to 12 hours post-burn or the lack of response in urine output until much later. Up until hour 23, when fluids could finally begin to be decreased, urine output averaged only 0.97 ml/kg/h, but the patient had already received a resuscitation volume of 5.70 ml/kg/%TBSA.

This information demonstrates that an increasing number of exceptions to the Parkland formula have been accumulating for many years. Although modern series document a significantly greater manifestation of this trend, and in apparently unselected patient samples, it appears likely that some mechanisms responsible for fluid creep may have been influencing fluid resuscitation in burn care for much longer than previously appreciated. The characteristic clinical presentation described above, although not universally present, suggests some factors contributing to the cause of fluid creep and some potential therapeutic interventions, as will be discussed below.

Fluid Creep and the Abdominal Compartment Syndrome

In the early 1980s, surgeons noted that increasing abdominal distension and bleeding was associated with oliguria and eventual renal failure, which could be reversed by abdominal decompression.[43] Kron et al demonstrated that clinical manifestations could be correlated with measurements of bladder pressure, which provided an objective indication for re-exploration.[44] Since then, ACS has become a well-characterized problem. The syndrome is considered secondary when it occurs in the absence of

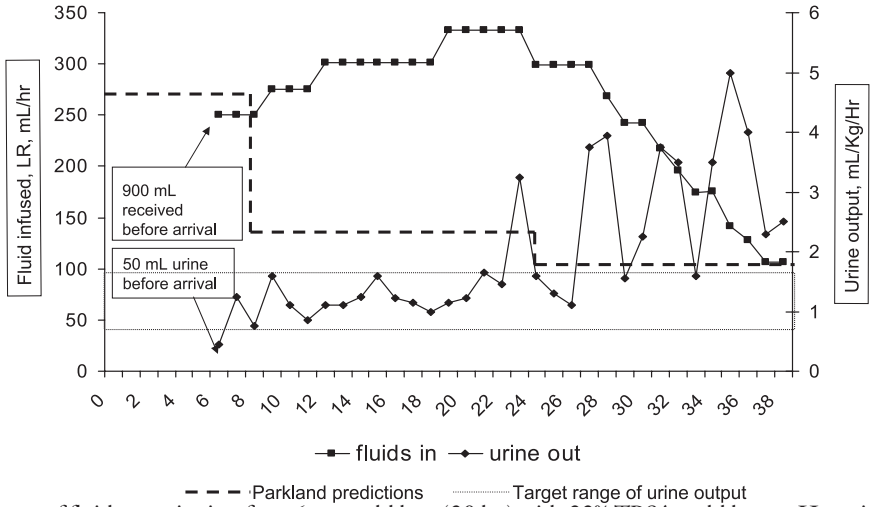

Figure 1. Time course of fluid resuscitation for a 6-year-old boy (20 kg) with 33% TBSA scald burns. He arrived at the burn center 6 hours post-injury, having received 900 ml of lactated Ringer's solution prior to arrival. Fluid resuscitation was started according to the Parkland formula (heavy dashed line); nurses were instructed to maintain urine output between 0.9 and 1.8 ml/kg/h (dotted line). Initial resuscitation was close to Parkland guidelines, but beginning at about 10 hours post-burn, fluid requirements increased progressively until about 22 hours post-burn, when urine output finally began to rise, and fluids were tapered in a stepwise manner according to protocol. The patient reached his calculated maintenance fluid rate of 106 ml/h at hour 36. Total resuscitation received was 11.38 ml/kg/%TBSA. He had no difficulties with compartment syndromes or respiratory distress.

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demonstrable intraabdominal pathology.[45] Secondary ACS in burn patients has been repeatedly described.[46–50] Its occurrence has been shown to correlate directly with volume of crystalloid resuscitation fluid in both burn and nonburn situations.[51] The incidence is unknown, but it may be very common in patients given sufficient amounts of fluid resuscitation.[52,53] It is worthy of note that both hypertonic crystalloid and colloid-based resuscitation appear to reduce development of ACS.[54,55]

Limited data suggest that other complications can also occur from excessive resuscitation, including massive pleural and pericardial effusions,[52] compartmental compression in unburned extremities, and the need to perform or prolong intubation in patients without inhalation injuries or facial burns.[56] Recently, elevated intraocular pressures have also been described in association with massive fluid resuscitation in burn patients.[57,58]

WHAT FACTOR(S) CAUSE FLUID CREEP?

