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Fluid Resuscitation in Burn Patients: Above and Beyond Baxter

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Fluid Resuscitation in Burn Patients: Above and Beyond Baxter

Abstract
Background: Information for immediate burn resuscitation and treatment has been available in many forms, most of which requires starting with the Parkland formula. Research in the last ten years has called that formula into question and has recommended either using it only as initial guidance or using another method all together.

Purpose: To present a summary, in an unbiased format, of the information available for immediate burn fluid resuscitation especially that which has been published in the past 25 years. The primary focus is on the Parkland formula and its validity either as initial guidance or as a method for immediate treatment.

Methods: An exhaustive search of available medical literature using CINHAL, Medline-OVID, Medline-plus and UpToDate. Of those articles highlighted, 20 were found to have information pertaining only to general guidelines, to particular types of burns or to a specific pediatric or geriatric population. The final 12 articles were found to have pertinent and current information regarding the immediate fluid resuscitation of new onset burns and the value of the Parkland or other formula in doing so. All tables and data analyses were directly transferred from annotated sources.

Results: The sum total of burn victims evaluated was over 1100 patients using various testing formats ranging from well-randomized to retrospective studies. The validity of each article is discussed and with the amount of available information, some are presented as supporting evidence only. Given the advances in knowledge of burn treatment and resuscitation, the author recommends additional studies comparing purposeful dehydration versus the Parkland formula, with emphasis on the means for monitoring the Parkland formula results.

Conclusion: Literature evidence has supported the Parkland formula in the past as a starting point for resuscitation, with the onus on the Provider for calculating appropriate amounts and adjusting based on careful monitoring. Recent studies have shown that the numbers from the Parkland formula are not reproducible. Therefore, the author recommends a larger study evaluating the Parkland formula as compared with Permissive Hypovolemia and other methods of resuscitation.

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Fluid Resuscitation in Burn Patients: Above and Beyond Baxter

A Clinical Research Project Submitted to the Faculty of the

School of Physician Assistant Studies

Pacific University

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For the Masters of Science Degree August 16, 2008

Faculty Advisor: Dr. Mark Pedemonte, MD
Clinical Project Advisor: Jonathon W Gietzen, MS PA-C
STATEMENT OF ACCEPTANCE:

This project is hereby accepted as a requirement for completion of the degree of: Masters of Science in Physician Assistant Studies at Pacific University School of Physician Assistant Studies.

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Biography

Kate Molyneux grew up in the Midwest and attended Wheaton College, Illinois where she majored in Biology. Upon graduating she received a commission into the United States Army as a Second Lieutenant in Aviation. After serving over 7 years as an officer and completing her Attack Helicopter Company Command, she left the active duty Army and moved with her husband, Dan, and her Siberian husky, Zeke, to Portland, Oregon. She held several medical jobs before being accepted to Pacific University’s Physician Assistant program. She enjoys being in the outdoors, hiking and fly-fishing.
Abstract

**Background:** Information for immediate burn resuscitation and treatment has been available in many forms, most of which requires starting with the Parkland formula. Research in the last ten years has called that formula into question and has recommended either using it only as initial guidance or using another method all together.

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**Keywords:** Burns, practice guidelines as topic, advances, crystalloid, colloid, thermal injuries, fluid, resuscitation, Parkland, state of the science, databases as topic, treatments, therapy, initial, injury, partial-thickness, burn unit, and management.
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To Dan—C’est seulement quand on a fini quelques chose d’import qu’on réalise ce qui est vraiment important.
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Table 1: Comparison of methods of fluid resuscitation.

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List of Abbreviations

TBSA.................................................................Total Body Surface Area
UOP...........................................................................Urine Output
ARF.................................................................Acute Renal Failure
TPN..............................................................Total Parenteral Nutrition
MV.................................................................Mechanical Ventilation
ARDS.....................................................Acute Respiratory Distress Syndrome
CHF............................................................Congestive Heart Failure
ACS...........................................................Abdominal Compartment Syndrome
Fluid Resuscitation in Burn Patients: Above and Beyond Baxter

I. Introduction

The American Burn Association has estimated that in 2007 over 500,000 patients per year were treated for various types of burns. The majority of these people had a thermal burn (46% fire/flame, 32% scald, 8% hot object), versus an electrical, chemical or other type of burn. Of that number only 8% were hospitalized and of that small percentage only 60% went to Burn Centers. [ABA, 2008] These numbers make for an interesting situation as most burn victims seek care at Emergency Departments, Urgent Care Centers and Private Physician offices, creating a need for Primary Care Providers to remain treatment-savvy.

It used to be that a severe burn was a death sentence, usually within hours or days. When exploring the history of burn resuscitation, the first recorded observations were made after the Rialto Theatre fire in New Haven, Connecticut in 1921 and after the infamous Coconut Grove fire at a club in Boston, Massachusetts in 1942. While caring for these burn victims, providers noticed that despite having survived the fire with large burns on their bodies, patients died from shock within the first 12-24 hours. Underhill and Moore identified the concept of thermal injury–induced intravascular fluid deficits in the 1930s and 1940s, and Evans soon followed with the earliest fluid resuscitation formulas in 1952. [Yowler, C.J. 2000] As previously mentioned, up to that point, burns covering as little as 10-20% of total body surface area (TBSA) were associated with high rates of mortality. Through the 1970s, even a 30% TBSA burn was associated with nearly 100% mortality, especially in older patients.

