

POTASSIUM REPLACEMENT IN OPEN HEART SURGICAL PATIENTS

by

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## ABSTRACT

The purpose of this descriptive study was to determine the temporal pattern of serum potassium fluctuation in open heart surgery patients during the immediate four hour postoperative period.

The subjects were selected as a convenience sample from a group of patients scheduled for open heart surgery. Arterial blood samples were obtained upon the subject's arrival in the Cardiothoracic Unit from the operating room, and every hour thereafter for four hours. Samples were analyzed by flame photometry for potassium concentration. Statistical analysis, using the paired t-test on selected samples, was not significant at the  $p = .05$  level. However, it was difficult to tell if the nonsignificance occurred from an actual lack of difference or from low sample size.

The data showed that the period of greatest decremental fluctuation was between hours one and three, with a leveling off between hours three and four.

An unexpected outcome of the serum collection was an observable change in color from  $T_0$  to  $T_4$ . The initial sample ( $T_0$ ) was darker than the final sample ( $T_4$ ). This might suggest that the initial sample may have been hemolyzed. If this was the situation, higher potassium concentrations may have been measured in vitro (at  $T_0$  particularly) than actually existed in vivo.

The major implication of this study was that postoperative open heart surgery patients may need to be monitored more closely than they presently are with respect to changes in serum potassium levels during the immediate four hours postoperatively.

## CHAPTER 1

### INTRODUCTION

The maintenance of health is dependent on the body's ability to maintain homeostasis, that is, its ability to keep the fluid volume and electrolyte composition within a defined range. The primary fluid in the body is water, and dissolved within this water are solutes, or electrolytes, which affect not only respiration, metabolism, digestion and excretion but also life itself. Thus, any disruption in the balance between fluids and electrolytes as would be seen under the conditions of illness, stress, surgical trauma etc. would affect the normal physiological activities of the body. As an example, patients who undergo cardiovascular surgery are prone to develop electrolyte imbalance due to both surgical trauma and the physiological aberrations caused by extracorporeal circulation. Hypokalemia is probably the most frequently encountered electrolyte abnormality in this situation (Hudak 1977). Again, this is due to intraoperative fluid replacement, and the hemodilution of the blood via extracorporeal circulation. Thus, the control of homeostasis literally rests in the hands of the individual administering the replacement therapy (Moran and Zimmerman 1967).

A potassium deficit affects cellular metabolism especially in muscle tissue (Meltzer, Abdellah and Kitchell 1976). In cardiac

muscle the resultant changes are seen as a decrease in myocardial contractility and a delay in electrical conduction (Hudak 1977). A potassium induced delay in conduction can cause ventricular arrhythmias, particularly ventricular fibrillation and death. The severity of the arrhythmias certainly points out the need for early recognition of this problem (Hudak 1977).

Postoperative open heart patients, specifically those undergoing a coronary artery bypass procedure, need to have supplemental intravenous (IV) potassium chloride replacement in order to maintain a plasma level of potassium between 3.5 and 4.5 mEq/L. This order for intravenous (IV) replacement is initiated immediately postoperatively by medicine and the order continues until the patient can take oral supplementation. The period of time during which the patients are on IV potassium replacement varies from one patient to another; it is during this period of time that nurses monitor patients closely for a variety of postoperative complications using both laboratory values and selected clinical indices in order to maintain a serum potassium level equal to, or greater than, 4.0 mEq/L.

There are two methods of potassium replacement presently in use by nurses to replace IV potassium. One method involves the replacement, every four hours of 0.2 mEq/L of potassium chloride for every 0.1 mEq/L that serum potassium values are less than 4.5 mEq/L. (This method is used at Arizona Health Sciences Center in Tucson, Arizona). The other method, less commonly in use, involves the

replacement of 1 mEq/L of potassium chloride for every 15cc of urine output on an hourly basis. (This method is used at St. Joseph Mercy Hospital in Ann Arbor, Michigan).

For reasons of economy and expediency clinicians are forced to rely on serum levels of potassium to determine hypokalemic states in the cardiac surgical patient. Unfortunately, the magnitude of potassium depletion cannot be accurately estimated from serum potassium measurements since most of the total body potassium is intracellular. An intracellular deficit of 100 mEq/L produces but a 1 mEq/L lowering of serum potassium. This estimate is derived from data of Relman and Schwartz (1952; 1953) as cited by Scribner and Burnell (1956). Since hypokalemia leads to metabolic alkalosis, an elevated bicarbonate concentration is frequently an indication of total body potassium depletion, even if serum potassium is close to normal (Ayres et al. 1974).