Whereas reports of ACS and other edema-related complications demonstrate unequivocally the potentially disastrous consequences of fluid creep, they provide little insight into its etiology. That these causes are almost certainly multiple can be inferred from several observations about this phenomenon. For one thing, heterogeneity in clinical practice among burn centers is the norm; despite professing adherence to the Parkland formula, burn centers practice fluid resuscitation differently. Both the widespread observations of fluid creep and the substantial differences in absolute fluid volumes required in different centers documented in Table 2 suggest that fluid creep transcends minor variations in resuscitation practice and is manifested differently among these centers. A number of possible explanations can be proposed, which may all contribute to some extent to the emergence of fluid creep as a clinical problem. These include the following.

The Parkland Formula Isn't Accurate, Especially for Very Large Burns

In Baxter's studies, patients with large burn injuries required disproportionately more fluid for resuscitation than those with smaller injuries.[30] The majority of patients with burns of ≥60% TBSA died,[20] and death was attributed to "resuscitation failure" in a majority of cases. In a recent review of burn resuscitation, Cancio et al found that fluid requirements correlated with both total and full-thickness burn size, ranging from approximately 4.0 ml/kg/%TBSA for moderate injuries to almost 6.0 ml/kg/%TBSA for burns of 80% to 100% TBSA,[59] and that patients with the largest injuries were most likely to fail resuscitation attempts.[60]

Today mortality from burn injuries is at an all-time low. Many patients with massive injuries survive, often following aggressive resuscitation well beyond Parkland confines. In turn, this success may have influenced practitioners' approach to resuscitation of patients with smaller injuries and encouraged less stringent adherence to formulas. But even if this is true, it would not explain the magnitude of increased fluid requirements in recent reports or the "runaway" nature of fluid creep observed in many patients.

Modern Clinicians are Careless

Inherent in the term *fluid creep* is the implication that clinicians are permitting resuscitation to escape their control through lack of attention or carelessness. In their review of resuscitations, Cancio et al noted that clinicians were less likely to reduce fluid infusions in the face of increased (>50 ml/h) urine output than they were to increase fluids in the face of inadequate (<30 ml/h) output.[59] Nonetheless, overall urine outputs were not excessive, which makes it unlikely that increased fluid requirements were the result of inattention to Parkland guidelines. Moreover, fluid creep often continues despite directed efforts to reduce fluid infusions. It is unquestionably true that burn unit staff members sometimes fail to reduce fluids in a timely manner, but errors occur in both directions. Recently, a computerized protocol for fluid resuscitation proved more accurate than technician-run resuscitation in an experimental model.[61] This may be a promising area for improving resuscitation in the future, but it appears unlikely that inadvertent over-resuscitation within burn centers explains the vast majority of fluid creep.

"Opioid Creep"

In 2004, a group at Harborview Burn Center in Seattle compared 11 patients treated during 1975 to 1979 to 11 similar patients treated in 2000 and found that fluid requirements more than doubled for the latter group (8.0 ± 2.5 vs. 3.6 ± 1.1 ml/kg/%TBSA; $P < .001$).[8] In a follow-up publication,[9] they demonstrated a corresponding increase in the use of narcotics and sedatives between these time periods: 1970s patients received a mean of 3.9 ± 2.2 opioid equivalents during the first 24 hours post-burn, compared with 26.5 ± 12.3 equivalents in the patients treated in 2000 ($P < .001$). Opioid dosage correlated with fluid requirements in these patients. These authors postulated that fluid creep is a con-

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sequence of the increasing use of narcotics during initial burn care.

