A COMPARISON OF NORMAL SALINE AND LACTATED RINGER'S IV SOLUTION IN THE TREATMENT OF SHOCK

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# TABLE OF CONTENTS

Abstract ..................................................................................................................................6  
Chapter 1  
   Introduction ...................................................................................................................7  
   Significance of Fluid Resuscitation ..............................................................................11  
   Problem Statement ........................................................................................................12  
   Project Purpose .............................................................................................................13  
Chapter 2  
   Fluid Composition and Distribution .............................................................................15  
   Body Fluid Distribution ................................................................................................15  
   Composition of Normal Saline .....................................................................................16  
   Composition of Lactated Ringer’s ...............................................................................18  
   Chapter Summary .........................................................................................................20  
Chapter 3  
   Overview of the Physiology of Shock ..........................................................................22  
   Categories of Shock ......................................................................................................25  
   Chapter Summary .........................................................................................................27  
Chapter 4  
   Considerations for Resuscitation ..................................................................................29  
   Chapter Summary .........................................................................................................36  
Chapter 5  
   Implications for Practice ...............................................................................................38  
   Chapter Summary .........................................................................................................40  
Chapter 6  
   Summary .......................................................................................................................42  
   Considerations for future work .....................................................................................45  
   Chapter Summary .........................................................................................................46  
References ..............................................................................................................................50
LIST OF TABLES

Table 1, Electrolyte composition for each fluid compartment .............................................48

Table 2, Comparison of hematologic parameters between animals receiving either normal saline or lactated Ringer’s for hypovolemic shock................................................................49
ABSTRACT

In most cases of shock reducing morbidity and mortality depends on adequate, appropriate, and timely fluid resuscitation. To develop an effective resuscitation plan the Acute Care Nurse Practitioner (ACNP) must consider several important factors.

Currently a wide variety of literature exists on the treatment of patients in need of fluid resuscitation due to shock; however there is limited agreement on a fluid or combination of fluids that provide the most benefit. The purpose of this project is to review the resuscitation literature related to the use of normal saline and lactated Ringer’s for shock resuscitation. The review examines the literature concerning the effect of these fluids on metabolic pH, coagulation factors, the inflammatory cascade, and cellular apoptosis.

Data show that large volumes of normal saline does cause a metabolic acidosis and dilutes circulating clotting factors, however this appears to be transitory. Lactated Ringer’s does not cause a metabolic acidosis, but more fluid is required for resuscitation from massive hemorrhage and it increases the rate of cellular apoptosis. Both fluids cause an increase in adhesion properties (CD18), an indication of inflammatory response.

Currently there is no ideal resuscitation fluid and consideration should be given to including both fluids for large volume resuscitation. A combination mitigates the potential consequences that occur with one fluid alone. It is important for the ACNP utilize the current literature to design a resuscitation strategy that meets the needs of the patient but minimizes the long term complications.
CHAPTER 1

Introduction

In most cases of shock altering morbidity and mortality depends on adequate, appropriate, and timely fluid resuscitation. (Committee on Trauma, 1997; Schierhout & Roberts, 1998; Jordan, 2000; Trunkey, 2001; EAST, 2003) However shock resuscitation is much more than administration of large volumes of fluid, restoration of blood pressure, and circulating volume. (EAST, 2003) Appropriate shock resuscitation involves an appreciation for the quantity of fluid that might be required and an understanding of the effect fluid volume and type will have on blood chemistry, metabolic pH, coagulation parameters, and platelet and cellular response. (Rhee et al., 2000; Tremblay, Rizoli, & Brenneman, 2001; Kellum, 2002; Kaplan et al., 2006) However limited human subject research exists on the effect that these physiologic changes have on morbidity or mortality. (Waters et al., 2001) It is valuable to understand the effects and interactions of these parameters if the Acute Care Nurse Practitioner (ACNP) is going to develop an individualized resuscitation strategy that will optimize patient survival. The role of the ACNP is expanding, providing care in emergency departments, intensive care units, and on hospitalist services. With these increasing responsibilities and the ability to impact more patients it is important to develop an appreciation for the evidence that supports critical decisions like fluid resuscitation.

There are three main categories of fluid that are used to help restore and maintain body systems during shock resuscitation. These include blood and blood products,
colloidal fluids, and crystalloid solutions. (Jordan, 2000; Tremblay et al., 2001; Kellum, 2002; Cook, 2003; F.A. Moore, McKinley, & Moore, 2004; Thompson, 2005)

Blood and blood products are the primary category of resuscitation fluids. In cases of severe hemorrhagic shock (hemoglobin [Hb] < 10g/dL or hematocrit [Hct] < 30%) the use of blood in conjunction with an isotonic volume expander is highly recommended. (Jordan, 2000; Tremblay et al., 2001; Messina, 2006; Moore et al., 2006) In these patients not only has circulatory volume declined but the oxygen carrying capacity of the blood has also been seriously depleted. The addition of blood, typically packed red blood cells, to the resuscitation regime is necessary in order to restore oxygen carrying capacity, thereby increasing the amount of oxygen available to the cells, and mitigating some of the hypoxic effects of shock. (Committee on Trauma, 1997; Messina, 2006) A similar logic applies to the use of blood in the resuscitation of the septic patient. (J.L. Vincent, 2003; J.L. Vincent & Gerlach, 2004) While the evidence supporting the widespread use of blood in the resuscitation of septic patients is considered uncertain, monitoring oxygen consumption and oxygen delivery values can assist the ACNP in targeting blood use in this specific patient population. (J.L. Vincent & Gerlach, 2004) However the use of blood, in either hemorrhagic or septic shock, can risk exposing the patient to an infection, trigger an unwanted allergic or hemolytic reaction, or significantly alter coagulation parameters. (Tremblay et al., 2001) Infusion of large quantities of blood can increase mortality or result in serious complications, such as disseminated intravascular coagulation (DIC), acute respiratory distress syndrome.
(ARDS), or systemic inflammatory response syndrome (SIRS). (Linker, 2006; Moore et al., 2006)

In some cases of hemorrhagic shock it may be necessary to administer other blood products, such as fresh frozen plasma. In these cases the supplemental blood products are used as a means of controlling coagulopathies that may result from the traumatic insult, environmental conditions, or the infusion of large volumes of crystalloids or blood which can either dilute or alter existing clotting factors. (Neff, 1993; Committee on Trauma, 1997; Tremblay et al., 2001)

Colloidal solutions are another major category of resuscitation fluids. Colloids are large molecular weight products whose solutes remain in the vascular space for 3-6 hours after infusion. (Levine & Braun, 2006) Over the past few years colloids have received attention as a possible replacement for crystalloid solutions in shock resuscitation. (Jordan, 2000; Kellum, 2002; Rizoli, 2003; Jacob et al., 2006) This increased attention is due primarily to their ability to remain in the vasculature therefore requiring smaller aliquots to increase overall circulating volume. Colloids also create an increase in intravascular oncotic pressure which can result in a migration of interstitial fluid into the vascular space. (Tremblay et al., 2001; Cook, 2003) This can have the effect of reducing edema and may be considered beneficial for patients in whom resuscitation with large volumes may prove detrimental, for example the head injured patient. Overall, however, colloids are a costly alternative to crystalloids. The cost of colloids is estimated at approximately $90 per unit while crystalloids are approximately $3 per liter. (Bisonni, Holtgrave, Lawler, & Marley, 1991; Schierhout & Roberts, 1998) The cost factor is cited
by several authors as being one reason that colloids have not reached the same level of support as crystalloids for large volume fluid resuscitation. (Jordan, 2000; Tremblay et al., 2001; Levine & Braun, 2006)