Since the effects of hypokalemia can drastically effect the normal physiological state, as previously described, it becomes critically important that the potassium which is lost be replaced exogenously. Inherent in the decision to correct hypokalemia by intravenous (IV) potassium replacement is a consideration of both the amount of potassium to be replaced, and the frequency with which potassium should be replaced.

The rate of potassium replacement is dependent on the severity of the hypokalemia. Carroll and Oh (1978) suggested that a safe and convenient rate of IV administration is about 10 mEq/hr, although as

much as 80 mEq in 15 minutes has been given in life threatening arrhythmias. Schwartz and Lyons (1977) suggested that replacement be based on the following formula: patient's weight in Kg x 3 mEq = maximum safe dose of IV potassium/24 hours. Thus, even among various investigators there is no consensus as to an absolute safe range for replacement administration.

The frequency of replacement represents as urgent a problem as the amount. In the methods of replacement, as described earlier in this paper, the replacement of IV potassium on a four hourly basis appears to be inadequate. Based on clinical observations nurses have stated that they are giving extra doses of IV potassium during the four hour interim. This would suggest that a more frequent determination of serum level, followed by IV replacement, might be in order.

#### Significance of Problem

This problem is significant to nursing since it is nurses who monitor and replace potassium, in the form of potassium chloride, in postoperative open heart surgery patients according to protocols established at their specific institutions. Strict adherence to standard guidelines fails to take into consideration other physiological events that need to be assessed, as well as the rapidity with which the patient recovers from surgery. Mandal et al. (1969) reported that the major causes of potassium excretion in the postoperative period are stress, hemodilution, diuresis, and improved cardiovascular state. Because of the extreme variability in presentation of these factors

as significant postoperative occurrences it is conceivable that some patients will be overreplaced with potassium chloride, while others will be underreplaced.

One method nurses rely upon to determine whether a patient is hypokalemic is to examine the laboratory reports of serum potassium concentration. However, since only two percent of the total body potassium is in the serum this tells the clinician nothing about the relationship between the whole body potassium and the serum potassium levels. Since potassium is primarily an intracellular ion, the bulk of the body's total potassium cannot be measured in a routinely available test. If massive losses of extracellular potassium occur, as seems to be the case in open heart surgery patients, intracellular potassium may leave the cells to support the serum concentration. This process cannot be measured directly and can only be inferred from an understanding of the clinical state and from such signs as dehydration, muscle weakness, tremors, and changes in electrocardiographic tracings (Widmann 1973).

The effects of a hypokalemic state have been documented. According to Guyton (1976) when the serum potassium ion concentration falls below approximately one half normal (2.5 mEq/L or less) muscle paralysis, or at least severe muscle weakness, often develops. This is caused by hyperpolarization of the nerve and muscle fiber membranes which prevents transmission of action potential. In terms of the myocardium, this state produces a generalized irritability that gives

rise to life threatening arrhythmias such as ventricular tachycardia and ventricular fibrillation. Adroque et al. (1971) maintained that the notable therapeutic effect of small amounts of IV potassium supports the importance of hypokalemia as responsible for the development of arrhythmias.

Nurses who understand the physiologic reasons for electrolyte imbalance in the immediate postoperative state will be able to both monitor cardiac patients more closely, and use criteria based on knowledge--not invalid or unreliable indicators--to assess the patient for hypokalemia, and in turn, will be able to adjust--in consultation with medicine--the amount of IV potassium being replaced.

In addition to recognizing the signs and symptoms of a hypokalemic state, nurses must also monitor the frequency with which intravenous potassium is replaced. Too infrequent a replacement of IV potassium might result in a continuance of the hypokalemic state with a possible worsening of the pathophysiological consequences. On the other hand, too frequent a replacement could result in a state of extracellular hyperkalemia characterized by abnormalities of rhythm and rate of conduction due to: 1) decreased resting membrane potential; 2) increased velocity of repolarization resulting in shortening of the action potential; and 3) decreased rate of diastolic depolarization (Carroll and Oh 1978). The problem remains then: what is the frequency with which IV potassium should be replaced?