Over the next 30 years, advances in resuscitation further expanded these observations and led to numerous strategies to treat burn shock. Currently, almost a dozen deaths per day reportedly result from residential fires. Children younger than 5 years and adults older than 65 years have a mortality from burns that is 6 times the national average. [Emedicine, 2008]
Modern times have led to a progressive treatment for burns, and in the most recent years we have not only come to a greater understanding of physiologically how tissue is affected when burned, but also, how to manage a patient when they have received a burn. Current survival expectations can exceed 94%, and survival is increased the smaller the burn area and the younger the age of the patient. [Hackenschmidt, A. 2007] When burn victims do die, the leading causes, especially with patients having 80% Total Body Surface Area (TBSA) burn are from multiple organ failure, sepsis or concomitant inhalation injury. [Hackenschmidt, A. 2007]

To combat this mortality, Burn Centers have been created that exist solely for burn evaluation, resuscitation, and treatment. These centers are important because there are so many aspects to manage with burn treatment as well as many complications associated with the treatment. Burns obviously affect the skin, but resuscitation includes management of airway, ventilation, fluid balance, pain management, temperature control, psychosocial support, early wound care and infection prevention. [Hackenschmidt, A. 2007] The most important thing to understand about burn patients is that a burn has not only a local effect to the thermally injured tissue, but burns also affect the body on a systemic level, all of which leads to massive fluid movements from the intravascular space into the interstitium. As the burn size approaches 15-20% total body surface area (TBSA), shock sets in if the patient does not undergo appropriate fluid resuscitation. [Emedicine 2008]

We also now understand much more about fluid movement in the body of a patient who has received a burn and how it will affect the patient on multiple levels. Hypovolemia is an enormous initial problem in a badly burned patient and this leads to inadequate tissue perfusion and eventually organ failure. Secondarily, many of the problems associated with a burn also cause or heighten edema, making it difficult to treat because the edema is multi-factorial.

Initially, a burn affects the tissue at the cellular level by causing a decrease in cellular transmembrane potential in both injured and non-injured tissue. Changing this potential leads to an increase in intracellular sodium, as the transmembrane Na-ATPase activity is decreased. The overall
effect drives water into the cells. A cycle of cell membrane rupture continues due to spreading decreased membrane potential and more subsequent intracellular sodium, and water accumulation.

At the same time, heat injury triggers inflammatory and vasoactive mediators. Margination occurs with neutrophils, macrophages and lymphocytes, all of which release mediators to influence capillary permeability. The immediate area is vasodilated with an increase in capillary permeability, resulting in edema within the first few minutes of injury. The intercellular communication spreads and vasodilation also occurs systemically. Complement proteins, kinins, histamines, platelet products, serotonin, prostaglandins and oxygen-derived free-radicals and neuropeptides (a cascade of chemical mediators) are released by the inflammatory response, causing a systemic reaction. Also, in accordance with the associated trauma, the sympathetic system is stimulated, leading to a stress response. One aspect of this response is that glucagon is released and fluid is lost through glycosuria related diuresis, further aggravating hypovolemia.

Physically, heat injuries work to also denature collagen fibers in the interstitium which causes expansion of the third space potential. The potential space develops a negative pressure which favors drawing fluids into the interstitium, which further heightens edema.

All of these effects are maximized at approximately 6-12 hours post-burn. At this point the capillaries begin to re-seal, thus decreasing fluid requirements. Most burn resuscitation formulas adjust fluids at this time for that reason, and at this point some formulas begin adding colloid. One should also note that in general, these reactions mainly occur with burn patients having >15% TBSA affected tissue. Burns with less than this amount will typically not stimulate the systemic inflammatory response.

As mentioned previously, the fluid losses and resulting hypovolemia and intravascular volume deficits often lead to poor organ perfusion. Under-resuscitation can convert areas of ischemic damage into deeper burn damage or can lead to acute renal failure (ARF) and death. On the other hand, over-resuscitation or rapid fluid bolus can lead to systemic or pulmonary edema, elevated compartment
pressures, areas that require escharotomies, Acute Respiratory Distress Syndrome (ARDS), and multiple organ dysfunctions.

The author’s interest in burns and burn treatment was piqued during a six-week rotation at the Oregon Burn Center. Though knowing little about managing the entirety of patient care for a burn victim, she noted that fluid resuscitation seemed to vary quite a bit for each patient though she was only familiar with the Parkland Formula.

In 1968, Dr. Charles Baxter, MD, described a particular method for burn victim resuscitation while working at the Parkland Hospital at Southwestern University Medical Center in Dallas, Texas. His paper focused on fluid resuscitation for burn victims after completing a study with 438 patients of his own. In a series of published journal articles, he recommended using Ringer Lactate solution at 4 mL/kg body weight/% total body surface area burned (TBSA). This volume is calculated for the first 24 hours of resuscitation, with half the volume being given in the first 8 hours from the time of the burn and the remaining fluid given over the following 16 hours. [Emedicine 2008]

