THE PHYSIOLOGICAL RESPONSE TO PLASMA EXCHANGE IN PATIENTS IN BURN SHOCK

by

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To the Graduate Council of The University of Utah:

I have read the dissertation of Melva D. Kravitz in its final form and have found that (1) its format, citations, and bibliographic style are consistent and acceptable; (2) its illustrative materials including figures, tables, and charts are in place; and (3) the final manuscript is satisfactory to the Supervisory Committee and is ready for submission to the Graduate School.

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ABSTRACT

The physiological consequences of major thermal injury center around profound, life-threatening shock occurring in conjunction with the burn and consisting of two pathological syndromes: hypovolemic and cellular shock. Intravascular hypovolemia following major thermal injury results from increased capillary permeability with subsequent loss of intravascular fluid into the interstitium. Investigations of burn shock have demonstrated the release of circulating factors which effect this change in capillary permeability. The purpose of this study was to evaluate the effect of a therapeutic regime involving the removal of the circulating factors by performing plasma exchange. Fourteen adult patients with burns of 40% total body surface area (TBSA) served as subjects. Seven were randomly assigned to the control group which received standard burn shock resuscitation. Seven were randomly assigned to the treatment group which received the same resuscitation in combination with plasma exchange. The study period was the first 48 hours postburn with the plasma exchange procedures performed as soon as was clinically feasible. A total of 937 measure-

ments of physiological variables were made on each patient. These included vital signs, cardiopulmonary parameters, respiratory status, and serum content analysis measured upon admission and every 4 hours thereafter during the study period. Hourly fluid intake and output records were compiled. Descriptive data included age, sex, percent TBSA burn and resuscitation requirements. Data were analyzed for statistical significance. The findings were as follows: the sample was unevenly distributed, with the treatment group more critically ill than the control on the basis of the variable of percent TBSA full-thickness injury ($p < .01$) and the incidence of documented inhalation injury. No significant difference was found between the groups on the variable of fluid requirement, either in subjects with or without associated inhalation injury. Plasma exchange significantly decreased platelet count ($p < .05$) in the treatment group when compared with the control but did not alter other serum chemistry values. The coagulopathy reported to occur in burn patients was not observed in this group of 14 subjects. The plasma exchange group was in significantly ($p<.05$) more normal base excess balance at both postburn hour 16 and 24 than the control. There was no evidence that plasma exchange performed during burn shock for the purpose of removing circulating factors was harmful in

any way to the treatment subjects. It is recommended that the study as designed be continued until the sample size permits statistical significance to be reached or rejected.

CONTENTS

CHAPTER I

INTRODUCTION AND STATEMENT OF THE PROBLEM

The physiological consequences of major thermal injury center around the profound, life-threatening hypovolemic shock which occurs in conjunction with cellular and immunological disruption within a few minutes of the injury. In contrast, the effects of minor and moderate burn injuries are limited to the skin. Individuals with minor and moderate burn injuries will experience discomfort until healing or skin grafting is accomplished, but these burns are not life-threatening. With a major burn injury, a systemic pathophysiology ensues which requires therapeutic intervention to sustain life. The American Burn Association (1) has defined a major burn injury as one that involves greater than 25% of the total body surface area (TBSA) because this is the extent of injury which produces a systemic insult. Major burns are not a skin problem; instead, systemic trauma resulting in cellular pathophysiology of all body systems produces the condition defined as burn shock.

The problem of burn shock was recognized only fairly

recently and the cause remains unknown. Currently, burn shock is treated with large volumes of intravenous resuscitation fluid. Since the 1940s, various fluid resuscitation formulas have succeeded in maintaining patients through the initial hypovolemic state of burn shock. In the past, treatment has been supportive rather than therapeutic. The sequence of events is as follows: Within minutes of a major burn injury, the normally semipermeable capillary system becomes an open system. Intravascular fluid leaks into the interstitial space, which results in hypovolemic shock. This process continues for about 24 hours postburn at which time the system regains its capillary integrity. Burn shock resuscitation involves the infusion of intravenous fluid at a rate faster than the rate of the leak of circulating volume fluid for the 24 hour postburn shock period. When fluid resuscitation does not occur, the rapidly progressive hypovolemia leads to death. Survival of a major burn injury requires prompt fluid resuscitation to support the patient through the burn shock phase. However, at this time, burn shock resuscitation is a supportive, rather than a therapeutic, intervention.

Pathophysiology of Burn Shock

Burn shock consists of two pathological syndromes: Hypovolemic shock and cellular shock. The major assumption of this study is that both are nonadaptive com-

pensatory mechanisms; therefore, altering either or both syndromes back toward homeostasis will be beneficial to the burn patient.

The syndrome of intravascular hypovolemia and decreased cardiac output following major burn injury results from increased capillary permeability with subsequent loss of intravascular fluid into the interstitium. The etiology of this increase in capillary permeability has not been defined. Loebl (2), in 1968, demonstrated that cross-perfusion from burned dogs to unburned animals led to a decreased cardiac output in the unburned animals, suggesting there are circulating factors in the burn serum responsible for burn shock. Investigations of burn shock have documented the release of mediators of the inflammatory response which can lead to loss of capillary seal following major thermal injuries. These substances include vasoactive amines (histamines, serotonin), products of platelet activation (thromboxanes), products of complement activation (C3a, C5a), prostaglandins, kinins and endotoxins. Moreover, increased metabolic hormones (catecholamines, glucocorticoids) are also associated with edema formation (3). More than one circulating etiological factor appears to be involved in the pathophysiology of hypovolemic shock following thermal injury.

The second aspect of burn shock is cellular shock.

Increasing data are being accumulated on the mechanisms occurring in the early postburn period at the cellular level. There appears to be depressed function of the sodium-potassium membrane pump and altered adenosine triphosphate (ATP) dynamics. Alteration of the levels of ionized magnesium and calcium in the cellular milieu suggests depressed energy utilization; magnesium and calcium fluxes occurring in the cell may be important in the generation of altered cellular permeability. Experiments by Baxter (4) using intracellular electrical potential measurements demonstrate membrane potential to be greatly decreased following thermal injury with failure to return to normal even after successful fluid resuscitation. The immunological alterations demonstrated by many investigators are another aspect of cellular shock associated with major thermal injury. The immune response is depressed and the release of histamine and serotonin increased. Burn toxins and circulating myocardial depressant factors have also been described.

Physiological Consequences of Fluid Resuscitation

The immediate consequence of successful fluid resuscitation is restoration of the circulating cardiovascular volume to a level compatible with life. Without fluid resuscitation, most patients with major thermal injury die of hypovolemic shock. There are a variety of resuscita-

tion formulae which are successful in restoring circulating volume but none are specifically administered for the purpose of restoring cellular function. Present therapy is limited to cardiovascular support rather than alteration of the burn shock syndrome.

Fluid resuscitation for burn shock focuses on infusing intravenous fluid at a rate which produces a minimum of 30-50 milliliters (mL) per hour of urine output. Various fluid resuscitation formulas are used to predict the amount of fluid which might be necessary to achieve the output criteria. The most widely used fluid resuscitation formula is the Parkland Formula (5) whereby Ringer's lactate is infused at a rate of 4 mL per kilogram (kg) of body weight per percent total body surface area (TBSA) burn during the first 24 hours postburn. Approximately one-half of this total fluid volume is given during the first eight hours postburn and one-fourth during each of the second and third eight hour periods.

Resuscitation formulas are used as guidelines only; the hourly volume of resuscitation fluid administered is determined by the clinical parameter of urine output. Baxter and Shires (5) report 70 to 80% of all burn patients require 4 mL/kg/% TBSA burn of resuscitation fluid during the first 24 hours postburn. Moreover, 95% of all burn patients required between 3.5 and 4.5 mL/kg/% TBSA burn. The problem is that even though 95% of all

thermally injured patients can be successfully resuscitated using the Parkland formula, the burn shock remains so severe for 24 hours postburn that the volume of fluid required merely supports the patient's circulatory system but does not alter the shock syndrome itself. Patients with major burns greater than 60% TBSA may require 20 to 30 liters of intravenous fluid during the first 24 hours postburn. This progresses to massive iatrogenic edema which leads to mechanical airway obstruction necessitating tracheal intubation, increased severity of the interstitial pulmonary edema associated with inhalation injury, prolonged ileus with bowel wall edema, compromised circulation to the extremities necessitating escharotomy or fasciotomy, and to a rapid depletion of serum protein with resultant lowered albumin levels. In addition, edema has been demonstrated to impair wound healing secondary to decreased oxygen tension at the cellular level.

The internal environment in which various cellular components of the body must exist is drastically altered from normal following thermal injury. Even though thermally injured patients demonstrate altered cellular function, these abnormalities can be returned to normal when the cell is removed from the burn environment. It is clinically not possible to remove these cells for the purpose of restoring them to normal; thus, therapeutic inter-

vention has to be aimed at restoring the burn environment toward normal. This information indirectly supports the use of any treatment modality which could "mimic" removal of the cell from the toxic environment.

With the development of in vivo blood cell separators, the separation and removal of specific blood components for therapeutic purposes is now a practical possibility in the clinical setting. Although the procedure is commonly referred to as plasmapheresis (to take away plasma (6)), plasma exchange is the preferred term for the procedure as used in burn patients since the volume of removed plasma is replaced with an equal volume of fresh frozen banked plasma. The removal of plasma followed by the return of the cellular components of blood was first described by Orosez (7) in 1913 for the purpose of correcting uremia in bilaterally nephrectomized dogs. During the Twentieth Century, whole blood exchange revolutionized the management of hemolytic diseases of the newborn. Ten years have elapsed since the introduction of in vivo blood cell separators into clinical medicine. These machines were initially developed for the collection of granulocytes and platelets from normal donors; however, their availability in general hospitals has led to their therapeutic use in a wide range of medical conditions. Plasmapheresis has a definitive role in the management of many immunoproliferative and autoimmune

disorders for the purpose of restoring a physiologic internal environment. Plasma exchange to reverse or alter burn shock has the same goal.

In summary, fluid resuscitation as it is currently accomplished is successful in 95% of all burn patients. However, its aim is to support the patient through burn shock which requires massive volumes of intravenous fluid and leads to iatrogenic complications. Plasma exchange seeks to restore the internal environment toward normal by removal of hypothesized circulating toxic factors and replacing them with banked fresh frozen plasma, which may alter the burn shock syndrome in a manner to restore the capillary seal. If plasma exchange accomplishes this aim, the burn shock and, thus, the massive volume of fluid required for resuscitation, will be altered.

Nursing Treatment of Burn Shock: State of the Art

Burn shock is not addressed specifically as a nursing problem in the literature. Burn nursing has traditionally occurred within a multidisciplinary setting with all members addressing all problems. Pruitt (8) states that the vast increase in burn care knowledge confirms the effectiveness of multidisciplinary care and research. A reflection of the overall philosophy of burn care is the idea that the people responsible for patient care are the ones in a position to identify clinical problems deserving

of study and resolution. Pruitt states an indigenous nursing staff is of primary importance in the list of factors essential for burn care and research because its members not only provide the intensive care necessary for optimum survival but assist in the identification of clinical problems.

The first burn center staffed by a multidisciplinary team in the United States opened at Brooke Army Medical Center at Fort Sam Houston, Texas, in 1947. By 1979, there were 172 burn facilities with 1,511 beds (9). The American Burn Association was established in 1967 with membership open to any professional with one year's experience in burn care. Marvin (9) reports that although the physician is regarded as the "captain of the ship," the nurse on the burn team traditionally holds the role of coordinator of all activities directed toward the care of burned patients. Thus there is no nursing research per se in burn care but rather a series of articles authored by members of the burn team which prominently includes nurses. This multidisciplinary approach to burn care and its practice in a physically designated area has resulted in a higher patient survival rate and a hospital time about one-half that of nonunit care (10). Archambeault-Jones and Feller (11) state patients with major burns require meticulous and comprehensive care for survival and the key member in structuring an environment

for recovery is the nurse. The concept that clinical nurses are responsible for structuring an environment is consistent with the current concept of nursing diagnosis. Yet the intensive care setting is where the nursing-medical diagnosis confusion abounds. Dracup (12) reports critical care nurses constantly deal with patients in physiological crises but physiological nursing diagnoses remain the most problematic. She gives as examples the diagnoses of "alterations in cardiac output" and "impaired gas exchange."

Guzetta and Dossey (13) have described nursing diagnosis in terms of its framework, process, and problems. They have identified the problems with using nursing diagnosis in critical care as multifaceted and complex. One problem which tends to overshadow all others is that of territory or, as these authors refer to it, the dependent vs. interdependent and independent role of the critical care nurse. They state that the dependent and independent roles theoretically can be defined yet the lines that separate these roles in practice become fuzzy. Burn nurses have the distinct advantage in that their role has been accepted as one of interdependence since 1947 by all members of the multidisciplinary team, including the nurse. Thus activities in a burn unit are burn nursing with burn shock resuscitation an integral part of that nursing.

Shock as a physiologic consequence of thermal injury

was recognized only fairly recently. Prior to the early 1900s, burns were considered a skin problem and therapy was focused on wound care. Then in 1897, Tommasoli started to treat patients with severe burns by saline infusion (14). Warden (15) correlates the dawn of modern burn care with three discoveries. The first was the discovery of anesthesia by Morton, the second was the elucidation of the nature and treatment of burn wound infection by Lister, and the third was the use of sodium chloride in the resuscitation of burn shock by Parascandolo in 1901. Fluid resuscitation is now universally recognized as the primary intervention in the emergent (first 48 hours postburn) phase. Wooldridge-King (16) lists the goals of fluid resuscitation as a) correction of antecedent fluid, electrolyte, and protein deficits; b) replacement of continuing losses and maintenance of fluids without overloading; and c) prevention of excessive edema formation. She also states that basic fluid therapy is ordered by the physician but the amount infused each hour is based on nursing judgment within established protocols. O'Malley and Snow (17) report burn unit nurses participate fully in moment-to-moment evaluation and treatment by initiating fluid changes and beginning ventilatory support when these measures are necessary. Christopher (18) describes a model for hemodynamic balance to describe burn shock.

Nurses working in burn intensive care areas perform nursing assessments which in effect determine the rate of intravenous fluid infusion for patients in burn shock. These decisions are based upon both knowledge and expectations; specifically, several formulas exist which predict these fluid requirements. The most commonly used formula is the Parkland formula which predicts that a patient with major thermal injury will require 4 mL of intravenous fluid for each percent TBSA burn per kg of body weight during the 24 hour postburn period.

The trained burn nurse assumes complete responsibility for determinig the rate of administration. This is appropriate since Gordon and Sweeney (19) list among areas of nursing diagnoses the states of altered skin integrity, fluid volume, and cardiac output. Nurses in burn intensive care units stabilize the patient's urine output by titrating the rate of intravenous fluid administration.

Nursing is a practice discipline which occurs in a variety of settings. One such setting is an intensive care unit; specifically, a burn unit. Here patients are critically ill as a result of a catastrophic injury which has allowed no time for adaptation, either physiologically or psychologically. The goal of intervention is to support the patient through a series of physiologic changes as the body attempts to establish compensatory

adaptations. Burn shock is not a physiologic change to which the body can adapt; an external source of adaptation is required for survival. The nursing intervention is to provide cardiovascular support via the administration of intravenous fluids at a rate to assure survival until the cessation of burn shock, which is usually self-limited in a 24-hour time-frame. Fluid resuscitation is currently routinely performed by highly skilled burn nurses. However the method of plasma exchange, a recent advance in therapy for burn shock, has necessitated a reevaluation of the methods previously used to resuscitate burn patients.

Plasma exchange is a procedure which involves removing the patient's plasma and replacing it with banked fresh frozen plasma. The nursing implications of this procedure when performed on a patient in burn shock are not known, yet the nurse remains responsible for the administration of appropriate fluid volumes to assure cardiovascular stability while at the same time assessing the effect of the procedure. The effects of plasma exchange on the patient's fluid requirements and cardiovascular status are unknown. Therefore, nursing research is essential to document the patient's response to plasma exchange. At this point, plasma exchange is an experimental procedure when used for the purpose of therapeutically altering burn shock.

A desired outcome of plasma exchange is to stop the loss of capillary seal and, in fact, restore capillary integrity. If this occurs, the amount of intravenous fluid required to support the cardiovascular system would decrease proportionately. The purpose of plasma exchange during burn shock is to reverse the loss of capillary seal; if this does not occur, there is no reason to continue to perform the procedure.

A review of the literature for the purpose of identifying a nursing model based on a higher theoretical framework than nursing diagnosis revealed that none of the nursing models were appropriate because none had been applied in the intensive care setting. The nursing models reviewed are strangely silent on the topic of devastating traumatic injury or disease during the initial posttrauma period. Rogers includes a cardiac patient in an example of the use of her continuum model, but the time-frame involves teaching the patient about the lifestyle changes necessary after an acute myocardial infarction. No mention is made of the patient during the time of the acute insult (20). Neuman's model focuses on the patient's perception of the illness and is noted to be particularly relevant to patients with hypertension (21). The core of Orem's self-care nursing model is that man has an innate ability to care for himself (22). Roy's adaptation model identifies the environment as the

source of stimuli to which the person must adapt with nursing actions either maintaining or promoting adaptation (23). Hollen proposes a holistic model of health which is based on the belief that health is choice (24). Guzzetta and Dossey (13) clarify the central concepts of the holistic model as one which includes the patient as an active participant at all times. The model is also inappropriate since concepts of the response to severe life-threatening acute trauma have not been validated in the intensive care setting where no decisions are made by the patient and all decisions are made by the health care team for a period often covering many days.

A review of literature on nursing research in the clinical intensive care areas revealed that nursing models are not utilized in the theoretical underpinnings of the research. Rather, the physiologic response to trauma was consistently found as the basis of the researcher's review of the literature. Another assumption of this study is that nursing models have not been tested in intensive care settings. This was especially evident in the coronary intensive care research efforts where measurements with Swan-Ganz catheters were used. In burn nursing clinical research, the focus tends to be on the metabolic alterations which occur as a result of the burn injury.

The consistent practice of conducting intensive care

unit physiological research without incorporation into a nursing model appears to be due to a temporal gap in existing nursing models when no time for, nor means of, adaptation occurs. In ICU settings, nurses need to adapt to the needs of a helpless, severely-traumatized patient. It is only much later that the nurse can work with the patient to facilitate adaptation to the magnitude and implications of the illness/injury.

Purpose

The purpose of this study was to determine the effect of plasma exchange on the pathophysiology of burn shock. This research is designed to answer the following specific questions:

1. Is the volume of resuscitation fluid decreased in thermally injured subjects when plasma exchange is combined with standard fluid resuscitation using the Parkland formula?

2. What is the effect of plasma exchange combined with standard burn shock resuscitation using the Parkland formula on measurable physiological variables in thermally injured subjects?

CHAPTER II

THEORETICAL FRAMEWORK

This chapter presents the theoretical framework of the study. The material is organized as follows so as to comprise a physiological shock framework. First is an overview of the physiologic response to thermal injury which includes the cardiovascular, cellular and immunologic responses. Second, the factors of pulmonary injury and increased evaporative water loss in response to thermal injury are presented. Next is a review of the principles of fluid resuscitation and the variety of formulas currently in use. Then plasmapheresis and its current clinical application is discussed. Following this is a review of the current use of plasma exchange in burn patients. To conclude the chapter, a summary is presented.

Pathophysiological Response to Thermal Injury

Burn shock appears to consist of both a hypovolemic and a cellular component. Hypovolemic shock results from an increase in capillary permeability which begins with the onset of thermal injury and persists for approximately 24 hours postburn, even when adequate resuscitation fluid

is given. Investigators have documented the release of many mediators of the inflammatory response which may play roles in the cardiovascular response to burns. Evidence has also accumulated suggesting that cellular metabolism is disrupted with onset of the burn wound resulting in altered membrane permeability and loss of normal electrolyte homeostasis. This cellular defect may be the pathophysiologic process responsible for the genesis of burn shock. Also, the many circulating factors demonstrated in burn serum may play a role in the generation of the cellular abnormalties known to occur. While recognizing that the cardiovascular or systemic response is intricately interwoven into the cellular response, they will nevertheless be discussed as separate entities for the purpose of describing their components.

Cardiovascular Response to Thermal Injury

The end result of a major burn injury is hypovolemic shock. This burn shock is proportional to the depth and extent of the injury. Burns involving 25 to 40% TBSA require cardiovascular support via intravenous fluid but patients usually tolerate the treatment in a fairly predictable manner. Burns involving greater than 40% TBSA are potentially lethal injuries which are often accompanied by a stormy clinical course. In general, the burn shock research model refers to an involvement of 40% TBSA burn

or greater.

Cope and Moore (25) in 1944, were among the first to describe the alteration in capillary permeability which results in a fluid shift to the interstitium. This was measured indirectly in that the fluid content of burn blisters was analyzed for protein content and found to be protein-rich. Almost simultaneously, Fox and Keston (26) in 1945 demonstrated massive redistribution of sodium in burned mice, with the sodium content of injured skin and muscle greatly increased in proportion to water gain. Many further studies were performed in experimental burns and in clinical burn treatment to document the magnitude of the capillary leak of intravascular fluid into the interstitium. Ganrot et al. (27) demonstrated the lymph/plasma ratio of all proteins except that of alpha-2-macroglobulin increased after experimental scalding of dogs, indicating an increased capillary permeability to proteins with molecular weights up to 300,000. These findings were significant because normally the interstitial fluid is essentially an ultrafiltrate of plasma in equilibrium with plasma but containing little protein and nearly equal amounts of sodium. Wachtel et al. (28) in 1983, used Wick catheters to obtain direct measurements of the interstitial fluid pressures while at the same time measuring serum oncotic pressures in six severely burned patients. The study showed no consistent

relationship between oncotic pressures of serum and interstitial fluid. Thus, after extensive thermal injury, a sequential series of fluid shifts occurs involving the redistribution of body water, salt, and protein. The increase in capillary permeability allows the intravascular fluid, except for the red blood cells and white blood cells, to leak into the interstitial spaces. This results in a marked decrease in the available circulating volume; thus the terminology, burn shock.

It has long been recognized that cardiac dysfunction is also a component of major thermal injury. Burn shock is accompanied by a sudden precipitous drop of the cardiac output which does not parallel the gradual reduction of blood volume. Furthermore, the infusion of intravenous fluids in amounts to restore the circulating volume does not return the cardiac output to preburn levels. This was demonstrated in 1957 by Dobson and Warner (29) using dye-dilution techniques to measure changes in cardiac output, plasma volume, and liver blood flow in burned dogs. Their most striking finding was the almost immediate and precipitous fall in cardiac output not associated in the initial stages with a significant reduction in plasma volume. The liver blood flow paralleled the decline in cardiac output in this study. Merriam (30) in 1962, using ventricular function curves as an index of myocardial contractility in burned dogs,

determined that the burn produced impairment of myocardial contractility but was unable to identify the mechanism. Many further studies were performed to measure the magnitude of myocardial dysfunction but it was not until the early 1970s, with the advent of the Swan-Ganz thermodilution catheter, that the full physiologic impact was described. Aikawa et al. (31) in 1978 presented pulmonary artery catheterization and thermodilution cardiac output determinations in 39 critically burned patients. Their findings included a) pulmonary artery wedge pressures, which reflect left ventricular function relative to its afterload, were found to be a more reliable indicator of circulating volume than the central venous pressure which reflects right ventricular function, and b) depressed myocardial function was present in these patients.

The consistent burn shock finding of inappropriately low cardiac output in the presence of vigorous intravenous fluid resuscitation led to the suggestion of a specific myocardial depressant factor. Baxter et al. (32) suggested in 1966 the presence of circulating material capable of selectively depressing myocardial function. Their work involved cross-perfusion of burned to normal dogs and showed a decrease in cardiac output of 45 to 70% in the unburned animals occurring within three to five minutes of cross-perfusion. Glenn and Lefer (33) in 1971 demon-

strated that intravenous infusion of isolated myocardial depressant factor into intact anesthetized cats in amounts equivalent to that present in the plasma of cats in shock resulted in a profound shock state 30 to 60 minutes post-infusion.

A similar myocardial depressant factor was described by Lefer et al. (34) in studies of a hemorrhagic shock cat model. They found the substance to be dialyzable and therefore of low molecular weight. In addition, a marked depression in the contractility of isolated cat cardiac muscle when exposed to plasma from cats in late hemorrhagic shock was noted. Further work by Lefer and Blattberg (35) revealed not only a myocardial depressant factor but also a reticuloendothelial depressing factor.

The source of the myocardial depressant factor remained elusive. Lefer and Martin (36) in 1970 suggested the pancreas as the primary site of production of the precursor of myocardial depressant factor, its activator, or the factor itself. Rosenthal et al. (37) suggested the burned skin as the source of the factor. After isolating a "toxic factor" from burned skin, its action was shown to be primarily on the myocardium. After isolating purified burn toxin and its competetin, their data suggested competition for the same myocardial receptor sites. Raffa and Trunkey (38) demonstrated even more specific effects in a study of the function of rabbit

interventricular septum depression after myocardial depressant factor exposure.

The chemical structure of the myocardial depressant factor was characterized by Goldfarb et al. (39) as containing L-leucine, an amino acid which is a demonstrated cardiac depressant. And, while most investigators focused on the immediate postburn period as the time of maximum effect of myocardial depressant factor, DeSantis et al. (40) report even greater activity at four to five days postburn.

The gut has also been implicated as the source of an endotoxin producing a shock syndrome. Caridis et al. (41) discuss persistent shock in nonseptic disorders due to endotoxin. They point out that endotoxin is continuously absorbed from the intestinal tract but is promptly cleared by the reticuloendothelial system. As mentioned in a previously cited reference (35) the reticuloendothelial system is depressed with shock; thus it is possible that the circulating endotoxin accumulates with progressive vascular collapse as the consequence.

Hamer-Hodges et al.(42) in 1974 demonstrated the role of intraintestinal Gram-negative bacterial flora in major thermal injury by comparing a burned rabbit model exposed either to Gram-negative or to Gram-positive exotoxin. The shock response was overwhelming in the group with exposure to Gram-negative flora but relatively mild

in the group with Gram-positive exposure. An additional finding was a separate vasoactive agent released from the burn into the circulation during a period of several hours. This agent was reported to cause a generalized increase in vascular permeability which allows the transmural movement of living bacteria and endotoxin from the intestinal lumen. The burn wound itself was also postulated as the source of the vasoactive substance by Cuevas et al. (43). Isolation of a substance from the venous blood of burned rabbits with a large burn followed by its injection into unburned animals produced a capillary leak which then allowed mobilization of endotoxin from the intestine. At the same time, Little and Stoner (44) failed to find a role for intestinal bacterial endotoxin in burn shock. Kremer et al. (45) in 1981 produced additional strong evidence for a specific burn toxin which has as its source the burned skin and as its action direct damage to mitochondria. Their conclusion is that one important aspect of burn treatment should be the elimination of the toxic substances if possible.

In summary, while there is agreement that myocardial dysfunction is present with all major burn injuries, the etiology of the depression remains to be described except in the most general terms. It is now accepted that there is no simple specific myocardial depressant factor but, rather, a cascade of events which are generally termed

the cellular response to burn injury and include both metabolic and immunologic factors. These factors initiate the cardiovascular sequence of loss of capillary seal and subsequent hypovolemic shock.

Cellular Response to Thermal Injury

Major trauma effects the entire physiologic system but the survival of the patient depends upon its ultimate impact at the cellular level. This is as true for major burn patients as for any other form of shock-trauma patient. The cellular response to burn injury will be discussed in two general categories: Metabolic response and immunologic response.

The basic syndrome is referred to as the "sick cell syndrome." Welt et al. (46) were among the first to describe this phenomenon as a membrane transport defect. In 1967 their work with erythrocytes in burn and other types of patients revealed an alteration in the steady state composition characterized by high intracellular concentrations of sodium, a defect in the active transport of this cation in the presence of adequate levels of adenosine triphosphate (ATP). Rosenthal and Tabor (47) in 1945, had reported an elevation of serum potassium in shocked animals with the source of the potassium being intracellular from both traumatized and nontraumatized areas.

Actual measurement of changes in transmembrane

potential of rat skeletal muscle in a hemorrhagic shock model was performed by Cunningham et al. (48) in 1971. The finding of a consistent depression of transmembrane potential difference and a gradual elevation of interstitial potassium in association with prolonged severe hypotension parallels the findings by others in burn patients. Further work by Cunningham et al. (49) measured the resting membrane potential difference of skeletal muscle in 26 normal human subjects, seven patients with mild illness, and 21 patients with severe debilitating medical disorders. As with the animal model, the combination of a low resting membrane potential and a high intracellular sodium concentration in the ill patients was found. Shires et al. (50) demonstrated the same findings in a group of 22 baboons in hemorrhagic shock but they carried the experiment one step further and demonstrated that the effects are reversible with adequate resuscitation measures. Trunkey et al. (51) found a marked decrease in primate muscle extracellular water and an increase in both intracellular sodium and water during hypovolemic shock. In addition, there was an associated decrease in resting membrane potential, a decrease in amplitude of the action potential, and prolongation of both the repolarization and depolarization time in association with a decreased muscle intracellular potassium concentration. Resuscitation reversed the

changes acutely. Trunkey et al. (52) demonstrated that these alterations are due to circulating factors rather than ischemia. This was done by primate cross-perfusion studies with three groups. Group 1 was an ischemic model, Group 2 was the control, and Group 3 was the circulating model. Differences between the groups confirmed the changes were limited to the circulating cross-perfusion animals.