### Purpose of Study

The purpose of this study was to measure serum potassium hourly during the immediate postoperative period to determine the temporal pattern of serum potassium levels in postoperative coronary artery bypass surgery patients. If the serum potassium pattern was found to decrease steadily in the immediate postoperative period more frequent analysis of serum potassium may be necessary during the initial three to four hour period than the protocol now established, in order to prevent untoward side effects associated with hypokalemia. At the present time the general practice at the institution where this study was conducted is to replace IV potassium chloride at the rate of 2 mEq/L for every 0.1 mEq/L that serum potassium concentration is less than 4.5 mEq/L (initial replacement is based on the initial blood draw when patients are received into intensive care from the operating room). Replacement potassium is subsequently done on the basis of analysis of serum potassium on bloods drawn at four hour intervals. It is this particular protocol which was investigated.

## CHAPTER 2

### THEORETICAL FRAMEWORK

This chapter contains the theoretical framework which includes: the regulation of potassium, its role in maintaining resting membrane potential; the Donnan Equilibrium; factors which regulate ionic movement; and the role of potassium in cardiac contractility which includes the state of hypokalemia. A selected review of the literature is included which describes the prevailing methods used to replace potassium ion in postoperative cardiac patients.

#### Potassium as an Electrolyte

Body fluid consists chiefly of water and certain dissolved substances sometimes referred to as salts, minerals, or crystalloids but more correctly called electrolytes (Metheny and Snively 1979). Electrolytes are so named because they ionize--develop electrical charges--when they are dissolved in water (Metheny and Snively 1979). These charges can be either negative or positive. Electrolytes can be found either intracellularly or extracellularly.

Potassium is found in both the intracellular and extracellular fluid, and it is the major intracellular electrolyte--the primary cation of the cell. Approximately 98 percent of potassium is found in the intracellular fluid, and two percent is found extracellularly.

Of the 98 percent found in the intracellular compartment, 70 percent (or about 3,000 mEq) is found in the skeletal muscle and 28 percent in the liver and red blood cells. The two percent found in the extracellular compartment (about 50 mEq) is represented by the serum potassium reading (Stroot, Lev and Schaper 1977).

### Functions of Potassium

Potassium is indispensable in the human body because it is necessary for the intricate chemical reactions needed for transformation of carbohydrate into energy and for reassembling amino acids into proteins (Metheny and Snively 1979). Physiological studies by Skou (1965) and by Katz and Epstein (1968) suggest that active ionic transport requires an ATP-ase, which itself requires the presence of sodium and potassium ions for its proper activity. These studies suggested that this sodium-potassium dependent ATP-ase could act by altering the relative affinity of adenosinephosphate for sodium and potassium at different phases of the transport cycle. However, the importance of ATP extends beyond its transport function, for ATP dependent processes provide the bulk of energy required to transport ions against electrochemical gradients (Maxwell and Kleeman 1972).

In vitro studies by Lubin (1964) showed that potassium appears to control the rate of protein synthesis. In experiments on the kinetics of incorporation of phenylalanine into a polypeptide if sodium or lithium were added at the start of the reaction, they antagonized the stimulating effect of potassium or ammonium ions. If addition of

the inhibiting ion was delayed several minutes, however, the inhibition was found to be much less pronounced. These results suggested that an initial process, a "priming reaction" occurred before the formation of the peptide bond (Lubin 1964). The importance of this priming reaction was the critical requirement for potassium.

Additionally, potassium plays a major role in neuromuscular activity where it is essential for the transmission of nerve impulses in both the heart and skeletal muscle. The transmembrane potential of most cells is determined primarily by the ratio of intracellular to extracellular potassium concentration. The electrical charge across the cell membrane is about 90mV; with the inside of the cell negative to the outside. The most important mechanism for the generation of this potential is the difference between the intracellular and extracellular potassium concentrations. Potassium attempts to diffuse out of the cell because of the higher concentration within the cell than in the extracellular fluid. Its anions, complex multivalent organic molecules, cannot penetrate the cell membrane; therefore, they remain behind as potassium diffuses out. The amount of potassium that can diffuse out is limited by the pull of the negative field belonging to the anions. The normal membrane potential is present when the gradient of potassium is about 30:1. In most clinical situations it is the extracellular potassium concentration that is most readily altered, therefore the transmembrane potential is affected more by the extracellular potassium concentration (Carroll and Oh 1978).