Since the late 1800’s crystalloids have been the fluid of choice for volume expansion. Physicians and scientists of that era stressed that adequate rehydration with fluid similar to body composition was essential to the survival of children with severe diarrhea. (Trunkey, 2001) Restoration of circulatory volume with isotonic crystalloid solutions became the mainstay of shock resuscitation during the late 1960s. (F.A. Moore et al., 2004) This rise in popularity is due, in large part, to improved resuscitation of wounded soldiers in Vietnam and the introduction of prehospital care in the United States. In both environments it was important to have universal intravenous (IV) fluids that required no special storage, had an extended shelf life, and could be rapidly administered. (Greaves, Porter, & Revell, 2002)

Crystalloids are sodium based IV solutions which contain the same electrolytes as those found in plasma, although not in the same concentrations. (Jordan, 2000; Kellum, 2002; Cook, 2003) Because crystalloids have an osmolality similar to that of intravascular fluids they can be rapidly administered to a patient in any type of shock with few contraindications. (Jordan, 2000; Greaves et al., 2002; Cook, 2003) Unlike colloids, crystalloids readily cross out of the intravascular space replenishing important interstitial fluids. In shock, interstitial fluid moves into the intracellular and intravascular spaces, depleting the fluid found in the interstitial space. Therefore, the ability of
crystalloids to migrate into interstitial space is an important component of adequate fluid resuscitation. (F.A. Moore et al., 2004; Moore et al., 2006)

The side effects of crystalloid migration from the vasculature must also be underscored. The primary side effect of this fluid migration is increased interstitial volume which is manifested as tissue edema. Excessive tissue edema can give rise to serious complications such as decreased cardiac function, secondary abdominal compartment syndrome, and increased gastric mucosal permeability. (Balogh et al., 2002; Jacob et al., 2006)

**Significance of Fluid Resuscitation**

It is valuable to understand the effect of fluid choice on stabilization of the shock state as well as the potential complications that may arise. Most advances in fluid resuscitation have been made during armed conflicts, beginning with the delivery of colloids and blood for resuscitation of injured soldiers in World War II and the Korean conflict. (F.A. Moore et al., 2004) While the rate of survival from battlefield wounds increased, the number of late deaths also dramatically increased due to acute renal failure from delivery of colloidal solutions which focused on intravascular repletion. It was during the Vietnam War that it was first realized that adequate resuscitation should include increasing both intravascular and extravascular fluid volumes. Initial resuscitation with massive volumes of crystalloids did replenish intracellular and extravascular fluid subsequently decreasing the mortality rate and the incidence of acute renal failure in this setting. However a new problem began to emerge as a late
consequence of large resuscitation with crystalloids, acute respiratory distress syndrome or ARDS.

Since the 1970s and 1980s it has become well understood that ARDS is just one of several complications that can occur with serious illness, significant trauma, or as a result of aggressive fluid resuscitation. Other consequences include systemic inflammatory response syndrome (SIRS), multiple organ failure (MODS), abdominal compartment syndrome, and death. (Shires et al., 2005) Many of these complications are believed to be triggered by inflammatory mediators that result from cellular damage and/or death, type of resuscitation fluid, or rate of fluid infusions. (Rhee et al., 2000; F.A. Moore et al., 2004)

Problem Statement

Currently a wide variety of literature exists on the treatment of patients in need of fluid resuscitation as a result of shock. (Committee on Trauma, 1997; Weil, 1999; J. Boldt, Haisch, Suttner, Kumle, & Schellhase, 2002; P. Rhee, Koustova, & Alam, 2003; EAST, 2003; Savage, Fitzpatrick, Kashyap, Clouse, & Kerby, 2005; Thompson, 2005; Kiraly et al., 2006; Jacob et al., 2006; Levine & Braun, 2006) This literature encompasses all of shock the shock states, ranging from traumatic hypovolemic shock to cardiogenic shock from right sided heart failure to septic shock from an overwhelming infection. Despite this wide variety limited agreement exists within the literature on the best fluid or fluid combinations, administration rates, or endpoints of shock resuscitation. (Rizoli, 2003; Hoyt, 2003; J. Boldt, 2003; F.A. Moore et al., 2004; Knotzer et al., 2006) Without adequate guidelines or consistent standards the patient is placed at risk of too
much, too little, or inappropriate fluid to meet their metabolic demands. Since
crystalloids are the initial fluid used in all types of shock resuscitation it is valuable to
have an understanding of the effects of crystalloids on patient response to treatment.
Normal saline and lactated Ringer’s are the two most commonly used crystalloid fluids
for shock resuscitation and neither is a physiological match for body fluid. In keeping
with an evidence based approach to patient care it is important to understand the effect
that each has on electrolyte derangement, metabolic pH, intravascular osmolarity, clotting
factors, the role each fluid plays in the stimulation of the inflammatory response and cellular death.

Acute Care Nurse Practitioners (ACNP) are specialized advanced practice nurses
whose background and training prepares them for roles as primary providers in hospital
settings, such as emergency departments or intensive care units. As more and more
ACNPs accept primary responsibility for initial patient management, especially of the
critically ill patient, it will be important to make evidence based treatment choices, be it
research or expert consensus, that maximizes patient outcomes and minimize complications. (Mckay, 2006; Galicyznski, 2006) However the lack of consensus
guidelines regarding infusion rate, fluid type, or the acceptable amount of metabolic
derangement produced by fluid resuscitation complicates the interventions that an ACNP
makes when caring for critically ill patients who require fluid resuscitation.

Project Purpose

The purpose of this project is to review the resuscitation literature related to the
use of the normal saline and lactated Ringer’s in the treatment of shock. Three main
types of shock will be discussed but the emphasis will be on the effects and outcomes of resuscitation from traumatic hypovolemic shock. This review will present information on the components of normal saline and lactated Ringer’s solutions, their distribution in the body, and their effect on electrolytes, metabolic pH, coagulation parameters, and the inflammatory response with minimum and maximum resuscitation amounts, and outcomes. Future directions for resuscitation research, geared at the development of resuscitation guidelines, will also be addressed.
CHAPTER 2

Fluid Composition and Distribution

Fluid is distributed throughout the body in three distinct compartments: intracellular, interstitial, and intravascular. Each of these compartments has a unique volume and electrolyte composition that must be appreciated in the development of a resuscitation strategy. Crystalloids can affect the balance of these body fluids in only two of the body fluid compartments, intravascular and interstitial. (Tremblay et al., 2001; Cook, 2003) Intracellular fluid volume is a function of the health of the cells and therefore can only be indirectly affected by fluid infusions. (Shires et al., 2005)

Body Fluid Distribution

The body is composed of nearly 60% water (Cook, 2003; Sherwood, 2004; Levine & Braun, 2006) with two thirds of the fluid volume residing inside the cells and the remaining one third in the extracellular compartment which includes the interstitial and intravascular space. Three-quarters of this extracellular fluid volume is in the interstitial space and the remaining one-quarter is in the vasculature. (Tremblay et al., 2001; Cook, 2003; Levine & Braun, 2006) For example, using this distribution one liter of body water would be disseminated with 667 ml intracellular, 250 ml interstitial and 83 ml intravascular. (Cook, 2003)