Cunningham et al. (53) studied the changes in intracellular sodium and potassium content of red blood cells in a group of burn patients during the first few hours after admission. Early sampling of burn patients revealed consistently normal red cell sodium levels regardless of the extent of the burn (range: 20-95% TBSA). Sayeed et al. (54) in their study of the effect of hemorrhagic shock on rat hepatic transmembrane potentials, supported the concept of hepatic cell volume being regulated by metabolically linked sodium extrusion but not by an equally coupled sodium-potassium pump. This failure of cellular energy-related electrogenic sodium extrusion is the suggested etiology of hepatic cell swelling with shock.

The cellular dysfunction of burn injury extends beyond the transmembrane potential disruption and the sodium-potassium pump impairment. Turinsky et al. (55) suggest that muscles underlying the burn in a rat model also show a loss of intracellular magnesium and phosphate.

Deets and Glaviano (56) have verified the effect of shock on muscle by demonstrating an elevated lactic dehydrogenase (LDH). Burned dogs showed a marked increase in total plasma LDH accompanied by a significant decrease in cardiac output and an increase in total peripheral resistance and hematocrit. Their finding of negative myocardial uptake of LDH indicated the cardiac muscle was the source of the circulating LDH.

In summary, the above studies suggest impairment of the basic cellular functions such as the sodium-potassium pump as the underlying cause of the diminished membrane potentials. The data suggest a decrease in the efficiency of the pump; a change which can be reversed by adequate resuscitation over time. This points to evidence for the presence of circulating factors versus ischemic factors.

Stress reactions to severe trauma also involve the response of the sympathetic nervous system and other homeostatic regulators. Catecholamines are found in elevated amounts in both serum and urine of burn patients. Okamoto et al. (57) report changes in lipid metabolism described as an elevation in plasma free fatty acids (FFA) and a decrease in plasma cholesterol and phospholipids simultaneously with the elevated catecholamines. Wilmore et al. (58) in 1974 conducted in-depth research of 20 burn patients and four normal individuals in a metabolic chamber environment for the purpose of studying the hypermeta-

bolic response to injury. They found all burn patients were hypermetabolic at all ambient temperatures and their core and mean temperatures were significantly elevated above control values. However, burn patients are internally warm, not externally cold. The metabolic rate increased with burn size in a curvilinear relationship, with oxygen consumption rarely exceeding two and one-half times basal levels. Burn patients treated in a warm environment (32 degrees C) demonstrated lower metabolic rates than when treated in a cool environment (22 degrees C). Despite this finding, it is apparent that evaporative water loss and surface cooling in the burn patient are not the primary stimulus for the hypermetabolic state. These authors found evidence for mediation by catecholamines as the etiology of the increased heat production in response to a direct effect on cellular calorigenic activity. Associated injuries in patients with greater than 40% TBSA burn exert little or no metabolic effect, for the thermal injury has already caused a maximal stress response. Burn patients were found to have reset their thermal regulatory set-point upward. Additional findings include: a) fasting blood glucose is above normal levels following the injury; and b) the hyperglycemia is related to the extent of the injury. Hauben et al. (59) report on eight burn patients with concommitant smoke inhalation injury, seven of whom demonstrated elevated levels of

plasma vasopressin (antidiuretic hormone (ADH)) during the shock phase of burn injury. The level of elevation was found to be related to the severity of the burn. Serum sodium and potassium levels did not show any significant alterations. Burn injuries are known to produce a sympathetic stress response. The reflex arc mobilizes neural and/or hormonal afferent stimuli to the hypothalmus. This produces a catecholamine response manifested clinically as hypermetabolism, hyperthermia, and hyperglycemia.

Evidence also exists that the burn wound itself directly mediates the response to injury at both the local and systemic level. Wilmore et al. (60) report that the body's priority response to injury is the wound itself and that the general systemic events appear to occur as if in response to tissue inflammation. That is, vasodilation, increased capillary permeability, and edema occur to promote healing. The distribution of the peripheral circulation following thermal injury transports both heat and glucose preferentially to the wound. The energy cost of these repairative and transport processes is reflected in the increased metabolism and hyperdynamic circulation previously reported by Wilmore et al. (58). The signal for the response is unknown since patients whose wounds have been denervated continue to have the posttraumatic metabolic response. Gump et al. (61) also analyzed blood flow

and oxygen consumption in patients with severe burns. They found that the extensive evaporative heat loss characteristic of burn patients is met, at least in part, by increased visceral heat production. Analysis of the data suggested that peripheral blood flow was increased beyond metabolic tissue requirements.

Studies describing the effect of injury and infection on visceral metabolism and circulation were also performed by Wilmore et al. (62). Thirty-one burn patients were studied to characterize the role of the liver and kidney. Seven of the patients were in the early phase of burn injury and all demonstrated splanchnic uptake of lactate and pyruvate greater than normal. Assuming complete hepatic conversion of lactate and pyruvate to glucose, these two substrates accounted for 30 to 50% of the glucose produced by the liver. The study showed that hepatic glucose production increases following thermal injury.

Hypothalamic function alterations following thermal injury were evaluated by Wilmore et al. (63) to determine the role of the central nervous system in directing the metabolic response to injury. Nine burn patients were studied in an environmental chamber and were found to have elevated human growth hormone (HGH) serum levels in the presence of hyperglycemia. Since HGH is normally suppressed by hyperglycemia, it is suggested that the injury produces an alteration in hypothalamic function which aug-

ments HGH elaboration at the same time it increases sympathetic discharge.

The relative significance of thermal and metabolic demands on burn hypermetabolism was evaluated by Aulick et al. (64) by studying 20 burn patients and five normal controls in an environmental chamber. They found that the hypermetabolic rate is not decreased during rest, sleep, or warmth in burn patients. Since the increased oxygen consumption could not be accounted for on the basis of the elevated body temperature alone, it was concluded that an elevated metabolic state, and not a thermoregulatory drive, is responsible for the increased heat production.

Glucose and lactate kinetics are also altered following burn shock. While tissue hypoxia produces lactic acidosis, its persistence in the presence of adequate tissue perfusion suggests an increased rate of glycogenolysis. Wolfe et al. (65) in a study on a guinea pig model, found the percentage of gluconeogenesis originating from lactate was elevated postburn. Wilmore et al. (66) in a discussion of glucose metabolism, report that an absolute or relative insulin deficiency in combination with an excess of glucocorticoid, glucagon, and/or catecholamine are the signals which promote gluconeogenesis. In the early burn phase, insulin concentrations are low but then rise toward normal with resuscitation. The hyperglycemia is a result of increased hepatic glucose production. The cel-

lular components of the injured tissue utilize glucose as their primary fuel and convert this sugar to lactate which is recycled to the liver and reprocessed to new glucose.

Evidence of hepatic response to injury is also characterized by alterations of the clotting factor. Burn patients are often classified as "hypercoagulable" in that plasma fibrinogen concentration is elevated while prothrombin time (PT) and activated partial thromboplastin time (PTT) are shortened. McManus et al. (67) studied the syndrome of disseminated intravascular coagulation (DIC) in burn patients. The syndrome results in incoagulability (PT, PTT), clotting factor consumption (Factors V, VIII, platelet count), and a resultant secondary fibrinolysis. A review of 274 burn patients revealed that five went on to develop clinically documented DIC. Baxter, in discussing this paper, reports laboratory findings reflecting progressive thrombocytopenia in conjunction with elevated fibrin split products and fibrinogen, as "normal" findings in 100 patients with 30% or greater TBSA burns.

In summary, extensive thermal injury initiates the most marked alterations in body metabolism associated with any illness. Much of the work explaining this response has been conducted by Wilmore and Aulick (3) who report the persistent tachycardia, hyperpnea, hyperpyrexia, and marked body wasting seen in the burn patient reflects heightened metabolic activity and accelerated body catabo-

lism. These systemic alterations occur as a result of the cutaneous inflammatory process and are thought to facilitate wound repair. The neural component of this alteration is in response to a sympathetic reaction which releases catecholamines and vasopressin in large amounts.

Immunologic Response to Thermal Injury

The immunologic response to burn injury is immediate, prolonged, and severe. The end result in patients surviving burn shock is an increased susceptibility to potentially fatal systemic burn wound sepsis. Alexander and Moncrief (68) reported in 1966 thermal injury results in a susceptibility to infection which continues to be the greatest single cause of death in patients surviving the initial shock. This discussion will be limited to the immunologic changes associated with the shock phase.

The role of these circulating factors in the generation of burn shock has been extensively studied. Serum or plasma from burned subjects has since been shown to induce a variety of phenomena associated with the burn state. Warden et al. (69) in 1974, evaluated leukocyte chemotaxis *in vitro* in 46 thermally injured patients. During the first 72 hours postburn, all patients demonstrated a decrease in leukocyte migration with the decrease inversely correlated with burn size. A further

study by the same group and reported in 1975 assessed the effect of normal serum upon burn-suppressed leukocytes and the effects of three commonly used topical chemotherapeutic agents upon the chemotaxis exhibited by granulocytes from normal controls (70). They found that placing the burn-suppressed leukocytes into serum obtained from normal donors returned the levels to 107% of normal activity. Additionally, burn serum was demonstrated to suppress normal leukocytes from unburned donors. The use of commercially available albumin did not restore chemotactic function. Both mafenide and silver sulfadiazine suppressed the chemotactic function of granulocytes obtained from normal controls. Further work by Miller and Baker (71) reports suppressive mononuclear cells are at least partially responsible for the decreased immunocompetence of burn patients. Ninnemann (72) reported the participation of both a serum-borne factor and a specific subset of B lymphocytes in the generation of such suppressor cells. Moreover, he has demonstrated the presence of prostaglandins, endotoxins, and interferon in the sera of thermally injured patients and suggests that these substances may be responsible for the above described phenomenon. Ninemann et al. demonstrated that lymphocyte function is compromised in the presence of burn sera (73). Rapaport and Bachvaroff (74) report that thermal injury is associated with significant

enhancements in the rate of generation of antibody-forming cells in response to T cell dependent antigens and that the effect is most pronounced in mice immunized within 24 hours postburn.

Altered white blood cell (WBC) superoxide activity was reported by Edgar et al. (75) when cells were incubated in burn serum. Loebel et al. (2) reported markedly shortened red blood cell (RBC) survival and an increase in RBC destruction when normal RBCs were placed in burn patients. A return to normal longevity of the RBCs was noted when the cells were placed into normal individuals. From these studies it can be concluded that, although thermally injured patients demonstrate altered leukocyte function, these abnormalities can be returned to normal when the leukocyte is removed from the burn environment.

A host of chemicals found to be present in burn plasma in altered concentrations may play a role in burn shock. These include vasoactive amines (histamine, serotonin), products of complement activiation (C3a, C5a), prostaglandins, kinins, endotoxin, and the metabolic hormones (catecholamines, glucocorticoids).

Heideman et al. (76) have demonstrated a decrease in the complement components C3a and C5a in the circulation following thermal injury and suggest that the injury non-specifically activates the complement system. Activation of complement in the injured tissue results in an inflam-

matory response due to the release of histamine and serotonin by C3a and C5a. This appears to alter capillary permeability, leading to edema formation. Gelfand et al. (77) found preferential activation and depletion of the alternative complement pathway in eight adult burn patients. The alternative pathway titer was reduced by more than 90%, suggesting preferential depletion of this pathway.

A consumptive opsoninopathy has been reported by Alexander et al. (78). While normally opsonin renders bacteria susceptible to phagocytosis, this study showed reduced ability of a group of patients' serum to opsonize bacteria. Bjornson et al. (79) likewise found consumption of C3, properdin, and Factor B following thermal injury and suggested a consumptive opsoninopathy had occurred. They were able to demonstrate that burn serum contained an inhibitor of C3 conversion which would lead to decreased opsonization and polymorphonuclear (PMN) neutrophil function.

The vasoactive amines (histamine and serotonin) initiate the inflammatory response along with kinin polypeptides and other chemical mediators (80). As a result of these vascular changes, fluid and fibrinogen leave the dilated, permeable vessels. Prostaglandins function in the inflammatory process by regulating the metabolism of the cells of inflammation (lymphocytes,

macrophages, and neutrophils). In addition to the release of effector substances, burn injury has been shown to cause platelet consumption and activation; release of thromboxanes; and inhibition of heart muscle contraction. Studies into the pharmacologic alteration of the histamine-serotonin release have been performed by Markley et al. (81) and Holliman et al. (82). Markley found that preinjury doses of purines and histamines produced an increased blood volume and lower hematocrit values after burning of mice. The mechanism remains obscure but two possibilities appear feasible: a) vasoconstriction decreased fluid loss into the interstitium, or b) the drug increased fluid loss at the site of injection, where it was held while fluids were lost at the site of injury, and then returned it to the circulation after the fluid loss due to injury had reached its peak. Holliman evaluated the effect of ketanserin, a specific serotonin antagonist, on burn shock in a pig model and found the ketanserin-treated groups demonstrated improved cardiac index, decreased pulmonary artery pressures, and smaller arteriovenous oxygen content differences compared to the control group. Donati et al.(83) have reported on the marginal effectiveness of the administration of the immunomodulating agents methysoprinol and timostimoline in partially restoring neutrophil function. Ishizawa et al. (84) have used thymosin to reverse the T lymphocyte depression seen

acutely postburn.

Another management approach is to alter the internal burn environment. In altering the environment, treatment possibilities include either plasmapheresis or hemodialysis to remove the various circulating toxins. Warden et al. (85) have presented preliminary results using plasma exchange therapy in 21 patients not responding to conventional burn management. Plasma exchange was initiated for a) fluid resuscitation failure, b) massive myoglobinuria following electrical injury, c) metabolic exhaustion, d) acute respiratory distress syndrome following delayed resuscitation, and e) documented sepsis. In all patients, clinical values returned toward normal as a result of plasma exchange. Among the 5 groups, the most spectacular results were seen in the inadequate resuscitation group. Preliminary work by Ninnemann(80) in the same group of patients suggests that this procedure also corrects at least some postburn immunologic problems. A brief report by Baxter(85) utilizing exchange transfusion in pediatric burn patients not responding to conventional fluid volumes showed reversal of the fluid requirements toward normal resuscitation volumes.

The significance of adrenal hormones in response to burn injury has been detailed in a case study by Stratta et al. (86) of an adrenalectomized patient. This 29 year old white male's past medical history was remarkable for a

bilateral adrenalectomy performed 13 years earlier for presumed Cushing's disease. Since that time he had been maintained on replacement corticosteroids. The patient presented with a 35.5% TBSA burn, 3.5% of which appeared to be full-thickness. He also had a serious inhalation injury confirmed by ^{133}Xenon perfusion scan. This patient demonstrated an inadequate response to fluid resuscitation and excessive third-space fluid losses, defective thermogenesis, profound nutritional abnormalities, impaired wound healing, and compromised immunologic function. The patient was discharged 114 days following injury with nearly complete burn wound closure and normal range of motion in all extremities.

Pulmonary Factors in the Response to Thermal Injury

There are two physiologic mechanisms responsible for the pulmonary response to burn injury. The first is in response to the hypermetabolism of burn injury and the second is in response to the direct trauma of an inhalation injury. Petroff et al.(87) report that uncomplicated burn patients have a minute ventilation twice that of healthy normal subjects. This hyperventilation is in large part due to the increased metabolic demands of the burn patient since oxygen consumption has been shown to be as much as twice basal levels.

The second component is due to inhalation of noxious

products of combustion. The damage is not from heat, since air is cooled by the time it reaches the bronchus unless live steam is inhaled. Inhalation injury refers to direct insult at the alveolar level secondary to chemical fume or smoke inhalation. The subsequent response involves interstitial edema as the inflammatory process is initiated. The edema is a diffusion defect which prevents the passage of oxygen across the lung. No immediate clinical signs or symptoms are evidenced except by history. The injury manifests itself as acute respiratory distress syndrome (ARDS) at 48 to 72 hours postinjury. The initial chest radiograph and arterial blood gas values will be within normal limits. The edema is progressive and, since the lungs have a total surface area of approximately 70 square meters in an adult (88), the amount of sequestered fluid can be three to five liters. The severity of the injury is proportional to the concentration and duration of contact with the noxious agent and is in no way correlated with the extent of the TBSA burn. Diagnosis is made by 133-Xenon lung scan and/or fiberoptic bronchoscopy.

Moylan et al. (89) evaluated the use of 133-Xenon in measurements of both the perfusion and the diffusion-ventilation phases of pulmonary function in 50 burn patients. They found uniform agreement between the 133-Xenon scan diagnosis of inhalation injury and patholo-

gical finding. The mortality rate in burn patients with inhalation injury is higher than in those patients with either injury alone. This series of patients had a 60% mortality.

Moylan et al. (90) studied a group of 25 burn patients undergoing fiberoptic bronchoscopy for the purpose of diagnosing inhalation injury. The positive finding of injury in 15 of the 25 patients studied revealed the usefulness of this technique. Three of the patients with airway injuries had skin burns of less than 5% TBSA. At the time of admission, only two patients had symptoms of ARDS.

Evaporative Water Loss as a Factor in the Response to Thermal Injury

One of the major purposes of intact skin is to serve as a barrier to evaporative water loss from the body. With major burn injury, this ability of the skin to regulate evaporative water loss is totally disrupted. In 1962 Moncrief and Mason (91) attempted to determine the magnitude of such a loss. They reported that the use of the parameter of insensible weight loss in burn patients had previously been used as an approximation of insensible water loss. Using the same parameter and a scale with an accuracy of $\pm$ 50 g, 19 patients were studied over four hour time periods. The data revealed evaporative water loss to be extensive in burned patients, being in the

range of 20 times normal in the early phase of injury and gradually decreasing as wound closure was achieved. Later studies by Wilmore et al. (58) report that while present, the evaporative water loss and surface cooling in the burn patient is not the primary stimulus for burn hypermetabolism but rather, the hypermetabolic response is related to endogenous metabolic activity. Vaporizational heat loss is a route of transfer of this excess heat from the body. The insensible water loss through the skin is not from evaporation of water from sweat glands but from water vapor formed within the body and lost through the skin (92).

Calculation of the amount of fluid lost via evaporative water loss includes losses from all sources. While normally the skin is the major source of insensible loss (75%) and the lungs are minor sources (25%), the amount is only about 600-800 ml per day. This changes dramatically with burn shock because not only does the skin's loss increase but so does the lung loss. Hypermetabolism and hyperventilation, especially in an intubated patient, may result in losses up to 1.5 L/day. Replacement of the losses is mandatory to prevent volume deficit. Moncrief (93) reports a minimum of 2,000 mL/day is necessary for basal requirements, and in larger burns 100 to 150 mL/m^2 BSA/ hour is average in adults. The actual criterion for evaluation is a serum sodium of 130 to 140 mEq/L since a

level below 130 mEq/L represents overhydration and above 140 mEq/L represents dehydration.

Each gram of evaporated water removes approximately 0.58 kcal of heat from the body. If thermal neutrality is to be maintained, the metabolic rate of the patient must increase to replace the lost heat. This may be accomplished, in part, by the shivering seen in burn patients. This increased heat need may be as much as 3,000 kcal per day over normal levels. The energy expended for such an increased demand would reduce that available for other metabolic functions. Harrison et al. (94) in 1964, measured simultaneously the insensible water loss and the metabolic rate of 21 patients with burns of varied severity. A strong relationship was found between insensible loss and percent TBSA burn irrespective of whether the wound was partial- or full-thickness. Both types of burns are equally poor barriers to water loss during the early postburn period. This study reported a total water loss, including urine, insensible loss, and exudate as 2.0 to 3.1 mL/kg/% burn. Roe and Kinney (95) report the evaporative water loss in two patients with 50% TBSA burn as about 5 L/day; this is an expenditure of 2,880 kcal/day merely to maintain a stable body temperature. They also report the serum sodium level as the most sensitive index of water balance. Birke et al. (96) measured evaporative water losses exceeding 7 L/day in a

group of 17 burn patients with the highest losses occurring during the first days after injury. During the initial stage, fluid was lost directly as exudate from the wound as well as via increased evaporation from the injured epithelium. Lamke and Liljedahl (97) studied 16 burn patients and found that evaporative water loss from normal, intact skin in burn patients was not altered. First degree burns emitted as little water as normal skin. Thus, in calculating fluid requirements, areas of partial- and full-thickness injury are the basis of the formula. Lamke (98) also reports that evaporative water loss can be minimized by maintaining environmental conditions at a warm (32 degree C) and relatively humid (25%) setting. The patient's core body temperature should be maintained at 38 degrees C and shivering avoided. Zawacki et al. (99) report that application of a waterproof film to the burn wound was associated with a marked reduction in insensible weight loss but no significant change in the elevated metabolic rate. Carnes et al. (100) report increased evaporative water loss as a phenomenon which continues even after the wound is clinically healed.

The cumulative information on evaporative water loss made it apparent that the loss was of significant clinical importance. Only by the administration of large volumes of fluid could the burn patient maintain fluid balance. A

formula was developed for the purpose of estimating the volumes of fluid which might be required to replace evaporative water loss (see page 89 for further discussion). The type of fluid administered depends upon the patient's serum sodium content, acid-base balance, general electrolyte status, and renal function. The route of fluid administration depends upon the patient's ability to ingest fluids, either orally or via an enteral feeding tube to the duodenum, after resolution of the paralytic ileus associated with major thermal injury. Initially, all fluid is administered by the intravenous route.

Resuscitation of Burn Shock

Burn shock and its associated hypovolemia have been a recognized component of burn care since 1930. The principles of burn shock therapy have been aimed at supportive rather than therapeutic interventions; that is, the goal of treatment is to support the patient's cardiovascular system with large volumes of fluid until burn shock ceases. This treatment, while usually effective, is not effective for all patients. A 1980 survey of burn survival by Curreri et al. (101) reports that 15% of 75 deaths in a population of 937 burn patients were the result of irreversible burn shock. Baxter (102) in 1981 reported on 954 patients with 54 deaths occurring in the first ten days postburn. Thirty-two of the 54 patients died within the first 24 hours postburn and 37 died within the first

48 hours. Sevitt (103) in 1972, reported 12% of 156 burn deaths as due to early shock or cardiac failure. Deaths due to burn injury represent a significant societal problem since Artz and Yarbrough (104) report there were 7,645 deaths due to burn accidents in the United States in 1960. The extent of the TBSA involved is the single most important factor influencing prognosis and treatment. Baxter (105) states patients with zero to 20% burns do not have to be resuscitated at all. With most burns in the physiologic age range, between 20 and 35% volume restoration of almost any kind, so long as it contains electrolytes, will suffice. Where optimal resuscitation, which Baxter defines as restoration of all physiologic systems at the earliest possible time, becomes critical is in the 35 to 60% burn. In burns exceeding 65% TBSA, other factors influence ultimate survival.

There are two components to fluid resuscitation formulas: The volume/time and the chemical content of the fluid administered. Caldwell(106) states that almost any solution containing sodium will serve to adequately resuscitate young and healthy patients. This fact does not help to define the ideal salt and water combination. The need for fluid has been well-established since death soon occurs in patients with large burns but without administered fluid. Leape (107), in assessing the volume/time factor, reported that the initiation of early fluid resus-

citation improved survival in a rat study. Untreated rats with a 50% TBSA burn all died by 24 hours, 92% by 12 hours postburn. Mean survival time in untreated animals was 7.4 hours. The administration of fluid at four hours improved survival time but was less than half the effect of giving fluid within the first hour. Animals given 30% body weight of fluid did better than those given 20%.

Recognition of the necessity for large volumes of resuscitation fluid has resulted in a great decrease in the early mortality of burn patients. Since the 1940s, formulas for burn resuscitation have been based on several pathophysiologic observations. First, immediately following thermal injury, there begins a rapid leakage of fluid from the vascular space into the interstitium. This fluid loss is greatest during the first six to eight hours postburn, after which it gradually declines so that by 24 to 36 hours postburn, capillary integrity is generally restored. While capillary leakage following minor burns in localized to the wound area, burns involving greater than 25% TBSA result in systemic leakage and total body edema. Isotope dilution studies (26) have demonstrated loss of up to 50% of the effective extracellular fluid (ECF) volume during unresuscitated burn shock (5). The initial disruption of capillary integrity permits even large protein molecules to permeate freely into the interstitium (27). For this reason, colloid-containing resus-

citation solutions are usually withheld until the restoration of capillary integrity at 24 to 36 hours postburn, at which time colloids may be effective in reexpanding the vascular compartment. The key ingredient of all resuscitation fluid appears to be the sodium ion, and various regimens have been shown to be effective in treating burn shock in proportion to their sodium content. Bull (108) reports there are several successful fluid regimens varying greatly in sodium content, both absolutely and relatively to water. The underlying problem remains that the circulatory volume needs to be maintained in spite of a continuing leak. When the volume is replaced as free water, water intoxication occurs. It is now known that sodium enters cells as the sodium-potassium pump becomes dysfunctional. This theoretically explains the tremendous salt load necessary in the burn shock period to prevent hyponatremia. In addition, Moncrief (109) reports a precipitous drop in cardiac output, to about 50% of resting normal values, precedes any measurable change in blood or plasma volume. Thus, the time after injury when cardiovascular support is necessary for survival is far shorter than would be expected based on the factor of capillary permeability alone. Moylan et al. (110) showed that the untreated burn dog model had cardiac outputs of 30% of normal by six hours postburn. This study also found the sodium dosage and the water dosage of resusci-

tation fluids to be independent determinants of early restoration of cardiac output.

The clinical criteria for the amount of fluid administered is urine output. Pruitt (111) is in agreement with other sources when stating the resuscitation fluid regimen is adjusted to obtain 30 to 50 mL of urine per hour in the burned adult. Greater hourly urine outputs are achieved at the expense of additional edema formation.

There are many resuscitation formulas. The first established formula was the Evans formula, followed by the Brooke formula. The one most widely used at the current time is the Parkland formula. The hypertonic saline method is used in some institutions as is the hypertonic, albuminated fluid-demand (HALFD) method. A British model, the dextran saline method or Mount Vernon formula, has also also been used in some burn centers. As reported by Baxter et al. (112), the various regimens have in common an almost identical quantity of isotonic volume for each percent TBSA of injury. However, they differ widely in the ratio of colloid to crystalloid volumes and in the time intervals recommended for effective administration. Burn shock differs from other types of hypovolemic shock in that it is primarily due to a loss of plasma rather than whole blood. In fact, hemoconcentration occurs as the less viscous fluid exits and leaves behind only red blood and white blood cells.

The hourly rate of fluid replacement depends on the specific resuscitation formula used to treat the patient. But, as Rogenes and Moylan (113) report, the formula is only a guideline. Observation of the patient for signs of fluid deficit or overload and electrolyte imbalance, combined with an understanding of the physiological consequences of thermal injury is essential for the nurse to regulate the fluid replacement. For, while the basic fluid therapy in major burns is prescribed by the physician, the amount of fluid administered each hour becomes a nursing decision.

The Evans formula (114) is a crystalloid and colloid formula with both products being given throughout the 48 hour period postburn. The formula was derived from a prospective resuscitation study of 68 burn patients. During the first 24 hours, colloid in the form of dextran 70 in normal saline solution is administered at the volume of 1 mL/kg/% TBSA burn/24 hours along with the crystalloid in the form of normal saline at a volume of 1 mL/kg/% TBSA burn/24 hours. In conjunction with this, the patient is given 2,000 mL of 5% dextrose in water (D5W) over the 24 hour period. Half of the fluid is given in the first eight hours postburn and the other half is given over the subsequent 16 hour period. In the second 24 hours, the colloid and crystalloid are given at a rate of 0.5 mL/kg/% TBSA burn/24 hours with the amount of maintenance fluid

remaining at 2,000 mL of D5W over the 24 hours. The maximum calculated burn is to be 50% TBSA.

The Brooke formula (115), which is also a crystalloid and colloid formula, is a modification of the Evans formula. The colloid is administered in the form of plasma at a rate of 0.5 mL/kg/% burn/24 hours. The crystalloid, in the form of lactated Ringer's solution, is administered at a volume of 1.5 mL/kg/% burn/24 hours along with maintenance water of 2,000 mL D5W over 24 hours. Half of the fluid is given in the first eight hours and half during the next 16 hours. During the second 24 hours, the colloid is administered at a volume of 0.25 mL/kg/% TBSA/24 hours and the crystalloid at 0.75 mL/kg/% TBSA burn/24 hours. The maintenance water volume remains at 2,000 mL/24 hours. The maximum burn size to be calculated is 50% TBSA.