To maintain effective resuscitation, Baxter monitored the urine output (UOP) and initially recommended an initial goal urine output of 50mL/hour and, once reached, to then reduce the fluids given to maintain UOP at this rate. He went on to recommend 50-100mL/hour UOP as the goal, and in further articles mentioned a goal of above 40mL/hour and later, 40-70mL/hour. He also repeatedly mentions that this formula will be applicable to at least 70% of patients, and that 12% will need more than the recommended fluid levels and 18% will need less. Finally, it is important to note that his patient set included burn victims with inhalation injuries and very large burns, all of which supported his formula and its application. [Engrav 2000]

The Baxter formula was embraced by the medical community and when it proved itself under multiple trials (by patient survival); it was considered the standard of care for most burn patients. Other formulas have been developed (see Table 1) and their use is varied from clinic to clinic, though the Parkland formula and Ringer’s Lactate as fluid of choice are both widely used and accepted.
Over the last 20 years, the Parkland Formula has gone through some transition to being used no longer as the optimal care standard, but as initial guidance only. Multiple studies have been performed that fail to reproduce the same results as gathered by Dr. Baxter. Several explanations have been postulated as to why this has happened: Did Baxter give enough detailed guidance for us to follow in a reproducible manner? Are providers no longer trusting the formula and giving more or less fluid based on their own gestalt or experience? Are opioids or “opioid creep” changing the amount of fluid we need to give? Is the nature of burn treatment changing with new pharmacological treatments? Are the types of burns changing? Do new monitoring technologies change how we view appropriate resuscitation? The ABA acknowledges that, “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.” [Pham 2008] Above all else, the medical community has begun to embrace evidence based medicine and seemingly, though it is necessary to tailor treatment to an individual, there should be a basis or standard for care that can be supported by reproducible studies.

The end point or points for resuscitation are also currently debated, but hourly urine output is a well-known and trusted parameter for guiding effective fluid management. Current ABA recommendations state that “the rate of fluid administration should be titrated to a urine output of 0.5 mL/kg/h or approximately 30-50 mL/h in most adults and older children (>50 kg). In small children, the goal should be approximately 1 mL/kg/. Failure to meet these goals should be addressed with gentle upward corrections in the rate of fluid administration by approximately 25%.” [Pham 2008]

Aside from closely monitoring UOP, gradually adjusting the fluid rate is much more favorable than injecting frequent boluses when UOP is low. This may cause elevations in hydrostatic pressure gradients for short periods that serve to shift more fluids to the interstitium and increase severity of the edema. It is considered appropriate to administer a bolus to patients early in the resuscitation to prevent hypotensive shock and at the same time, UOP at rates greater than 30-50 mL/h should be
avoided. Fluid overload in the critical hours of early burn management may lead to unnecessary edema and pulmonary dysfunction. It can also require morbid escharotomies and extend ventilator support. One must consider the whole patient picture and not the minute-by-minute changes because the overall clinical response and general trends in these numbers are much more useful for adjusting fluid.

Furthermore, specific burn populations usually require higher resuscitation volumes. Patients with inhalation injuries, which are generally considered to be one of the greatest risks for mortality, require volumes sometimes as much as 30-40% higher (close to 5.7 mL/kg/%TBSA) than predicted by the Parkland formula. Extremely large burns (upwards of 70% TBSA) also require significantly more fluid. Baxter does acknowledge circumstances where the formula may be adjusted upward, such as inhalation injuries and gross burn state, but he refers back to his results saying that hyper-resuscitation will only be needed in 12% of the cases.

Ia. Purpose

The author will present a summary, in an unbiased format, of the information available regarding burn fluid resuscitation within the first 24-hour period, especially that which has been published in the past 25 years. The primary focus is on the Parkland formula and its validity either as initial guidance or as a method for immediate treatment, but it is necessary to also discuss possible explanations for increased fluid need and new methods for fluid resuscitation.

Ib. Hypothesis

The author suspects that this review will question continued use of the Parkland Formula, even as initial guidance. I also believe that some complications such as Fluid Creep and Abdominal Compartment Syndrome (ACS) will be avoided in the future if the standard of care is adjusted as per current evidenced based medicine findings.
While working for six weeks at the Oregon Burn Center, the author saw first-hand multiple examples of excellent and appropriate resuscitation and continued care. Survival after extensive burns was impressive, especially those with inhalation injury. Unfortunately, most practitioners do not have the delicate expertise that the author witnessed, and Emergency Department staff needs reliable methods for providing care to an injury with which they may not be familiar. Regardless, the point of having standards is to provide the best patient care available, and obviously, if a method is inappropriately applied or outdated, we must re-evaluate our standard of care.

II. Methods

An exhaustive search of available medical literature was conducted using CINHAL, Medline-OVID, Medline-plus and UpToDate, with the keywords: burn, burns, practice guidelines as topic, advances, crystalloid, colloid, thermal injuries, fluid, resuscitation, Parkland, state of the science, databases as topic, treatments, therapy, initial, injury, partial-thickness, burn unit, and management. The inclusion criteria were all English language articles, published after 1985, evaluating the Parkland Formula and/or current burn resuscitation methods. Literature from 1985 through the present was reviewed and graded based on how well they answered the hypothesis. Exclusion criteria included articles dated before 1985, those that addressed specific populations or types of burns, and articles that focused on resuscitation evaluation methods. The results were analyzed and of those articles highlighted, 20 were found to have information pertaining only to general guidelines, to background information, to particular types of burns or to a specific population. The final 12 articles were found to have pertinent and current information regarding the immediate fluid resuscitation of new onset burns and the value of the Parkland or other formula in resuscitation. All tables and data analyses were directly transferred from annotated sources and the new compiled results were analyzed.
III. Results