Each of these compartments consists of both fluid and electrolytes in various concentrations. (Table 1) To maintain the correct distribution of fluid the osmotic pressure or tension between compartments must remain nearly equal. Osmotic pressure is the result of the attraction each of these electrolytes has for fluid. While the number of
Electrolytes in each fluid compartment is not the same, 400 intracellular and 308 extracellular, the osmotic pressure exerted by the electrolyte combinations is nearly equal with serum osmolality being maintained somewhere between 280-300 mOsm/L. (Cook, 2003)

Either through fluid losses or gains the concentration of electrolytes in these physiologic compartments can be altered resulting in a change in the corresponding osmotic pressure which will cause fluid to shift from one compartment to another. Based on the principle of homeostasis a migration of fluids will occur from an area of lower osmotic pressure to one of higher osmotic pressure in an attempt to return the system to its balanced state. (Sherwood, 2004) To prevent this change in osmotic pressure from occurring with fluid administration it is important to use an isotonic solution, like normal saline or lactated Ringer’s solutions. While these fluids will move freely from intravascular to interstitial space, the resulting change in electrolyte concentrations and corresponding osmotic pressure will be minimal due in part to their intrinsic electrolyte concentrations. (Jordan, 2000)

**Composition of Normal Saline**

Normal saline is one of the two crystalloid solutions commonly used for fluid resuscitation. Normal saline is considered an isotonic solution because it has an osmotic pressure of 308 mOsm/L which is similar to that found in intravascular and interstitial fluid. This similarity in osmotic pressure reduces the likelihood of a rapid shift in fluid following a large infusion. (Cook, 2003; Ho, Karmakar, Contardi, Ng, & Hewson, 2001) Normal saline or 0.9% NaCl consists of 154 mmol/L of Na⁺ and 154 mmol/L of Cl⁻. (Ho
et al., 2001; Freeman & Natanson, 2005) Although the osmolality of normal saline is
not exactly the same as serum, this small difference will not cause a fluid shift. The
process of osmosis requires there be a 10% difference between fluid compartments before
a fluid shift will occur. (Cook, 2003)

While normal saline is isotonic and does not create an imbalance in body fluid or
electrolytes, there are some limitations. Normal saline has slightly higher amounts of
sodium and chloride than body fluid and aggressive fluid resuscitation can result in
large amounts of non-buffered solution are added to the vasculature dilution of
circulating bicarbonate occurs which lowers pH, creating a metabolic acidosis. The
severity of the acidosis is proportional to the volume of normal saline that is infused. In a
study of 66 patients undergoing abdominal aortic aneurysm repair metabolic pH was
found to drop from 7.43 to 7.35 in 33 patients who received an average of 7 liters of
normal saline during surgery. The authors point out that this metabolic acidosis was
transient, with pH normalizing soon after resumption of routine crystalloid infusion.
(Waters et al., 2001)

Normal saline distributes though the body in a fashion similar to body fluids, 75%
interstitially and 25% intravascularly. Since only 25% of the infused volume remains in
the vascular space large volumes may be required to raise and maintain adequate
circulating volume and blood pressure. It is important to point out that aggressive fluid
therapy can result in tissue edema which, in turn, can impair cardiovascular function,
increase the opportunity for bacterial translocation in the gut due to increased intestinal
permeability, and potentiate secondary abdominal compartment syndrome. These complications are more prevalent when patients are resuscitated to hemodynamic values at the high end of normal. Values in this range include pulmonary capillary wedge pressures (PCWP) greater than 15 mmHg, oxygen delivery at a tidal volume greater than 600mL/min, or more than 3 mL of crystalloid are infused for every mL of blood loss.(Balogh et al., 2002; Savage et al., 2005) It should also be mentioned that aggressive fluid therapy increases the likelihood of ARDS, MODS, and SIRS.

Composition of Lactated Ringer’s

The other commonly used crystalloid solution for fluid resuscitation is lactated Ringer’s. Sidney Ringer, studying the properties of various physiologic fluids in the mid-1800s, felt that potassium was necessary for any fluid that would be used to treat significant fluid losses and subsequently developed Ringer’s solution from a normal saline base. In 1910 after numerous studies on children with severe diarrhea it was determined that not only was there a significant electrolyte loss but there was also a loss of bicarbonate. Based on this research Alexis Hartmann added sodium lactate, a natural precursor to bicarbonate, to Ringer’s formula and today we know it as lactated Ringer’s solution.(Trunkey, 2001)

Lactated Ringer’s consists of 130 mmol/L of Na⁺, 4 mmol/L of K⁺, 3 mmol/L of Ca²⁺, and 109 mmol of Cl⁻. (Ho et al., 2001; Freeman & Natanson, 2005) The lactate in the solution is metabolized in the liver by two routes, gluconeogenesis and oxidation. Both of these processes remove a hydrogen atom from the lactate molecule, leaving an OH⁻ free to combine with circulating CO₂ to form bicarbonate, HCO₃. In a normally
functioning liver, one liter of lactated Ringer’s can produce approximately 29 mmol of bicarbonate. (Ho et al., 2001) Consideration should be given to avoiding the use of lactated Ringer’s in diabetic patient’s who are taking the medication metformin. Metformin alters the ability of the liver to metabolize lactate, resulting in a metabolic alkalosis. (James, 2006) In an evaluation of pH change with lactated Ringer’s infusion, Water’s and colleagues studied patients undergoing abdominal aortic aneurysm repair. The study found that the pH change after receiving an average of 7 liters of lactated Ringer’s was very minimal, from 7.42 to 7.40. (Waters et al., 2001) The minimal change in metabolic pH with large infusions is what makes lactated Ringer’s the fluid of choice for resuscitation of the hypovolemic trauma patient. (Committee on Trauma, 1997; Trunkey, 2001)

There are limitations when considering the use of lactated Ringer’s for fluid resuscitation. As with normal saline, only 25% of infused volume will remain in the intravascular space, necessitating large volumes to maintain adequate blood pressure and perfusion to the cells. Lactated Ringer’s also has an osmolality slightly lower than body fluid. (Cook, 2003) When delivered as maintenance therapy the difference in osmolality is less than the 10% necessary for osmosis. However, it has been shown that large volumes of lactated Ringer’s can reduce serum osmolality enough to potentiate cerebral edema in the head injured patient. (Thompson, 2005) Utilizing a rabbit shock model, Tommasino and colleagues found that resuscitation with lactated Ringer’s restored the blood pressure, central venous pressure, and osmolality much like the comparison fluids in the study. However unlike the comparison fluids the intracranial pressure increased
from 1.1 mmHg to 5.2 mmHg in the hour following resuscitation in the lactated Ringer’s group. (Tommasino, Moore, & Todd, 1988) The conclusion by the authors is that even a small change to the osmolality of the blood appears to cause significant changes in intracranial fluid volumes resulting in increased intracranial pressure.