Hutcher and Haynes (116), in comparing the two formulas find the difference to be mainly in the ratio of crystalloid to colloid, the Evans being 1:1 whereas the Brooke is 3:1. Both formulas require similar amounts of sodium and both use 50% TBSA as the maximum calculated burn. Reckler and Mason (117) evaluated the records of 50 burn patients resuscitated with the Brooke formula and found that while this formula satisfactorily predicted the clinically required volume administration in burns smaller than 50%, larger burns on the average required in excess

of the predicted amounts.

The Parkland formula (4) utilizes Ringer's lactate at a volume of 4 mL/kg/% TBSA burn for 24 hours postburn. No colloid is administered. One half of the fluid is given in the first eight hours postburn and the second half is given over the subsequent 16 hours. The calculation is by absolute percent of burn with no "maximum calculation." In the second 24 hours, D5W is administered at a rate to maintain the serum sodium at 140 mEq/L. Plasma is given between 24 and 30 hours postburn in the following amounts: 40-50% burn, 250 to 500 mL; 50-70% burn, 500 to 800 mL; and greater than 70% burn, 800 to 1,200 mL with rapid infusion (118). Baxter (119), in a retrospective analysis of 438 adult burn patients, found the formula to accurately predict the fluid requirements at 4 mL ($\pm$0.3 mL)/kg/% TBSA burn/24 hours in 70% of the cases. The use of Ringer's lactate rather than the previously reported normal saline was of concern in that it could theoretically aggravate the existing lactic acidosis of shock. Canizaro et al. (120) performed 639 lactate and pyruvate determinations in 84 patients resuscitated with Ringer's lactate. The findings included a significant decrease in lactate and excess lactate levels and a return toward normal of pH and base excess values during the period of shock while Ringer's lactate solution was being infused.

The amount of edema formation with the previously

discussed formulas is massive. Efforts to deliver the requisite salt in a smaller volume of water resulted in the development of a hypertonic resuscitation formula. The fluid used contains 250 mEq of sodium/L and is administered during the first 24 hours at a rate to maintain urine output at 30 to 40 mL/hour. In the second 24 hours, one-third isotonic salt solution is administered orally. No colloid is given during the 48 hour period. If possible, the isotonic salt solution is administered orally; either way, fluid intake is restricted to 3,500 mL in the second 24 hours. Monafo et al. (121) report that the initial hypertonic sodium solution contained 300 mEq sodium/L but that this caused hypernatremia with serum sodium levels greater than 165 mEq/L and alkalosis. Subsequently, the solution is now intended to contain 250 mEq/L of sodium, 150 mEq/L of chloride, and 100 mEq/L of racemic lactate. Moylan et al. (122) compared hypertonic lactate saline solution with isotonic resuscitation according to the Brooke formula in a dog model and found that the hypertonic resuscitation produced natriuresis and no gain in weight. Shimazaki et al. (123) measured body fluid changes during hypertonic lactated saline (HLS) solution therapy for burn shock in 12 patients compared to 26 patients receiving Ringer's lactate and colloid solutions. While finding that the total infusion volume during the first 48 hours postburn in the HLS

group was only one-half to two-thirds of the other group, the intrinsic complications of hyperosmolarity and hypernatremia were of clinical significance. Caldwell et al. (124) treated 13 burn patients with a solution containing 300 mEq/L of sodium, 100 mEq/L of chloride, 200 mEq/L of lactate, and an osmolality of 600 mosm/L. The total volume of fluid given in the first 48 hours was 23% less and the sodium load administered 86% greater than would have been given using the Brooke formula. All patients developed hypernatremia and increased serum osmolality. Fox (125) administered solutions containing from 75 to 300 mEq/L of sodium in various dosages to scalded mice and found a wide range of solutions was effective. The most effective solution appeared to be composed of 225 mEq/L of sodium. Hypotonic solutions were less effective at all dosage levels.

A modification of the hypertonic resuscitation is the use of a hypertonic, albumin-containing fluid demand regimen (HALFD). This method, as described by Jelenko et al. (126), consists of a resuscitation fluid composed of a 240 mosm/L hypertonic fluid plus 12.5 g/L of albumin. A comparison between randomly selected groups of burn patients resuscitated using hypotonic fluid alone, hypertonic fluid alone, or hypertonic plus albumin resulted in the latter group requiring smaller amounts of resuscitation fluid. The parameter evaluated was mean arterial pressures.

A British formula for fluid resuscitation (127) reports a formula calculated upon (percent TBSA burn x weight in kg) divided by 2. This volume is given in each of the following successive periods: four hours, four hours, four hours, six hours, six hours, 12 hours over the first 36 hours postburn. This formula, the Mount Vernon formula, recommends the use of reconstituted dried human plasma as the main transfusion fluid (128). Although the fluid of choice is plasma, Dextran 70 in normal saline or Hartmann's solution can be used if necessary. The goal is 50 to 100 mL/hour of urine output. This formula is predictive of much less total volume than any other currently used formula.

Hall and Sorensen (129) treated 43 patients for burn shock by fluid resuscitation using a dextran saline solution in 21 patients and Ringer's lactate in 22 patients. They found the volume of fluid intake over the first 48 hours was the same in both groups. Hemoconcentration was much greater in the Ringer group, but acid-base balance was restored to normal more rapidly than in the dextran group. No clinical differentiation could be made between the progress of the patients in the two groups.

It becomes apparent that in the clinical setting there are a variety of fluid resuscitation formulas which enable clinicians to bring patients through burn shock. All formulas stress that they are guidelines only; the

hourly volume of fluid administered is determined by the clinical parameter of urine output and that is kept to a minimum of 30 to 50 mL/hour. Even so, the volumes of fluid administered are extremely large. For example, the Parkland formula of resuscitating a 70 kg patient with a 50% TBSA burn would predict a fluid need of 14,000 mL in the first 24 hours postburn. Patients with burns greater than 60% TBSA may require 20 to 30 L of intravenous fluid during the first 24 hours. The hypovolemic burn shock is the problem but the iatrogenic complications are also a problem. The massive edema associated with burn shock resuscitation can lead to mechanical airway obstruction necessitating tracheal intubation, increased severity of the interstitial pulmonary injury associated with inhalation injury, prolonged ileus with bowel wall edema, compromised circulation to the extremities necessitating escharotomy or fasciotomy, and to a rapid depletion of serum protein with resultant lowered albumin levels. In addition, edema has been demonstrated to impair wound healing secondary to decreased oxygen tension at the cellular level. At the end of the resuscitation period, mobilization of fluid can cause cardiac congestion and pulmonary edema. In addition, a major cause of mortality in patients with very large burns is failure to resuscitate.

These reported investigations reveal that the in-

ternal milieu in which various cellular components of the body must exist is drastically altered following thermal injury. Although thermally injured patients demonstrate altered cellular function, these abnormalities can be returned to normal when the cell is removed from the burn environment. Clinically it is impossible to remove these cells; thus, therapeutic intervention has to be aimed at returning the burn environment to normal. This concept indirectly supports the use of plasma exchange as potentially beneficial in removing circulating toxic substances thereby returning the cellular environment toward compatibility with homeostasis.

Plasmapheresis as a Therapeutic Intervention

The removal of plasma and the return of cellular components of the blood was first described by Abell et al. in 1913 to relieve uremia in bilaterally nephrectomized dogs (7). The term pheresis derives from a Greek word, aphairesis, which means "taking away (6)." Although the procedure is commonly referred to as plasmapheresis, plasma exchange is a better term for the procedure as used in burn patients since the volume of removed plasma is replaced with an equal volume of fresh frozen banked plasma. In the past, small scale whole blood exchange was carried out using manual exchange. During the Twentieth Century, this technique of whole

blood exchange revolutionized the management of hemolytic diseases of the newborn. Ten years have elapsed since the introduction of in vivo blood cell separators into clinical medicine. These machines were initially developed for the collection of granulocytes and platelets from normal donors; however, their availability in general hospitals has led to their therapeutic use in a wide range of medical conditions. Current technology now allows two liters of plasma to be exchanged per hour.

Linker (130) describes a plasmapheresis procedure as performed on a continuous flow cell separator. Blood is removed from a patient and anticoagulated with a citrate solution. The blood then enters a centrifuge and is separated into cellular components and plasma. The cellular components are returned to the patient along with the replacement fluid of choice. The plasma is collected in a reservoir. The amount of the large-volume plasma exchange is a factor which has to be individualized to each patient. Plasma volume in humans is normally 40 mL/kg of body weight. By exchanging increasing numbers of plasma volume, Linker reports an intravascular marker will be depleted to an increasing extent (Table 1). A plasma exchange of 1.5 times the calculated plasma volume will deplete an intravascular substance by about two-thirds. Exchanging a larger volume gives small additional yield. An assumption implicit in these con-

Table 1. Relationship of Plasma Exchange Volume and Removal of Intravascular Substance

Plasma Volume = 40 mL/kg		
No. Plasma Volumes	Volume (mL)	Percent Remaining
0.5	1,400	65
1.0	2,800	45
1.5	4,200	35
2.0	5,600	30

From: Linker, C.: Plasmapheresis in Clinical Medicine. West Jrn Med 1983; 138:60-69.

clusions is, as Berkman (131) reports, that no net shift occurs between the extravascular and intravascular space and that there is no further major synthesis of the factor being removed.

Taft (132) reports the most efficient pheresis procedures are those involving cells of density significantly less than that of the predominant erythrocyte population. In plasma exchange, the extent of depletion of components not present in the replacement fluid depends on the rate of replacement, their extravascular concentration and synthetic rate. Since apheresis procedures have access only to the intravascular compartment, the success of the treatment is largely related to volume of blood processed and the rapidity with which clearance occurs.

As reported by Linker (130), plasmapheresis is a field of medicine that has been created by the availability of a new technology. There are currently three different pieces of equipment designed for on-line cell and/or plasma separation, procurement, or removal. Silvergleid (133) lists these as Haemonetics' Model 30 (Haemonetics Corp., Braintree, Mass.), IBM's 2997 (IBM Biomedical Systems, Princeton, New Jersey), and Fenwal's CS 3000 (Fenwal Laboratories, Deerfield, Illinois). All three are designed to create an interface between different constituents of the blood based on the differential effect of centrifugation, and to effect collection

and/or removal of the desired component based on harvesting at that interface. The Haemonetics Model 30 relies on a disposable bowl in which separation occurs; is an operator-dependent function; and is a discontinuous, or intermittent procedure. The procedure can be performed through one venipuncture. Both the IBM 2997 and the Fenwal CS 3000 are based on continuous flow. In addition, the IBM is partially, and the Fenwal almost completely, automated and therefore less dependent upon operator judgment. Two venipunctures are necessary to perform the continuous exchange.

Despite the design of the unit, the potential for operator error exists. This is a relatively new procedure often performed by inexperienced personnel. Werynski et al. (134) report that setting the plasma flow rate above a certain critical value can result in hemolysis. The physical feature of hemoconcentration is a significant variable in this excessive value. Wiltbank et al. (135) and Malchesky et al. (136) in an attempt to overcome plasmapheresis based on centrifugation and thereby limited in efficiency by the sedimentation rate of blood cells, developed a new approach using cross-flow filtration. By using a microporous membrane, having pore dimensions between 0.4 and 0.8 um and flowing the blood across a laminar field parallel to the membrane while maintaining a positive transmembrane pressure, plasma

filtration without red blood cell damage and/or membrane clogging occurred. The problem with the system was the time necessary to accomplish even a small plasmapheresis; it was found not to be of value with large-volume exchanges. Filters with specific macromolecular weight cut-offs are also being evaluated. Kayashima et al. (137) conducted an evaluation of three kinds of hollow fiber type membrane filters used as a second stage membrane filtration unit in an effort to return essential substances. They found they could, in fact, return substances such as albumin to the patient. This preliminary work demonstrates the possible clinical application of selective removal filters and the need for further research. This area of research, referred to as cascade filtration, is being actively pursued. Gurland (138) reports a tremendous decline in the membrane surface area of plasma filters. Early models had a membrane surface area of 6,500 cm^2; the smallest currently available commercial devices (Dideco, Travenol and Cobe) require only about 1,500 cm^2. The clinical significance is related to the amount of blood in the filter at any given time and to cost.

The increasing availability of cell separators has made it possible to investigate the use of large-volume plasma exchange to modify diseases associated with high levels of circulating antibody or antigen-antibody com-

plexes. Jones (139) reports a large variety of sizes of immune complexes and that some complexes may be more harmful than others. At the present time, the state of the art is that molecular weight alone determines upon which side of the membrane filter a cell will locate. Feng (140) reports that the American Red Cross currently lists 61 disease states treatable by therapeutic plasmapheresis, and the list is still expanding. The majority of reports about the use of plasmapheresis are highly anecdotal, and there is a paucity of controlled trials. Kleit (141) in an editorial, states that randomized controlled studies in apheresis will be expensive, complicated, time consuming, and possibly lethal to some patients. Some of the issues to be resolved, as reported by Wenz and Barland (142), include patient selection; frequency, intensity, and duration of the procedure; amount and type of replacement fluids; serological monitoring, and outcome criteria for continued use.

The use of plasmapheresis in clinical practice includes its use by Wood et al. (143) for two patients with refractory myasthenia gravis, one rhesus-sensitized woman, one procedure to diminish the anti-A titre in a patient requiring bone marrow transplant, and one procedure for S concentration reduction of a sickle cell disease patient. This group reported improvement and no complications associated with plasma exchange. Valbonesi et al. (144) re-

port that patients with high titers of circulating immune complexes are most likely to benefit from plasmapheresis. Seventeen patients with immune complexes were plasmapheresed; prepheresis, 14 of the patients had high complex levels while three patients had no evidence of circulating immune complex. The 14 high circulating level patients showed clinical and immunochemical improvement postpheresis while the other three patients showed no change. Blacklock et al. (145) have treated 26 patients with Goodpasture's Syndrome or dysproteinemias and concluded that the clinical improvement warranted the exchanges. Wenz and Rubinstein (146) treated one patient with acquired agammaglobulinemia and produced a clinical remission of five month's duration. Robinson and Tovey (147) treated 14 high-risk cases of Rh alloimmunized women with intensive plasma exchange throughout their pregnancies in weekly procedures. Successful outcome was achieved in nine of the 12 cases. Ginder et al. (148) used plasma exchange three times in a patient with mixed cryoglobulinemia with some success until the patient's death. Hepatic failure has been treated by Fujita et al. (149), Kayashima et al. (150), and Smith et al. (151) with mixed success in small groups of patients. Evans et al. (152) discuss a case study of the successful use of plasmapheresis in a patient with systemic lupus erythematosus. There are a variety of other reports but, as previously stated, the data is from

much too small a sample to be the basis for conclusions. Silvergleid (133) reports five general categories, based on the mechanics of the disease, which might theoretically benefit from plasmapheresis. These are diseases associated with a) abnormal (or excess) plasma proteins, toxins, or metabolic products; b) autoantibodies; c) alloantibodies; d) immune complexes; and e) miscellaneous disorders.

Complications of plasmapheresis have been reported to occur infrequently. Linker (130) reports that fibrinogen, the third component of complement (C3), and immune complexes are depleted 75 to 85% after a 1.5 volume exchange. Immunoglobulins are removed with a 65% depletion. Electrolytes, uric acid, and selected proteins such as factor VIII are removed very inefficiently. Erythrocyte loss is predicted to be in the range of 30 mL per procedure. The platelet count will often be slightly reduced, but thrombocytopenia to levels less than 50,000 ul occurs in about 10% of cases (130). Complications may also attend the infusion of large amounts of plasma. Silvergleid (133) identifies the possibilities of citrate toxicity, cardiac arrhythmias, hepatitis, anaphylaxis, and hemolysis. Also mentioned is the fact that approximately 24 deaths directly attributable to plasma exchange have been reported. The source is a personal communication and no further information is provided. Huestio

(153) in an editorial, reports 42 deaths that seem to have been associated with hemapheresis. Sixteen of these deaths occurred in the United States, 20 occurred in France, three occurred in Canada, and three in other countries. The replacement fluid was either albumin (6 cases), fresh frozen plasma (23 cases), or both (7 cases). The major causes of death are cardiac, respiratory, or anaphylactic.

McLeod (154) discusses the immunologic factors in blood transfusions as consisting of two distinct etiologies when plasma is the solution being infused. First, the plasma can serve as a source of antibodies that may react with cells in the recipient's bloodstream (intravascular hemolysis). In addition, plasma proteins may serve as a source of antigen thus leading to the potential for antigen-antibody reactions in subsequent transfusions. Hepatitis is also a risk factor associated with transfusion.

The anticoagulant used in the tubing of most plasmapheresis machines is an acid citrate dextrose (ACD) solution, a solution known to bind serum calcium. Watson et al. (155) and Morse et al. (156) have reported decreased ionized calcium during therapeutic plasma exchange. Hypocalcemia may lead to a decrease in the strength of cardiac contractions. The problem is manifested on the electrocardiogram as a lengthening of the QT interval and is as-

sociated with fibrillation.

Hypokalemia has also been reported in association with plasma exchange. This problem is manifested on the electrocardiogram as a prolonged PR interval, low amplitude T-waves, premature ventricular contractions, and fibrillation. Hypotension associated with hypovolemia can occur if blood is removed from the patient too rapidly.

Access sites and the tubing itself are also potential sources of complications. The tubing itself may become a source of free air leading to air embolus if there are leaks in the system. In addition, severe uncontrolled hemorrhage occurs if the access tubing becomes disconnected from the plasmapheresis machine tubing. Sterile technique is practiced at all interfaces between the patient and machine to prevent bacterial contamination.

Crismon (157) reports that plasmapheresis is a new type of therapy that holds promise for the treatment of an array of critical disorders. Considered experimental until recently, the procedure's impact upon critical care nursing is growing, as nurses become involved in the treatment of plasmapheresis patients. The critical care nurse must be prepared to continuously monitor the patient's status during the procedure. Crismon states that the critical care nurse normally monitors the patient's condition and carries out nursing duties while another

person (a nurse or technician) who has received special training in operation of the pheresis equipment performs the treatment. Cona(158) reports that pheresis operators are usually trained at the facility where they will be working. The training is generally supplied by the company from which the instrument is purchased.

Plasma Exchange in Burn Patients

There is currently only one burn center performing plasma exchange in burn patients. Clinical evaluation of plasma exchange was begun at the Intermountain Burn Center, Salt Lake City, Utah, in 1979. Initial results of this experience were published by Warden (85) and Warden et al. (159) in 1983. Plasma exchange in burn patients was performed on a group of patients when they failed to resuscitate from burn shock using conventional therapy. Irreversible burn shock results from failure of fluid resuscitation and is almost invariably fatal. Because of the implied role of circulating serum factors in the generation of burn shock, the use of plasma exchange was evaluated retrospectively in patients with major thermal injuries who had failed to respond to conventional therapy and had undergone plasma exchange.

Twenty-two patients with a mean burn size of 47.9% TBSA and a mean age of 22.7 years underwent exchange for ongoing burn shock after standard fluid resuscitation failed. Fourteen of these patients were adults and under-

went plasma exchange; eight of the patients were children who underwent exchange transfusion of whole blood and platelets. A therapeutic response was documented in 95.4% of the patients. The improvement was characterized by a sharp decrease in fluid requirements from a mean of 260% above the predicted hourly volume to within calculated requirements by 2.3 hours following the exchange. Markedly improved urine output and resolution of lactic acidosis were also demonstrated. No major complications occurred.

The results of this study demonstrated that an altered internal environment exists following thermal injury. Whether the mechanism of action of plasma exchange involves the removal of circulating toxic factors, the replenishment of specific deficiencies, or a combination of the two remains to be determined. Conclusions from this study were: a) plasma exchange can be performed safely in critically injured burned patients; b) plasma exchange arrests ongoing burn shock through an as yet undefined mechanism resulting in a dramatic reversal of fluid requirements, a brisk diuresis, a resolution of lactic acidosis, and a restoration of capillary integrity; and c) plasma exchange facilitates resuscitation from burn shock in a select group of patients who do not respond to conventional volume therapy.

Although this report is preliminary and involves a

heterogeneous patient population without adequate controls, the return toward normal of various clinical parameters in nearly all of these patients was encouraging. Plasma exchange in order to provide a potential alternative in burn shock resuscitation by returning the altered internal milieu toward normal was indicated. The nurse administering the fluid volume would need to determine the effect of plasma exchange on the fluid requirements. Thus, a reseach question arises: Does plasma exchange performed during burn shock alter the predicted resuscitation fluid requirements a burn nurse may expect to deliver to a patient in burn shock?

Summary

Burn shock appears to consist of both a hypovolemic and a cellular component. Hypovolemic shock results from an increase in capillary permeability which begins with the onset of thermal injury and persists for approximately 24 hours postburn, even when supportive therapy in the form of fluid resuscitation is provided. Investigations have documented the release of many mediators of the inflammatory response which may play roles in the cardiovascular response to burns. These include vasoactive amines, metabolic hormones, products of arachidonic acid metabolism, kinins, polypeptides, endotoxin, fibronectin, and others. Evidence suggests that with onset of the burn

wound, cellular metabolism is also disrupted. This results in altered membrane permeability and loss of normal electrolyte homeostasis associated with the flux of sodium and water into the cells and the loss of intracellular potassium. This cellular effect may be the pathophysiologic process responsible for the genesis of burn shock. These circulating factors altering fluid dynamics not only effect the capillary permeability but also lead to decreased vascular colloid osmotic pressure and a deranged capillary hydrostatic pressure. The result is an excess of fluid in the interstitial space in the form of edema and a decreased circulating volume. Also, the many circulating factors present in burn serum may play a reciprocal role in the generation of the cellular abnormalities observed.

Preliminary investigations into plasma exchange in the treatment of burn shock inpatients who have not responded to conventional management report marked improvement in several clinical settings, including refractory resuscitation failure, acute respiratory distress, myoglobinuria associated with major electrical injury, and the syndrome of metabolic exhaustion or presepsis. In treating patients suffering resuscitation failure, plasma exchange has demonstrated an immediate decrease in fluid requirements, resolution of lactic acidosis, and a return to a normal resuscitation schedule.

The current paradigm of supportive burn therapy assumes that optimal care consists of the administration of fluids at the same rate and in the same volume and composition in which they are lost. This paradigm is outdated in view of advances in knowledge and state of the art technology available. A therapeutic paradigm imvolves restoring cardiovascular and physiological integrity as early as possible postburn. The combination of plasma exchange with supportive therapy is the treatment paradigm supporting this study.

CHAPTER III

DESIGN AND METHODOLOGY

This chapter will present the design and methods of procedure.

Design

The design chosen to answer the research questions of this study was experimental with random assignment of 14 consenting burn subjects to one of two treatment groups. One group of subjects received standard resuscitation according to the Parkland formula. A second group of subjects received standard resuscitation in conjunction with plasma exchange as the independent variable.

Methodology

Subject Selection

All patients between 15 and 60 years of age admitted to the Intermountain Burn Center and suffering acute burns of greater than or equal to 40% TBSA were considered for inclusion as subjects in the study. Because of the difficulty in estimating burn size in outlying hospitals, no patient was admitted to the study as a sub-

ject prior to initial evaluation in the burn center itself. Estimation of burn size was carried out using the Lund and Browder Chart (Appendix A) and included estimates of both partial- and full-thickness burns. To be included in the study, subjects had to have burn wound involvement of 40% or greater TBSA injury.

Human Subjects

Human subjects' approval was obtained from the Human Subjects Committee of the University of Utah Medical Center prior to data collection. Upon arrival at the burn center, the extent of the wound was determined and standard burn care initiated. After determining that the patient had a burn injury of 40% TBSA or greater, the patient and family were interviewed by a burn physician for consent to participate in the study. Informed consent from the patient and next-of-kin was necessary for the patient to be included in the study. Consent was obtained using a specially written consent form which had been approved by the Human Use Committee of the University of Utah Medical Center. The consent form included descriptions of both the invasive monitoring and of the plasma exchange procedure to be performed. No claims of documented efficacy for plasma exchange therapy were made. Risks were explained verbally and in writing. Patient participation was voluntary with the option to withdraw from and/or ask questions about the study at any time.

Anonymity was maintained. In addition, the subjects were told that if they were entered into the control group and subsequently showed evidence of resuscitation failure, they would have the option of undergoing plasma exchange as a therapeutic procedure.

Because this study involved legally minor subjects, the consent for entry into the study was signed by the legal next-of-kin when the patient's age was 15 to 18 years.

Complications and Risks of the Study

The risks associated with participation in the study were essentially threefold: complications associated with placement of catheter lines, complications associated with the plasma exchange procedure, and complications associated with the drawing of blood samples.

The complications associated with placement of the two additional lines directly related to the study were identified as a risk. The Swan-Ganz catheter was placed for monitoring of cardiac parameters and obtaining mixed venous blood gas samples; the additional 14-gauge venous line was placed for the plasma exchange procedure access. Both of these lines were placed under the direct supervision of one of the physician-directors of the Burn Center. Potential risks from Swan-Ganz catheter placement in any patient include pneumothorax, hemothorax, hydro-

thorax, arterial puncture, cardiac tamponade, and arrhythmias secondary to placement of the catheter. All of these complications are exceedingly rare. In order to minimize their occurrence further, an effort was made to place all catheters through an internal jugular rather than the subclavian approach. The internal jugular approach was attempted because of the lower risk of pneumothorax and the greater ease in treating an arterial puncture. In order to minimize the possibility of arrhythmia, all subjects had continuous ECG monitoring during placement of the Swan-Ganz catheter. Lidocaine and cardiopulmonary resuscitation equipment were immediately available. Placement of the 14-gauge line for plasma exchange was performed in a femoral vein which has few complications.

Potential complications associated with the plasma exchange procedure were also identified as risks. The procedure carries with it the associated risks of hypotension due to excessive volume withdrawal, air embolism from operator error, and hepatitis from the volume of fresh frozen plasma infused. Complications related to the withdrawal of excessive volume were controlled by the continuous flow technique employed. Fluid balance was maintained at or near zero at all times during the procedure. The risk of air embolus was decreased by using only fully-trained and experienced pheresis technicians who

were additionally alerted by both audible and visible alarms built into the machine to signal an air-in-line warning. The infusion of large quantities of fresh frozen plasma carried the theoretical risk of transfusion reaction, although this was less than if whole blood had been used. In addition, the possibility of transmission of viral hepatitis existed.

Complications associated with the withdrawal of multiple blood samples were also considered. Because the subjects had an indwelling arterial line throughout the study period, there were no complications associated with the performance of venipuncture for the withdrawal of blood samples. The total volume of blood to be withdrawn during the course of the experiment was calculated to be approximately 350 mL (Appendix B). Existing protocols in the Burn Center required a similar battery of blood tests to be obtained on all patients with major burns every six hours; thus, the 350 mL represented an increase of approximately 33% in the quantity of blood to be drawn from study patients. The difference was between 120 and 150 mL in the 48 hour study period.

Invasive Monitoring

Upon admission to the burn center, all patients with burns of 40% TBSA or greater routinely undergo placement of the following invasive lines:

1. Nasogastric tube: Placement is via the naris whenever possible; oral placement is an option. A 2-part tube of appropriate size is placed, secured, documented to be in physiologic position by radiographic exam, and connected to low (20 to 40 mm Hg) constant suction.

2. Foley bladder catheter: Placement of a catheter of the appropriate size is accomplished using sterile technique. When in position, as verified by urine return, the cathether is conneced to a down-drain bag with a built-in urimeter.

3. Large-bore intravenous lines for fluid resuscitation: At least one 14-gauge catheter is placed into the internal jugular, subclavian or femoral vein using sterile technique. The site selected for line placement is based upon the location of the burn wound and the mobility and preference of the patient. Lines are sutured in place and position verified by radiographic exam.

4. Arterial line: An arterial line is placed into either the radial or femoral artery. A 20-gauge catheter is routinely used for the radial artery and an 18-gauge line for the femoral artery. The line is then attached to a pressure transducer with flush system connected to a patient monitor (Mennen Model 480, Clarence, NY) and sutured into place.

In addition to the above lines, subjects in this study underwent the placement of a Swan-Ganz thermodilu-

tion catheter (Model 93A-131-7F, Edwards, Inc., Santa Ana, Ca.). The catheter was threaded through a hollow plastic catheter introducer (Cordis, Inc., Miami, Fla.) into either the internal jugular, subclavian, or femoral vein. The balloon-tipped Swan-Ganz catheter is equipped with pulmonary artery and central venous ports and an electronic thermister. Pulmonary artery pressure is monitored by attachment of the catheter's distal port to a pressure transducer connected to a patient monitor equipped with oscilloscopic display of pressure tracings, digital readout of pressures, and a strip recorder. While continuously monitoring pressures, the catheter is flow-directed into the proximal pulmonary artery and measurements of wedge pressure obtained. Appendix C lists normal values and formulas used for the calculation of cardiopulmonary profiles. During catheter placement, the electrocardiogram (ECG) is monitored continuously for the occurrence of arrhythmias; cardiopulmonary resuscitation equipment and personnel certified in cardiopulmonary resuscitation techniques are available at the bedside. Once in position in the pulmonary artery, the catheter is sutured into position and placement confirmed by a portable chest radiograph.