A total of 12 articles addressed the validity of the Parkland Formula between 1985 and 2008. (See Table 2) These articles either addressed particular types of patients and applicability of the Parkland Formula, the validity of Baxter’s results using the Parkland Formula, or compared the Parkland formula to a variation formula. Hypernatremic resuscitation was not considered in any of the articles because the idea has only been recently introduced and has not had sufficient review and study reproduction. Each article was evaluated on the following criteria: 1.) randomization, 2.) cohort study, 3.) sample size, 4.) applicability of burns, 5.) average amount of fluid used, 6.) whether it supported the Parkland formula and 7.) recommendation for higher or lower than the Parkland formula. (See Table 1) 1154 patients were included in the studies and the average sample size was 98 patients, 5 of the studies were randomized and 4 were cohort studies.

Navar et al [Navar,P.D. 1985] performed a retrospective chart review and examined the amounts of fluids administered, using the Baxter formula for 171 patients with at least 25% TBSA burn, some with inhalation injuries and some without inhalation injury. Both groups were matched, electrical burns and early death patients were excluded. Their UOP goal was 30-50mL/kg/h. The fluid requirement average was 5.76 +/- 0.39 mL/kg/%TBSA for those with smoke inhalation injury and 3.98 +/- 0.19 mL/kg/%TBSA without inhalation injury. They concluded that inhalation injury markedly increases the need for fluids, well in excess of the Parkland formula (44% on average); and those patients without inhalation injury supported the findings of the Parkland formula. It is important to note that Baxter specified that patients with inhalation injury have some of the greatest fluid requirements, yet he did not adjust his formula for that specific injury.

Herndon et al [Herndon,D.N. 1988] compared resuscitation needs in three groups, two of which apply to our study: 20 patients with 30% TBSA with inhalation injury and 14 patients with burns alone that exceeded 50% TBSA. For inhalation injury patients, on the average 3.8 +/- 1.5 mL/kg/%TBSA of fluid was required. For a burn alone it was 2.3 +/- 1.2 mL/kg/%TBSA of fluid that was needed. It is
important to note that children were included in this study and the investigators did not report figures separately. This study placed most of its focus on pulmonary studies, but did effectively represent that under- or over-resuscitation of inhalation injuries is dangerous and inhalation injured burn patients will require more fluids than others.

Darling et al [Darling, G.E. 1996] also examined the fluid needs of 100 adult patients with inhalation injuries in a retrospective study. Their purpose was to determine whether there is a relationship between pulmonary complications and fluids received and to contrast the amount of fluid received compared to the amount predicted. On average they required 6.52 +/- 0.26 mL/kg/%TBSA. They concluded that the higher fluid requirement is a reflection of the increased severity of the injury, which predisposes the patient to other complications.

Dai et al [Dai, N.T. 1998] conducted a retrospective review that compared adult fluid resuscitation for inhalation injuries and found 3.1 +/- 1.0 mL/kg/%TBSA in a group of 26 patients with inhalation injuries and 2.3 +/- 0.8 mL/kg/%TBSA for 36 patients without inhalation injury. UOP goal was 0.5-1.0 mL/kg/hour as specified within the limitations of the Parkland formula. They found that results were significantly lower in fluid requirement than stipulated by Baxter and by previous studies, in fact they compare their results to the modified Brooke formula which is nearly half of the Parkland.

Engrav et al [Engrav, L.H. 2000] took an unusual approach as they reviewed records from 7 Burn Centers including their own and gathered data on 50 adult patients, some of which had inhalation injuries and some without. The 16 patients with inhalation injury required 5.2 +/- 2.3 mL/kg/%TBSA and the 34 patients with burn alone required 4.8 +/- 2.0 mL/kg/%TBSA. They noted that, of the burn victims without inhalation injury, the average fluid requirement was significantly affected by the 13 patients with full-thickness burns who required 5.3 +/- 2.2 mL/kg/%TBSA. In their clinical practice, they had observed that they seemingly used more than as specified by the Parkland formula and this proved true when they tested that hypothesis. Not only did the inhalation injuries require more fluid, but also the full-thickness burns were outside of the fluid requirements as defined by Baxter.
Cartotto et al [Cartotto,R.C. 2002] conducted a retrospective cohort study to determine how well the Baxter formula actually predicted the amount of fluid that would be needed for appropriate fluid resuscitation. They found that despite careful monitoring in accordance with the Parkland formula, all the patients received much more than predicted. This was especially apparent in patients with large, full thickness burns who received 6.7 +/- 2.8 mL/kg/%TBSA.

Friedrich et al [Friedrich,J.B. 2004] conducted a cohort study of 11 burn patients from 1975-1978 and 11 patients from 2000, all matched by age, sex and %TBSA, to discover whether “fluid creep” (i.e. resuscitating more than the Baxter formula or in past historical estimate) was a new phenomenon that was becoming consistent in their practice. They encouraged the burn community to explore reasons why practitioners were now using much more fluid than that of 20 years ago, and postulated several explanations. On average their current patients received 8.0 +/- 2.5 mL/kg/%TBSA. They did not compare ICU stays or mortality and morbidity results which would have allowed them to show that many specialty units were and still are using much more than the Parkland Formula recommends without significantly increasing mortality. However, most significant was that the patients had no difference in their UOP, which was Baxter’s basis for adjusting fluid resuscitation.