Chapter Summary

The body is composed of 60% water, distributed in three main compartments – intracellular, interstitial, and intravascular. These fluid compartments contain a mixture of electrolytes that, en masse, exert an osmotic pressure that maintains fluid balance. Fluid loss, from vomiting, diarrhea, insensible loss, bleeding or the shifting of fluid into the interstitial spaces as a result of acute or chronic disease alters the electrolyte balance resulting in changes in osmotic pressure. Depending on extent of the electrolyte change, fluid may shift between compartments to maintain homeostasis. Despite the reason for the loss a shift in fluid balance will occur with as little as a 10% difference in osmotic pressure between fluid compartments. To prevent unexpected or unwanted fluid shifts the choice of fluid for replacement in the hypovolemic patient should reflect, as closely as possible, normal electrolyte balance.

Normal saline and lactated Ringer’s are considered isotonic solutions, with osmotic pressures similar to that found in the body. However the varying amounts of electrolytes in these fluids have the capacity to change body pH and create significant tissue edema following large infusions. Normal saline contributes to a metabolic acidosis when given in large quantities, but studies have demonstrated that this is transient when infusion rates are slowed. While lactated Ringer’s does not contribute to metabolic
acidosis, large quantities delivered to head injured patients has been shown to increase cerebral edema. It is important to understand that neither fluid is innocuous and must be administered judiciously.
CHAPTER 3

Overview of the Pathophysiology of Shock

Shock occurs when the rate of arterial blood flow can no longer meet the metabolic demands of body tissues. (Sherwood, 2004; Messina, 2006) Shock is considered the conclusion of a cascade of events which may have any of a variety of onsets, but ends with decreased cellular perfusion, anaerobic metabolism, and cellular death. (Sherwood, 2004; Mitchell, 2005) The severity of the disease is defined, primarily, as it relates to the degree and pathology of the shock state. There are several pathologies that can lead to shock, including hypovolemia, heart failure, and a loss of vascular integrity. However despite the onset, the final phase in each is generalized hypotension, which is followed by decreased tissue perfusion, changes in cellular metabolism, and cell death. (Sherwood, 2004; Mitchell, 2005) Early in the process the tissue hypoxia is reversible with adequate fluid resuscitation. However the longer the shock state persists the higher the rate of cell death, the greater the number of long term complications and the higher the likelihood of mortality. (Erstad, 2005) The long term complications associated with shock can include SIRS, MODS, and ARDS.

Shock can be divided into three subjective phases or stages. It begins with the compensatory phase, which if left untreated or unrecognized moves to the progressive stage, then can continue to the irreversible phase. (Mitchell, 2005) The compensatory phase is initiated when the blood pressure begins to decline. This initial change in blood pressure, which for most individuals can occur with as little as a 10% change in circulating fluid volume, triggers a cascade of neuronal and hormonal mechanisms
designed to maintain the proper functioning of vital organs. This decline in blood pressure can be the result of fluid loss as occurs with hemorrhage, pooling as occurs with loss of vascular tone, or sequestration. Independent of the initial causative event the change in blood pressure results in a drop in cardiac output. The change in blood pressure stimulates the baroreceptor reflex to increase sympathetic activity, triggering an increase in heart rate. (Sherwood, 2004; James, 2006) This heart rate increase is a physiologic response designed to maintain cardiac output despite a decreased circulating blood volume. The increased heart rate is typically the first change that is noted in a patient’s condition.

The increased sympathetic activity also results in constriction of the peripheral circulation, a mechanism designed to improve venous return to the heart thereby preserving blood flow to the brain and other vital organs. In addition to increasing heart rate the sympathetic stimulation also increases myocardial contractility. The improved contractility, when combined with the increases in heart rate and venous return, enhance cardiac output thereby improving tissue perfusion which is manifested by an increase in blood pressure.

Depending on the extent of the initial hypotension, a fluid shift may also occur in the capillary beds. When arterial pressure changes extend into the capillary system, interstitial fluid moves into the vasculature in a process called autotransfusion. This fluid shift is aided by the synthesis and release of albumin and C-reactive protein by the liver. These plasma proteins increase osmotic pressure in the vasculature creating an influx of fluid from the interstitial space. (Sherwood, 2004)
The decreased circulating volume and hypotension also trigger sodium and water conservation by the kidneys through decreased urinary output. The increase in sympathetic tone causes constriction of the renal arteries which reduces blood flow to the kidneys, thus decreasing filtration and reducing output. This low flow state causes the kidney to release vasopressin, a potent vasoconstrictor, and activates the renin-angiotensin-aldosterone hormone pathway which results in further decrease of blood flow to the kidneys as well as generalized vasoconstriction. All of these actions are focused on improving systemic blood pressure, blood flow, and maintaining tissue perfusion. (Sherwood, 2004; Mitchell, 2005)

If the underlying cause is unrecognized or untreated the compensatory mechanisms will ultimately begin to fail and the shock state will move to the progressive stage. No longer are the reflex mechanisms, including increased sympathetic tone, able to maintain cardiac output, resulting in various levels of tissue hypoxia. It is in this stage that the cells begin to change from aerobic to anaerobic metabolism, resulting in a significant loss in the amount of energy available to maintain cellular activity. In aerobic conditions the cells generate 36 mols of adenosine triphosphate (ATP) for every glucose molecule that is processed, but in anaerobic conditions the amount of energy derived from each glucose molecule drops to 2 mols of ATP. (Sherwood, 2004) In the anaerobic state the degradation of glucose cannot proceed further than glycolysis due to a lack of oxygen. Without oxygen pyruvic acid, the byproduct of glycolysis, is converted to lactic acid for disposal from the cell. Releasing the lactic acid into the vasculature lowers body pH. The increased vasomotor response which had been maintaining the blood pressure
and cardiac output is blunted by the lower body pH, resulting in vasodilation and pooling in the microcirculation. (Mitchell, 2005) At this point, survival is still possible with aggressive fluid resuscitation and management of the underlying disease or traumatic state.

In the last stage, irreversible shock, there is not only widespread tissue hypoxia but also widespread cellular death. At this point nearly all cells are forced to utilize anaerobic metabolism, producing only 2 mols of ATP and disposing of large quantities of lactic acid. Massive cellular death leads to widespread organ failure, including complete renal failure and depressed myocardial function. Most patients in this stage do not survive. Those who do survive have significant long term complications necessitating extensive hospitalization and rehabilitation.

**Categories of Shock**

There are four main categories of shock, hypovolemic, cardiogenic, constrictive, and distributive. (Freeman & Natanson, 2005) Of these only three – hypovolemic, cardiogenic, and distributive shock – produce alterations in actual circulating volume. It is this alteration in circulating volume that results inadequate tissue perfusion, a change in cellular metabolism, and ultimately cellular death.

Hypovolemia is a relative or actual loss of circulating volume, often due to fluid losses to the external environment. (Erstad, 2005) In the case of bleeding the loss is visible and can, to some extent, be quantified to assist in determining the extent of replacement that will be required. However insensible losses due to dehydration, from extended exposure to a hot, dry climate, are more difficult to assess and quantify for
replacement. However, both create a real loss of circulating volume, resulting the signs and symptoms of hypovolemic shock.

In cardiogenic shock the ability of the heart to pump blood has been greatly reduced, which can be the result of a myocardial infarction or cardiac dysrhythmia. Because the cardiac ejection fraction is significantly decreased there is limited forward motion of blood and consequently the pressure in the vascular system is inadequate to maintain perfusion at the cellular level. By increasing the volume available, even low cardiac output conditions can begin to produce adequate circulation and potentially improve the shock condition. Cardiogenic shock presents very similarly to hypovolemic shock, and like hypovolemic shock ultimately results in inadequate tissue perfusion, anaerobic metabolism, and cellular death.