Resuscitation

All subjects underwent initial resuscitation according to the Parkland formula. This formula called for

the intravenous infusion of lactated Ringer's solution (Appendix D) at a rate of 4 mL/kg/% TBSA burn. Half of the calculated volume was given over the initial eight hours following thermal injury and the remainder over the ensuing 16 hours. Standard guidelines for assessing the success of fluid resuscitation were used with the primary criteria being urine output. Subjects underwent the insertion of a Foley bladder catheter as soon as was clinically feasible; hourly urine output determinations were made thereafter for a 48 hour period. Fluid volumes were adjusted to maintain urine output at a range of 30-50 mL per hour. Subjects whose urine output was less than this value were given additional fluid in volumes sufficient to improve urine output; subjects whose urine output was in excess of this amount underwent appropriate decreases in fluid infusion.

Patients transported to the burn center from long distances had their fluid resuscitation begun prior to transport. In no case was fluid resuscitation withheld or adjustments in fluid resuscitation made according to the planned entry of the patient into the study.

Documentation of Inhalation Injury

All subjects suffering potential exposure to toxic products of combustion were evaluated for inhalation injury. The evaluation was based on clinical findings but,

in all cases, objective documentation was by ^{133}xenon perfusion scan. In addition, subjects who underwent endotracheal intubation had fiberoptic bronchoscopy performed. Diagnosis of inhalation injury was based upon the presence of two of the following three criteria:

1. Clinical findings consisting of oropharyngeal burns; carbonaceous sputum; respiratory distress or wheezing; facial burns, singed vibrissae and facial hair; or upper airway edema.

2. The presence of a positive ^{133}xenon scan consisting of retention of isotope beyond 90 seconds in segmental areas of the lung or diffuse retention for longer than 120 seconds.

3. Bronchoscopic evidence of inhalation injury consisting of tracheal or broncheolar edema, erythema, desquamation, or carbonaceous deposits.

In addition, arterial blood gas analysis was performed on admission to the burn center for the purpose of assessing respiratory parameters and documenting carboxyhemoglobin content. An admission chest radiograph was also obtained on all subjects.

Randomization of Subjects to Plasma Exchange

The population of burn patients admitted to the burn center was considered to be a true sample of all burn patients from a large geographical area based on two

factors. The first factor is that the burn center has a policy to accept all burn patients for admission. The second factor is that the burn center is the regional referral center for all hospitals in the intermountain area. Thus, since essentially all hospitalized patients with major burns are transferred to this burn center and, since the burn center refuses no admissions, a basic assumption is that the criteria for achieving representative sampling of burn patients appeared to be met.

Random assignment of subjects into the treatment group or control group was accomplished using a table of random numbers (Appendix E). Prior to the beginning of the study, 96 numbers were sequentially paired. Each pair was then numbered sequentially one through 48. Using the pair number, reference was made to a standard table of random numbers with the first number of each pair being assigned either to the treatment or control group. The second number of each pair was then designated to the other group. Based on these assignments, a series of 96 envelopes were numbered sequentially; a card designating that individual's group assignment was placed inside; and the envelope was sealed. A box containing all 96 envelopes in proper numerical sequence was placed at the nurses' station. On admission to the burn center, patients who qualified for the study were approached by a physician for consent. After obtaining consent, the en-

velope in the front of the box was opened by a staff member to learn to which group the subject was assigned.

The rationale for pairing the subjects was to offset both the seasonal nature of burn admissions and the not infrequent occurrence of multiple admissions from a single fire or other catastrophe. If random assignment of 96 individual numbers had been performed, it would have been possible for many numbers in series to be assigned to the same group. If this occurred during the winter months when patients have a higher incidence of inhalation injury due to burn injuries sustained in a house fire, a bias regarding the plasma exchange treatment could have resulted.

Similarly, if a number of patients injured in a single accident were admitted simultaneously, the pairing system assured that they were evenly and randomly assigned to the two treatment groups. Finally, since the pairing system assured that both the control and treatment groups contained an equal number of subjects, the performance of periodic review of results facilitated analysis of the data. Placing individual assignments in sealed envelopes sequentially numbered assured that the order of treatment assignment was not subject to bias. Arrangement for assignment of 96 subjects was made to assure that the number of studies necessary to reach statistical significance would not exceed the number ini-

tially randomly assigned. Because of limited knowledge regarding the effect of plasma exchange on burn patients, there was no way to predict the number of trials necessary to reach a conclusion prior to beginning the study. Continual review of results was built in to the design so that the endpoint of the study was statistical significance.

Performance of Plasma Exchange

Subjects randomized to undergo plasma exchange had the procedure performed as soon as was clinically feasible. That is, all access lines were immediately placed and plasma obtained in readiness for the procedure to begin as soon as consent was obtained. Patients who were not admitted to the burn center in time to begin plasma exchange by the fifteenth postburn hour were not considered for entry into the study protocol.

Plasma exchange was performed using an IBM Model 2997 continuous blood cell separator (IBM Systems, Endicott, N.Y.). The performance of the procedure was under the technical direction of the medical director of the University of Utah Medical Center pheresis center and blood bank. The procedure was performed by plasmapheresis technicians at the subject's bedside in the burn center.

The IBM 2997 separates whole blood into its major components with the advantage over discontinuous cell se-

parators of requiring virtually no extraneous volume from the patient to prime the machine. Blood flow to and from the patient is controlled by variable speed roller pumps. A centrifuge separates the blood into its components based upon their specific gravities. Strategically placed pipettes within the machine collect the various components of the blood as it is separated in the centrifuge. Anticoagulant is injected into the blood as it is removed, in a whole blood-to-anticoagulant ratio of 10:1. Acid citrate dextrose (ACD) formula A (Fenwal Labs., Deerfield, Ill.) is employed as an anticoagulant. Blood is withdrawan through one of the large intravenous catheters and entered into the blood separation channel (Ethox, Inc., Buffalo, N.Y.) in place in the machine. As blood is spun, the plasma component is removed and collected in storage bags for research use. Erythrocytes, platelets, and white cells are returned to the patient through a second large bore intravenous line. Simultaneously, the volume of plasma removed from the patient is replaced mL for mL with type-specific fresh frozen plasma from the University Hospital Blood Bank. The fresh frozen plasma used is prepared from whole donor blood in which the plasma is separated by centrifugation and frozen at -30 degrees C within six hours of collection. Fresh frozen plasma has a dating period of 12 months after which time it is deficient in Factor VIII

and must be discarded. The fresh frozen plasma is quickly thawed immediately prior to use to prevent loss of labile coagulation factors.

Subjects undergoing plasma exchange had a calculated volume of exchange equal to one and one-half times their calculated blood volume. This was based on the following calculation (160): For males, blood volume equals 7% of the body weight in kilograms; for females, blood volume equals 8% of body weight. The plasma exchange procedure was regulated so as to be completed in the shortest possible time. Because of mechanical limitations, the procedure takes a minimum of two to five hours. Regulation also kept the patient's balance of exchange fluid approximately equal to zero thus preventing over- or underhydration during the course of the exchange procedure. Continuous monitoring of blood pressure and other vital signs was performed throughout the procedure. Parkland fluid resuscitation continued throughout the period of plasma exchange and was modified according to the standard parameter of urine output.

Completion of Resuscitation

Following resuscitation from burn shock, patients with major burns have increased requirements for maintenance fluid. All subjects in this study had hourly urine output determinations, with fluid requirements modified

as needed. When a subject was able to maintain a urine output of 30 to 50 mL per hour for two hours with the volume of fluid infusion equal to calculated maintenance, fluid resuscitation ws considered complete and burn shock reversed.

Maintenance fluid requirements in burn patients are predicted by using two standard calculations. The first calculates evaporative water losses from the burn wound (161):

$(25 + \%\ \text{TBSA burn})\ (\text{BSA } m^2) = \text{evaporative loss in mL/hour.}$

Formula components:

25 = constant as described in reference by Warden et al. (161).

% TBSA burn = percent total body surface area burn as described by Lund and Browder (Appendix A).

$\text{BSA } m^2$ = body surface area as described by Dubois (162). This formula, the "Height - Weight Formula," estimates the surface area of subjects when their height and weight are known and is expressed as:

$$\text{BSA} = W^{0.425} \times H^{0.725} \times C$$

with BSA being surface area in square centimeters, W the weight in kilograms, H the height in centimeters, and C the constant, 71.84. A chart has been plotted from this formula (Appendix F).

The second formula calculates other maintenance fluid

requirements (urine output, stool, respiratory losses) and is expressed as:

$$(1500 \text{ mL})\ (\text{BSA } m^2) = \text{Maintenance requirements in mL per 24 hours}$$

or

$$(62.5 \text{ mL})\ (\text{BSA } m^2) = \text{Maintenance requirements in mL per hour}$$

Total maintenance fluids for burn patients are equal to the addition of the two formulas or:

$$(25 + \% \text{ TBSA burned} + 62.5)\ (\text{BSA } m^2) = \text{mL per hour.}$$

Thus, when a subject sustained an adequate urine output of 30 to 50 mL per hour for two consecutive hours on the predicted amount of infused maintenance fluid, resuscitation criteria were met. In addition to urine output, completion of resuscitation was monitored by evaluation of the subject's clinical status using other parameters including vital signs and serum laboratory reports. Upon completion of resuscitation, all subjects received an infusion of type-specific fresh frozen plasma equal to 20% of their calculated blood volume. All subjects were then given standard maintenance therapy consisting of 5% dextrose in 0.2% normal saline (D5.2NS) at a rate calculated to equal maintenance needs.

Data Collection

Subjects entered into the study had a number of

blood chemistry determinations made at specified times throughout the 48 hour course of the study. Blood samples were withdrawn by burn center staff through the arterial line, utilizing a three-way stopcock and sterile technique. The line was flushed with normal saline following each withdrawal. Blood was aspirated into sterile plastic syringes and transferred to the appropriate tube (Vacutainer Systems, Rutherford, N.J.) for transportation to the pathology laboratory at University Hospital. There the samples underwent standard automated techniques employed for the determination of specific values. Appendix G presents normal ranges of laboratory values. For determination of arterial and mixed venous gas contents, blood was drawn into sterile preheparinized plastic syringes (Concort Labs, Keene, N.H.), placed in ice, and transported immediately to the pulmonary laboratory at University Hospital. Appendix C presents normal values for blood gas determinations.

Serum determinations were made serially on each subject admitted to the study. Appendix H lists the variables and the intervals postburn that samples were obtained.

Physiologic variables measured serially by burn center staff included:

1. Vital signs: Heart rate, respiratory rate, core body temperature utilizing the Swan-Ganz catheter connec-

ted to the Edwards cardiac output instrument, and systemic blood pressure using the arterial line transducer connected to the Mennen monitoring instrument.

2. Swan-Ganz measurements: Pulmonary artery mean and systolic/diastolic pressures; pulmonary capillary wedge pressures; central venous pressures; and cardiac output determinations. Determinations of cardiac output were made by the technique of thermodilution using sterile D5W maintained in ice at a temperature of 0 degrees C. A 10 mL aliquot of iced D5W was injected into the proximal port of the Swan-Ganz catheter following verification of its position by pressure tracing and portable chest radiograph. Measurement of blood temperature at the distal pulmonary artery port was made by the thermistor incorporated into the catheter. Calculation was made using the Edwards Model 9520 cardiac output computer. All determinations were made in triplicate within one minute intervals and the mean of the three values used as the recorded value. The normal values for these parameters are presented in Appendix C.

3. Intake: All infusions were measured and recorded according to content, amount, and route administered.

4. Output: All output, including urine, nasogastric tube drainage, stools, emesis and estimated blood loss were measured and recorded.

5. Ventilatory status including settings of venti-

lator and timing of changes made in settings. These parameters include fraction of inspired oxygen (Fi02), tidal volume, mode of therapy, ventilator rate, and positive and expiratory pressure (PEEP) setting.

Cardiac profiles were calculated by computer technicians using the Telemed Cardiopulmonary System (Tenet Company, Salt Lake City, Utah) to determine arterial venous oxygen difference, oxygen consumption, oxygen availability, oxygen extraction, pulmonary vascular resistance index, systemic vascular resistance index, cardiac index, stroke index, and percent of shunt. The formulas used to calculate these values are presented in Appendix C.

Data collected on each subject also included age; sex; percent TBSA burn with division into partial- and full-thickness injury; etiology of injury; time postburn intravenous resuscitation was begun; time postburn admitted to burn center; presence of inhalation injury; concommitant injury; preexisting disease and current medications; weight; height; body surface area; calculated fluid and sodium requirements according to Parkland formula and maintenance formula; actual fluid and sodium requirements; amount of intake and output; survival; and, in the treatment group, plasma exchange data.

The nursing staff of the burn center carried the primary responsibility for adherence to the research pro-

tocol. The member of the burn center staff assigned to deliver care to the patient was responsible for incorporating the research protocol activities into the subject's burn care. Assignment of staff is the responsibility of the charge nurse on each shift. The nursing staff works 12-hour shifts so that at least four different nursing shifts were responsible for the care of the subject during the 48 hour study period. All staff caring for critically ill patients on admission are experienced burn center personnel. In addition, the two medical directors, the clinical specialist, and the head nurse of the burn center were available as a resource at all times during the study period. To clarify the specific tasks associated with the study, a list of the nurse's hourly responsibility during the plasma exchange research study was developed (Appendix I). This list was included in the envelopes containing the assignment to group card so that it was immediately available to the nurse whose patient entered into the protocol.

Termination of the Study

All study parameters were followed for a total of 48 hours from the time of burn injury. At that time, the Swan-Ganz catheter was removed if the subject was sufficiently stable to warrant discontinuing this method of monitoring. The arterial line was also removed at that time if clinical circumstances permitted.

The participation in the study by an individual was terminated at any time during the course of the study under the following circumstances:

1. If the subject expressed a desire to withdraw participation in the study.

2. If the subject's family expressed a desire for the subject to be withdrawn from the study.

3. If significant complications arose as a result of procedures incorporated into the study which were not considered routine procedures; i.e., Swan-Ganz catheter placement, plasma exchange procedure.

4. If plasma exchange could not be started by 15 hours postburn.

If a study subject died before the 48 hour postburn period had elapsed, that subject remained in the study for the purpose of analysis of all data gathered up to the time of death.

Other Burn Therapy

Entrance into and participation in this study did not, in any way, compromise other aspects of burn care. All standard protocols used in the burn center were continued in subjects entered into the study. These included aggressive cimetadine and antacid prophylaxis to guard against the development of gastric stress erosions; aggressive nutritional support including vitamin therapy;

early excision and autografting of all full- and deep partial-thickness burns; and early, vigorous physical therapy.

Resuscitation Failure

Subjects entered into the plasma exchange protocol who were randomized to be controls continued to be at risk for developing resuscitation failure. Resuscitation failure was defined as a subject who, at 18 hours postburn, still required in excess of twice the calculated volume of resuscitation fluid to maintain urine output at the minimum acceptable level of 30 mL/hour. In addition, subjects who required formal resuscitation with lactated Ringer's solution for longer than 36 hours postburn were considered resuscitation failures. Subjects in the control population who developed resuscitation failure were dropped from the control protocol; at that time, they underwent a course of plasma exchange as a therapeutic maneuver. Any monitoring devices in place were continued throughout the 48 hour period. Inclusion of such subjects in the control group was continued but the development of failure to resuscitate placed them in a subgroup for statistical analysis.

Statistical Analysis Technique

Data collection was performed using two 24-hour flow sheets for each subject. The data were collected on each

subject immediately after the conclusion of the 48 hour study period. Data were analyzed using the Statistical Package for the Social Sciences Program. A UNIVAC 1100 computer processed the statistical programs. Statistics utilized to describe the sample were descriptive in nature and included means, standard errors, ranges and frequencies (%). In addition, t-test analysis was performed on 321 selected variables measured to determine whether or not significant differences occurred between the control and treatment groups. Because of the exploratory nature of the work and the small number of subjects studied, statistical significance is defined at the .05 level. The technique of survival statistics was also performed on both groups.

CHAPTER IV

RESULTS

An experimental study designed to evaluate the effect of plasma exchange on subjects in burn shock was conducted. Subjects assigned to the control group received standard burn shock resuscitation while the experimental group (PLA/EX) received standard burn shock resuscitation plus plasma exchange. Built into the design of the study was a means to periodically evaluate the data. This chapter presents the statistical analyses of data from an initial sample of 14 subjects. These data are presented in tabular form beginning with the description of the sample. Following the descriptive data, the two specific questions concerning the physiological response to treatment by group will be presented.

The Sample

Student's t-tests of 2-tail probability were conducted to identify statistical differences between the two groups on all variables. The list of all measured variables is presented in Appendix I.

Fourteen patients with 40% TBSA burn or greater were

admitted to the study between July 1982, and December 1983. Ten (71%) male and four (29%) females were included (Table 2). The cause of injury in all cases was flame. Five subjects (36%) had documented associated inhalation injury. The mean age was 37.6 years (range: 20-52). The mean percent total body surface area (TBSA) burn was 51.2 (range: 40-83) with a mean full-thickness component of 28.4% TBSA (range: 0-46). The mean body weight was 77 kg (range: 56-93) with a mean body surface area (BSA) of 1.9 m^2 (range 1.55 to 2.25). Thirteen of the 14 subjects (93%) survived burn shock. Eleven subjects (79%) survived the burn injury.

The two subject groups were compared for differences on these variables (Table 3). The control group consisted of six males (86%) and one female (14%); the PLA/EX group consisted of four males (57%) and three females (43%). The incidence of inhalation injury was documented in one control subject (14%) and four PLA/EX subjects (57%). The mean age of control subjects was 36.7 years (range: 23-52). The PLA/EX group had a mean age of 38.4 years (range: 20-49). The control group had a mean burn size of 48.9% TBSA (range: 40-83).

PLA/EX subjects had a mean burn size of 53.6% TBSA (range: 44-71). There was no statistical difference ($p>.05$) between the groups on these variables. A statistically significant difference was found on the variable

Table 2 - Descriptive Characteristics of Sample (n=14)*

Variable	No. (%)	Mean	SE	Range
Sex				
Male	10 (71)			
Female	4 (29)			
Cause of Injury				
Flame	14 (100)			
Inhalation Injury	5 (36)			
Age, Years		37.6	2.98	20-52
% TBSA Burn		51.2	3.47	40-83
% Full-Thickness TBSA Burn		28.4	3.41	0-46
Weight, kg		77.0	3.07	56-93
BSA m^2		1.9	0.05	1.55-2.25
Survival of Burn Shock	13 (93)			
Survival of Burn Injury	11 (79)			

*Represents number of cases (No.), frequencies (%), mean, standard error (SE), and range.

Table 3 - Descriptive Characteristics of Groups*

Variable	No.(%)	Mean	SE	Range	Probability
Sex					
Male					
Control	6 (86)				
PLA/EX	4 (57)				
Female					
Control	1 (14)				
PLA/EX	3 (43)				
Inhalation Injury					
Control	1 (14)				
PLA/EX	4 (57)				.111
Age, Years					
Control	7	36.7	4.86	23-52	
PLA/EX	7	38.4	3.81	20-49	.787
% TBSA Burn					
Control	7	48.9	6.00	40-83	
PLA/EX	7	53.6	3.78	44-71	.521
% Full-Thickness TBSA Burn					
Control	7	18.3	3.35	0-25	
PLA/EX	7	38.4	2.33	27-46	.000
Weight, kg					
Control	7	79.0	3.63	66-93	
PLA/EX	7	74.9	5.12	56-75	.522
BSA, m^2					
Control	7	1.95	0.07	1.70-2.25	
PLA/EX	7	1.89	0.08	1.55-2.20	.555

*Represents number of cases (No.), frequenciess (%), mean, standard error (SE), range, and t-test level of significance.

of percent full-thickness TBSA burn with controls having a mean of 18.3% TBSA full-thickness involvement (range: 0-25) compared to 38.4% (range: 27-46) for PLA/EX subjects ($p<.01$). The mean body weight for controls was 79.0 kg (range: 66-93) compared to a mean of 74.9 kg (range: 56-75) in the PLA/EX group. Body surface area (BSA) was a mean of 1.95 m^2 for control (range: 1.70-2.25) and 1.89 m^2 for PLA/EX subjects (range: 1.55-2.20). No statistical difference between groups was present in either of these variables ($p>.05$).

Resuscitation Requirements

The first proposed question in this study was as follows:

> Does plasma exchange performed during burn shock alter the predicted resuscitation fluid requirements a burn nurse may expect to administer to a patient in burn shock?

The Student's t-test was used to analyze the resuscitation data. The mean and standard error are reported in this situation where the precision of the sample mean as an estimate of the population mean was intended. The control had intravenous (IV) fluid started by a mean of 1.29 hours postburn (range: 1 to 2 hours). All PLA/EX subjects had IVs infusing by one hour postburn (Table 4). The postburn hour (PBH) of arrival in the burn center was 4.43 for the control (range: 1-7) and 3.43 for the PLA/EX group (range: 2-5). During the first 24 hours postburn,

Table 4. Resuscitation Requirements First 24 Hours Postburn

Variable	Control Group (n=7) Mean	SE	Range	PLA/EX Group (n=7) Mean	SE	Range	Probability
PBH IV Started	1.29	.18	1-2	1.00	.00	1.00	.172
PBH Arrival in Burn Center	4.43	.81	1-7	3.43	.53	2-5	.326
Fluids to Resuscitate, 1st 24 hrs mL/kg/hr	3.23	.51	1.83-5.15	3.37	.47	1.90-4.99	.845
Fluids to Resuscitate to seal mL/kg/hr	3.30	.59	1.49-4.68	2.91	.49	1.32-5.67	.620
Fluids to Resuscitate, 1st 8 hrs mL/kg/hr	1.35	.22	0.50-2.24	1.88	.26	0.65-2.83	.139
Fluids to Resuscitate, 2nd 8 hrs, mL/kg/hr	1.12	.28	0.15-2.22	0.82	.24	0.09-1.60	.426
Fluids to Resuscitate, 3rd 8 hrs, mL/kg/kr	0.66	.15	0.24-1.34	0.73	.21	0.19-1.77	.768
PBH to Resucitation	27.9	3.14	14-37	22.30*	4.03	9-35	.305
Sodium Infused to Resuscitation, mEq/kg/%TBSA burn	0.61	.09	0.31-0.95	0.67*	.13	0.31-1.10	.698
Urine Output to Resucitation mL/hr	62.00	7.95	38-96	105.00*	10.87	77-142	.009**

*n=6; **p<.01

the control group received a mean of 3.23 mL/kg/hr of resuscitation fluid (range: 1.83-5.15). The PLA/EX group received a mean of 3.37 mL/kg/hr during the first 24 hours postburn (range: 1.90-4.99). The mean amount of IV fluid to resuscitate subjects until the time when clinical criteria for sealing was met was a mean of 3.30 mL/kg/hr for the control (range: 1.49-4.68) and 2.91 mL/kg/hr for the PLA/EX group (range: 1.32-5.67). Fluids to resuscitate during the first eight PBH period were 1.35 mL/kg/hr for the control (range: 0.50-2.24) and 1.88 mL/kg/hr for the PLA/EX group (range: 0.65-2.83). Fluids to resuscitate during the second eight PBH period were 1.12 mL/kg/hr for the control (range: 0.15-2.22) and 0.82 mL/kg/hr for the PLA/EX group (range: 0.09-1.60). Fluids to resuscitate during the third eight PBH period were 0.66 mL/kg/hr for the control (range: 0.24-1.34) and 0.73 mL/kg/hr for the PLA/EX group (range: 0.19-1.77). The time to resuscitation for the control was 27.9 hours postburn (range: 14-37) and 22.3 hours postburn for the PLA/EX group (range: 9-35). One PLA/EX subject died at PBH 36 without meeting the clinical criteria for sealing. The amount of sodium infused for resuscitation of the control was a mean of 0.61 mEq/kg/% TBSA burn (range: 0.31-0.95). The PLA/EX group received a mean of 0.67 mEq/kg/% TBSA burn (range: 0.31-1.10). Urine output to resuscitation was a mean of 62 mL per hour for the control (range: 38-96) and 105 mL

per hour for the PLA/EX group (range: 77-142). This variable was significantly different ($p<.01$).

In comparing the control and PLA/EX groups, no difference was found in any of the variables associated with resuscitation requirements ($p>.05$). Comparison of the control to a group designated experimental survivors was then conducted. Survival in the group was dependent upon clinical criteria of a normal response to burn injury. All control subjects responded as expected to burn shock resuscitation and none were deemed resuscitation failures. In the experimental PLA/EX group, three subjects (43%) failed to survive in the group. One patient died at 36 hours and two patients failed to resuscitate and had repeat plasma exchange procedures within 48 hours of the burn. Failure to survive in the group was not statistically significant ($p>.05$) between the groups. A subgroup of experimental subjects was identified and designated as experimental survivors (EXP-SUR). Comparison of the control to EXP-SUR group is reported in Table 5. Differences between the four EXP-SUR subjects and the seven control subjects failed to achieve statistical significance ($p>.05$) on resuscitation variables due to low t-test power.

The second 24 hours of burn shock was also studied regarding fluid requirements (Table 6). The predicted maintenance was determined using previously described

Table 5. Resuscitation Requirements First 24 Hours Postburn

Variable	Control Group (n=7) Mean	SE	Range	EXP-SUR Group* (n=4) Mean	SE	Range	Probability
PBH IV Started	1.29	.18	1-2	1.00	.00	1-1	.172
PBH Arrival in Burn Center	4.43	.81	1-7	3.25	.75	2-5	.318
Fluids to Resuscitate 1st 24 hrs mL/kg/hr	3.23	.51	1.83-5.15	3.46	.75	1.90-4.99	.808
Fluids to Resuscitate to seal, mL/kg/hr	3.30	.59	1.49-4.68	2.80	.71	1.32-5.67	.600
Fluids to Resuscitate 1st 8 hrs mL/kg/hr	1.35	.22	0.50-2.24	2.06	.29	1.53-2.83	.094
Fluids to Resuscitate 2nd 8 hrs mL/kg/hr	1.12	.28	0.15-2.22	0.86	.42	0.09-1.60	.621
Fluids to Resuscitate 3rd 8 hrs mL/kg/hr	0.66	.15	0.24-1.34	0.48	.14	0.19-0.83	.402
PBH to Resuscitation	27.9	3.14	14-37	17.30	3.71	9-27	.065
Sodium Infused to Resuscitation mEq/kg/%TBSA burn	0.61	.09	0.31-0.95	0.60	.18	0.31-1.10	.955
Urine Output to Resuscitation mL/hr	62	7.95	38-96	98	15.26	77-142	.090

*Experimental survivors.

Table 6. Resuscitation Requirements Second 24 Hours Postburn

Variable	Control Group (n=7) Mean	SE	Range	PLA/EX Group (n=6) Mean	SE	Range	Probability
Predicted Maintenance Rate mL/hr	267	17.72	217-360	267	15.48	206-318	.986
Volume Delivered 2nd 24 hrs, mL/hr	337	38.27	226-481	392	60.09	239-608	.460
Volume Resus. Time to PBH 48 mL/hr	376	45.04	276-549	380	64.20	235-601	.959
Urine Output 2nd 24 hrs mL/hr	106	30.25	48-258	84	8.65	63-112	.519
Urine Output Resus. time-PBH 48, mL/hr	131	26.16	57-213	86	9.93	68-126	.150
Predicted FFP Need, mL	858	76.81	660-1264	911	45.44	750-1120	.563
FFP Administration, mL	866	79.77	660-1250	1004	138.00	800-1680	.413
PBH Administered	31.6	2.30	23-40	21.5	2.566	14-29	.014

methods (Appendix J). The controls were predicted to need 267 mL/hr of IV fluid (range: 217-360) and the PLA/EX group 267 mL/hr (range: 206-318). The actual volume delivered during the second 24 hours postburn was a mean of 337 mL/hr in the control (range: 226-481) compared with a mean of 392 mL/hr for the PLA/EX group (range: 239-608). The volume delivered from the time the subject met the clinical criteria of sealing until PBH 48 was a mean of 376 mL/hr for the control (range: 276-549) and 380 mL/hr (range: 235-601) for the PLA/EX group. Hourly urine output for the second 24 hour period was a mean of 106 mL/hr (range: 48-258) for the control and 84 mL/hr (range: 63-112) for the PLA/EX group. Urine output from the time of sealing until PBH 48 was a mean of 131 mL/hr for the control (range: 57-213) and 86 mL/hr (range: 68-126) for the PLA/EX group. The amount of FFP to be delivered to each subject was determined using previously described formulas (Appendix J). The mean amount for the control was 858 mL (range: 660-1,264) and the PLA/EX group mean was 911 mL (range: 750-1,120). The actual mean amount of FFP delivered was 866 mL for the control (range: 660-1,250) and 1,004 mL for the PLA/EX group (range: 800-1,680). The postburn hour of administration was a mean of 31.6 hours for the control (range: 23-40) and 21.5 hours for the PLA/EX group (range: 14-29). There was no statistical difference be-

tween groups ($p>.05$) on any of the variables presented in Table 6 except for PBH of administration of FFP. There the control and PLA/EX groups differed significantly ($p<.01$). The EXP-SUR group was again compared with the control and the data are presented in Table 7. No statistically significant differences between the groups were found ($p>.05$) except for the variable PBH of FFP administration where statistical significance was again reached ($p<.05$).