This experience exemplifies greatly increased emphasis on the assessment and treatment of pain in hospitalized patients over the past decade in every patient population.[62] Opiates are the mainstay of pain control in burn patients,[63,64] and these agents have significant cardiovascular effects. Rouby et al found that administration of morphine to critically ill patients can "partially antagonize adrenergically mediated cardiovascular response to stress."[65] But even high doses of narcotics appear to be well tolerated in patients with acute burns,[66] so it appears unlikely that opiates alone could explain the dramatic magnitude of fluid creep observed in recent years. In addition, high doses of narcotics are routinely given to patients in a variety of other clinical conditions, without apparent propensity to fluid sequestration.

The Influence of Goal-Directed Resuscitation

Over the past 20 years, critical care practitioners have attempted to adjust resuscitation to achieve the goals of normalizing base deficit (BD) and lactic acid (LA) levels and achieving supranormal levels of cardiac index (CI) and oxygen delivery (DO_2) and/or consumption (VO_2). The finding that BD and LA levels correlate with magnitude of injury and mortality in trauma patients[67,68] and initial studies which demonstrated that survival correlated with attainment of supranormal levels of CI, VO_2, and DO_2[69] led to protocols to push patients to these goals, with use of Swan-Ganz catheters, inotropes, and fluid support.[70,71] In initial trials this approach appeared effective.[72,73] However, in both meta-analyses[74,75] and carefully controlled large multicenter trials, "goal-directed" therapy has not been shown to be superior to treatment based on standard clinical parameters,[76,77] and it clearly requires increased volumes of fluid and blood,[78] with a higher incidence of ACS.[79]

Very similar experience has been documented in burn patients. Base deficit and LA levels correlate with both mortality[39,80] and fluid requirements for resuscitation.[81] Traditional resuscitation often fails to normalize LA and BD[82] and may not reflect changes in CI and VO_2.[83] Goal-directed resuscitation was associated with improved survival in one case-control study of burn patients.[84] In contrast, other groups were unable to determine whether resuscitation aimed at normalizing BD was effective or beneficial,[6,85] and in two other trials, attaining target values of preload, CI, or VO_2 required more fluid—as much as *four times* Parkland predictions—without obvious improvements in survival.[86,87] In a trial involving 50 adult patients randomized to receive either strict Parkland or goal-directed resuscitation, Holm et al found no differences in mortality, intensive care unit or ventilator days, pH, or serum lactate levels.[88] Cardiac index was increased in the goal-directed group only at 24 hours post-burn, and all parameters were identical by 48 hours. Patients in the goal-directed group required 56% more fluid than Parkland patients. Authors concluded that these findings "may be due to the fact that a pure crystalloid resuscitation is incapable of restoring cardiac preload during the period of burn shock"—exactly the same conclusion reached by Baxter 25 years earlier.

It now appears clear that patients' ability to attain at least normal values of CI, DO_2/VO_2, BD, etc. is predictive of survival following trauma and burns but that it may be impossible to turn "nonresponders" into "responders" by specific physiologic manipulations.[89,90] In addition, these studies confirm the classic observations of Baxter and others,[18] that restoration of preload and cardiac function and resolution of acidosis appear to require 24 to 48 hours to occur, regardless of the resuscitation used. "Pushing" these parameters with increased preload or inotropes results in greatly increased fluid requirements without obvious improvements in outcome. Although use of invasive monitoring may still be indicated in some high-risk patients[91] and in patients with respiratory failure, heart disease, or inadequate response to standard treatment,[75] even in these circumstances data derived from Swan-Ganz catheters may be more useful in avoiding major errors than in driving resuscitation to specific "supraphysiologic" endpoints.

But although routine practice of goal-directed resuscitation thus appears to be unnecessary or even harmful, it nonetheless seems likely than many burn clinicians—who double as trauma and critical-care doctors—have been influenced by these experiences and may often be tempted both to measure base deficit, lactate, and other variables and to respond to worrisome values by increasing fluid infusions, even when vital signs and urine output are adequate. This may contribute significantly to fluid creep in many situations, but it still doesn't explain the tendency for fluid creep to persist despite attempts to reduce fluid infusions.