Cancio et al [Cancio,L.C. 2004] responded to the question regarding resuscitation volume affecting in-hospital mortality. They concluded that higher volumes of fluid resuscitation were not directly correlated with increased mortality, and instead, it was based more on age, %TBSA burned and base deficit. This team did use a modified Brook formula and divided their groups into more or less than 4 mL/kg/%TBSA, so the volume is still relatively close to the Parkland Formula. Their high volume group with 56 patients still averaged 6.10 +/- 0.22 mL/kg/%TBSA.

Mitra et al [Mitra,B. 2006] conducted a retrospective, randomized review to elucidate whether the Parkland formula should still be the ‘gold standard’ for fluid resuscitation, if there was a significant difference to how it was applied, and whether this difference should have been used as guidance to
establish a revision of fluid resuscitation. This study used 49 patients that received 5.58 +/- 2.28 mL/kg/%TBSA.

Arlati et al [Arlati,S. 2007] explored the potential for a new method of treatment they dubbed “permissive hypovolaemia” as they compared two cohort groups of patients, 12 of whom were given the Parkland formula and 12 of whom received hypovolemic fluid levels for resuscitation. The Parkland formula patients received 4.6 +/- 0.3 mL/kg/%TBSA and the hypovolemic patients received 3.2 +/- 0.7 mL/kg/%TBSA. Note that the Parkland formula was used only as initial guidance. The study looked for complications of or injury due to over- or under-resuscitation.

Klein et al [Klein,M.B. 2007] analyzed 72 patients with an average received volume of 5.2 mL/kg/%TBSA. The team noted that other studies have suggested that patients today are receiving more fluid than in the past. Their purpose was to find significant predictors of negative outcomes after resuscitation. They concluded that higher volumes equaled higher risk of injury and complications.

Blumetti et al [Blumetti,J. 2008] conducted a retrospective analysis of 483 burn patients to measure adequate resuscitation. Using Baxter’s guidelines based on UOP of 0.5-1.0 mL/kg/hr only 14% of these patients were adequately resuscitated by the Parkland formula, with an average of 5.8 mL/kg/%TBSA. They concluded that the Parkland formula should only represent a “starting” point for resuscitation.

IV. Discussion

The focus of this study was to compare recent data presented in current medical literature to determine whether the medical community should retain Baxter’s Parkland Formula as a standard of care in new onset burns. Patients vary, but past research and current knowledge of burns and burn treatment should lead us to a standard of care for burn victims. Baxter was clear in his point that his formula should apply 70% of the time, including in those patients with inhalation injuries or large, deep burns, and the articles reviewed clearly did not support this number or something near it.
Navar’s study [Navar,P.D. 1985] may have initially appeared to support the Parkland formula because his 120 patients with a burn only were consistent with what Baxter proposed (with 3.98 +/- 0.19 mL/kg/%TBSA). However, this article showed clearly that in the 51 cases with inhalation injury as well as burn, the patients required well above the Parkland at 5.76 +/- 0.39 mL/kg/%TBSA. They collected data from patients with at least 25% TBSA burn and thoroughly confirmed inhalation injury with xenon-133 scanning, bronchoscopy or both. His team used the Parkland formula as their initial fluid estimate and adjusted drip rate based on clinical response and maintenance of UOP of 30-50mL/hour. One downfall of this study is that they used pediatric patients, but to compensate for this, they separated the data by age, showing that fluid requirements were consistently significantly higher (p=0.05 or greater) in inhalation injuries in groups from age 6-62. They noted that inhalation injury and massive burns have been acknowledged to be the greatest requiring of fluid, but no one has yet proposed an adjustment to the Baxter formula. Intriguingly, they also stated that their results concur with previous articles estimating inhalation injury fluid requirement, and they called for standardization of a 5.5-5.75 mL/kg/%TBSA initial assessment adjustment for inhalation injuries. This study produced strong evidence that Baxter, though he acknowledged that massive burns and inhalation injuries may require the most fluid, likely overestimated the applicability of the formula to this type of patient.

Likewise, Herndon’s study [Herndon,D.N. 1988] examined inhalation injury and required fluid amounts to prevent lung injury. This study disagreed with most of the current studies in that the fluid requirement for all of the patients (inhalation injury or only burn) was significantly lower than elsewhere reported. It is interesting to see a parallel though: the inhalation injury patients were within Baxter standards at 3.8 +/- 1.5 mL/kg/%TBSA and the non-inhalation injuries averaged 2.3 +/- 1.2 mL/kg/%TBSA, which shows a significant increase of need (by 65%) of the patients who had inhalation injuries. Also, this study included children and did not provide a breakdown of the ages, so it was impossible to separate the data. Finally this study was not designed to test the Parkland formula,
in fact, the study result showed that patients survived with fluid amounts significantly lower than insisted upon by Baxter.