Data regarding the plasma exchange (PLA/EX) procedure are presented in Table 8. The mean time of actually starting the procedure was PBH 10 (range: 7-19). The mean time of ending PLA/EX was PBH 15 (range: 10-23). Using previously described formulas (Appendix J) the calculated amount of volume to be exchanged was determined to be a mean of 8,278 mL (range: 6,720-9,555). The actual exchanged volume was a mean of 7,539 mL (range: 6,000-9,300). The urine volume during PLA/EX was a mean of 229 mL/hr (range: 119-507).

The past medical history of the subjects was reviewed to determine any concomitant injury or illness. One subject (7%) had preexisting cardiac problems (Table 9). Two subjects (14%) had gastrointestinal disease; three subjects (21%) had a history of alcohol abuse; one subject (7%) had a history of drug abuse; and two subjects (14%) had intercurrent trauma. Seven of the nine problems

Table 7. Resuscitation Requirements - Second 24 Hours Postburn

Variable	Control Group (n=7) Mean	SE	Range	EXP-SUR Group (n=4) Mean	SE	Range	Probability
Predicted Maintenance Rate mL/hr	267	17.72	217-360	264.0	28.85	206-318	.933
Volume Delivered 2nd 24 hrs, mL/hr	337	38.27	226-481	369.0	86.04	239-608	.749
Volume Resus. time-PBH 48 mL/hr	376	45.04	276-549	359.0	83.78	235-601	.869
Urine Output 2nd 24 hrs mL/hr	106	30.25	48-258	72.0	5.25	63-84	.311
Urine output Resus. Time-PBH 48, mL/hr	131	26.16	57-213	71.0	2.02	68-77	.064
Predicted FFP Need, mL	858	76.81	660-1264	887.0	50.34	750-992	.757
FFP Administered	866	79.77	660-1250	1063.0	207.02	800-1680	.424
PBH Administered	31.6	2.30	23-40	21.8	2.87	15-29	.032

Table 8 - Plasma Exchange Procedure

Variable	PLA/EX Group (n=7) Mean	SE	Range
PBH Started	10	1.55	7-19
PBH Ended	15	1.54	10-23
Calculated Volume to be exchanged, mL	8278	389.22	6720-9555
Exchanged Volume, mL	7539	487.33	6000-9300
Urine Volume During PLA/EX, mL/hr	229	53.14	119-507

Table 9 - Past Medical History

Variable	No.(%)	Group Assignment	
		Control No.(%)	PLA/EX No.(%)
History of Cardiac Disease	1 (7)	0 (0)	1 (14)
Pulmonary Disease	0 (0)	0 (0)	0 (0)
Diabetes	0 (0)	0 (0)	0 (0)
Renal Disease	0 (0)	0 (0)	0 (0)
Gastrointestinal Disease	2 (14)	1 (14)	1 (14)
Neurologic Disease	0 (0)	0 (0)	0 (0)
Hepatic Disease	0 (0)	0 (0)	0 (0)
Alcohol Abuse	3 (21)	1 (14)	2 (28)
Drug Abuse	1 (7)	0 (0)	1 (14)
Intercurrent Trauma	2 (14)	0 (0)	2 (28)

occurred in PLA/EX subjects.

Physiologic Variables and the Effect of Plasma Exchange

The second specific research question was:

Does plasma exchange performed during burn shock alter measurable physiologic variables?

The total number of measured variables collected on each subject entered into the research protocol was 945 (Appendix H). For the purpose of this study, 321 selected representative variables are reported. This includes the previously described data plus the measured physiologic variables for PBH 8, 16, 24, and 48. The data were statistically analyzed for difference between groups using the Student's t-test. Because this was a clinical study occurring in the ICU area, one limitation of the study was that there were times when variables were not measured or were not recorded. The number (N) and percent (%) of total cases is therefore included in the tables to represent the actual sample size of each reported variable. The representative times were chosen to identify early burn shock effect (PBH 8), postplasma exchange effect (PBH 16), end of burn shock phase (PBH 24), and restoration of cardiovascular integrity (PBH 48).

Hematology

The white blood cell (WBC) count was initially elevated in both the control and the PLA/EX group (Table 10).

Table 10 - Hematology

Variable	PBH	Group	Mean	SE	Range	No.(%)
WBC, K/uL	8	Control	19.9	3.39	8.0-32.0	6 (86)
	16		14.1	3.37	2.7-24.3	6 (86)
	24		10.6	2.86	3.9-22.0	6 (86)
	48		4.6	1.38	1.8-10.8	6 (86)
	8	PLA/EX	27.8	6.61	17.6-53.5	5 (72)
	16		21.9	3.65	10.8-34.7	7(100)
	24		18.1	3.67	3.6-27.9	7(100)
	48		7.7	1.53	4.5-11.8	4 (57)
RBC, m/uL	8	Control	5.5	0.23	4.82-6.03	5 (72)
	16		5.6	0.31	4.60-6.75	6 (86)
	24		5.8	0.34	4.80-6.95	6 (86)
	48		4.4	0.19	3.70-4.90	6 (86)
	8	PLA/EX	5.0	0.62	3.20-6.80	5 (72)
	16		5.4	0.32	3.80-6.00	7(100)
	24		5.0	0.37	3.60-6.20	7(100)
	48		4.8	0.18	4.30-5.20	4 (57)
HGB, g/dL	8	Control	17.6	1.04	14.6-21.3	6 (86)
	16		17.2	0.88	13.9-19.6	6 (86)
	24		17.4*	0.77	14.5-19.3	6 (86)
	48		13.1	0.51	12.0-15.0	6 (86)
	8	PLA/EX	14.7	1.63	9.5-18.9	5 (72)
	16		15.7	0.96	11.4-18.2	7(100)
	24		14.4	0.72	11.4-16.4	7(100)
	48		13.9	0.46	13.0-15.0	4 (57)
HCT, %	8	Control	52	2.85	42.8-60.9	6 (86)
	16		51	2.71	40.9-58.3	6 (86)
	24		52*	2.54	42.9-59.1	6 (86)
	48		40	1.45	35.8-45.5	6 (86)
	8	PLA/EX	43	5.05	27.8-55.2	5 (72)
	16		47	2.88	33.2-51.7	7(100)
	24		44	2.92	32.8-55.5	7(100)
	48		43	1.66	38.7-46.7	4 (57)
Platelets, K/uL	8	Control	295*	28.29	234-403	6 (86)
	16		223*	13.67	175-266	6 (86)
	24		193*	13.44	138-224	6 (86)
	48		94*	8.59	67-126	6 (86)
	8	PLA/EX	215	18.14	162-274	5 (72)
	16		133	11.76	81-169	7(100)
	24		101	21.74	45-215	7(100)
	48		55	12.10	19-71	4 (57)

*$p<.05$

Both groups had WBC counts within normal limits (3.6 to 9.0 k/μL) (Appendix G) by PBH 48. At no measured time was a statistically significant difference identified ($p>.05$) on this variable. The red blood cell (RBC) count was within normal limits (WNL = 4.71 to 5.77 m/μL) for both groups throughout the measured times with the exception of the PBH 48 control which was 4.4 m/uL. No statistical difference was found between the groups on this variable ($p>.05$). Hemoglobin (HGB) was significantly different ($p<.05$) between the groups at PBH 24 when the control mean was 17.4 g/dL and the PLA/EX mean was 14.4 g/dL. Both groups maintained HGB levels at values within normal limits (WNL) (14.5-17.1 g/dL) until PBH 48 when both decreased. Hematocrit (Hct) was significantly different between the groups at PBH 24 when the control mean value was 52% and the PLA/EX mean was 44%. Other PBH means were not different between the groups ($p>.05$). Both groups ranged within normal limits (43 to 52%) except for PBH 48 in the control when the mean was 40%. Platelets were significantly lower ($p<.05$) in the PLA/EX group at all times, including preplasma exchange. The mean pre-exchange value was 295 k/μL for the control and 215 k/μL for the PLA/EX group. The control dropped below the lower limits of normal (140 to 440K/μL) by PBH 48 and the PLA/EX dropped below by PBH 16.

Chemistries

Serum sodium mean levels remained WNL (137 to 146 mEq/L) for both groups at all reported times until PBH 48 when both groups dropped below the lower normal limit (Table 11). A statistically different ($p<.01$) sodium level occurred between the group means at PBH 16. The control mean sodium was 137 mEq/L compared to a mean 145 mEq/L in the PLA/EX group. No statistically significant difference ($p>.05$) existed in other PBH means.

Potassium means were significantly different between the groups at PBH 16 and PBH 24. The control potassium mean was 4.3 mEq/L at both times compared to the PLA/EX mean of 3.2 mEq/L at PBH 16 and 3.1 mEq/L at PBH 24 ($p<.05$). The control group mean potassium remained WNL (3.8-5.3 mEq/L) until PBH 48, at which time the mean of 3.5 mEq/L was below the normal lower limit. The PLA/EX group mean potassium was below the lower normal limits at all measured PBH intervals.

Chloride mean values were slightly elevated from normal (100-109 mEq/L) at PBH 8, 16, and 24. PLA/EX values remained WNL at all measures. A statistically significant difference ($p<.05$) was found between the groups at PBH 24 when the mean control was 111 mEq/L compared to 106 mEq/L for the PLA/EX group. No difference was found at other measures ($p>.05$).

Total carbon dioxide (CO_2) was lower in the control

Table 11 - Chemistries 1

Variable	PBH	Group	Mean	SE	Range	No.(%)
Sodium, mEq/L	8	Control	137	0.99	134-141	6 (86)
	16		137*	2.56	134-140	6 (86)
	24		137	2.75	133-150	6 (86)
	48		133	1.63	127-139	6 (86)
	8	PLA/EX	143	2.50	137-151	6 (86)
	16		145	2.03	139-152	7(100)
	24		143	1.92	136-149	7(100)
	48		131	3.75	121-144	5 (72)
Potassium, mEq/L	8	Control	4.1	0.20	3.6-4.8	6 (86)
	16		4.3*	0.23	3.7-5.2	6 (86)
	24		4.3*	0.22	3.5-4.8	6 (86)
	48		3.5	0.18	3.0-4.0	6 (86)
	8	PLA/EX	3.5	0.42	2.5-5.0	6 (86)
	16		3.2	0.13	2.7-3.8	7(100)
	24		3.1	0.17	2.5-3.6	7(100)
	48		3.7	0.28	3.0-4.0	5 (72)
Chloride, mEq/L	8	Control	111	1.20	106-114	6 (86)
	16		111	1.36	105-115	6 (86)
	24		111*	0.58	109-113	6 (86)
	48		105	1.34	100-109	6 (86)
	8	PLA/EX	108	2.60	102-118	6 (86)
	16		108	1.11	104-113	7(100)
	24		106	1.13	104-112	7(100)
	48		101	1.18	97-104	5 (72)
Total CO2, mEq/L	8	Control	17	1.95	10-23	6 (86)
	16		19	1.17	17-23	6 (86)
	24		18*	0.70	16-21	6 (86)
	48		24	1.75	19-28	6 (86)
	8	PLA/EX	22	2.71	10-29	6 (86)
	16		24	2.29	17-33	7(100)
	24		26	1.44	20-32	7(100)
	48		24	2.16	20-31	5 (72)
BUN, mg/dL	8	Control	13	1.33	10-19	6 (86)
	16		11	0.96	7-14	6 (86)
	24		15	1.88	8-20	6 (86)
	48		10	1.26	6-14	6 (86)
	8	PLA/EX	13	1.34	7-17	6 (86)
	16		14	1.82	7-22	7(100)
	24		13	1.09	9-17	7(100)
	48		9	1.97	3-14	5 (72)

*$p<.05$

at all PBH means but a statistically significant difference ($p<.05$) occurred only at PBH 24 when the control mean was 18 mEq compared to 26 mEq/L for the PLA/EX group mean. Normal CO_2 levels (21-27 mEq/L) were not reached by the control until PBH 48 whereas the PLA/EX means remained WNL at all PBH intervals.

Blood urea nitrogen (BUN) levels remained WNL (6-20 mg/dL) for both groups at all measured intervals. There was no statistical difference between the control and PLA/EX group BUN measures at any reported PBH.

Serum glucose means remained above normal limits (84-119 mg/dL) at all PBH intervals in both groups (Table 12). A statistically significant difference ($p<.05$) between the group means existed at PBH 48 when the control mean glucose level was 172 mg/dL compared to 206 mg/dL for the PLA/EX group mean. No difference was found ($p>.05$) at other PBH measures.

Serum creatinine levels remained WNL (0.9 to 1.4 mg/dL) for both groups at all PBH measures. No difference was found between the control and PLA/EX group mean at any measured PBH on this variable ($p>.05$).

Uric acid means were not significantly different between the control and PLA/EX group at any PBH. The mean levels remained WNL (4.6-8.5 mg/dL) for both groups until PBH 48 when the control mean decreased to 3.9 mg/dL and the PLA/EX mean to 3.7 mg/dL.

Table 12 - Chemistries 2

Variable	PBH	Group	Mean	SE	Range	No.(%)
Glucose, mg/dL	8	Control	141	17.29	91-211	6 (86)
	16		157	10.44	126-194	6 (86)
	24		173	12.80	135-214	6 (86)
	48		172*	11.15	141-222	6 (86)
	8	PLA/EX	171	20.90	97-223	6 (86)
	16		205	24.56	115-300	7(100)
	24		164	16.25	87-208	7(100)
	48		206	9.37	189-230	5 (72)
Creatinine, mg/dL	8	Control	1.1	0.08	0.9-1.4	5 (72)
	16		1.1	0.08	0.9-1.4	6 (86)
	24		1.3	0.17	0.9-1.9	6 (86)
	48		1.1	0.09	0.9-1.5	6 (86)
	8	PLA/EX	1.1	0.12	0.7-1.4	6 (86)
	16		1.3	0.19	0.8-2.2	7(100)
	24		1.3	0.12	0.9-1.7	7(100)
	48		0.9	0.10	0.7-1.2	4 (57)
Uric Acid, mg/dL	8	Control	6.2	0.44	5.1-7.3	5 (72)
	16		5.2	0.47	4.3-7.1	6 (86)
	24		5.1	0.51	3.7-6.6	5 (72)
	48		3.9	0.28	3.2-5.0	6 (86)
	8	PLA/EX	5.6	1.17	3.4-7.4	3 (43)
	16		6.3	0.84	3.4-9.7	7(100)
	24		5.6	0.73	3.2-8.3	7(100)
	48		3.7	1.02	2.2-6.7	4 (57)
Calcium, mg/dL	8	Control	7.9*	0.19	7.4-8.4	5 (72)
	16		7.3	0.19	6.7-7.9	6 (86)
	24		7.2	0.37	6.4-8.6	5 (72)
	48		6.8	0.21	6.3-7.6	6 (86)
	8	PLA/EX	6.8	0.16	6.4-7.1	4 (57)
	16		6.8	0.27	6.1-8.2	7(100)
	24		6.6	0.25	6.0-7.9	7(100)
	48		6.0	0.43	5.3-7.2	4 (57)
Phosphate, mg/dL	8	Control	3.5	0.43	2.4-4.8	5 (72)
	16		3.6	0.30	2.6-4.7	6 (86)
	24		2.9	0.21	2.2-3.3	5 (72)
	48		1.7	0.19	1.2-2.5	6 (86)
	8	PLA/EX	3.1	0.48	2.1-4.4	4 (57)
	16		2.9	0.61	1.0-6.0	7(100)
	24		2.7	0.32	1.3-3.9	7(100)
	48		1.4	0.28	0.9-2.2	4 (57)

*$p<.05$

Total calcium means were significantly different ($p<.05$) at PBH 8 when the control mean was 7.9 mg/dL compared to 6.8 mg/dL for the PLA/EX group. No other PBH mean was significantly different on the variable ($p>.05$). Both the control and PLA/EX means were below the lower limit of normal (8.6-10.7 mg/dL) at all PBH intervals.

Serum phosphate mean levels were not significantly different ($p>.05$) between the groups at any PBH interval. Mean values remained WNL (2.4 to 4.1 mg/dL) until PBH 48 when both groups decreased below the lower limit of normal.

Total bilirubin and direct bilirubin were both found not to be significantly different ($p>.05$) between group means at any PBH interval (Table 13). Total bilirubin means remained WNL (0.3 to 1.9 mg/dL) as did direct bilirubin means (0.0 to 0.3 mg/dL).

Total protein mean values were not significantly different ($p>.05$) between the control and PLA/EX group at any PBH interval. The means in both groups at all PBH intervals remained below the lower limits of normal (6.4-8.1 g/dL).

Albumin mean values were not significantly different ($p>.05$) between the groups. At no time did the mean levels reach the lower limits of normal for albumin (4.0 to 5.1 g/dL).

Cholesterol mean levels were initially WNL (128-288

Table 13 - Chemistries 3

Variable	PBH	Group	Mean	SE	Range	No.(%)
Total Bili-	8	Control	1.0	0.16	0.6-1.5	5 (72)
rubin,	16		0.9	0.14	0.5-1.3	6 (86)
mg/dL	24		0.9	0.26	0.4-1.7	5 (72)
	48		1.2	0.57	0.5-4.0	6 (86)
	8	PLA/EX	0.9	0.19	0.5-1.4	4 (57)
	16		1.5	0.32	0.3-2.4	7(100)
	24		1.3	0.30	0.5-2.7	7(100)
	48		1.2	0.36	0.5-2.1	4 (57)
Direct Bili-	8	Control	0.18	0.04	0.1-0.3	5 (72)
rubin,	16		0.12	0.02	0.1-0.2	6 (86)
mg/dL	24		0.12	0.02	0.1-0.2	5 (72)
	48		0.13	0.02	0.1-0.2	6 (86)
	8	PLA/EX	0.15	0.03	0.1-0.2	4 (57)
	16		0.19	0.06	0.0-0.5	7(100)
	24		0.16	0.02	0.1-0.2	7(100)
	48		0.13	0.05	0.0-0.2	4 (57)
Total Protein	8	Control	4.5	0.36	3.4-5.0	4 (57)
g/dL	16		3.3	0.36	2.0-5.0	6 (86)
	24		3.4	0.60	1.8-5.5	5 (72)
	48		3.5	0.20	3.0-4.0	6 (86)
	8	PLA/EX	3.5	0.44	2.6-4.7	4 (57)
	16		3.8	0.37	2.0-5.0	7(100)
	24		3.8	0.30	2.8-5.2	7(100)
	48		3.4	0.28	3.0-4.0	4 (57)
Albumin,	8	Control	2.7	0.28	1.9-3.2	5 (72)
g/dL	16		2.0	0.24	1.0-3.0	6 (86)
	24		2.0	0.38	1.1-3.4	5 (72)
	48		1.9	0.17	1.0-2.0	6 (86)
	8	PLA/EX	2.0	0.36	1.3-3.0	4 (57)
	16		2.4	0.22	1.0-3.0	7(100)
	24		2.3	0.20	1.6-3.1	7(100)
	48		2.0	0.13	2.0-2.0	4 (57)
Cholesterol,	8	Control	157	24.25	97-242	5 (72)
mg/dL	16		119	12.40	84-158	6 (86)
	24		111	17.06	66-147	5 (72)
	48		98	8.16	74-122	6 (86)
	8	PLA/EX	145	23.14	95-200	4 (57)
	16		117	5.48	90-133	7(100)
	24		114	6.26	89-144	7(100)
	48		114	12.74	90-149	4 (57)

mg/dL) for both groups at PBH 8 but then decreased below the lower limit of normal at all subsequent PBH intervals. No significant difference was found on this variable between the control and PLA/EX group ($p>.05$).

GGTP mean values remained WNL (5-85 IU/L) at all PBH intervals (Table 14). A statistically significant difference ($p<.01$) was found between the groups at PBH 24 when the control mean was 32 IU/L and the PLA/EX was 11 IU/L. No significant difference was found at other PBH intervals ($p>.05$).

Alkaline phosphatase (ALK PHOS) means were not significantly different between groups ($p>.05$) at any PBH interval. The mean values were WNL (40-139 IU/L) at all PBH intervals in both the control and PLA/EX group.

LDH mean values were above normal (138-328 IU/L) in the control group at PBH 8 and 24. The PLA/EX group had elevated LDH means at all PHB intervals. No statistically different mean values were found between the control and PLA/EX group ($p>.05$).

SGOT mean values were above normal (11-43 IU/L) at PBH 8 and 24 in the control and all PBH in the PLA/EX group. No statistical difference was found between the control and PLA/EX group on this variable.

SGPT mean values remained WNL (11-85 IU/L) in both groups at all PBH intervals. No significant difference was found between the groups.

Table 14 - Chemistries 4

Variable	PBH	Group	Mean	SE	Range	No.(%)
GGTP, IU/L	8	Control	30	11.00	11-73	5 (72)
	16		23	5.35	8-47	6 (86)
	24		32*	2.56	25-41	5 (72)
	48		13	2.02	9-20	5 (72)
	8	PLA/EX	17	4.33	9-29	4 (57)
	16		12	2.03	6-22	7(100)
	24		11	1.26	8-18	7(100)
	48		9	1.20	7-11	3 (43)
ALK PHOS, IU/L	8	Control	74	3.61	60-80	5 (72)
	16		53	7.61	26-81	6 (86)
	24		54	13.84	27-105	5 (72)
	48		57	4.21	44-68	5 (72)
	8	PLA/EX	57	19.44	15-108	4 (57)
	16		54	3.91	39-69	7(100)
	24		55	3.21	42-67	7(100)
	48		71	12.49	53-95	3 (43)
LDH, IU/L	8	Control	404	52.13	311-519	4 (57)
	16		305	38.97	202-440	6 (86)
	24		343	59.65	230-558	5 (72)
	48		289	38.31	225-407	5 (72)
	8	PLA/EX	513	170.32	213-999	4 (57)
	16		365	36.58	188-498	7(100)
	24		414	78.26	273-852	7(100)
	48		482	112.64	296-685	3 (43)
SGOT, IU/L	8	Control	46	9.76	30-82	5 (72)
	16		30	3.66	18-44	6 (86)
	24		46	13.72	25-99	5 (72)
	48		25	2.46	21-33	5 (72)
	8	PLA/EX	51	16.62	25-99	4 (57)
	16		45	8.29	17-79	7(100)
	24		52	12.69	17-99	7(100)
	48		57	22.05	24-99	3 (43)
SGPT, IU/L	8	Control	35	8.88	20-69	5 (72)
	16		30	4.88	15-45	6 (86)
	24		38	9.87	5-67	5 (72)
	48		20	3.62	12-33	5 (72)
	8	PLA/EX	32	5.92	22-46	4 (57)
	16		29	3.22	12-39	7(100)
	24		31	6.71	12-56	7(100)
	48		42	25.70	11-93	3 (43)

*$p<.01$

Lactic acid mean values were above normal (0.5-2.2 mEq/L) at all PBH intervals in both the control and PLA/EX groups (Table 15). No statistically significant difference was found between the groups at any PBH interval.

Coagulation Studies

Prothrombin time (PT), patient, was prolonged above normal values (10.0-14.4 seconds) in the control group at PBH 24 and in the PLA/EX group at PBH 8 (Table 16). Mean values for PT, control, were WNL (32 to 48 seconds) at all PBH intervals for both control and PLA/EX group. No statistical difference was found between the two groups on this variable ($p>.05$). Partial thromboplastin time (PTT) patient and PTT control remained WNL in both the control group and the PLA/EX group at all PBH intervals. No significant difference between the means of control and PLA/EX group was found ($p>.05$). Fibrinogen mean values remained WNL (150-350 mg/dL) in both the control and PLA/EX groups until PBH 48 when the control mean was elevated to 552 mg/dL and PLA/EX mean was 490 mg/dL. No statistically significant difference was found at any PBH between group means ($p>.05$).

Pulmonary Variables

The fraction of inspired oxygen (FiO_2) mean was above that of room air (21%) at all PBH intervals in both groups (Table 17). There was a statistically significant dif-

Table 15 - Chemistries 5

Variable	PBH	Group	Mean	SE	Range	No.(%)
Lactic Acid, mEq/L	8	Control	3.4	0.87	1.6-6.6	5 (72)
	16		3.5	0.90	1.0-7.0	6 (86)
	24		4.1	0.85	1.9-7.0	6 (86)
	48		2.6	0.24	2.0-4.0	6 (86)
	8	PLA/EX	4.5	1.22	2.1-8.5	5 (72)
	16		7.5	1.70	3.0-16.0	7(100)
	24		5.2	0.77	2.7-7.6	7(100)
	48		2.8	0.35	2.0-4.0	5 (72)

Table 16 - Coagulation Studies

Variable	PBH	Group	Mean	SE	Range	No.(%)
PT patient, Sec.	8	Control	12.6	0.47	11.0-13.7	5 (72)
	16		14.0	0.39	13.2-15.7	6 (86)
	24		15.1	0.49	13.2-16.4	6 (86)
	48		13.0	0.47	11.0-15.0	6 (86)
	8	PLA/EX	14.9	1.82	12.1-22.0	5 (72)
	16		14.0	0.58	12.4-16.3	7(100)
	24		14.1	0.58	12.2-16.2	7(100)
	48		13.3	0.34	12.0-14.0	5 (72)
PT Control, Sec.	8	Control	12.2	0.18	11.8-12.7	5 (72)
	16		12.3	0.13	11.9-12.7	6 (86)
	24		12.4	0.11	12.1-12.8	6 (86)
	48		12.3	0.15	12.0-13.0	6 (86)
	8	PLA/EX	13.2	0.87	11.9-16.6	5 (72)
	16		12.7	0.39	11.7-14.8	7(100)
	24		12.7	0.41	11.7-14.9	7(100)
	48		12.5	0.26	12.0-13.0	5 (72)
PTT Patient, Sec.	8	Control	32	0.68	30-33	5 (72)
	16		36	1.77	32-42	6 (86)
	24		38	2.75	27-45	6 (86)
	48		34	1.51	30-41	6 (86)
	8	PLA/EX	40	3.91	30-54	5 (72)
	16		42	2.35	35-53	7(100)
	24		42	2.62	33-52	7(100)
	48		36	2.28	30-42	5 (72)
PTT Control, Sec.	8	Control	38	1.14	34-40	5 (72)
	16		38	1.02	34-41	6 (86)
	24		39	0.43	37-40	6 (86)
	48		38	0.49	37-40	6 (86)
	8	PLA/EX	41	2.58	37-51	5 (72)
	16		39	0.72	37-42	7(100)
	24		40	1.06	36-45	7(100)
	48		39	0.45	38-40	5 (72)
Fibrinogen, mg/dL	8	Control	235	21.96	196-297	4 (57)
	16		249	15.86	197-290	6 (86)
	24		319	34.00	255-380	4 (57)
	48		552	39.39	450-694	6 (86)
	8	PLA/EX	202	42.94	60-320	5 (72)
	16		209	14.41	153-274	7(100)
	24		256	23.36	170-265	7(100)
	48		490	65.33	322-626	4 (57)

Table 17 - Pulmonary

Variable	PBH	Group	Mean	SE	Range	No.(%)
FiO2, %	8	Control	32	3.26	21-40	7(100)
	16		34*	2.71	21-40	7(100)
	24		32	3.26	21-40	7(100)
	48		28	3.56	21-40	7(100)
	8	PLA/EX	49	8.62	35-10	7(100)
	16		43	2.64	35-50	7(100)
	24		41	5.52	21-70	7(100)
	48		31	5.02	21-50	6 (86)
Resp. Rate/ min.	8	Control	17	2.01	9-24	7(100)
	16		21	1.44	15-24	7(100)
	24		19	2.05	11-25	7(100)
	48		21	1.99	14-29	7(100)
	8	PLA/EX	18	2.39	9-24	7(100)
	16		18	1.54	14-26	7(100)
	24		18	2.27	9-25	7(100)
	48		16	1.24	12-20	6 (86)
Core Body Temp., Degrees C	8	Control	37.4	0.32	36.5-39.0	7(100)
	16		38.0	0.20	37.0-39.0	7(100)
	24		38.1	0.30	37.5-39.8	7(100)
	48		37.7	0.25	37.0-39.0	7(100)
	8	PLA/EX	36.8	0.25	36.0-37.4	6 (86)
	16		38.3	0.31	37.0-39.0	7(100)
	24		37.7	0.35	35.9-38.6	7(100)
	48		37.7	0.16	37.0-38.0	6 (86)
% Intubated	8	Control	4 (57)			
	16		4 (57)			
	24		4 (57)			
	48		3 (43)			
	8	PLA/EX	4 (57)			
	16		5 (72)			
	24		4 (57)			
	48		4 (57)			

*p<.05

ference between the groups at PBH 16 when the control mean FiO_2 was 34% compared to 43% for the PLA/EX group. No other PBH intervals were statistically different ($p>.05$). The mean respiratory rate for both groups at all PBH intervals was WNL and not statistically different between groups ($p>.05$).