In the case of distributive shock, the loss of circulating volume is not due to the environmental losses or decreased cardiac output but rather to a change in the permeability of blood vessels resulting in a leak of fluid into interstitial spaces. The most common type of distributive shock is septic shock, which affects over 100,000 individuals each year with a mortality rate of 40-80%. (Messina, 2006) The mechanism for vasodilation in septic shock is related to the toxins produced by the invading bacteria not a loss of sympathetic tone as with hypovolemic and cardiogenic shock. These toxins also blunt cardiovascular activity thereby reducing cardiac output. The decreased vascular tone that accompanies distributive shock ultimately results in an inability to provide oxygen and nutrients to the cells, resulting in decreased tissue perfusion, anaerobic metabolism, and cellular death.
Chapter Summary

Shock is defined as decreased perfusion at the cellular level. The causative factor can be generalized into one of three mechanisms, hypovolemia, heart failure, or loss of vascular tone. In the early stages of shock the tissue hypoxia is reversible. However a prolonged state of shock leads to increased cellular death, more long term complications, and a higher mortality.

Shock can be generalized into three subjective stages, compensatory, progressive, and irreversible. Each stage of shock has its own unique set of signs and symptoms, and associated physiologic responses. In the initial stage the body responds by activating various neuronal and hormonal reflexes. The initial reflex is to increase sympathetic stimulation through activation of the baroreceptors, which results in vasoconstriction and an increase in heart rate. The kidneys, stimulated by the low cardiac output and hypotension, retain fluid and sodium and release potent vasoconstrictors in an effort to maintain intravascular volume. As the shock progresses these compensatory mechanisms begin to fail, leaving the body to increase reliance on anaerobic metabolism to maintain cellular activity. Increasing reliance on anaerobic metabolism reduces cellular efficiency and the byproduct of lactic acid lowers body pH which contributes to decreased cardiac output and end organ failure.

There are three major categories of shock which produce an actual reduction in circulating volume. These are hypovolemic, cardiogenic, and distributive shock. Each category of shock is associated with unique signs and symptoms in the compensatory and progressive stages. However, all types of shock ultimately result in a reduction in tissue
perfusion, increased reliance on anaerobic metabolism, and cellular death. Since each of these categories is related to a reduction of circulating volume each is managed with fluid resuscitation.

Overall the ability of the body to compensate and recover from shock is related to the underlying cause of the shock and the underlying health of the patient. For all categories of shock proper fluid resuscitation reduces the progression that leads to inadequate tissue perfusion, alterations in cellular metabolism, and finally cellular death. The ACNP can contribute to the successful outcome from shock with early recognition and early aggressive fluid resuscitation with appropriate fluid and blood products.
CHAPTER 4

Considerations for Resuscitation

The goal of fluid resuscitation in shock is to restore circulating fluid volume to a point that will optimize cardiac output, improve oxygen availability at the cellular level, and thereby preserve function in major organs. (Jordan, 2000; Jacob et al., 2006) However, there are no clear definitions for what constitutes adequate or aggressive fluid resuscitation or guidelines regarding what type of fluid and how quickly it should be delivered. (Revell, Greaves, & Porter, 2003; Holte, Jensen, & Kehlet, 2003; EAST, 2003; Cotton, Guy, Morris, & Abumrad, 2006) The definitions most often utilized for aggressive fluid resuscitation are, at best, situational. Aggressive or large volume resuscitation is defined in the literature as the infusion of as much fluid as required to return the blood pressure to near normal levels in the shortest amount of time.(Soucy et al., 1999; Solomonov, Hirsh, Yahiya, & Krausz, 2000) This lack of uniform definitions or guidelines can make the development of a fluid resuscitation strategy difficult. In addition to fluid type and rate, it is important to also consider the complications of edema, increased intracranial pressure, ARDS, SIRS, and MODS. (Rizoli, 2003; Hoyt, 2003; P. Rhee et al., 2003)

Since there is little agreement in the literature on endpoints many healthcare providers utilize the systolic blood pressure. It is one of the easiest endpoints to monitor for improvement, by providing an indirect, non-invasive measurement of peripheral vascular resistance. However the blood pressure may not be the most reliable indicator of shock resuscitation. (EAST, 2003) It would, however, be sufficient to state that for
most patients an improvement in peripheral vascular resistance is associated
improvement in pressure at the cellular level, enhancing the migration of oxygen and
energy substrates into the cells. However, it is important to underscore the need to
balance improving systolic blood pressure with the possibility that it can worsen
hemorrhage in patients with penetrating wounds and it may result in significant edema in
the septic patient. (Revell et al., 2003; EAST, 2003) To measure adequate fluid
resuscitation, it is important not only to obtain normovolemia but also evaluate metabolic
pH, clotting factors, neutrophil activity, and cellular apoptosis. These endpoints of fluid
resuscitation success are detailed below.

The majority of work in the area of fluid resuscitation has been conducted in
hypovolemic shock as a result of trauma; therefore the results presented here will be most
applicable to the hypovolemic shock state. Here the debate has focused on the metabolic
consequences of fluid resuscitation. Normal saline is considered by the College of
Surgeons Committee on Trauma to be responsible for metabolic acidosis when used in
large quantities for the resuscitation of traumatic hypovolemia. (Committee on Trauma,
1997; EAST, 2003) The metabolic acidosis results from a dilution of serum bicarbonate
by the normal saline without providing an adequate buffer replacement. This ultimately
results in an imbalance in serum chloride levels and a hyperchloremic normal anion gap
metabolic acidosis. (Ho et al., 2001) Metabolic acidosis can depress myocardial
function, decrease the body’s response to inotropic medications and, when combined
with hypothermia, can result in increased morbidity and mortality. (Ho et al., 2001)
Hyperchloremia has also been shown to contribute to renal vasoconstriction, leading to a
decrease in glomerular filtration and potentially contributing to fluid retention. (Thompson, 2005) However, there are no human outcome studies that evaluate the effect of this acidosis on morbidity or mortality. (James, 2006)

The fluid of choice by the College of Surgeons for traumatic hypovolemic shock is lactated Ringer’s. (Committee on Trauma, 1997; Hoyt, 2003; EAST, 2003) This preference for lactated Ringer’s is based on the ability of the body to metabolize the lactate into byproducts that result in an increase of 29 mmol of bicarbonate per liter of solution. (Ho et al., 2001) The replacement of serum bicarbonate through this process buffers in the electrolyte changes that can cause metabolic acidosis thereby making lactated Ringer’s a more commonly used treatment for traumatic hypovolemic shock.