Influence of Excessive Crystalloid Infusion on Starling Forces

Considerable evidence, both theoretical and clinical, supports the idea that excessive administration of crystalloid and the abandonment of colloid replenishment at the end of resuscitation are major contributors to fluid creep.

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The forces that control transcapillary fluid flux are summarized in Starling's equation[92]; their alterations in burn injury have recently been reviewed by Demling.[93] The greatest edema formation occurs almost immediately post-burn within the wound, caused by near-total permeability to even very large (350 Å) molecules, permitting leakage of fluid which is essentially identical to plasma.[94] This effect is transient; both its duration and its magnitude are proportional to burn size.[95,96] This initial leakage of proteins largely eliminates the oncotic pressure gradient necessary for maintenance of intravascular volume. Simultaneously, the densely configured collagen-hyaluronate interstitial matrix, which ordinarily acts as a "safety valve" to edema formation,[97] is disrupted, increasing compliance and producing osmotically active fragments and negative ("sucking") interstitial pressure, which also favors rapid fluid sequestration.[98] Although this gradient is neutralized within a few hours, compliance continues to increase as interstitial gel is hydrated, allowing ongoing accumulation of fluid with little change in hydrostatic pressure.[99] In contrast to early edema formation, subsequent fluid sequestration occurs prominently outside the wound. Depletion of plasma proteins alone can mimic burn edema, and infusions of albumin or dextran can almost completely prevent edema in unburned tissues.[100,101]

With this in mind, it is easy to see that any excessive fluid given in the early post-burn period would increase capillary hydrostatic pressure and further reduce oncotic pressure,[102] both contributing to a cycle of accelerated capillary leakage which requires ever-greater amounts of crystalloid to satisfy. This mechanism could explain why fluid creep is manifested so prominently by edema in unburned tissues, including the abdomen, as well as the otherwise paradoxical observation that fluid requirements are usually fairly close to Parkland predictions for the first 8 hours post-injury—when capillary leakage should be greatest—but become increasingly problematic after this period.[10] Cancio et al found that while "resuscitation failure" correlated with burn size, it could not be predicted on patient characteristics alone.[60] Other factors—including, perhaps, the volume of initial fluid therapy—appeared to play a role. This mechanism could explain why the fluid requirements documented in some recent reports are continuing to escalate to volumes far in excess of Parkland calculations, seemingly without limit.[8,9] In this scenario, fluid creep becomes self-perpetuating and creates its own physiology of edema formation.

Finally, this mechanism may also explain why fluid creep is being reported at this point in time. Over the past decade, three trends have emerged that all favor a tendency to over-resuscitate in the early post-burn period. First is the practice of goal-directed resuscitation, discussed previously, which still influences many clinicians. Second is the success of ubiquitous outreach education in burn care, which has improved burn triage but also contributed to a now-common problem of excessive resuscitation given by first responders and inexperienced physicians, who often greatly overestimate burn size[42,103] and sometimes run intravenous infusions "wide open." Thus, patients often arrive at a burn center having received much of their first 8-hour Parkland requirements in just an hour or two.[10]

Third is the current prejudice against use of colloid, which has developed in recent years. Several meta-analyses of trials comparing resuscitation regimens have concluded that use of colloids is deleterious to patients in a variety of situations,[104] including burn patients, for whom the odds ratio for mortality with albumin usage has been calculated to be as high as 2.40 (95% confidence limits: 1.11, 5.19).[105]

Though widely regarded as authoritative, these publications have been criticized for being based largely on very old, heterogenous, unblinded studies,[106] which appears to be true for burns. Reviews from the Cochran Collaboration have evaluated only four small trials involving burn patients,[107–110] only one of which showed increased mortality with albumin usage—the 1983 study by Goodwin et al.[109] Authors found that colloid-resuscitated patients required less fluid than those who received crystalloid alone (2.98 vs 3.81 ml/kg/%TBSA) but also demonstrated progressive increases in lung water up to 7 days post-burn. Mortality was higher in the colloid group (11 of 40 patients) than in the crystalloid group (3 of 39 patients), though all patients died later of causes not obviously related to fluid resuscitation. This small study has influenced thinking about burn resuscitation for >20 years and has contributed, perhaps excessively, to the interdiction of colloid use in many centers. As refutation of this attitude, a recent major multicenter trial of routine albumin use for resuscitation in almost 7,000 intensive care unit patients found no increased risk of death or other adverse outcomes.[111] Burn patients were excluded from this trial, but a more recent randomized trial involving burn patients yielded the same conclusion and revealed no difference in rates of multiple organ failure.[112]