The study of inhalation injuries continued with Darling’s study [Darling,G.E. 1996] of inhalation injuries and increased fluids exacerbating lung problems. Certainly, complications associated with inhalation injury are the most common and are severe, and this group used a controversial method of resuscitation by including colloid introduction at 8 hours post-burn. Some have reported that this may increase pulmonary injury, which this report acknowledges. Also, this study must be considered cautiously because 86% of all patients studied were smokers, and thus were prone to greater lung injury. Overall, fluids ranged from 4.03-14.69 mL/kg/%TBSA with a mean of 6.52 +/- 0.26 mL/kg/TBSA with a percent deviation from the Parkland being as much as 267%. They also concluded that the patients that developed pneumonia, ARDS or who later died received higher levels of fluid than those who survived, but statistically, this difference was not significant (based on the p value). However, predicted fluid requirement was found to have a strong association with death (p = 0.0027). They recommend a re-evaluation of fluid resuscitation and invasive monitoring for >15% TBSA burned with inhalation injury.

An intriguing evaluation of the Parkland formula was demonstrated in Dai’s study [Dai,N.T. 1998] by a retrospective analysis on 62 patients, 26 with inhalation injury and 36 without inhalation injury. The average fluid needs were 3.1 +/- 1.0 mL/kg/%TBSA and 2.3 +/- 0.8 mL/kg/%TBSA respectively. Dai concluded that in general patients required much less than was suggested by Baxter. It is interesting, as in Herndon’s article, that there was a significantly greater need in patients with inhalation injury (74% versus Herndon’s report of 65%). If nothing else, one must wonder if the Parkland formula was reproduced appropriately (which they comment on as a difficulty in this study), and if not, one may conclude at a minimum that inhalation injuries always require significantly more fluids that those without such injuries.
Engrav et al [Engrav,L.H. 2000] questioned why current burn-related resuscitation has seemed to deliver much more fluid than recommended by Baxter. They conducted a literature review and found two articles that support the Parkland formula and two that do not (the same articles are referenced here as well: see Herndon, Darling, Dai and Navar articles). They reviewed 50 cases that were collected from multiple Burn Centers who received an average of 5.2 +/- 2.3 mL/kg/%TBSA and concluded that patients typically receive more fluid than by the Parkland standard. Most importantly, they called for a study to confirm this finding and they discussed several possibilities for an explanation.

In the Cartotto et al article [Cartotto,R.C. 2002], the team made a direct evaluation of the Parkland formula and concluded that in most cases, Baxter’s formula underestimated the amount of fluid required for appropriate resuscitation. Cartotto’s team only surveyed 31 patients, which is a smaller sample size. They also admitted to struggling at times to interpret what Baxter had in mind with the directions to reproduce the formula, but they did not believe that this would lead to the vastly different results that they found. They also showed that the Parkland formula was accurate for the first 8 hours of resuscitation, so by their estimation, the formula should remain in place as a time-honored guide to initial resuscitation. They recommend a study with 5.6-7.7 mL/kg/%TBSA given to patients with large full thickness burns to be conducted.

Friedrich et al [Friedrich,J.B. 2004] tested whether increased fluid resuscitation, termed “fluid creep”, was a new phenomenon. They compared two sets of 11 patients from 1975-78 and 2000. Both sets were matched for age, sex and %TBSA, and the first group was in line with Baxter, but the second group received 100% more than specified by the Parkland formula. They concluded that it was only recently that providers have started increasing fluid resuscitation amounts, but we are left with a question that still lingers—why?

Cancio et al [Cancio,L.C. 2004] observed 56 patients who received 6.10 +/- 0.22 mL/kg/%TBSA. This team started with the modified Brooke formula (see Table 1), but the fluid was
then adjusted based on a UOP of 30-50 mL/kg/hour. Their purpose was to identify those patients who required above 4mL/kg/%TBSA and to find whether resuscitation volume affects mortality in-hospital. They too concluded that inhalation injury required significantly more fluid (5 mL/kg/%TBSA).

Another research team that evaluated whether deviations from the Parkland formula were widespread and if this should be used as a basis for a revision of fluid resuscitation was Mitra et al. [Mitra,B. 2006] Their 49 patients were given 5.58 mL/kg/%TBSA with minimal complications. Interestingly, in this study, a large proportion of the fluid excess was given in the first 8 hours. Overall mortality was the same as other centers and lower than other studies, without significant numbers of complications. Previous studies indicated that giving fluid over the Parkland formula led to over-resuscitation type injuries, but this study showed little or no difference with fluid-type complications.

A ground-breaking approach was taken by Arlati et al [Arlati,S. 2007] as they introduced the burn world to “permissive hypovolaemia”. Two cohort groups of 12 patients each, one of whom received the Parkland formula and one that received an average of 3.2 +/- 0.7 mL/kg/%TBSA were monitored by the multi-organ dysfunction score (MODS) to evaluate organ function damage. Surprisingly, patients tolerated this form of resuscitation well and permissive hypovolemia led to less edema and fewer complications than the Parkland. They concluded that this method reduces organ and system disturbance and prevents fluid overload injuries.

Klein et al [Klein,M.B. 2007] compared the variables that contributed to increased injury post-burn, including outcome from fluid received, %TBSA, age, weight and intubation status. They did use the Parkland formula, but they also had an average UOP of 1.1 mL/kg/hr, which was a higher goal for resuscitation than Baxter recommended. Their retrospective cohort study showed that for every extra 5L of fluid given, the odds ratio for pneumonia, sepsis, ARDS, multi-organ failure and death increased significantly (minimum OR = 1.49), and all patients who received greater than 25% more than predicted fluid volumes experienced adverse outcomes. Clearly, massive over-hydration or “fluid creep” led to undesirable effects.
Blumetti et al [Blumetti, J. 2008] conducted a review of the accuracy of the Parkland formula based on a retrospective study of 483 patients at the same institution over the past 15 years. Overall, they stated, “the actual burn resuscitation infrequently met the standard set forth by the Parkland formula” (only 13% of the time), and usually the amount was higher.