However it should be noted that animal studies have demonstrated an increase in intracranial pressure when lactated Ringer’s is used for hypovolemic shock resuscitation in a non-brain injured model. (Prough et al., 1985; Tommasino et al., 1988) In a 1988 study, Tommasino and colleagues compared the effects of lactated Ringer’s and 6% hetastarch on brain edema, intracranial pressure (ICP), and cerebral blood flow in a hypovolemic rabbit model. The 36 rabbits were divided into three groups with two of the groups receiving an intervention that involved bleeding at a rate of 2 ml/hr with simultaneous infusion of either lactated Ringer’s or hetastarch. This ongoing fluid replacement was designed to maintain a central venous pressure and blood pressure at or near baseline readings in the treatment groups. The control group received lactated Ringer’s at 4 ml/kg/h and no intervention. One hour after initiation of the treatment the lactated Ringer’s group showed a rise in ICP from a baseline of 1.1 mmHg to 5.2 mmHg,
with all other parameters at or near baseline. The osmolality in the lactated Ringer’s
group had only decreased by 4 mOsm. The rise in ICP is not, according to the authors,
based on hemodynamics alone but rather a combination of increased cerebral blood
volume and increased brain water content. The authors conclude that even small
decreases in cerebral plasma osmolarity can result in an increase in the percentage of
fluid and a decrease in specific gravity in the brain. (Prough et al., 1985; Tommasino et
al., 1988) Therefore a patient with a head injury is at increased risk of edema and
worsening patient prognosis when lactated Ringer’s is utilized as the primary
resuscitation fluid. (Thompson, 2005)

In an evaluation of the effect of fluid volume on blood pH, Healey et al compared
normal saline and lactated Ringer’s in the resuscitation of two groups of rats. (Healey et
al., 1998) One group of animals received moderate fluid resuscitation while the other
group received massive fluid resuscitation. Blood was collected at regular intervals
during the study period, and then analyzed for pH, electrolytes, glucose, blood urea
nitrogen (BUN), and creatinine. Data were also recorded on the total volumes of isotonic
crystalloid or isotonic crystalloid/blood mixture required for resuscitation.

In the group of rats receiving only moderate resuscitation, described as two hours
of stable hypotension followed by resuscitation with crystalloids only, the blood pressure
increased more quickly and fluctuated less with normal saline. (Healey et al., 1998)
These rats also required less resuscitation fluid than those in the lactated Ringer’s group,
402% of lost blood vs. 585% of lost blood, respectively. In the lactated Ringer’s group
the final pH was 7.44 with a serum bicarbonate of 25.2. In the normal saline group the
final pH was 7.39 with a serum bicarbonate of 21.5. The authors found no significant differences between these groups in any of the other measured parameters. All the animals in both groups survived the two week follow on period. In the setting of moderate fluid resuscitation, defined as stabilization achieved with crystalloids alone, these authors found no significant difference in final pH or blood chemistry between normal saline and lactated Ringer’s.

In the same study the authors compared the outcome of massive fluid resuscitation, defined as resuscitation requiring both blood and crystalloids to increase and maintain blood pressure, with either normal saline or lactated Ringer’s and blood. The massive resuscitation model consisted of an initial blood loss to a mean arterial pressure (MAP) of 60 mmHg followed by ongoing blood loss with simultaneous replacement of a crystalloid (lactated Ringer’s or normal saline)/blood mixture for two hours, maintaining the MAP at 60 mmHg. This was followed by termination of blood loss and resuscitation to a MAP of >90 mmHg and monitoring survival for two weeks. (Healey et al., 1998) In this model the authors found that more volume was required in the lactated Ringer’s group to reach a MAP >90 mmHg, 1049% of blood lost vs. 964% blood lost in the normal saline group. The final pH in the normal saline group was 7.14 and serum bicarbonate 9.4, while in the lactated Ringer’s group the pH was 7.39 with a serum bicarbonate of 19.7. In this massive hemorrhagic and resuscitation model, only 50% of the rats in the normal saline group survived the two week monitoring period. Results from this arm of the study showed that in the setting of hemorrhage requiring
massive fluid resuscitation, there is significant acidosis and chemical derangement with normal saline when compared to lactated Ringer’s.

In an effort to understand the effect of crystalloid resuscitation on coagulation factors, Kiraly and associates developed a model of uncontrolled hemorrhage requiring fluid resuscitation. (Kiraly et al., 2006) The authors measured different coagulation parameters in 20 anesthetized swine after liver injury. In this model the animals bleed for 30 minutes following a grade V liver laceration before being randomly assigned to receive either normal saline or lactated Ringer’s. At 30 minute intervals after the liver laceration blood was taken for analysis of serum lactate, hematocrit, electrolytes, partial thromboplastin time (PTT), prothrombin time (PT) and fibrinogen. The authors found that animals resuscitated with normal saline were more acidotic than those resuscitated with lactated Ringer’s, the pH began to demonstrate decline at the first 30 minute mark and remained lower throughout the study period. However, it was not until 60 minutes into the resuscitation that the base excess and bicarbonate levels demonstrated a difference between groups. The results demonstrate that normal saline results in a significant metabolic acidosis.

This same study also involved the evaluation of coagulation parameters. Here the authors found that resuscitation with normal saline resulted in dilution of coagulation factors and a difference in all measured parameters. (Table 2) For example, at 120 minutes post injury both the PTT and PT were significantly lower and fibrinogen levels were significantly higher in the lactated Ringer’s group. Data from this study indicate that
resuscitation with lactated Ringer’s leads to greater hypercoagulability and less blood loss than resuscitation with normal saline in uncontrolled hemorrhagic shock.

In 2000, Rhee and associates evaluated the activity of neutrophils in whole blood drawn from 20 healthy human volunteers when diluted with varying amounts of normal saline, lactated Ringer’s, or colloid solutions. The purpose of this study was to develop an understanding of the effect of fluid infusion on the inflammatory cascade. (Rhee et al., 2000) The authors found that both normal saline and lactated Ringer’s caused an increase in neutrophil activity as well as adhesion properties (CD18), indicating activation of the inflammatory response. The response was dose-related, with increasing volumes of fluid increasing the neutrophil activity. In an attempt to identify the likely cause of the neutrophil response the authors held sodium concentrations constant and measured pH, electrolyte concentrations, and osmolality. They found no difference in the pH, electrolyte concentrations or osmolality that could account for the increased activity. The authors postulated that there may be a safe dose range for crystalloid resuscitation fluids, with large amounts of fluid contributing to an increase in the inflammatory response. (Rhee et al., 2000)

Another consideration when developing a fluid resuscitation strategy is the effect of fluid choice on cell apoptosis. In 2005, Shires and colleagues subjected 80 rats to a hemorrhagic model with an initial MAP of 40 mmHg followed by a 75 minute shock period where the MAP was maintained between 40-60 mmHg, followed by resuscitation with one of six different fluids or no resuscitation. (Shires et al., 2005) The animals received 80ml/kg of fluid during the one hour resuscitation period. Following one hour
of stabilization the liver and lungs were harvested for evaluation of apoptosis. The authors found that the initial hemorrhagic event caused a significant increase in apoptosis when compared to baseline. The results also demonstrated a one-third increase in apoptosis in both the liver and lung in the group resuscitated with lactated Ringer’s when compared to the normal saline group. Although the underlying mechanism was not clear, these authors concluded that aggressive fluid resuscitation had a significant impact on the cells and that lactated Ringer’s may significantly contribute to cellular destruction. (Shires et al., 2005)

Chapter Summary

The goal of fluid resuscitation is to restore adequate circulating volume. The restoration of circulating volume improves peripheral vascular resistance which translates to improvement at the cellular level. However there are limited guidelines regarding what endpoints indicate optimal fluid resuscitation. While monitoring the blood pressure is a good indirect measure in some patients it may not truly reflect increased perfusion at the cellular level. When developing a resuscitation strategy consideration must be given to the effect of resuscitation on intracranial pressure, metabolic pH, clotting factors, neutrophil activity, and cellular apoptosis. It should be noted that the majority of studies in the area of resuscitation have conducted in the animal model. How these results translate to humans is unclear. Therefore the findings discussed here are limited in their application.