Core body temperature was recorded as a pulmonary variable because it is one of the known variables necessary to calculate blood gas analyses. All mean core body temperature values were WNL (36.0-39.0 degrees C) at all PBH intervals and no statistically significant difference was found between the control and PLA/EX group ($p>.05$). The percent of patients intubated at each PBH interval is presented in Table 17. A total of nine patients (64%) required intubation. There is no significant difference between the groups on this variable ($p>.05$).

Arterial blood gas determinations were made on all patients (Table 18). Oxygen saturation (02 SAT) mean was WNL (>93%) in both the control and PLA/EX group at all PBH intervals. No significant difference was found on this variable between groups at any PBH interval ($p>.05$). Appendix C presents normal values for blood gas analysis.

PO_2 mean value was above normal (68-78 mmHg) at all PBH intervals in the control group and until PBH 48 in the PLA/EX group. No statistical difference was found between group mean PO_2 levels ($p>.05$). PCO_2 mean value was at or

Table 18 - Arterial Blood Gas Analysis

Variable	PBH	Group	Mean	SE	Range	No.(%)
O2 SAT, %	8	Control	96	1.96	86-98	6 (86)
	16		97	0.52	95-99	7(100)
	24		97	0.89	93-99	6 (86)
	48		96	0.68	94-99	7(100)
	8	PLA/EX	93	3.06	76-99	7(100)
	16		97	0.46	95-99	7(100)
	24		96	0.48	94-97	7(100)
	48		95	0.48	94-97	6 (86)
PO2, mmHg	8	Control	150	22.85	62-213	6 (86)
	16		118	12.06	73-159	7(100)
	24		116	12.65	70-159	6 (86)
	48		88	8.14	71-132	7(100)
	8	PLA/EX	132	23.01	39-205	7(100)
	16		137	32.94	83-330	7(100)
	24		86	6.32	71-118	7(100)
	48		77	4.13	63-92	6 (86)
PCO2, mmHg	8	Control	29	4.66	12-40	6 (86)
	16		29	2.30	20-36	7(100)
	24		28*	1.47	23-33	6 (86)
	48		31	1.25	28-35	7(100)
	8	PLA/EX	34	2.08	27-42	7(100)
	16		32	2.72	20-41	7(100)
	24		33	1.50	26-38	7(100)
	48		33	2.55	27-42	6 (86)
pH	8	Control	7.44	0.06	7.28-7.69	6 (86)
	16		7.43	0.03	7.30-7.50	7(100)
	24		7.44	0.02	7.39-7.52	6 (86)
	48		7.47	0.02	7.40-7.50	7(100)
	8	PLA/EX	7.39	0.04	7.23-7.58	7(100)
	16		7.48	0.04	7.40-7.70	7(100)
	24		7.49	0.02	7.43-7.55	7(100)
	48		7.47	0.02	7.40-7.50	6 (86)
Bicarbonate, mEq/L	8	Control	18.0	1.47	13.7-23.3	6 (86)
	16		19.1*	1.00	16.0-23.0	7(100)
	24		18.7*	0.85	15.1-20.7	6 (86)
	48		22.9	1.12	20.0-28.0	7(100)
	8	PLA/EX	20.9	1.82	14.3-26.3	7(100)
	16		23.8	1.69	17.0-31.0	7(100)
	24		25.0	1.51	17.9-30.2	7(100)
	48		24.1	2.37	19.0-32.0	6 (86)

*$p<.05$

below normal values (31-41 mmHg) at all measured PBH intervals. PLA/EX group mean values were WNL at all PBH intervals. A statistically significant difference was found between PCO_2 levels at PBH 24 when control mean was 28 mmHg compared to a mean PLA/EX value of 33 mmHg ($p<.05$). Other PBH means did not significantly differ between groups ($p>.05$). Arterial pH values were different from normal (7.35 to 7.45) in the control at PBH 48 and in the PLA/EX group at PBH 16, 24, and 48. These differences were not significant between the control and PLA/EX group at any PBH interval.

Bicarbonate levels were below normal (22.0-26.0 mEq/L) in the control at PBH 8, 16, and 24 and in the PLA/EX group at PBH 8. A statistically significant difference was found between groups at two PBH intervals, PBH 16 and 24 ($p<.05$). At PBH 16, the control mean bicarbonate value was 19.1 mEq/L compared to 23.8 mEq/L in the PLA/EX group. At PBH 24, the control mean was 18.7 mEq/L compared to 25.0 mEq/L for the PLA/EX group. Other PBH interval means were not significantly different ($p>.05$).

Mixed venous blood gas determinations were analyzed for each patient (Table 19). Oxygen saturation (O_2 SAT) was maintained WNL (60-85%) in both groups at all PBH intervals (Appendix C presents normal values for mixed venous blood analysis). A significant difference ($p<.05$) was found between the groups at PBH 16 when the control

Table 19 - Mixed Venous Blood Gas Analysis

Variable	PBH	Group	Mean	SE	Range	No.(%)
O2 SAT, %	8	Control	75	2.80	70-83	4 (57)
	16		75*	1.53	70-81	7(100)
	24		69	2.16	64-76	6 (86)
	48		74	2.02	68-80	6 (86)
	8	PLA/EX	69	8.20	36-97	6 (86)
	16		65	3.74	50-77	7(100)
	24		69	3.08	59-79	7(100)
	48		67	4.21	53-76	5 (72)
PO2, mmHg	8	Control	37	3.19	31-43	4 (57)
	16		39	2.40	28-46	7(100)
	24		37	2.45	30-46	6 (86)
	48		37	1.97	32-46	6 (86)
	8	PLA/EX	45	11.37	19-99	6 (86)
	16		33	2.67	25-46	7(100)
	24		34	2.03	27-39	7(100)
	48		33	3.91	23-44	5 (72)
PCO2, mmHg	8	Control	27*	4.26	20-39	4 (57)
	16		33	2.36	25-42	7(100)
	24		32*	0.68	30-34	6 (86)
	48		35	1.28	31-38	6 (86)
	8	PLA/EX	42	2.38	32-47	6 (86)
	16		40	3.47	21-49	7(100)
	24		37	2.15	29-45	7(100)
	48		36	2.52	31-45	5 (72)
pH	8	Control	7.46	0.04	7.39-7.56	4 (57)
	16		7.41	0.03	7.30-7.50	7(100)
	24		7.41	0.02	7.36-7.49	6 (86)
	48		7.44	0.02	7.40-7.50	6 (86)
	8	PLA/EX	7.36	0.04	7.20-7.43	6 (86)
	16		7.44	0.04	7.30-7.60	7(100)
	24		7.46	0.01	7.39-7.49	7(100)
	48		7.43	0.02	7.40-7.50	5 (72)
Bicarbonate, mEq/L	8	Control	18.8	1.64	15.5-23.3	4 (57)
	16		20.2*	0.87	18.0-24.0	7(100)
	24		20.3*	1.13	17.8-25.1	6 (86)
	48		23.8	1.08	21.0-28.0	6 (86)
	8	PLA/EX	23.5	1.97	17.1-28.9	6 (86)
	16		26.2	1.61	22.0-32.0	7(100)
	24		26.4	1.22	21.5-31.1	7(100)
	48		24.0	2.49	18.0-33.0	5 (72)

*$p<.05$

mean O_2 SAT was 75% compared with a PLA/EX group mean of 65%. Other PBH interval means were not significantly different ($p>.05$). PO_2 mean values were also kept either at or above normal values at all PBH intervals. There was no significant difference between the groups at any PBH mean value ($p>.05$).

PCO_2 mean control values were below the normal range (38-50 mmHg) at all PBH intervals. The PLA/EX values were WNL at PBH 8 and 16 and below normal at PBH 24 and 48. There was a significant difference between the groups at PBH 8 and 24 ($p<.05$). At PBH 8, the control PCO_2 was 27 mmHg compared to 42 mmHg for the PLA/EX group. At PBH 24, the control PCO_2 was 32 mmHg compared to 37 mmHg for the PLA/EX group. No significant difference was found between the groups at other PBH intervals for this variable ($p>.05$).

Serum pH mean levels were different from normals (7.32-7.42) at PBH 8 and 48 in the control and at PBH 16, 24, and 48 in the PLA/EX group. No significant difference was found between the group means at any PBH interval ($p>.05$). Bicarbonate levels were less than the lower limit of normal (22-29 mEq/L) in the mean control values at PBH 8, 16, and 24. All PLA/EX group means were WNL at all PBH intervals. A significant difference was found between the groups at PBH 16 and 24. The control mean bicarbonate at PBH 16 was 20.2 mEq/L compared to 26.2

mEq/L for the PLA/EX group. At PBH 24, the control mean was 20.3 mEq/L compared to the PLA/EX group value of 26.4 mEq/L. Other PBH intervals did not show a significant difference.

Base Excess

Arterial blood gas (ABG) base excess mean values were WNL (-3 to 3) at all PBH control intervals except PBH 8 when the mean value was -3.5 (Table 20). The PLA/EX group means remained WNL at all PBH intervals. There was a significant difference between the groups ($p<.05$) at PBH 16 and 24. At PBH 16, the control mean base excess was -3.0 compared to 1.9 for the PLA/EX group. At PBH 24, the control mean base excess was -3.1 comapred to 3.0 for the PLA/EX group. No significant difference was found between the groups at other PBH intervals measured ($p>.05$). The mixed venous blood base excess mean was WNL at all PBH intervals for the control and all except PBH 24 for the PLA/EX group. There was a significant difference between groups on PBH 16 and 24 ($p<.05$). The control PBH 16 mean was -2.8 compared to 2.7 for the PLA/EX group. The control PBH 24 mean value was -2.6 compared to 3.5 for the PLA/EX group. There was no significant difference between the groups at other PBH intervals.

Cardiopulmonary Profile

The physiological variables either measured by or

Table 20 - Base Excess

Variable	PBH	Group	Mean	SE	Range	No.(%)
ABG Base Excess	8	Control	-3.5	1.29	-7.6 to 0.5	6 (86)
	16		-3.0*	1.08	-7.0 to 0	7(100)
	24		-3.1*	1.10	-6.8 to 0.9	6 (86)
	48		0.6	1.43	-3.0 to 6.0	6 (86)
	8	PLA/EX	-2.7	2.44	-12.2 to 6.3	7(100)
	16		1.9	1.80	-6.0 to 8.0	7(100)
	24		3.0	1.56	-3.7 to 8.2	7(100)
	48		1.8	2.26	-5.0 to 9.0	6 (86)
MVBG Base Excess	8	Control	-2.3	1.14	-5.0 to-0.	14 (57)
	16		-2.8*	1.07	-6.0 to 1.0	7(100)
	24		-2.6*	1.42	-5.9 to 3.5	6 (86)
	48		0.6	1.25	-3.0 to 5.0	6 (86)
	8	PLA/EX	-1.5	2.38	-10.9 to 4.6	6 (86)
	16		2.7	1.68	-4.0 to 8.0	7(100)
	24		3.5	1.07	-0.4 to 7.3	7(100)
	48		0.8	2.40	-5.0 to 9.0	5 (72)

*p<.05

calculated from the Swan-Ganz catheter monitor system are referred to as a cardiopulmonary profile. The normal parameters are presented in Appendix C.

The pulmonary artery (PA) mean pressure was WNL (9-18 mmHg) at all PBH intervals for both control and PLA/EX groups (Table 21). There was no significant difference between the groups on any PBH mean value ($p>.05$). The pulmonary artery wedge pressure (PAWP) was WNL (6-15 mmHg) at all PBH intervals for the control and all except PBH 8 for the PLA/EX group when the mean value was 5 mmHg. There was no statistical difference between the control and PLA/EX group on any PBH mean value for PAWP ($p>.05$).

Cardiac output was WNL (3.5-6.5 L/min) for the control from PBH 8 through 24 but was above normal at 6.9 L/min by PBH 48. The PLA/EX group remained WNL at all PBH intervals. There was no statistical difference between the control and PLA/EX group on this variable ($p>.05$). Cardiac index as an indicator of cardiac output per m^2 BSA likewise showed no statistical difference ($p>.05$). Stroke work index was WNL (41-51 mL/beat/m^2 BSA) for both groups at all PBH intervals. No statistical difference was found between the PBH mean values for this variable ($p>.05$).

Systemic vascular resistance index (SVRI) was above normal values (1970-2390 Dynes/second/m^2 BSA/cm^5) at PBH 8

Table 21 - Cardiopulmonary Profile

Variable	PBH	Group	Mean	SE	Range	No.(%)
PA mean mmHg	8	Control	11	2.59	5-19	5 (72)
	16		14	1.86	7-21	7(100)
	24		15	1.46	10-19	6 (86)
	48		17	2.91	6-28	6 (86)
	8	PLA/EX	17	2.44	10-25	5 (72)
	16		13	2.26	5-20	7(100)
	24		17	2.92	10-27	7(100)
	48		16	3.86	7-26	5 (72)
PAWP, mmHg	8	Control	7	1.00	4-10	5 (72)
	16		7	1.55	3-13	6 (86)
	24		8	1.34	5-11	5 (72)
	48		10	2.26	1-16	6 (86)
	8	PLA/EX	5	1.32	3-8	4 (57)
	16		7	1.76	1-15	7(100)
	24		8	2.31	0-18	7(100)
	48		8	3.39	2-20	5 (72)
Cardiac Output, L/Min	8	Control	5.4	0.66	3.4-7.2	5 (72)
	16		6.5	1.01	3.7-11.7	7(100)
	24		4.9	0.52	2.9-6.6	6 (86)
	48		6.9	1.02	4.4-9.8	6 (86)
	8	PLA/EX	4.7	0.87	1.3-7.4	6 (86)
	16		5.4	0.63	3.5-8.3	7(100)
	24		5.8	0.45	4.5-7.8	7(100)
	48		5.6	0.41	4.3-6.8	5 (72)
Cardiac Index, L/Min/ m2 BSA	8	Control	2.7	0.45	1.8-3.2	3 (43)
	16		3.2	1.03	1.5-7.0	5 (72)
	24		2.4	0.30	1.6-3.1	5 (72)
	48		3.5	0.67	2.0-5.0	4 (57)
	8	PLA/EX	2.6	0.52	0.6-4.3	6 (86)
	16		3.0	0.43	2.0-5.0	7(100)
	24		3.2	0.35	2.0-4.3	7(100)
	48		3.1	0.33	3.0-4.0	5 (72)
Stroke Work Index, mL/ beat/ m2 BSA	8	Control	23.8	7.05	16.7-30.8	2 (28)
	16		36.0	14.46	19.0-65.0	3 (43)
	24		24.6	7.38	14.3-38.9	3 (43)
	48		29.4	5.77	19.0-44.0	4 (57)
	8	PLA/EX	24.9	6.62	8.1-39.9	4 (57)
	16		23.6	4.59	11.0-36.0	5 (72)
	24		24.6	4.99	15.3-38.5	4 (57)
	48		24.8	1.88	21.0-32.0	5 (72)

for both control and PLA/EX and then returned to WNL for the remaining PBH intervals (Table 22). There was no statistical significance between the groups on this variable ($p>.05$). Pulmonary vascular resistance index (PVRI) was below normal values (225-315 Dynes/second/m^2 BSA/cm^5) in the control at PBH 8, 16, and 48 and in the PLA/EX group at PBH 16 and 48. No statistical difference in PVRI was found at any PBH interval. Systemic blood pressure (BP) mean was WNL (70-105 mmHg) at all PBH interval means in both groups. Systemic BP diastolic was also WNL (60-90 mmHg) in both groups at all PBH intervals. There were no significant differences between the group means on the variables of mean BP or diastolic BP ($p>.05$).

Heart rate was above normal values (80-120 beats/min) at PBH 8 in the control and at all intervals in the PLA/EX group. The difference was not significant at any PBH interval between groups ($p>.05$).

Arterial-venous oxygen difference (A-VO_2 DIFF) was above normal values (4.6-5.4 mL O_2/100 mL) at PBH 8 and 24 and below normal at PBH 16 and 48 in the control (Table 23). The PLA/EX group was above normal at PBH 8, 16, and 24 and WNL at PBH 48. There was not a significant difference between the mean PBH interval values ($p>.05$).

Oxygen consumption was above the normal of 240 mL/min in both groups at all PBH intervals. The difference between the control and PLA/EX group on the mean O_2 con-

Table 22 - Cardiopulmonary Profile 2

Variable	PBH	Group	Mean	SE	Range	No.(%)
Systemic	8	Control	2967	1166.00	1801-4133	2 (28)
Vascular	16		1919	399.36	903-3287	5 (72)
Resistance	24		2051	219.91	1432-2667	5 (72)
Index,	48		2032	536.69	916-3103	4 (57)
Dynes/sec/	8	PLA/EX	3865	2052.84	1142-9953	4 (57)
m2 BSA/	16		2360	282.75	1498-3116	6 (86)
cm5	24		2166	250.81	1336-2832	5 (72)
	48		2462	186.03	1865-2886	5 (72)
Pulmonary	8	Control	174	44.50	129-218	2 (28)
Vascular	16		158	30.57	37-198	5 (72)
Resistance	24		248	104.98	108-666	5 (72)
Index,	48		149	30.83	104-208	3 (43)
Dynes/sec/	8	PLA/EX	373	205.92	92-985	4 (57)
m2 BSA/	16		189	37.25	35-277	6 (86)
cm5	24		246	99.63	71-531	4 (57)
	48		192	85.33	65-519	5 (72)
Systemic BP,	8	Control	100	0.00	100	1 (14)
mean, mmHg	16		87	12.01	72-111	3 (43)
	24		71	5.49	62-81	3 (43)
	48		80	6.38	62-91	5 (72)
	8	PLA/EX	84	12.01	69-108	3 (43)
	16		86	4.65	75-100	5 (72)
	24		84	5.51	75-94	3 (43)
	48		96	3.93	91-104	3 (43)
Systemic BP	8	Control	68	3.17	52-76	7(100)
Diastolic,	16		68	5.82	51-92	7(100)
mmHg	24		67	5.22	47-88	7(100)
	48		63	5.18	45-80	7(100)
	8	PLA/EX	66	7.08	41-89	6 (86)
	16		71	3.50	58-83	7(100)
	24		70	3.51	58-82	7(100)
	48		76	3.37	62-87	6 (86)
Heart Rate,	8	Control	105	8.90	78-140	7(100)
Beats/Min.	16		114	9.90	81-147	7(100)
	24		126	8.09	89-151	7(100)
	48		121	5.04	106-142	7(100)
	8	PLA/EX	121	9.69	80-160	7(100)
	16		133	8.93	104-164	7(100)
	24		128	5.80	111-153	7(100)
	48		125	4.64	108-140	6 (86)

Table 23 - Cardiopulmonary Profile 3

Variable	PBH	Group	Mean	SE	Range	No.(%)
A-V O2 Diff, mLO2/ 100mL	8	Control	6.4	2.35	4.0-8.7	2 (28)
	16		4.1	0.68	3.0-5.0	3 (43)
	24		5.7	0.88	3.9-6.6	3 (43)
	48		3.8	0.33	3.0-5.0	4 (57)
	8	PLA/EX	5.7	0.63	4.0-7.0	4 (57)
	16		6.1	0.76	4.0-9.0	6 (86)
	24		7.2	0.75	5.2-8.8	4 (57)
	48		5.2	0.65	3.0-7.0	5 (72)
O2 Consumption, mL/min	8	Control	256	40.00	216-296	2 (28)
	16		303	70.50	162-374	3 (43)
	24		309	65.04	222-436	3 (43)
	48		277	73.31	132-451	4 (57)
	8	PLA/EX	279	71.02	73-376	4 (57)
	16		317	83.69	155-727	6 (86)
	24		427	59.15	333-596	4 (57)
	48		280	18.52	224-324	5 (72)
O2 Available mLO2/min/ m2 BSA	8	Control	537	80.00	457-617	2 (28)
	16		735	147.22	490-999	3 (43)
	24		551	66.56	431-661	3 (43)
	48		589	121.46	379-822	4 (57)
	8	PLA/EX	488	120.17	140-653	4 (57)
	16		530	62.63	390-814	6 (86)
	24		585	92.27	468-860	4 (57)
	48		489	23.20	416-550	5 (72)
O2 Extracted, %	8	Control	27	7.20	20.0-34.4	2 (28)
	16		20	2.51	17.0-25.0	3 (43)
	24		27	3.10	20.8-31.1	3 (43)
	48		23	1.77	19.0-28.0	4 (57)
	8	PLA/EX	31	2.76	24.4-36.9	4 (57)
	16		31	4.25	17.0-49.0	6 (86)
	24		38	0.80	36.3-39.9	4 (57)
	48		27	6.96	2.0-44.0	5 (72)
A-a O2 Diff, mLO2/ 100 mL	8	Control	33	13.87	9-65	4 (57)
	16		48*	10.84	10-75	5 (72)
	24		43	10.60	15-72	5 (72)
	48		39	15.38	3-99	7(100)
	8	PLA/EX	144	86.83	33-490	5 (72)
	16		113	19.09	34-157	6 (86)
	24		112	34.18	2-291	7(100)
	48		65	25.51	7-160	6 (86)

*$p<.05$

Table 24 - Cardiopulmonary Profile 4

Variable	PBH	Group	Mean	SE	Range	No.(%)
Shunt (QS/QT), %	8	Control	14	2.50	11-16	2 (28)
	16		22	2.80	16-30	5 (72)
	24		26	6.74	9-47	5 (72)
	48		26	2.72	18-30	4 (57)
	8	PLA/EX	22	4.66	11-33	4 (57)
	16		22	3.17	9-33	6 (86)
	24		31	7.49	19-53	4 (57)
	48		28	3.85	18-35	4 (57)
CVP, mmHg	8	Control	8	1.14	5-11	5 (72)
	16		9	2.01	3-15	6 (86)
	24		10	1.94	5-15	5 (72)
	48		9	1.86	1-14	6 (86)
	8	PLA/EX	8	2.29	2-17	6 (86)
	16		7	2.13	1-15	6 (86)
	24		9	2.03	2-15	7(100)
	48		5	2.32	1-14	5 (72)

CHAPTER V

DISCUSSION

The purpose of this research was to analyze the data collected on a group of 14 subjects entered into an experimental design study for the evaluation of the effect of plasma exchange during burn shock. The study was designed to allow periodic review for the purpose of determining the number of cases necessary to achieve statistical significance in a prospective manner. This study reports the preliminary findings and specifically addresses two nursing research questions.

The Sample

The sample was found not to be evenly distributed on the very important variable of percent TBSA burn full-thickness injury ($p<.01$). The control had an 18.3% full-thickness injury (range: 0-25) compared to the PLA/EX group's 38.4% full-thickness injury (range: 27-46). Thus, the subjects in the PLA/EX group were significantly more injured than the control. This made the other study parameters more difficult to interpret since an equal result between two groups of subjects when one group is

much more severely injured does not necessarily carry the same implications for both groups. In addition, while not achieving statistical significance, the clinical significance of having four of the PLA/EX patients (57%) with inhalation injury compared to one patient (14%) in the control further unbalances the severity of clinical injury. Thus, the first conclusion is that the sample as now distributed is uneven, with the PLA/EX group being much more critically ill than the control on the basis of two variables: percent TBSA full-thickness injury and the incidence of inhalation injury.

Resuscitation Requirements

There was no statistically significant difference between the groups in terms of fluid requirements in total nor at PBH 8, 16, and 24. However, the argument could be made that since the PLA/EX group was more severely injured, the equal requirement means the PLA/EX therapy kept the requirements down. The identification of a subgroup of subjects, EXP-SUR, was made and this data compared to the control. Statistical significance was not achieved on the fluid variable but the EXP-SUR group did require less total fluid to resuscitate while, at the same time maintaining a significantly higher hourly urine output ($p<.01$). In addition, the EXP-SUR group required more fluid than the control in the first eight hours and less in the subsequent two eight-hour periods. The power

of the t-test indicates the problem is one of small sample size combined with wide ranges on the variables measured. Thus, the second conclusion: The initial trend appears to support the notion that PLA/EX decreases fluid requirements during burn shock but significance has not been reached due to insufficient sample size.

Physiologic Variables

The effect of PLA/EX on measurable physiologic variables was also analyzed. Again, the power of the t-test indicated an insufficient sample in all but a few variables. The variables which have reached significance with the current sample size are astonishingly strong.

Hematology

The parameters of WBC, RBC, HGB, and HCT initially all showed the hemoconcentration effect of burn shock. Platelets were significantly ($p<.05$) diminished in the PLA/EX group thus demonstrating the reported removal of platelets as a side-effect of the PLA/EX procedure. Thus, the third conclusion: Plasma exchange significantly decreases platelet counts.

Chemistries

Chemistry values were not significantly different nor were there trends toward differences on most variables. As expected, no electrolyte imbalances occurred because

all subjects were resuscitated with lactated Ringer's solution. The BUN and creatinine levels remained within normal limits in both groups, indicating adequate renal perfusion. Glucose levels were slightly elevated, an expected finding secondary to the stress response. Two other variables which differed from normals but were expected in burn subjects were the findings of low albumin levels and elevated lactic acid levels. Thus, conclusion four: PLA/EX does not appear to alter serum chemistry values from those expected in other burn patients.

Coagulation Studies

Coagulation studies, which included prothrombin time and partial thromboplastin times, and fibrinogen, were not different from normal laboratory control values, from normal ranges, nor between study subjects. Thus, the following conclusion is made: The coagulopathy reported to occur in burn patients was not observed in this group of study subjects.

Pulmonary Variables

The total group of patients (n=14) sustained flame injury which resulted in five patients (36%) sustaining inhalation injury. A total of nine patients (64%) required intubation. One patient died at 36 hours postburn from an overwhelming inhalation injury. Arterial and mixed venous blood gas analysis determinations were ana-

lyzed for each subject. Except for occasional statistically significant differences in the pCO_2 mean values, there was no difference between groups. Again, since the samples are uneven for incidence of inhalation injury (1/7 for control; 4/7 for PLA/EX group), it can be argued that equal results are actually an indicator of the benefits of PLA/EX in minimizing the clinical response to inhalation injury. The FiO_2 was significantly higher at PBH 16 in the PLA/EX group but not at other PBH intervals. In addition, the clinical expectation of patients with severe inhalation injury is that they will require excessive amounts of resuscitation fluid. This was not the case for this group of subjects with inhalation injury. Thus the next conclusion: Statistical significance was not reached in the fluid requirements of subjects with inhalation injury. This appears to be a function of insufficient sample size. The base excess was significantly different ($p<.05$) at PBH 16 and 24 in both MVBG and ABG determinations with the PLA/EX being in a balance corrected toward 0 while the control was in a much more severe negative base excess. Thus the following conclusion: The PLA/EX group was in significantly ($p<.05$) more normal base excess balance at both PBH 16 and 24 than was the control group.

Cardiopulmonary Profile

There were no statistically significant differences

between the control and the PLA/EX group on the measured cardiopulmonary profiles. Again, this appears to be a function of sample size as indicated by the minimal power of the t-test. Since it is clinically and statistically known that the PLA/EX group is much more severely injured, if both groups have the same cardiac index, the results may be implied to be better in the PLA/EX group. Thus, the following conclusions: There were no statistically significant differences between the control and the PLA/EX group on the measured cardiopulmonary profiles. This appears to be due to insufficient sample size.

Conclusions

1. The sample as now distributed is uneven, with the PLA/EX group being much more critically ill than the control on the basis of two variables: Percent TBSA full-thickness injury ($p<.01$) and the incidence of documented inhalation injury.

2. Significance has not been reached on the variable of fluid requirement. This appears to be a function of insufficient sample size as reflected by the low power of the t-test.

3. PLA/EX significantly decreases platelet count ($p<.05$).

4. PLA/EX does not appear to alter serum chemistry values from the expected values of subjects with burn

injury.

5. The coagulopathy reported to occur in burn patients was not observed in this group of subjects.

6. Statistical significance was not reached on the fluid requirements of subjects with inhalation injury. This appears to be a function of insufficient sample size.

7. The PLA/EX group was in significantly ($p<.05$) more normal base excess balance at both PBH 16 and 24.

8. There is no evidence that the PLA/EX is harmful in any way to experimental subjects.

It is recommended that the study as designed be continued until statistical significance is reached or rejected.