In summary, these findings are significantly different from the original Baxter formula of 4.0 +/- 0.3 mL/kg/%TBSA, despite the depth of injury and with or without inhalation injury concomitantly.

These findings should be viewed with caution because the study groups were small in the majority of the studies (n=77 or below in 10 of the 12 reports). However, when the information from all patients was combined, 1154 far outweighed the 438 initially studied by Baxter. Unfortunately, not every study was conducted directly to evaluate the Parkland formula. Also, one must question if all providers who used the Parkland formula were actually applying it uniformly, of no fault of their own. Baxter has not been clear on the UOP goal and as evidenced by the articles that applied the Parkland formula, their interpretation of his method became important. Furthermore, colloid use was not addressed by Baxter at all, though the use of Albumin was alluded to in one of his articles, and was frequently used at clinics world-wide with various reported results, all of which served to confound results when using the formula. Moreover, as indicated in several articles, Baxter did not describe if fluid should be gradually adjusted at 8 hours or if drip rate should be changed at once and consequently, would rapid adjustment have the same effect as adding a bolus?

In evaluating fluid resuscitation, we must also continue exploring reasons why providers are increasing initial 24-hour fluid resuscitation, also dubbed “fluid creep”. First of all, Cancio [Cancio, L.C. 2004] suggested that providers may be more likely to increase fluids, rather than decrease them, based on appropriate adjustment occurring 37% and 27% of the time in that order. Blumetti [Blumetti, J. 2008] also suggests that part of the variation of the formula is “failure to implement management of the formula”, in other words, that careful monitoring was not or could not be
performed at the appropriate time. Thirdly, it is suggested by the Engrav article [Engrav, L.H. 2000] that potentially the nature of the burns we treat has changed, methamphetamine explosion burns, for example, seemed to require more fluids. The same article suggests that new, more invasive techniques for monitoring may be requiring more fluid.

Another possible explanation for fluid creep was introduced by Sullivan et al [Sullivan, S.R. 2004] and has been termed “opioid creep”. They described how analgesics blunt physiologic response to fluid resuscitation, requiring more for the same effect. Modern medicine has provided not only a wider spectrum of pain medication from which to choose, but also, providers have recognized that in the past, we were reluctant to give narcotics and sedative-hypnotics. Sullivan’s report demonstrated a clear linear response (P < 0.01) between amount of opioid equivalents and fluids given. The increase of amount and number of analgesics caused hypotension and thus, increased fluid needs. This is only one initial explanation for a problem that could easily be multi-factorial.

Unfortunately, as with any other literature review, this particular study has its limitations. In general, studies relating to burn victims have low sample sizes, which overall reduces the validity of the study. Some studies attempt to compensate by using animal subjects. Moreso, though some studies exist on uniform burns emplaced on animal subjects, pain control is obviously not titered per patient and normally the animals are kept sedated as per current abuse prevention laws and study criteria. Therefore, the difficulties of evaluating opioid creep, for example, are limited to human subjects only, and obviously cannot have a control group without analgesics. Also, not all information was provided in each article to make a full evaluation as pertains to this study (i.e. not separating child patients from adult patients).

V. Conclusion

Based on this review of recent medical literature, the author found data to potentially question the continuing usefulness of the Parkland Formula. Baxter did an incredible work by keeping the
records and observations and developing his formula, knowing that it would benefit all providers. However, if nothing else, from this study, one may conclude that something has changed in burn treatment, making it necessary to review the Parkland formula’s effectiveness. We may never know why this change occurred, but evidence based medicine demands that we have a supported explanation for our treatment standards and the Parkland formula may have decreased in applicability.

As with most literature reviews, and from a quality control standpoint, burn centers would benefit from another, larger size retrospective review of their outcomes and management approaches. This may help identify patterns of success and/or failure that could then be adjusted within the practice preferences of the physicians who staff that particular burn center.

Furthermore, it would be ideal for a specific large-scale study to be performed to further evaluate the summary of these findings, mainly because the results were so varied. A great deal of the inconsistency appeared to stem from low sample numbers which will always be a challenge when dealing with burn patients, but if several Burn Centers participate cooperatively, a study that includes at least 200 patients could be accomplished. The author recommends a randomized, cohort study comparing permissive hypovolemia with a UOP goal of 50-100 mL/hour. The point of this study is to evaluate the method that provides the best results, regardless of extent of injury. Other smaller, retrospective studies have been conducted, but the ABA needs more conclusive evidence before it may change its policies.