Several animal studies have evaluated the effect of normal saline and lactated Ringer’s on metabolic pH. All the studies have demonstrated that normal saline does
result in a metabolic acidosis when delivered at either high volume or fast rate. However, in a study of patients undergoing abdominal aneurysm repair it was found that this metabolic acidosis is transient and the pH returns quickly to normal once fluid volume or rate are slowed. In an evaluation of the effect normal saline and lactated Ringer’s on bleeding times the researchers found that lactated Ringer’s lowered PT and PTT times and it resulted in a significant rise in fibrinogen levels. This is something that needs to be considered in a patient where hypercoagulation might complicate the healing process.

Other studies on lactated Ringer’s and normal saline have demonstrated increased neutrophil activity when increasing amounts of the crystalloids are added to the blood of health volunteers. This data translates to a significant increase in neutrophil activity in patients who have been injured or are in septic shock, increasing the potential for SIRS in these already compromised patients.

The use of crystalloids for fluid resuscitation has been shown to be both beneficial and deleterious in the treatment of hypovolemic shock. However, use of crystalloids is also associated with changes in metabolic pH that can result in blunting of the compensatory mechanisms and increased resuscitation time. Crystalloids are also associated with coagulopathies, neutrophil activation and initiation of the inflammatory cascade, and with increased cellular apoptosis.
CHAPTER 5

Implications for Practice

The role of the ACNP in the healthcare community is evolving. Trained to provide care in the in-patient environment, the ACNP serves as the primary provider of care to patients in areas ranging from the emergency department to the intensive care unit. The ACNP is in a unique position to straddle both the medical and nursing environments, able to impact patient outcomes through direct care as well as through education of families and staff. (Lome, 2005) In many settings the role of the ACNP is to provide a continuity of care that may be currently fragmented by the number and variety of specialists involved in the patient’s care. Inclusion of the advanced practice role in the care continuum often results in an improvement in patient satisfaction and in the quality of patient care. (Lome, 2005; Howie & Erickson, 2002)

The ACNP utilizes diagnostic reasoning in patient care activities that is evidence based. (Shapiro & Rosenberg, 2002) It is important to understand that it is this foundation of evidence based practice that guides the actions of the ACNP. An advanced practice nurse working in the medical environment must be prepared with the most current information to support his/her practice. It is important the physicians view advanced practice nurses as peers and staying current with scientific evidence is one way to solidify that relationship.

It was this innate quality of inquiry lead to the development of this project, a desire to find the evidence to support the use of one crystalloid IV fluid over another. It was the desire to understand under what conditions lactated Ringer’s would be better than
normal saline, or under what conditions the use of normal saline is most desirable. When fluid resuscitation is required it is important for the ACNP to understand the conditions that make one solution a better choice for the patient. In the case of lactated Ringer’s and normal saline the ACNP must consider the possibility of a head injury, an abdominal injury, and the approximate fluid loss that will require replacement. The ACNP should also note the patient’s comorbid conditions that might preclude the use of one fluid. Issues of coagulopathies, underlying metabolic derangement, or state of the shock condition must also be considered. Each of these plays an important role in determining the rate, volume, and type of fluid to be used.

In patients with an obvious or suspected head injury it is important to reduce the use of lactated Ringer’s. Animal studies have demonstrated an increase in cerebral edema when lactated Ringer’s is used in large quantities for resuscitation. (Prough et al., 1985; Tommasino et al., 1988) Abdominal injuries increase the possibility of either an abdominal compartment syndrome or infection from increased permeability in the gut following large infusions of either of the crystalloid solutions. (Balogh et al., 2002; Jacob et al., 2006) Having an appreciation of the amount fluid lost will assist the ACNP in the judicious use of blood products in addition to fluid therapy.

In patients with an underlying metabolic acidosis prior to fluid resuscitation it may be wise to utilize lactated Ringer’s as the primary fluid to avoid worsening of the acidosis that has been shown to occur with large volumes of normal saline. However in studies of patients undergoing cardiothoracic surgery the metabolic acidosis was a short lived phenomenon, which can be rapidly reversed by decreasing the rate of infusion.
(Prough & White, 2000) However, even if the acidosis is short lived and have no significant effect on patient outcome, it may interfere with the diagnostic process and delay the potential diagnosis. (Thompson, 2005)

In patients with an underlying coagulopathy or in whom a hypercoagulable state would be detrimental to outcome it may be advisable to initiate fluid resuscitation with normal saline. As demonstrated by Kiraly et al. normal saline dilutes the coagulation factors and reduces the likelihood of coagulopathies. (Kiraly et al., 2006) Administration of blood products also precludes the use of lactated Ringer’s solution. To avoid coagulation during blood administration the fluid in the tubing must be normal saline.

The ACNP must also evaluate the ramifications of stimulating the inflammatory cascade by delivering crystalloid solution too rapidly. (P. Rhee et al., 2003) Using blood drawn from health human volunteers Rhee and colleagues found a significant dose related response to when either normal saline or lactated Ringer’s was added to the blood. The authors found that both normal saline and lactated Ringer’s caused an increase in neutrophil activity as well as adhesion properties (CD18), indicating activation of the inflammatory response. While this may seem insignificant in some patients it may contribute to worsening of the underlying condition that initiated the shock state.

**Chapter Summary**

Overall the choice of fluid for resuscitation should be based on the best scientific evidence available. To date there have been very few randomized controlled human trials that compare normal saline to lactated Ringer’s in any patient population. (J. Boldt, 2003;
Thompson, 2005) Without human studies it is very difficult to fully appreciate the short and long term consequences of using either fluid for shock resuscitation. The animal studies that are available have demonstrated that both normal saline and lactated Ringer’s IV fluid can cause metabolic derangement when delivered in large quantities or at a rapid rate. How these findings translate to humans is unknown, but equipped with this knowledge the ACNP can make an evidence based decision on fluid resuscitation. Therefore it is imperative that the ACNP remain current with what studies and reviews are available on the topic and establish guidelines for use of appropriate fluid choice in resuscitation based on the best available evidence.
CHAPTER 6

Summary

It would seem from this evaluation of the literature that the delivery of crystalloid fluids for resuscitation in the treatment of shock is not as innocuous as it may seem. As demonstrated by Healy and associates as well as Rhee and associates the volume of crystalloids perhaps more than the type of fluid may play a significant role in determining the overall effect of the resuscitation on the patient. (Healey et al., 1998; P. Rhee et al., 2003) At rates and volumes necessary for treatment in the compensatory and early progressive stages without the addition of blood products, both normal saline and lactated Ringer’s are equivalent with neither producing any lasting untoward effects. Moderate infusions are defined as rates that raise the blood pressure at a slow but steady rate or that raise the systolic blood pressure to nearly 100 mmHg without the addition of blood or blood products. (Soucy et al., 1999; Solomonov et al., 2000) Infusion of normal saline at this rate and in this setting does not produce metabolic acidosis, as has long been considered the case. Neither normal saline nor lactated Ringer’s produces an increase in the inflammatory response when delivered at controlled rates early in the shock cycle. (Rhee et al., 2003; Cottom et al., 2006)