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STRATEGIES FOR PREVENTION AND TREATMENT OF FLUID CREEP

On the basis of the information above, it can be argued that an early redefinition of the Parkland formula that excluded colloid use, the influence of goal-directed resuscitation, and the trends that have favored overzealous early resuscitation and the exclusion of colloids have combined to produce a trend toward increased burn resuscitation requirements, which has recently been characterized as fluid creep. If so, then these mechanisms also suggest remedies that should halt or reverse progression of this problem. However, this hypothesis is unproven; the causes of fluid creep are likely multiple, so any protocol to control it should address as many of these potential causes as possible. In addition, the magnitude of this problem in clinical practice, its still poorly understood etiologies, and its serious adverse consequences argue strongly for the performance of randomized trials to evaluate all of these therapies.

Potential therapeutic strategies include the following:

1. Restrict Early Fluid Resuscitation

Although the prompt institution of fluid resuscitation after burn injury is an important contributor to improved survival,[113] excessive initial resuscitation is a likely contributor to fluid creep, which may not be apparent until much later. As pointed out by Cancio et al, fluid requirements may fall below Parkland predictions for the first few hours after injury,[59] and infusions can often be adjusted downward during this period. Close communication with first responders and referring physicians—possibly including telemedicine or other visual evaluation[42]—is essential and helps burn professionals regulate resuscitation as soon as possible after injury. Use of widely accessible programs for calculating burn size and fluid requirements may also help inexperienced clinicians avoid overresuscitation.[114–116]

2. Consider Routine Colloid, or "Colloid Rescue"

Although recent literature fails to prove that colloid-based resuscitation increases mortality or complications in burn patients, it also does not demonstrate any benefit of its routine use. Many patients are successfully resuscitated with crystalloid alone, without excessive volumes. However, edema-related complications correlate with the absolute volume of fluids infused; the volumes required with colloid-assisted resuscitation appear to be less than those with crystalloids alone,[32,35,59] and this has been associated with lower abdominal pressures and incidence of clinical ACS.[55] A few centers have also used limited amounts of synthetic colloids such as hetastarch for routine burn resuscitation, with good results.[117,118] Thus, administration of colloid may reduce the consequences of fluid creep even if it does not directly address its causes.

One potential approach to controlling fluid creep, therefore, would be to adhere to the original Parkland formula and infuse a colloid bolus at the end of 24 hours post-burn. This is still practiced in some units[27,40] and should be considered in situations where resuscitation is not straightforward. Alternatively, some centers administer colloids to patients who develop increasing fluid requirements during resuscitation, as a means of "escape" from fluid creep. This mechanism likely explains the efficacy of plasmapheresis to arrest progressive acute resuscitation failure.[119] Yowler and Fratianne institute resuscitation with albumin at 12 hours post-burn when fluid requirements exceed 120% of normal.[40] In a recent report on burn management during Operation Iraqi Freedom, Chung et al noted increasing clinical problems with "resuscitation morbidity"; as a result, they have developed a protocol to utilize 5% albumin solution in any patient whose 24-fluid requirements are projected to exceed 6 ml/kg/%TBSA.[120] This has reduced the incidence of ACS to zero.

3. Use Resuscitation Protocols

Concerns over the occurrence of fluid creep has increased confusion and variation in both physician and nursing practices of fluid resuscitation in many burn centers. In response to these concerns, we have developed a strict protocol for resuscitation at the University of Utah, which includes a pathway for colloid "rescue" in patients with increasing fluid requirements. This protocol is illustrated in Figure 2. We have found this helpful in reducing excessive resuscitation and improving staff awareness of fluid resuscitation guidelines.