APPENDIX A

LUND AND BROWDER CHART WITH DESCRIPTION OF DEPTH OF INJURY

Lund and Browder (163) developed a formula for the estimation of the total body surface area burn and published the results in 1944. Up to that time, "Berkow's table" had been used but these investigators reported that the data assembled for the table were for metabolic work and had been collected primarily to secure a correct total body surface area. For this purpose, differences in points of division between one region and another were unimportant in securing a valid total. In the use to which surface area proportions are put with burns, such definitions are of great importance. Also, it is of great importance to subdivide the surface into as many clearly demarcated areas as possible so as to permit the easiest possible visual comparison. Body surface area in relation to age is another factor which Lund and Browder incorporated into the chart. The table and diagrams were estimated to be applicable, without serious error, to at least 99.5% of all cases of burns. The Lund and Browder chart has been used in Burn Centers since its introduction in 1944. The chart was incorporated into the medical record charting system of this Burn Center upon its opening in 1976 (Figure 1). By convention, red is the color used to designate full-thickness injury; blue is used to designate partial-thickness injury. First degree burns are not included in the estimation of total body surface area burn.

University of Utah
Hospital
Burn Unit

BURN ESTIMATE AND DIAGRAM
AGE vs. AREA

Area	Birth 1 yr.	1-4 yr.	5-9 yr.	10-14 yr.	15 yr.	Adult	2°	3°	Total	Donor Areas
Head	19	17	13	11	9	7				
Neck	2	2	2	2	2	2				
Ant. Trunk	13	13	13	13	13	13				
Post. Trunk	13	13	13	13	13	13				
R. Buttock	2½	2½	2½	2½	2½	2½				
L. Buttock	2½	2½	2½	2½	2½	2½				
Genitalia	1	1	1	1	1	1				
R. U. Arm	4	4	4	4	4	4				
L. U. Arm	4	4	4	4	4	4				
R. L. Arm	3	3	3	3	3	3				
L. L. Arm	3	3	3	3	3	3				
R. Hand	2½	2½	2½	2½	2½	2½				
L. Hand	2½	2½	2½	2½	2½	2½				
R. Thigh	5½	6½	8	8½	9	9½				
L. Thigh	5½	6½	8	8½	9	9½				
R. Leg	5	5	5½	6	6½	7				
L. Leg	5	5	5½	6	6½	7				
R. Foot	3½	3½	3½	3½	3½	3½				
L. Foot	3½	3½	3½	3½	3½	3½				
						TOTAL				

Cause of Burn _____

Date of Burn _____

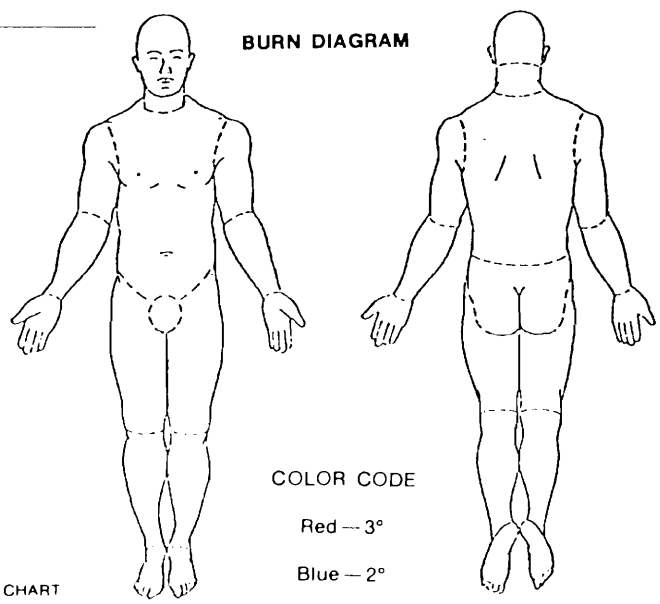
Time of Burn _____

Age _____

Sex _____

Weight _____

BURN DIAGRAM



COLOR CODE

Red — 3°

Blue — 2°

LUND AND BROWDER CHART

UHMC 1182 A 4-77

Figure 1. Burn estimate and diagram. Reprinted with permission of U of U Medical Center.

Depth of Burn Injury

Burn injury involves the destruction of the integumentary system. The skin is divided into three layers (Figure 2). The epidermis, or nonvascular outer layer of the skin is about the thickness of a sheet of paper. It is composed of epithelial cells that provide a protective barrier to the skin, hold in fluids and electrolytes, regulate heat, and keep harmful agents in the external environment from injuring or invading the body. The dermis, lying below the epidermis, is about 30 to 45 times thicker than the epidermis. The dermis contains connective tissues with blood vessels and highly specialized structures consisting of hair follicles, nerve endings, sweat glands, and sebaceous glands. Under the dermis lies the subcutaneous tissue containing major vascular networks, nerves, and lymphatics. The subcutaneous tissue acts as a shock absorber and heat insulator for the underlying structures: muscles, tendons, bones, internal organs, etc.

In the past, burns were defined by degrees: first degree, second degree and third degree. The American Burn Association currently advocates a more explicit physiological definition categorizing the burn according to depth: partial- and full-thickness. Table 25 reflects the comparison of the classification system (164).

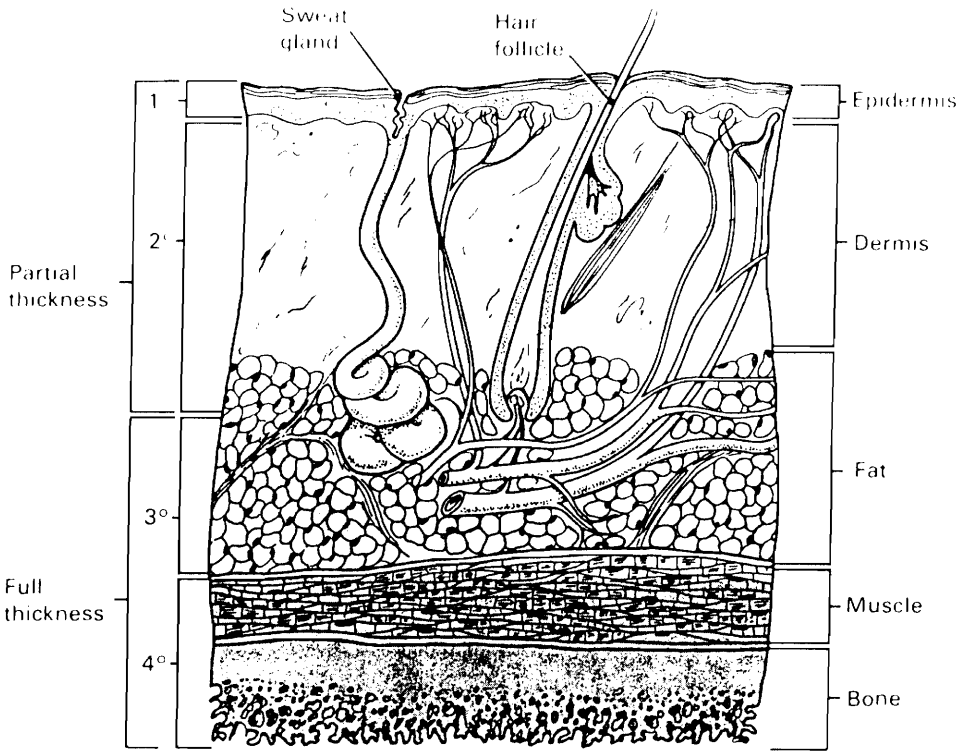


Figure 2. Cross-section of skin indicating burn and structures involved.

Table 25. Classification of Burns

Classification	Clinical Appearance and Cause	Morphology
Partial thickness 1st degree (Superficial)	Characterized by erythema. Blanches on pressure. Pain and mild swelling present. No vesicles or blisters (although after 24 hours skin may blister and peel). Caused by superficial sunburn or quick heat flash.	Only superficial devitalization with local hyperemia.
2nd degree (deep)	Fluid-filled vesicles. Red, shiny, wet (if vesicles have ruptured). Very painful due to nerve injury. Mild to moderate edema. Caused by flash, scald, or flame burn.	Involves both epidermis and dermis to varying depth. Some skin elements remain viable from which epithelial regeneration occurs.
Full thickness 3rd and 4th degree	Dry, waxy white, leathery or hard. Thrombosed vessels often visible. Insensitive to pain and pressure. Due to nerve destruction. Can involve muscles, tendons and bones. Caused by flame, scald, chemicals, tar or electric current.	All skin elements destroyed as well as nerve endings. Coagulation necrosis present.

APPENDIX B

BLOOD REQUIREMENTS FOR LAB VALUES

Table 26. Blood Requirements for Lab Values to be Drawn During the Randomized Trial of Plasma Exchange Therapy in Patients with Major Burns

Lab Value	Frequency of sample, hours	Total number of samples	Amount of Blood per sample, mL	Total volume required, mL
Arterial blood gas	2	24	2	48
Mixed venous blood gas	2	24	2	48
CBC, with platelets	4	12	3	36
PT, PTT, fibrinogen	4	12	3	36
Electro-lytes, BUN, Creatinine	4	12	3	36
SMA-20	4	12	7	84
Lactic acid	4	12	5	60
		Total		348

APPENDIX C

CARDIOPULMONARY PARAMETERS

Arterial and Mixed Venous Blood Gas Analysis

The values reported in this study were determined by the Pulmonary Laboratory, University of Utah Medical Center. All values have been adjusted for the elevation above sea level and the barometric pressure at the time of analysis. Normal values for this laboratory are presented in Table 27.

Hemodynamic Parameters

Hemodynamic parameters are measured directly using instrumentation previously described. The normal values for these parameters are presented in Table 28.

Computed Cardiopulmonary Parameters

The computation of cardiopulmonary parameters is performed within the Cardiopulmonary Profile Program developed by Tenet Information Services, Salt Lake City, Utah. Normal values are presented in Table 29. The Cardiopulmonary Profile Program is designed to optimally utilize values from arterial blood gases, mixed venous blood gases and other data obtained from a Swan-Ganz catheter. The values are derived using the following procedures.

Table 27. Arterial and Mixed Venous Blood Gas Normal Values Breathing Room Air

Value	Arterial Normal Range	Mixed Venous Normal Range
$P0_2$, mmHg	68 to 78	35 to 40
0_2 Saturation, %	> 93	60 to 85
pH	7.35 to 7.45	7.32 to 7.42
$PC0_2$, mmHg	31 to 41	38 to 50
Base Excess	-3 to 3	-3 to 3
Bicarbonate mEq/L	22 to 26	22 to 29
Carboxyhemoglobin, %	<2	

Table 28. Hemodynamic Parameters

Value	Parameter
Systemic Blood Pressure	
Mean, mmHg	70-105
Diastolic, mmHg	60-90
Pulmonary Artery Pressure	
Mean, mmHg	9-18
Pulmonary Artery Wedge Pressure, mmHg	6-15
Central Venous Pressure, mmHg	2-6
Heart Rate Beats/min	80-120
Temperature, Degrees centigrade	36-38.5
Cardiac Output, L/min	3.5-6.5
Cardiac Index, $L/minute/m^2$ BSA	2.8-4.2

Table 29. Cardiopulmonary Profile Predicted Values

Profile	Predicted Value
A-V O_2 Difference	4.6 to 5.4 mL O_2/100 mL
O_2 Consumption	240 mL/min
O_2 Availability	550 to 650 mL O_2/min/m^2 BSA
O_2 Extraction	23 to 27%
Systemic Arterial Mean Pressure	70 to 105 mmHg
Pulmonary Artery Pressure Mean	9 to 16 mmHg
Pulmonary Vascular Resistance Index	225 to 315 Dynes/second/m^2 BSA/cm^5
Systemic Vascular Resistance Index	1970 to 2390 Dynes/second/m2 BSA/cm5
Stroke Work Index	41 to 51 mL/beat/m^2 BSA
QS/QT (Shunt)	17 to 31%
A-a O_2 Difference	< 8

Arterial to Venous Oxygen Difference

Arterial to venous oxygen difference is calculated if the following criteria are met:

1. Arterial PO_2 or arterial oxygen content are reported.

2. Mixed venous PO_2 or mixed venous oxygen content is reported:

$A\text{-}VO_2$ diff = Art. O_2 cont. - venous O_2 cont.

Oxygen Consumption

Oxygen consumption is calculated if the following criteria are met:

1. No measured value is entered.

2. Measured cardiac output is entered.

3. The criteria for $A\text{-}VO_2$ diff. are met.

$\dot{V}O_2$ = Cardiac output (meas.) X 1000 X $A\text{-}VO_2$ diff.

Oxygen Availability

Oxygen availability is calculated if the following criteria are met:

1. Arterial O_2 content and/or arterial PO_2 are entered.

2. Cardiac output is entered or calculated.

3. Patient height and weight are entered.

O_2 availability = (art. O_2 content) (Cardiac index).

Oxygen Extration

Oxygen extraction is calculated if the criteria for $A\text{-}VO_2$ differences are met:

$$O_2 \text{ ext} = \frac{\text{art. } O_2 \text{ content} - VO_2 \text{ cont.}}{\text{art. } O_2 \text{ cont.}} \times 100\%$$

Systemic Arterial Pressure Mean (MAP)

$$MAP = \frac{\text{Systolic Pressure} + 2\,(\text{Diastolic Pressure})}{3}$$

and

$$MAP = \text{Diastolic Pressure} + \frac{(\text{Systolic} - \text{Diastolic Pressure})}{3}.$$

Pulmonary Artery Pressure Mean (Mean PAP)

Pulmonary artery pressure mean is calculated if the following criteria are met:

1. Systolic pulmonary artery pressure is reported.
2. Diastolic pulmonary artery pressure is reported.

$$\text{Mean PAP} = \frac{(\text{Systolic PAP} - \text{Diastolic PAP}) + \text{Diastolic PAP}}{3}$$

Pulmonary Vascular Resistance Index

Pulmonary vascular resistance index is calculated if the following criteria are met:

1. Systolic arterial blood pressure is reported.
2. Diastolic arterial blood pressure is reported.
3. Wedge pressure is reported.
4. Cardiac output (either measured or calculated) is reported.
5. Patient weight and height are reported.

$$PVR = \frac{79.96 \text{ (mean PAP - Wedge Pressure)}}{\text{Cardiac Index}} .$$

Systemic Vascular Resistance Index

Systemic vascular resistance index is calculated if the following criteria are met:

1. Systemic systolic blood pressure is reported.
2. Systemic diastolic blood pressure is reported.
3. Central venous pressure is reported.
4. Cardiac output is reported.
5. Patient height and weight are reported.

$$SVR = \frac{79.96 \text{ (mean SAP - Central Ven. Pressure)}}{\text{Cardiac Output}} .$$

SAP = Systemic arterial pressure,

$$\text{mean SAP} = \frac{(\text{Systolic SAP} - \text{Diastolic SAP}) + \text{Diastolic SAP}}{3}$$

$$\text{SVR index} = \frac{79.96\ (\text{mean SAP} - \text{Central Ven. Pressure})}{\text{Cardiac Index}}.$$

Cardiac Index

This is reported if the following criteria are met:

1. The criteria for QT are met.
2. Patient height and weight are entered.

$$\text{Cardiac index} = \frac{(\text{Cardiac Ouptut})}{\text{Body Surface Area}}.$$

Stroke Volume Index

This is calculated if the following criteria are met:

1. The criteria for cardiac output are met.
2. Patient heart rate is entered.
3. Patient height and weight are entered.

$$\text{Stroke index} = \frac{(\text{Stroke Volume})}{\text{Body Surface Area}}$$

$$\text{Stroke volume} = \frac{\text{(Cardiac Output)}}{\text{Heart Rate}} .$$

Shunt (QS/QT)

Shunt is calculated if the following criteria are met:

1. Criteria for capillary content are met.

2. Arterial PO_2 or arterial oxygen content are reported.

3. Mixed venous PO_2 or mixed venous oxygen content are reported:

$$QS/QT = \frac{\text{Pul. Cap. } O_2 \text{ cont.} - \text{Art. } O_2 \text{ cont.}}{\text{Pul. Cap. } O_2 \text{ cont.} - \text{Ven. } O_2 \text{ cont.}} \times 100.$$

APPENDIX D

COMPOSITION OF SOLUTIONS AND FLUIDS

Table 30. Composition of Lactated Ringer's Solution Compared with Extracellular Fluid

Electrolyte	Extracellular* Fluid	Lactated** Ringer's
Sodium, mEq/L	135-145	130
Potassium, mEq/L	3.2-4.5	4
Chloride mEq/L	95-105	109
Lactate, mEq/L***	24-28	28

NOTE. *Normal values may vary slightly from one test laboratory to another; ** Plus 80-100 mL free water per liter; *** Lactate is converted by liver into bicarbonate.

APPENDIX E

RANDOM NUMBER ASSIGNMENT SEQUENCE

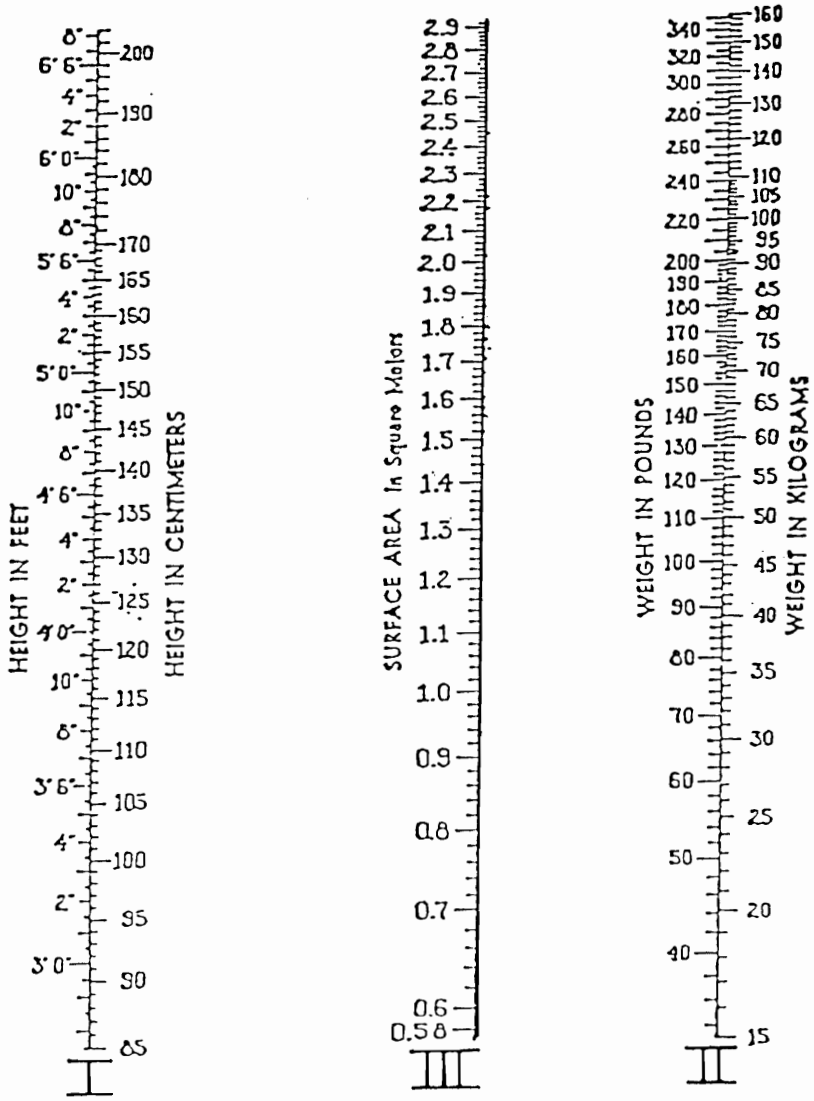
Table 31. Means of Assigning Random Numbers

Case No.	Assignment	Case No.	Assignment
1.	Control	49.	Control
2.	Exchange	50.	Exchange
3.	Control	51.	Exchange
4.	Exchange	52.	Control
5.	Control	53.	Exchange
6.	Exchange	54.	Control
7.	Control	55.	Control
8.	Exchange	56.	Exchange
9.	Control	57.	Control
10.	Exchange	58.	Exchange
11.	Control	59.	Control
12.	Exchange	60.	Exchange
13.	Control	61.	Control
14.	Exchange	62.	Exchange
15.	Exchange	63.	Exchange
16.	Control	64.	Control
17.	Control	65.	Exchange
18.	Exchange	66.	Control
19.	Exchange	67.	Exchange
20.	Control	68.	Control
21.	Control	69.	Control
22.	Exchange	70.	Exchange
23.	Exchange	71.	Exchange
24.	Control	72.	Control
25.	Control	73.	Control
26.	Exchange	74.	Exchange
27.	Control	75.	Control
28.	Exchange	76.	Exchange
29.	Control	77.	Exchange
30.	Exchange	78.	Control
31.	Exchange	79.	Exchange
32.	Control	80.	Control
33.	Exchange	81.	Exchange
34.	Control	82.	Control
35.	Control	83.	Control
36.	Exchange	84.	Exchange
37.	Exchange	85.	Control
38.	Control	86.	Exchange
39.	Exchange	87.	Control
40.	Control	88.	Exchange
41.	Control	89.	Exchange
42.	Exchange	90.	Control
43.	Control	91.	Control
44.	Exchange	92.	Exchange
45.	Exchange	93.	Control
46.	Control	94.	Exchange
47.	Control	95.	Control
48.	Exchange	96.	Exchange

APPENDIX F

BODY SURFACE AREA CHART

Directions: To find body surface of a patient, locate the height in inches (or centimeters) on scale I and the weight in pounds (or kilograms) on Scale II and place a straight edge (ruler) between these two points which will intersect Scale III at the patient's body surface area.



APPENDIX G

PATHOLOGY LABORATORY VALUES

Table 32. Normal Ranges of Laboratory Values

Laboratory Value	Normal Range
Hematology	
White blood cell	3.6-9.0 K/µl
Red blood cell	4.71-5.77 m/µL
Hemoglobin	14.5-17.1 g/dL
Hematocrit	43.0-52.0%
Platelets	140-440 K/µL
Chemistries	
Sodium	137-146 mEq/L
Potassium	3.8-5.3 mEq/L
Chloride	100-109 mEq/L
Carbon dioxide	21-27 mEq/L
Blood urea nitrogen	6-20 mg/dL
Glucose	84-119 mg/dL
Creatinine	0.9-1.4 mg/dL
Uric acid	4.6-8.5 mg/dL
Calcium	8.6-10.7 mg/dL
Phosphate	2.4-4.1 mg/dL
Total bilirubin	0.3-1.9 mg/dL
Direct bilirubin	0.0-0.3 mg/dL
Total protein	6.4-8.1 g/dL
Albumin	4.0-5.1 g/dL
Cholesterol	128-288 mg/dL
GGTP	5 to 85 IU/L
Alkaline phosphatase	40-139 IU/L
LDH	138-328 IU/L
SGOT	11-43 IU/L
SGPT	11-85 IU/L
Lactic acid	0.5-2.2 mEq/L
Coagulation	
Prothrombin time	10.0-14.4 seconds
Partial thromboplastin time	32-48 seconds
Fibrinogen	150-350 mg/dL

APPENDIX H

VARIABLE LIST

Group assignment
0=control
1=treatment
Card number
Age
Sex
0=male
1=female
% TBSA burn
% Full-thickness burn
Inhalation injury
0=no
1=yes
Type of injury
1=flame
2=scald
3=chemical
4=tar/asphalt
5=other
Time postburn IV
Fluid resuscitation started
$\leq$ 1 hour=1
n hour=n
Hours postburn of arrival in burn center
Total fluids to resuscitation expressed as
cc/kg/% TBSA burn/first 8 hrs postburn
cc/kg/% TBSA burn/second 8 hrs postburn
cc/kg/% TBSA burn/third 8 hrs postburn
Time to resuscitation
Total sodium infused expressed as
mEq/kg/% TBSA burn/time to resuscitation
Weight in kg
Body surface area
Urine output expresed as mean cc/hr/time to resuscitation
Past medical history
0=no history of disease
1=history of disease
Cardiac
Pulmonary
Diabetes
Renal
Gastrointestinal
Neurologic
Hepatic
ETOH abuse
Drug abuse
Other
Intercurrent trauma
0=yes
1=no

Survival of burn shock
0=yes
1=no
Survival of burn injury
0=yes
1=no
Group survival
0=yes
1=no
Plasma exchange group
Postburn hour started
Postburn hour stoppped
Calculated volume:
males = (7% body weight in kg X 1.5)
females = (8% X kg X 1.5)
Urine volume during procedure expressed as cc/hr
Predicted maintenance rate expressed in cc/hr
Actual volume received in second 24 hours expressed in mean cc/hr
Actual volume received from resuscitation time through postburn hour 48 expressed in mean cc/hr
Urine output expressed in mean cc/hr during 2nd 24 hours
Urine output expressed in mean cc/hr during resuscitation time
Calculated amount FFP
Delivered amount FFP
Postburn hour of administration
Blood products required
0=no
n=amount
Postburn hour administration started
Death in first 48 hours
0=no
n=postburn hour of death
Death due to burn=days
0=no
n=postburn day of death
Cause of death
0=no death
1=overwhelming inhalation injury
2=metabolic exhaustion
3=sepsis
4=failure to resuscitate
Failure to survive in group
0=no failure
1=failure to survive
Reason
0=no failure
1=death
2=technical difficulties
3=failure to resuscitate.

The following variables were measured at admission and every four hours thereafter (PBH 4,8,12,16,20,24,28,32, 36,40,44 and 48).

Blood Analyses

White blood cell count
Hemoglobin
Hematocrit
Platelets
Red blood cell count
Prothrombin time-patient
Prothrombin time-control
Partial thromboplastin time-patient
Partial thromboplastin time-control
Fibrinogen
Sodium
Potassium
Chloride
Total carbon dioxide
Blood urea nitrogen
Glucose
Creatinine
Uric acid
Total calcium
Phosphate
Total bilirubin
Direct bilirubin
Total protein
Albumin
Alkaline phosphatase
Lactate dehydrogenase (LDH)
Serum glutamic-oxaloacetic transaminase (SGOT)
Serum glutamic-pyruvate transaminase (SGPT)
Cholesterol
Lactate
GGTP

Respiratory

Fraction inspired oxygen
Method
- 0=room air
- 1=nasal prongs
- 2=mask
- 3=intubated
- 4=manually ventilated with mask
- 5=manually ventilated with intubation
- 6=ventilated with Bear

Tidal volume
- 0=spontaneous
- n=cc of air via ventilator

Mode
0=spontaneous
1=assist/control
2=intermittent mandatory ventilation
3=T-piece
4=manually delivered
5=CPAP
Positive end-expiratory pressure (PEEP)
Spontaneous respiratory rate

Arterial Blood Gas

Body temperature
Oxygen saturation
P02
PC02
pH
HC03
Base excess

Mixed Venous Blood Gas

Oxygen saturation
P02
PC02
pH
HC03
Base excess

Cardiac Parameters

Pulmonary artery mean pressure (PA mean)
Pulmonary artery wedge pressure (PAWP)
Cardiac output (C.O.)
Cardiac index (C.I.)
Stroke work index (SWI)
Systemic vascular resistance index (SVRI)
Pulmonary vascular resistance index (PVRI)
Systemic blood pressure - mean
Systemic blood pressure-diastolic
Heart rate
Arterial-venous oxygen difference
Oxygen consumption
Oxygen available
Oxygen extracted
Shunt (QS/QT)
A-a oxygen difference
Central venous pressure
Carboxyhemoglobin

APPENDIX I

NURSES' RESPONSIBILITY FOR PLASMA EXCHANGE RESEARCH PROTOCOL

Admission

Blood Draws Upon Admission:

1. ABG, MVBG, CBC with differential, SMA-6, SMA-20, Lactic Acid, PT, PTT, Fibrinogen (to lab on regular slips).

Plasma Exchange:

1. Draw (1) above pre- and postexchange. Send to lab with appropriate requisition slips.
2. Put plasma in fridge in dirty utility room after labeling it.
3. Do all cardiac parameters immediately pre- and postexchange.

48-Hour Routine:

1. S-G: Record all Swan-Ganz parameters including CVP.
2. C.O.: Do 3 cardiac output measures and record average measure.
3. C.P.: Cardiac parameters. So S-G and C.O. plus ABGs and MVBG and send slip to computer technician for cardiopulmonary profile.
4. V.S.: TPR, B.P.