Until an appropriate study is completed, providers could use the initial guidance from Baxter, expecting that much more fluid will be required even in the first 8 hours (especially for larger burns or inhalation injuries); or more preferably, start at a higher level such as 5.5 mL/kg/%TBSA. The majority of the studies suggested this higher amount (on average) and did not show strong evidence of complication due to fluid overload. In either instance, using UOP with frequent monitoring and adjustment continues to be appropriate as supported by current literature.
Table 1: Methods of Fluid Resuscitation for New Onset Burn, [Emedicine 2008]

<table>
<thead>
<tr>
<th>Formula</th>
<th>Fluid in First 24 Hours</th>
<th>Crystalloid in Second 24-Hours</th>
<th>Colloid in Second 24-Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkland</td>
<td>RL at 4 mL/kg per percentage burn</td>
<td>20-60% estimated plasma volume</td>
<td>Titrated to urinary output of 30 mL/h</td>
</tr>
<tr>
<td>Evans (Yowler, 2000)</td>
<td>NS at 1 mL/kg per percentage burn, 2000 mL D5W*, and colloid at 1 mL/kg per percentage burn</td>
<td>50% of first 24-hour volume plus 2000 mL D5W</td>
<td>50% of first 24-hour volume</td>
</tr>
<tr>
<td>Slater (Yowler, 2000)</td>
<td>RL at 2 L/24 h plus fresh frozen plasma at 75 mL/kg/24 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brooke (Yowler, 2000)</td>
<td>RL at 1.5 mL/kg per percentage burn, colloid at 0.5 mL/kg per percentage burn, and 2000 mL D5W</td>
<td>50% of first 24-hour volume plus 2000 mL D5W</td>
<td>50% of first 24-hour volume</td>
</tr>
<tr>
<td>Modified Brooke</td>
<td>RL at 2 mL/kg per percentage burn</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MetroHealth (Cleveland)</td>
<td>RL solution with 50 mEq sodium bicarbonate per liter at 4 mL/kg per percentage burn</td>
<td>Half NS titrated to urine output</td>
<td>1 U fresh frozen plasma for each liter of half NS used plus D5W as needed for hypoglycemia</td>
</tr>
<tr>
<td>Monafo hypertonic Demling</td>
<td>250 mEq/L saline titrated to urine output at 30 mL/h, dextran 40 in NS at 2 mL/kg/h for 8 hours, RL titrated to urine output at 30 mL/h, and fresh frozen plasma 0.5 mL/h for 18 hours beginning 8 hours postburn</td>
<td>One-third NS titrated to urine output</td>
<td></td>
</tr>
</tbody>
</table>

*D5W is dextrose 5% in water solution
Table 2: Comparison of Results from Reviewed Articles

<table>
<thead>
<tr>
<th>Author, year</th>
<th># Patients and Characteristics</th>
<th>Average Fluid Used (mL/kg/%TBSA)</th>
<th>% Pts Received less or more than Parkland</th>
<th>Supporting Baxter</th>
<th>Higher or Lower than Baxter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baxter et al, 1968</td>
<td>438</td>
<td>4.0 +/- 0.3</td>
<td>12%</td>
<td>(original data)</td>
<td>n/a</td>
</tr>
<tr>
<td>Navar et al, 1985</td>
<td>171 w/ smoke inhalation 120 w/o</td>
<td>5.76 +/- 0.39 w/ 3.98 +/- 0.19 w/o</td>
<td>30%</td>
<td>No</td>
<td>higher</td>
</tr>
<tr>
<td>Herndon et al, 1988</td>
<td>20 w/ 14 w/o</td>
<td>3.8 +/- 1.5 w/ 2.3 +/- 1.2 w/o</td>
<td>41%</td>
<td>No</td>
<td>lower</td>
</tr>
<tr>
<td>Darling et al, 1996</td>
<td>100 w/</td>
<td>6.52 +/- 0.26</td>
<td>100%</td>
<td>No</td>
<td>higher</td>
</tr>
<tr>
<td>Dai et al, 1998</td>
<td>26 w/ 36 w/o</td>
<td>3.1 +/- 1.0 2.3 +/- 0.8</td>
<td>100%</td>
<td>No</td>
<td>lower</td>
</tr>
<tr>
<td>Engrav et al, 2000</td>
<td>50</td>
<td>5.2 +/- 2.3</td>
<td>58%</td>
<td>No</td>
<td>higher</td>
</tr>
<tr>
<td>Cartotto et al, 2002</td>
<td>31</td>
<td>6.7 +/- 2.8</td>
<td>84%</td>
<td>No</td>
<td>higher</td>
</tr>
<tr>
<td>Friedrich, 2004</td>
<td>11 (1975-1978) 11 (2000)</td>
<td>3.6 +/- 1.1 8.0 +/- 2.5</td>
<td>50%</td>
<td>No</td>
<td>higher</td>
</tr>
<tr>
<td>Cancio, 2004</td>
<td>56</td>
<td>6.10 +/- 0.22</td>
<td>100%</td>
<td>No</td>
<td>higher</td>
</tr>
<tr>
<td>Mitra, 2006</td>
<td>49</td>
<td>5.58 +/- 2.28</td>
<td>72.9%</td>
<td>No</td>
<td>higher</td>
</tr>
<tr>
<td>Arlati, 2007</td>
<td>12 (Parkland) 12 (Permissive Hypovolaemia)</td>
<td>4.6 +/- 0.3 3.2 +/- 0.7</td>
<td>50%</td>
<td>No</td>
<td>lower</td>
</tr>
<tr>
<td>Klein, 2007</td>
<td>72</td>
<td>5.2</td>
<td>22%</td>
<td>No</td>
<td>higher</td>
</tr>
<tr>
<td>Blumetti, 2008</td>
<td>483</td>
<td>5.8-6.1</td>
<td>57%</td>
<td>No</td>
<td>neither</td>
</tr>
</tbody>
</table>
References