4. Other Resuscitation Alternatives

Hypertonic saline has been used for burn resuscitation for decades[1,121] and routinely requires less fluid than isotonic crystalloid. In addition, Oda et al reported that patients resuscitated with hypertonic lactated saline had less intra-abdominal hypertension than patients given LR.[54] Hypertonic resuscitation has been recommended for use in children[122] and the elderly[123] who tolerated excessive fluid volumes poorly. However, routine hypertonic resuscitation carries risks of hypernatremia and hyperosmolarity and requires careful monitoring. Its use has been

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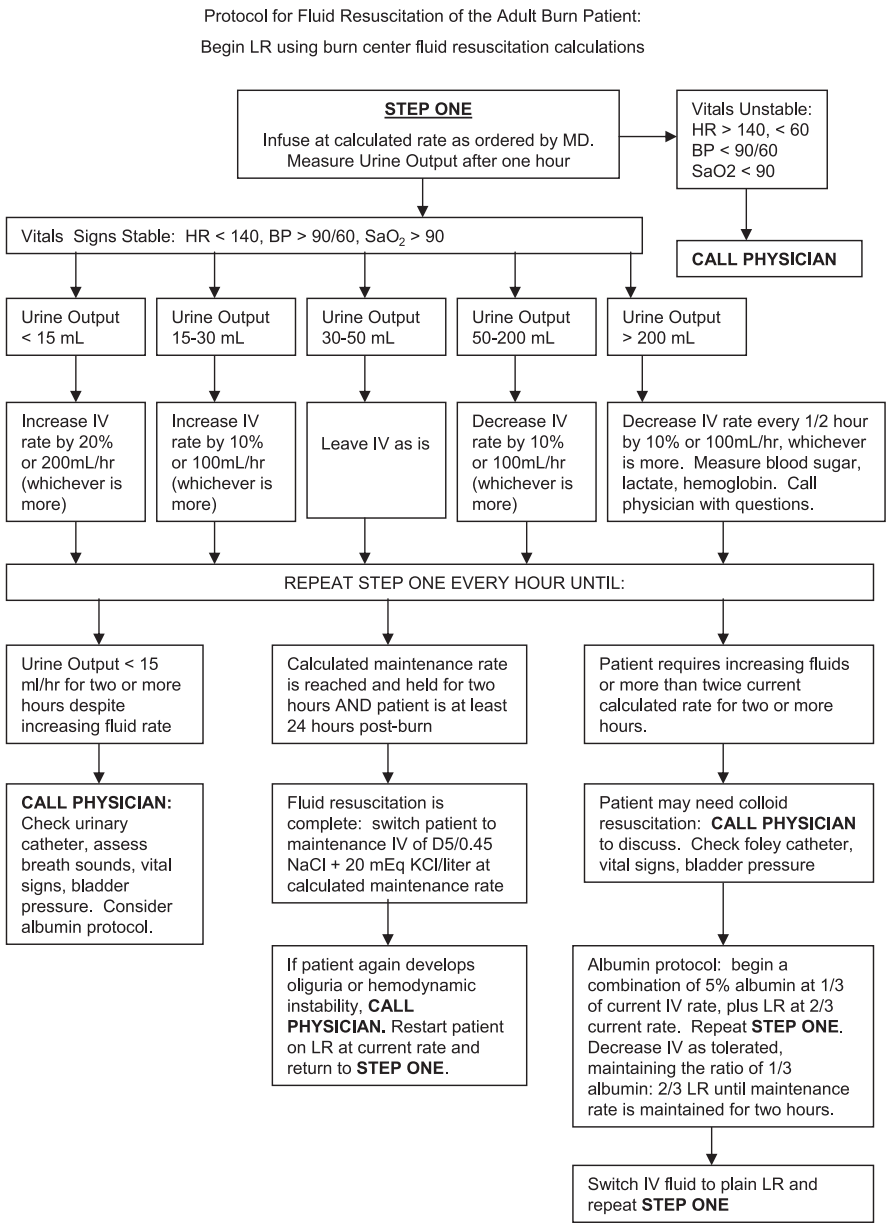