Postburn Hour

1. V.S., S-G, C.O., C.P., labs (1), (2), (3)
2. V.S., C.O., S-G
3. V.S.
4. V.S., S-G., C.O., C.P., lab (1)
5. V.S.
6. V.S., C.O., S-G
7. V.S.
8. V.S, S-G, C.O., C.P., lab (1)
9. V.S.
10. V.S., C.O., S-G
11. V.S.
12. V.S., C.O., S-G, C.P., lab (1)
13. V.S.
14. V.S., C.O., S-G,
15. V.S.
16. V.S., C.O., S-G, C.P., lab (1)
17. V.S.
18. V.S., C.O., S-G
19. V.S.
20. V.S., C.O., S-G, C.P., lab (1)

21. V.S.
22. V.S., C.O., S-G
23. V.S.
24. V.S., C.O., S-G, C.P., lab (1)
25. V.S., START 24 hour urine
26. V.S.
27. V.S.
28. V.S., C.O., S-G
29. V.S.
30. V.S., lab (1)
31. V.S.
32. V.S., C.O., S-G, C.P.
33. V.S.
34. V.S.
35. V.S.
36. V.S., C.O., S-G, lab (1)
37. V.S.
38. V.S.
39. V.S.
40. V.S., C.O., S-G, C.P.
41. V.S.
42. V.S., lab (1)
43. V.S.
44. V.S., C.O., S-G
45. V.S.
46. V.S.
47. V.S.
48. V.S., C.O., S-G, C.P., lab (1), end 24 hour urine

APPENDIX J

RESUSCITATION CALCULATIONS

A. Fluid Balance

1. Total volume received during resuscitation=mL
2. Total urine output during resuscitation=mL
3. Resuscitation fluid received=

[Total volume received - (urine output+basal fluid requirements)]mL

4. Volume of fluid/kg body weight/% TBSA burn to resuscitate patient:

$$\frac{\text{Total volume}}{\text{kg X \% TBSA burn}} = \text{mL/kg/\% TBSA burn.}$$

B. Sodium Balance

1. Total sodium received=mEq/Kg% TBSA burn
2. mEq of sodium/kg body weight/% burn to resuscitate patient:

$$\frac{\text{Total mEq Sodium}}{\text{kg X \% TBSA burn}} = \text{mEq Sodium/kg/\% TBSA burn.}$$

C. Basal Fluid Requirements

1. Body surface area using nomogram (Appendix F)
2. Basal fluid requirements=
   a. $1500/mL/m^2$ BSA = mL per 24 hrs

   b. $\frac{1500\ mL/m^2\ BSA}{24\ hrs}$ = mL per hr.

D. Colloid Replacement:

1. Adult males: 20% (5% X kg) = mL fresh frozen plasma (FFP)
2. Adult females: 20% (8% X kg) = mL FFP.

REFERENCES

1. American Burn Association Committee on Specific Optimal Criteria for Hospital Resources for Care of Patients with Burn Injury. San Antonio, American Burn Association, 1976.

2. Loebl EC, Baxter CR, Curreri PW: The mechanism of erythrocyte destruction in the early post-burn period. Ann Surg 1973; 178: 681-686.

3. Wilmore DW, Aulick LH: Metabolic changes in burned patients. Surg Clin No Am 1978; 58: 1173-1187.

4. Baxter CR: Fluid volume and electrolyte changes of the early postburn period. Clin Plast Surg 1974; 1: 693-709.

5. Baxter CR, Shires, T: Physiological resposne to crystalloid resuscitation of severe burns. Ann NY Acad Sci 1968; 150: 874-894.

6. Hernandez B: Platelets: A short course. RN 1980; 43: 36-41.

7. Orosz JJ: A short history of bloodletting. Int Soc Art Org 1981; 5: 226-228.

8. Pruitt B: Multidisciplinary care and research for burn injury: 1976 Presidential address, American Burn Association meeting. J Trauma 1977; 17: 263-269.

9. Marvin JA: Burn nursing as a specialty. Heart Lung 1979; 8: 913-917.

10. Artz CP, Baxter CR, Jackson DM, Sorenson B: Trauma workshop report: Burns. J Trauma 1970; 10: 1058-1061.

11. Archambeault-Jones C, Feller I: Burn nursing is nursing. Crit Care Nurs 1978; 1: 77-92.

12. Dracup K: Nursing diagnosis: A rose by any other name (editorial). Heart Lung 1983; 12: 211.

13. Guzzetta CE, Dossey BM: Nursing diagnosis: Framework, process and problems. Heart Lung 1983; 12: 281-291.

14. Thomsen M: Historical landmarks in the treatment of burns. Br J Plas Surg 1977; 30: 212-217.

15. Warden GD: The burned upper extremity -- historical persepctives. In Salisbury RE, Pruitt BA

(eds) Burns of the upper extremity: Major problems in clinical surgery. Philadelphia, W.B. Saunders Co., 1976, pp 16-23.

16. Wooldridge-King M: Nursing considerations of the burned patient during the emergent period. Heart Lung 1982; 11: 353-361.

17. O'Malley P, Snow N: Fluid resuscitation. Nurs 1976; 6: 43.

18. Christopher KL: The use of a model for hemodynamic balance to describe burn shock. Nurs Clin No Am 1980; 15: 617-627.

19. Gordon M, Sweeney MA: Nursing diagnosis: Methodological problems and issues. Adv Nurs Sci 1979; 2: 1-15.

20. Whelton B: An operationalization of Martha Rogers' theory throughout the nursing process. Int J of Nsg Stud 1979; 16: 7-20.

21. Utz SW: Applying the Neuman model to nursing practice with hypertension clients. Cardiovasc Nurs 1980; 16: 29-34.

22. Anna D, Christensen DG, Hohon SA, Ord L, Wells SR: Implementing Orem's conceptual framework. J Nsg Admin 1978; 8: 8-11.

23. Flaskerud JH, Halloran EJ: Areas in agreement in nursing theory development. Adv Nsg Serv 1980; 3: 1-7.

24. Hollen PA: A holistic model of individual and family health based on a continuum of choice. Adv Nsg Serv 1981; 3: 27-42.

25. Cope O, Moore FD: A study of capillary permeability in experimental burns and burn shock using radioactive dyes in blood and lymph. J Clin Invest 1944; 23: 241-257.

26. Fox CL, Keston AS: The mechanism of shock from burns and trauma traced with radiosodium. Surg Gynecol, and Obstet 1945; 80: 561-567.

27. Ganrot K, Jacobson S, Rothman U: Transcapillary passage of plasma proteins in experimental burns. Acta Physiol Scand 1974; 91: 497-501.

28. Wachtel TL, Frank HA, Sanders R, Hargens AR,

Peters RM: Definition of the Starling forces in Wick catheter in burned patients. J Burn Care and Rehab 1983; 4: 331-336.

29. Dobson EL, Warner GF: Factors concerned in the early stages of thermal shock. Circ Res 1957; V: 69-74.

30. Merriam TW: Myocardial function following thermal injury. Circ Res 1962; XI: 669-673.

31. Aikawa N, Martyn JAJ, Burke JF: Pulmonary artery catheterization and thermodilution cardiac output determination in the management of critically burned patients. Am J Surg 1978; 135: 811-817.

32. Baxter CR, Cook WA, Shires GT: Serum myocardial depressant factor of burn shock. Surg Forum 1966; 17: 1-4.

33. Glenn TM, Lefer AM: Significance of splanchnic proteases in the production of a toxic factor in hemorrhagic shock. Circ Res 1971; XXIX: 338-349.

34. Lefer AM, Cowgill R, Marshall FF, Hall LM, Brand ED: Characterization of a myocardial depressant factor present in hemorrhagic shock. Am J Physio 1967; 213: 492-498.

35. Lefer AM, Blattberg B: Comparison of the effects of two factors present in plasma of shocked animals. J Reticuloendothel Soc 1968; 5: 54-60.

36. Lefer AM, Martin J: Origin of myocardial depressant factor in shock. Am J Physiol 1970; 218: 1423-1427.

37. Rosenthal SR, Hawley PL, Hakim AA: Purified burn toxic factor and its competitin. Surg 1972; 71:, 527-536.

38. Raffa J, Trunkey DD: Myocardial depression in acute thermal injury. J Trauma 1978; 18: 90-93.

39. Goldfarb RD, Weber P, Estes JE: Characterization of circulating shock-induced cardiodepressant substances. Fed Proc 1978; 37: 2724-2728.

40. DeSantis D, Phillips P, Spath MA, Lefer AM: Delayed appearance of a circulating myocardial depressant factor in burn patients. Ann Emerg Med 1981; 10: 22-24.

41. Caridis DT, Reinhold RB, Woodruff PWH, Fine J:

Endoxaemia in man. Lancet 1972; 1: 1381-1385.

42. Hamer-Hodges D, Woodruff P, Cuevas P, Kaufman A, Fine J: Role of the intraintestinal gram-negative bacterial flora in response to major injury. Surg Gynecol, Obstet 1974; 138: 599-603.

43. Cuevas P, Ishiyama M, Koizumi S, Woodruff P, Kaufman A, Fine J: Role of endotoxemia of intestinal origin in early death from large burns. Surg Gynecol, Obstet 1974; 138: 725-730.

44. Little RA, Stoner HB: Studies on the mechanism of shock: Failure to find a role for intestinal bacterial endotoxin in burn shock. Br J Exp Pathol 1972; 53: 381-389.

45. Kremer B, Allgower M, Graf M, Schmidt KH, Schoelmerich J, Schoenenberger GA: The present status of research in burn toxins. Inten Care Med 1981; 7: 77-87.

46. Welt LG, Smith, EKM, Dunn MJ, Czerwinski A, Proctor H, Cole C, Balfer JW, Gitelman HJ: Membrane transport defect: the sick cell. Trans Assoc Am Physicians 1967; 80: 217-226.

47. Rosenthal SM, Tabor H: Electrolyte changes and chemotherapy in experimental burn and tramatic shock and hemorrhage. Arch Surg 1945; 51: 244-252.

48. Cunnigham JN Jr, Shires GT, Wagner Y: Cellular transport defects in hemorrhagic shock. Surg 1971; 70: 215-222.

49. Cunningham JN, Carter NW, Rector FC Jr, Seldin DW: Resting transmembrane potential difference of skeletal muscle in normal subjects and severely ill patients. J Clin Invest 1971; 50: 49-59.

50. Shires GT, Cunningham JN, Baker CRF, Reeder SF, Illner H, Wagner IY, Maher J: Alterations in cellular membrane function during hemorrhagic shock in primates. Ann Surg 1972; 176: 288-295.

51. Trunkey DD, Illner H, Wagner IY, Shires GT: The effect of hemorrhagic shock on intracellular muscle action potentials in the primate. Surg 1973; 74: 241-250.

52. Trunkey DD, Illner H, Arango, A, Holiday R, Shires GT: Changes in cell membrane function following shock and cross-perfusion. Surg Forum 1974; 1: 1-3.

53. Cunningham JN, Shires GT, Wagner Y: Changes in intracellular sodium and potassium content of red blood cells in trauma and shock. Am J Surg 1971; 122: 650-654.

54. Sayeed MM, Adler RJ, Chaudry IH, Baue AE: Effect of hemorrhagic shock on hepatic transmembrane potentials and intracellular electrolytes, in vivo. Am J Physiol 1981; 240: R211-R219.

55. Turinsky J, Gonnerman WA, Loose LD: Impaired mineral metabolism in postburn muscle. J Trauma 1981; 21: 417-423.

56. Deets DK, Glaviano VV: Plasma and cardiac lactic dehydrogenase activity in burn shock. Proc Soc Exp Biol Med 1973; 142: 412-416.

57. Okamoto R, Glaviano VV, Pindok M: Myocardial lipases and catecholamines in burn shock. Proc Soc Exp Biol Med 1971; 137: 347-353.

58. Wilmore DW, Long JM, Mason AD Jr, Skreen RW, Pruitt BA Jr: Catecholamines: Mediator of the hypermetabolic response to thermal injury. Ann Surg 1974; 180: 653-668.

59. Hauben DJ, LeRoith D, Glick SM, Mahler D. Nonoliguric vasopressin oversecretion in severely burned patients. Isr J Med Sci 1980; 16: 101-105.

60. Wilmore DW, Aulick LH, Mason AD Jr, Pruitt BA Jr: Influence of the burn wound on local and systemic responses to injury. Ann Surg 1977; 186: 444-458.

61. Gump FE, Price JB Jr, Kinney JM: Blood flow and oxygen consumption in patients with severe burns. Surg Gynecol, Obstet 1970; 130: 23-28.

62. Wilmore DW, Goodwin CW, Aulick LH, Powanda MC, Mason AD Jr, Pruitt BA Jr: Effect of injury and infection on visceral metabolism and circulation. Ann Surg 1980; 192: 491-500.

63. Wilmore DW, Orcutt TW, Mason AD, Pruitt BA: Alterations in hypothalamic function following thermal injury. J Trauma 1975; 15: 697-703.

64., Aulick LH, Hander EH, Wilmore DW, Mason AD Jr, Pruitt BA Jr: The relative significance of thermal and metabolic demands on burn hypermetabolism. J Trauma 1979; 19: 559-566.

65. Wolfe RR, Miller HI, Spitzer JJ: Glucose and lactate kinetics in burn shock. Am J Physiol 1977; 232: E415-E418.

66. Wilmore DW, Aulick HL, Goodwin CW: Glucose metabolism following severe injury. Acta Chir Scand 1979; 498: 43-47.

67. McManus WF, Eurenius K, Pruitt BA Jr: Disseminated intravascular coagulation in burned patients. J Trauma 1973; 13: 416-422.

68. Alexander JW, Moncrief JA: Alterations of the immune response following severe thermal injury. Arch Surg, 1966; 93: 75-83.

69. Warden GD, Mason AD Jr, Pruitt BA Jr: Evaluation of leukocyte chemotaxis in vitro in thermally injured patients. J Clin Invest 1974; 54: 1001-1004.

70. Warden GD, Mason AD, Pruitt BA Jr: Suppression of leukocyte chemotaxis in vitro by chemotherapeutic agents used in the management of thermal injuries. Ann Surg 1975; 181: 363-36 .

71. Miller, CL, Baker CC: Changes in lymphocyte activity after thermal injury: The role of suppressor cells. J Clin Invest 1979; 63: 202-210.

72. Ninnemann JL: Immunosupression following thermal injury through a B cell activation of suppressor T cells. J Trauma 1980; 20: 206-213.

73. Ninnemann JL, Fisher JC, Wachtel TL: Thermal injury associated immunosuppression: Occurrence and in vitro blocking effect of convalescent serum. J Immunol 1979; 122: 1736-1741.

74. Rapaport FT, Bachvaroff RJ: Kinetics of humoral responsiveness in severe thermal injury., Ann Surg 1976; 184: 51-59.

75. Edgar MA, Heck E, Okita R, Masters BS, Baxter CR: Defective superoxide production in polymorphonuclear leukocytes from burned patients. Proc Am Burn Assoc, New Orleans, 1979.

76. Heideman M, Kaijser B, Gelin L: Complement activation and hematologic, hemodynamic and respiratory reactions early after soft tissue injury. J Trauma 1978; 18: 696-700.

77. Gelfand JA, Donelan M, Burke JF: Preferential activation and depletion of the alternative complement pathway by burn injury. Ann Surg 1983; 198: 58-62.

78. Alexander JW, McClellan MA, Ogle CK, Ogle JD: Consumptive opsoninopathy: Possible pathogenesis in lethal and opportunistic infections. Ann Surg 1976; 184: 672-678.

79. Bjornson AB, Altemeier WA, Bjornson HS: Changes in humoral components of host defense following burn trauma. Ann Surg 1977; 186: 88-96.

80. Ninnemann, JL: Immunologic defenses against infection: Alterations following thermal injuries. J Burn Care Rehab 1982; 3: 355-398.

81. Markley K, Smallman E, Thornton SW: Protection against burn, tourniquet and endotoxin shock by histamine, 5-hydroxytryptamine and 5-hydroxytryptamine derivatives. Br J Pharmacol 1971; 42: 13-24.

82. Holliman CJ, Meuleman TR, Larsen KR, Port JD, Stanley TH, Pace NL, Warden GD: The effect of ketanserin, a specific serotonin antagonist, on burn shock hemodynamic parameters in a porcine burn model. J Trauma 1983; 23: 867-871.

83. Donati L, Lazzarin A, Signorini M, Candiani P, Klinger M, Moroni M: Preliminary clinical experiences with the use of immunomodulators in burns. J Trauma 1983; 23: 816-831.

84. Ishizawa S, Sakai H, Sarles HE, Larson DL, Daniels JC: Effect of thymosin on T lymphocyte function in patients with acute thermal burns. J Trauma 1978; 18: 48-52.

85. Warden GD: The use of plasma exchange in the management of thermally injured patients. In Ninnemann, JL (ed): Traumatic injury: Infection and other immunologic sequelae. Baltimore, University Park Press, 1983.

86. Stratta RJ, Saffle JR, Holliman CJ, Kravitz M, Ninnemann JL, Warden GD. Thermal injury in an adrenalectomized patient. J Trauma 1983; 23: 934-938.

87. Petroff PA, Hander EW, Mason AD: Ventilatory patterns following burn injury and effect of Sulfamylon. J Trauma 1975; 15: 650-656.

88. Guyton AC: Textbook of medical phsyiology (4th

ed). Philadelphia, W.B. Saunders Company, 1971, p. 477.

89. Moylan JA Jr, Wilmore DW, Mouton DE, Pruitt BA Jr: Early diagnosis of inhalation injury using 133-Xenon lung scan. Ann Surg 1972; 176: 477-484.

90. Moylan JA, Adib K, Birnbaum M: Fiberoptic bronchoscopy following thermal injury. Surg Gynecol, Obstet 1975; 140: 541-543.

91. Moncrief JA, Mason AD: Water vapor loss in the burned patient. Surg Forum 1962; 13: 38-41.

92. Shires GT, Canizaro PC. Fluid, electrolyte and nutritional management of the surgical patient. In Schwartz SI, Lillehei RC, Shires GT, Spencer FC, Storer EH (eds), Principles of surgery (2nd ed.). New York, McGraw-Hill, 1974, pp. 65-96.

93. Moncrief JA: Burns. In Schwartz SI, Lillehei RC, Shires GT, Spencer FC, Storer EH: Principles of surgery (2nd ed.). New York, McGraw-Hill, 1974, pp. 253-274.

94. Harrison HN, Moncrief JA, Duckett JW, Mason AD: The relationship between energy metabolism and water loss from vaporization in severely burned patients. Surg 1964; 56: 203-211.

95. Roe CF, Kinney JM: Water and heat exchange in third-degree burns. Surg 1964; 56: 212-220.

96. Birke G, Liljedahl SO, Olsson KE, Plantin LO: Total exchange and insensible loss of water in severe burns during the first two weeks. Acta Chir Scand (Suppl) 1970; 136: 125-132.

97. Lamke LO, Liljedahl SO: Evaporative water loss from burns, grafts, and donor sites. Scand J Plast Reconstr Surg 1971; 5: 17-22.

98. Lamke LO: Evaporative water loss from burns under different environmental conditions. Scand J Plast Reconstr Surg 1971; 5: 77-81.

99. Zawacki BE, Spitzer KW, Mason AD, Johns LA: Does increased evaporative water loss cause hyper-metabolism in burned patients? Ann Surg 1970; 171: 236-240.

100. Carnes RW, Sollecito WA, Salisbury RE: Evaporative water loss from healed burn wounds. J Burn Care

Rehab 1981; 2: 239-247.

101. Curreri PW, Luterman A, Braun DW, Shires GT: Burn injury: Analysis of survival and hospitalization time for 937 patients. Ann Surg 1980; 192: 472-478.

102. Baxter CR: Guidelines for fluid resuscitation. J Burn Care Rehab 1981; 2: 279-286.

103. Sevitt S: Reflections on mortality and causes of death after injury and burns. Injury 1972; 4: 151-156.

104. Artz CP, Yarbrough DR III: Major body burn. JAMA 1973; 223: 1355-1357.

105. Baxter CR: Fluid resuscitation, burn percentage and physiologic age. J Trauma 1979; 19 (11 Supplement): 864-865.

106. Caldwell FT Jr: Hypertonic vs hypotonic resuscitation. J Trauma 1979; 19 (11 Supplement): 874.

107. Leape LL: Urgency of fluid administration in resuscitation of burn shock. J Surg Res 1971; 11: 513-514.

108. Bull, JP: Current trends in research on burns. Proc R Soc Med 1972; 65: 27-30.

109. Moncrief JA: Burns. New Eng J Med 1973; 288: 444-454.

110. Moylan JA, Mason AD Jr., Rogers PW, Walker HL. Postburn shock: A critical evaluation of resuscitation. J Trauma 1973; 13: 354-358.

111. Pruitt BA: Complications of thermal injury. Clin Plast Surg 1974; 1: 667-691.

112. Baxter CR, Marvin J, Curreri PW: Fluid and electrolyte therapy of burn shock. Heart Lung 1973; 2: 707-713.

113. Rogenes PR, Moylan JA: Restoring fluid balance in the patient with severe burns. Am J Nurs 1976; 76: 1952-1957.

114. Evans EI, Purnell OJ, Robinett PW, Batchelor A, Martin M: Fluid and electrolyte requirements in severe burns. Ann Surg 1952; 135: 804-817.

115. Reiss E, Stirman JA, Artz CP: Fluid and electrolyte balance in burns. JAMA 1953; 152: 1309-1313.

116. Hutcher N, Haynes BW Jr: The Evans formula revisited. J Trauma 1972; 12: 453-458.

117. Reckler JM, Mason AD: A critical evaluation of fluid resuscitation in the burned patient. Ann Surg 1971; 174: 115-118.

118. Baxter CR, Marvin JA, Curreri PW: Early management of thermal burns. Postgrad Med 1974; 55: 131-138.

119. Baxter CR: Problems and complications of burn shock resuscitation. Surg Clin No Am 1978; 58: 1313-1322.

120. Canizaro PC, Prager MD, Shires GT: The infusion of Ringer's lactate solution during shock: Changes in lactate, excess lactate, and pH. Am J Surg 1971; 122: 494-501.

121. Monafo WW, Chuntrasakul C, Ayvazian V: Hypertonic sodium solutions in the treatment of burn shock. Am J Surg 1973; 126: 778-783.

122. Moylan JA, Reckler JM, Mason AD Jr: Resuscitation with hypertonic lactate saline in thermal injury. Am J Surg 1973; 125: 580-584.

123. Shimazaki S: Yoshioka T: Tanaka N, Sugimoto T, Onji Y: Body fluid changes during hypertonic lactated saline solution therapy for burn shock. J Trauma 1977; 17: 38-43.

124. Caldwell FT, Casali RE, Flanigan WJ, Bowser B: What constitutes the proper solution for rescuscitation of the severely burned patient? Am J Surg 1971; 122: 655-661.

125. Fox CL: Hypertonic balanced sodium solution in burn shock. Int Surg 1975; 60: 348-351.

126. Jelenko C III, Williams JB, Wheeler ML, Callaway BD, Fackler VK, Albers CA, Barger AA: Studies in shock and resuscitation, I: Use of a hypertonic, albumin-containing, fluid demand regimen (HALFD) in resuscitation. Crit Care Med 1979; 7: 157-167.

127. Bhantooa D: Fluid replacement with special reference to burned patients. Nurs Times 1977; 73: 337-

338.

128. Muir I: The use of the Mount Vernon formula in the treatment of burn shock. Intensive Care Med 1981; 7: 49-53.

129. Hall KV, Sorensen B: The treatment of burn shock: A comparative controlled trial of treatment by colloid infusion (dextran-saline) and by exclusively electrolyte infusion (Ringer lactate). Scand J Plast Reconstr Surg 1973; 7: 67-73.

130. Linker C: Plasmapheresis in clinical medicine. West J Med 1983; 138: 60-69.

131. Berkman E: Issues in therapeutic apheresis. New Eng J Med 1982; 306: 1418-1420.

132. Taft EG: Therapeutic apheresis. Hum Pathol 1983; 14: 235-240.

133. Silvergleid AJ: Applications and limitations of hemapheresis. Annu Rev Med 1983; 34: 69-89.

134. Werynski A, Malchesky PS, Sueoka A, Asanuma Y, Smith JW, Kayashima K, Herpy E, Sato H, Nose Y: Membrane plasma separation: Toward improved clinical operation. TransAm Soc Art Org 1981; 27: 539-543.

135. Wiltbank TB, Castino F, Grapka BH, Daniels JR, Solomon BA, Friedman LI: Filtration plasmapheresis in vivo. Transfusion 1981; 21: 502-510.

136. Malchesky PS, Wojcicki J., Nose Y: Advances in blood component separation and plasma treatment for therapeutics. J Parenter Sci Technol 1983; 37: 2-4.

137. Kayashima K, Sueoka A, Smith JW, Matsubara S, Abe Y, Ueno M, Shinagawa S, Katsume C, Malchesky PS, Nose Y: Development of new hollow fiber membrane macromolecular filters. TransAm Soc Art Org 1982; 28: 66-69.

138. Gurland HJ: Thoughts and progress. Art Org 1983; 7: 142-143.

139. Jones JV: Plasmapheresis: Current research and success. Heart Lung 1980; 9: 671-674.

140. Feng CS. Therapeutic plasmapheresis: "Blood-letting" makes a return. Postgrad Med 1982; 72: 251-255.

141. Kleit SH: Apheresis. Am J Kidney Dis 1983; 2:

573-575.

142. Wenz B, Barland P: Therapeutic intensive plasmapheresis. Semin Hematol 1981; 18: 147-162.

143. Wood L, Jacobs P, Dubovsky DW, Kernoff LM, Gunston KD, Botha I, Robertson L: The role of continuous-flow blood fraction separators in clinical practice. South Afr Med J 1981; 59: 99-104.

144. Valbonesi M, Garelli S, Mosconi L, Manca F, Cantarella S, Celada F: Patients with high titers of circulating immune complexes are most likely to benefit from plamapheresis treatment. Int J Art Org 1981; 4: 234-236.

145. Blacklock HA, Hill RS, Bridle M, Simpson IJ, Matthews JRD, Woodfield DG: Therapeutic plasmapheresis by continuous flow centrifugation. New Zealand Med J 1980; 92: 145-148.

146. Wenz B, Rubinstein A: Partial immunologic reconstitution of a patient with acquired agammaglobulinemia: A transient phenomenon accompanying therapeutic plasmapheresis. Blood 1982; 59: 233-235.

147. Robinson EAE, Tovey LAD: Intensive plasma exchange in the management of severe Rh disease. Br J Haematol 1980; 45: 621-631.

148. Ginder PA, Middendorf DF, Abdou, NI: Plasmapheresis: A therapeutic option for treatment of selected patients. J Kansas Med Soc 1982; 83: 140-142.

149. Fujita Y, Ohiwa T, Kubota Y, Shimizu H, Yoshida S, Hosoya R, Nishimura K: Clinical trial of plasmapheresis in hepatic failure. TransAm Soc Art Intern Org 1982; 28: 225-228.

150. Kayashima K, Smith JW, Barna R, Matsubara S, Abe Y, Ueno M, Katsume C, Valenzuela R, Clough JD, Malchesky PS, Nose Y: Improved white blood cell functions: Additional effects of membrane plasmapheresis. TransAm Soc Art Intern Org 1982; 28: 312-317.

151. Smith JW, Matsubara S, Horiuchi T, Kayashima K, Shinagawa S, Malchesky PS, Nose Y: Sorption-filtration therapy for chronic liver disease: in vitro testing and clinical correlation. TransAm Soc Art Intern Org, 1982; 28: 215-217.

152. Evans DTP, Giles M, DeL. Horne DJ, d'Apice AJF,

Riglar A, Toh BH: Cerebral lupus erythematosus responding to plasmapharesis and platelet pheresis. Postgrad Med J 1981; 57: 247-251.

153. Huestis DW: Mortality in therapeutic haemapharesis (letter). Lancet 1983; 1: 1043.

154. McLeod BC: Immunologic factors in reactions to blood transfusions. Heart Lung 1980; 9: 675-681.

155. Watson DK, Penny AF, Marshall RW, Robinson EAE: Citrate induced hypocalcaemia during cell separation. Br J Haematol 1980; 44: 503-507.

156. Morse EE, Hohnadel DC, Genco, P, Katz AJ: Decreased ionized calcium during therapeutic plasma exchange pharesis. Johns Hopkins Med J 1980; 146: 260-263.

157. Crismon CH: Plasmapheresis. Dimens Crit Care Nurs 1984; 3: 17-23.

158. Cona JA: Establishing a therapeutic pheresis program. Art Org 1981; 5: 229-233.

159. Warden GD, Stratta RJ, Saffle JR, Kravitz M, Ninnemann JL: Plasma exchange in patients failing to resuscitate from burn shock. J Trauma 1983; 23: 945-951.

160. Warden GD, Saffle JR, Kravitz M: A two-stage technique for excision and grafting of burn wounds. J Trauma 1982; 22: 98-103.

161. Warden GD, Wilmore DW, Rogees, PW, Mason AD, Pruitt BA: Hypernatremic state in hypermetabolic burn patients. Arch Surg 1973; 106: 420-427.

162. DuBois D, DuBois EF: A formula to estimate the approximate surface area if height and weight be known. Arch Int Med 1916; 17: 863-871.

163. Lund CC, Browder NC: The estimation of areas of burns. Surg Gynecol, Obstetr 1944; 79: 352-358.

164. Elster SE: Burn client (Chap 13). In Lewis SM, Collier IC (eds), Medical-surgical nursing: Assessment and management of clinical problems. New York, McGraw-Hill Book Company, 1983, pp. 269-292.