However, research has demonstrated that when patients require massive and rapid fluid resuscitation, volumes and rates designed to increase the blood pressure quickly and usually requiring the consideration of blood or blood products, a difference between normal saline and lactated Ringer’s becomes more evident. (Healey et al., 1998; Shires et al., 2005; Thompson, 2005) When large amounts of normal saline are administered, a
metabolic acidosis is likely to develop. As a general rule, metabolic acidosis blunts cardiac activity, lessens the effect of inotropic medications, and potentially increases mortality. (Ho et al., 2001) However it is not clear, in either animal or human studies, if the acidosis is actually harmful or a temporary nuisance that resolves when the volume and rate of infusion is decreased. (Prough & White, 2000) There are also no human outcome studies to suggest that this metabolic acidosis will increase morbidity or mortality in any patient population. (James, 2006)

Large volume resuscitation with lactated Ringer’s presents a slightly different problem, it can result in a hypercoagulable state, which can be beneficial in the early care of the trauma patient, but might prove detrimental to patients once they have been stabilized or those with septic shock. Hypercoagulation can contribute to decreased organ perfusion once the patient has been stabilized with damage control surgery by affecting the microcirculation. (Boldt, 2003; Moore et al., 2006) The process of delivering oxygen to the cells takes place in the microcirculation, so any clots or clumping of blood products will reduce the availability of the oxygen at the cellular level which could potentially worsen the shock. Lactated Ringer’s has also been associated with increased intracranial pressure in patients with the potential for a head injury. (Prough et al., 1985; Tommasino et al., 1988) While not well studied, it should be noted that in diabetic patients using metformin the ability of the liver to metabolize the lactate may be altered and the result could be a metabolic alkalosis from large infusions of lactated Ringer’s. (James, 2006)
It would appear that development of a resuscitation strategy must include a great deal of thought. The ACNP must evaluate the potential for the development of significant complications, such as ARDS, SIRS, and MODS, which can occur with either normal saline or lactated Ringer’s when delivered in large quantities or over extended periods of time. As well as the impact these complications will have the patient’s eventual recovery. There must also be an appreciation for the dilutional effect of large quantities of intravenous fluid on clotting factors. Some thought must also be given to the effect of metabolic acidosis or alterations in electrolyte concentrations in the blood. With changes in electrolyte concentrations comes the possibility of changes in serum osmolality and ultimately the shifting of fluid from one compartment to another. The effect of this fluid shift may be minor, an increase in peripheral edema, or significant, increased intracranial pressure or abdominal compartment syndrome.

It appears that either fluid can be safely and effectively utilized when large volumes of crystalloids are necessary. The answer to large volume fluid replacement may be using the fluids in combination thereby reducing the potential side effects of either fluid. Since both result in physiologic changes in the intravascular and interstitial spaces the patient must be carefully monitored during fluid resuscitation. Care should be taken to reduce excessive tissue edema that may result in secondary abdominal compartment syndrome or increase the likelihood of sepsis as a result of increased permeability in the gut. (Moore et al., 2006) It is also important to monitor the onset of respiratory compromise in the face of increasing edema or abdominal compartment
syndrome. Early consideration should be given to the addition of packed red blood cells or platelets to help maintain adequate circulating oxygen capacity and clotting factors.

Considerations for future work

Recent work by Vincent and colleagues has reintroduced the use of fluid boluses as a way of increasing circulating volume. By delivering fluid in this fashion there is more control over volume which could potentially reduce the long term consequences that occur with large volume infusions. (J.L. Vincent & Weil, 2006) In addition to reducing long term sequelae fluid boluses reduce the inflammatory response that can result from large volume or continuous intravenous infusions. Although not yet studied well studied, fluid boluses may also reduce the dilutional effect of fluid infusion on coagulation parameters and electrolytes. Currently bolus therapy is used successfully in mild hypovolemia and in the rehydration of children. Vincent & Weil point out that fluid boluses provide a much more controlled resuscitation effort and allow the body to begin the compensation process. (J.L. Vincent & Weil, 2006) Fluid boluses allow the natural neuronal and hormonal mechanisms of the body the opportunity to continue to contribute to the stabilization of the shock state.

Another consideration for future research is the use of medications early in the treatment of shock. The medications that are being discussed for use in shock include vassopressors for blood pressure support and inotropic drugs to increase the contractility of the heart. (Miller, Meredith, & Chang, 1998; Lim, Lee, & NG, 2000; Sakr et al., 2006) Currently the typical resuscitation of the patient in shock, either hypovolemic or septic shock, is the delivery of large volumes of fluid to obtain and maintain an adequate
systemic pressure. But, as noted earlier, there are multiple short and long term sequelae that can arise from the type of treatment regime. Certainly one way around some of the issues related to large volume therapy is to introduce medications that would support the systemic pressure and reduce the fluid requirement. Cotton et al and Moore et al have demonstrated an improved survival in patients with liver trauma, uncontrolled hemorrhage, traumatic brain injury, and chest trauma with the use of a vasopressor to control hypotension. In an observational study of dopamine administration for systemic pressure support in septic patients, Sakr and associates found that the addition of dopamine did not improve survival in this patient population. (Sakr et al., 2006) These studies evaluated different vasopressors which may account for the different findings.

Similarly, in 1998 Miller and associates evaluated the effect of adding an inotropic agent to the care of hypovolemic trauma patients. (Miller, 1998) The objective of the study was to determine if the inotropic agent would support cardiac function and perfusion as well as fluid resuscitation alone. The study findings indicated that the use of inotropic agents was not as effective as fluid therapy alone in this patient population. This study was not very large which might account for the lack of strong findings. However, in many institutions trauma patients received very little in the way of inotropic medications during resuscitation. This is certainly an area that might well be worth another evaluation.

Chapter Summary

Currently there is no ideal fluid for volume resuscitation in the shock patient. Both lactated Ringer’s and normal saline contribute to complications that may exacerbate
a current condition or increase the potential for long term complications. The prudent ACNP should develop a level of understanding for the risks and benefits of all types of fluids and treatments that are available for the management of the shock patient. While currently the emphasis is on large volume fluid therapy, there are other alternatives that have proven to be effective. Alternatives like bolus therapy or vassopressors to support blood pressure or inotropic medications to improve cardiac function that should be considered during the development of a resuscitation strategy.

The management of the patient in shock is multifactorial. It is imperative that the ACNP utilize evidence based information in the development of an effective fluid strategy. In evaluating the literature it appears that a good fluid resuscitation strategy includes the judicious use of all IV fluids, close monitoring for physiologic changes, adjusting therapies as needed and consider bolus therapy when possible. Clearly there are several avenues for more research, areas that may be well suited to the advanced practice nurse in a research capacity.
Table 1

<table>
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<th>Interstitial</th>
<th>Intravascular</th>
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Electrolyte composition for each fluid compartment (Cook, 2003)
Table 2

<table>
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<th>Measured Parameter</th>
<th>Fluid Type</th>
<th>Results (mean ± SD)</th>
<th>Statistical Significance p value</th>
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<td>Baseline pH</td>
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<td>pH 120 min post injury</td>
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Comparison of hematologic parameters between animals receiving either normal saline or lactated Ringer’s for hypovolemic shock. (Kiraly et al., 2006) (* signifies statistical significance with a p<0.05)
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