Figure 2. Protocol for fluid resuscitation of adult burn patients. In response to requests from nursing, this protocol was developed to permit nursing staff to manage fluid resuscitation of acute burn patients. Initial fluid rates are calculated by the Parkland formula. Nurses begin hourly infusion, measure urine output, and adjust fluids according to patient response. Development of unstable vital signs, inadequate response to fluids, or persistently high fluid requirements prompt a call to the physician. A pathway to begin colloid replacement exists for patients who display increasing fluid requirements or develop evidence of torso compartment syndrome.

associated with increased mortality in at least one study.[124] A recent Cochrane Database review found insufficient evidence to support either beneficial or deleterious effects of hypertonic resuscitation.[125]

Considerable recent research has also evaluated use of highly concentrated sodium solutions for resuscitation. The combination of 7.5% NaCl/dextran 70 (HSD) has been used for resuscitation of trauma patients in the field[126] and been advocated for situations such as combat or mass casualties, where large volumes of crystalloid may be unavailable.[127] In experimental models, infusions of HSD produced short-term repletion of intravascular volume while minimizing visceral edema.[128,129] However, in a clinical trial, a bolus of HSD did not reduce overall 24-hour fluid requirements.[130] Although these data do

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not clarify the value of HSD for routine burn resuscitation, they suggest that this agent might be useful to "rescue" patients demonstrating progressive fluid creep and edema-related complications.

Finally, it may be possible to regulate resuscitation pharmacologically. A number of investigators have attempted to reduce the severity of burn shock by blocking specific chemical mediators of acute inflammation, including use of vasodilators such as hydralazine, the serotonin antagonist ketanserin, and anti-inflammatory drugs such as hydrocortisone and ibuprofen.[18,93,131,132] The antioxidant vitamin C, given in high doses in the early post-burn period, has been shown to decrease fluid requirements in clinical burn resuscitation.[133] In experimental models, other scavengers of oxygen radicals have also been helpful in reducing fluid requirements for burn resuscitation.[134] Although none of these manipulations have found their way into widespread clinical use, the emergence of fluid creep as a clinical problem may renew interest in pharmacologic control of fluid resuscitation.

5. Monitor Resuscitation and Complications

Recent experience demonstrates that ACS is not itself a lethal complication in burn patients, although it is often associated with a poor prognosis from associated injury.[50] Early decompressive laparotomy can improve survival markedly, especially if ACS is diagnosed promptly.[47,49] Routine monitoring of bladder pressure should be performed in patients with large injuries, those who demonstrate oliguria or increasing ventilator requirements in the face of ongoing resuscitation, or those who require excessive resuscitation volumes, variously estimated at 6 ml/kg/%TBSA,[124] 250 ml/kg,[7] 500 ml/h,[53] or 20 liters of total fluid.[46] Established ACS is often a surgical emergency requiring immediate laparotomy, but impending ACS, heralded by increasing bladder pressures, can be treated by escharotomy, paracentesis, or fluid restriction. In addition, the value of colloid or hypertonic saline as a "rescue" therapy in such circumstances should be evaluated.

CONCLUSIONS

The recent emergence of fluid creep as a significant clinical problem in burn treatment has prompted review of classic investigations into the pathophysiology of burn shock that form the foundations of modern burn resuscitation. In many ways, this complication is a result of the progress made in burn care in recent decades, as patients with larger and larger injuries are considered salvageable and are subjected to aggressive initial care. Pruitt has suggested "pushing the pendulum back" in practicing fluid resuscitation. As an alternative, this experience should be viewed as an opportunity to move forward in burn treatment, by revisiting the principles of burn resuscitation and reevaluating current practice protocols. Although the exact causes of fluid creep remain undetermined, a number of strategies can be utilized to control its magnitude and complications. This experience also further underscores the need for multicenter randomized trials of resuscitation protocols to develop the best methods of caring for severely burned patients.

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