During excitation, the release of acetylcholine at synapses and motor end plates results in a decrease in the magnitude of the membrane potential to a critical value referred to as the threshold potential. In the skeletal muscle the normal resting potential is about  $-88\text{mV}$  and the normal threshold potential is about  $-65\text{mV}$ . When the threshold potential is reached there is a rapid reversal of the membrane potential, i.e., the cell interior becomes positive, and the membrane potential then returns to the resting state. This sequence of changes in membrane potential contributes to the action potential. The propagation of these changes to adjacent cells is responsible for the transmission of neural impulses and for the initiation of muscle contraction (Rose 1977).

The excitability of neuromuscular tissue is defined as the difference between the resting and threshold potentials. Thus, any factor, which alters either of these potentials affects excitability (Rose 1977).

Another important function that potassium performs is its role in buffering in order to maintain the acid-base balance of the fluid system. Potassium levels fluctuate, producing a rise in serum levels during acidosis and a fall in plasma levels during alkalosis. In either situation the potassium level changes to compensate for a change in hydrogen ion levels.

In acidotic states the hydrogen ion content in the extracellular fluid is elevated. In an attempt to compensate for this

disequilibrium, the cell begins to "absorb" the excess hydrogen ions. However, in order to make room for the hydrogen ions, potassium moves out of the cell into the surrounding interstitial fluid, and eventually into the intravascular fluid. The result is an elevated serum potassium level. Plasma potassium levels increase about 0.6 mEq/L for each 0.1 unit fall in blood pH. This elevated potassium reading is called a false positive because the total body potassium level is not actually elevated (Stroot et al. 1977).

In alkalotic states the opposite is true. There is a low level of hydrogen ions in the plasma, and the cells attempt to compensate by releasing hydrogen ions in order to increase the acidity of the blood and avoid alkalinity. The net result is an extracellular movement of potassium from the plasma into the cells, thereby decreasing the level of serum potassium. Plasma potassium falls about 0.6 mEq/L for each 0.1 unit rise in blood pH (Stroot et al. 1977).

#### Movement of Potassium

Basic to an understanding of ionic movement is an understanding of the Gibbs-Donnan membrane equilibrium, which defines the state of equilibrium that exists when solutions of two electrolytes with a common ion are separated by a membrane permeable to this common ion but impermeable to one of the other ions (Jensen 1976).

Imagine a semipermeable membrane separating two solutions, one containing potassium chloride and the other a potassium salt of a protein, this latter being the non permeable ion. If the protein

solution is placed on the inner surface of the membrane, and the potassium chloride solution on the outer surface, there will be a spontaneous net diffusion of the potassium and chloride ions in an attempt to restore a concentration equilibrium. The potassium and chloride ions will freely diffuse inward until the ionic activity product (that is, the sum of all cations is equal to the sum of all anions) of the potassium chloride is the same on the inside as it is on the outside of the membrane. At equilibrium the Gibbs-Donnan relationship defines only the unequal distribution of the diffusible ions across a semipermeable membrane. This concept will be basic to understanding membrane potentials (Jensen 1976; Bland 1963).

There is a reciprocal relationship between the electrolytes sodium and potassium which is responsible for the development and maintenance of the electrochemical gradients for these ions across the cell membrane (Jensen 1976). This mechanism which is responsible for the normal movement of potassium between the intra and extracellular compartments is regulated by the sodium-potassium pump.

The sodium-potassium pump is an active transport system located in the cellular membrane, and powered by ATP which is derived from the metabolic processes occurring within the cell (Jensen 1976; Guyton 1977). The carrier mechanism attempts to maintain a dynamic equilibrium between these two ions by actively transporting sodium out of the cell, and potassium into the cell according to the body's

needs. The maintenance of these electrochemical gradients, in turn, is an essential feature in the development of membrane potentials.

Electrical potentials exist across the membrane of essentially all cells of the body and some cells such as nerve and muscle cells are "excitable"--that is, capable of transmitting electrochemical impulses along their membranes (Guyton 1976). The sodium-potassium pump exemplifies this type of gradient. A nerve membrane in a relaxed state has a positive charge on the outside and a negative charge on the inside. When the membrane becomes more permeable due to excitation and ionic flux, a small number of potassium ions move out of the cell and simultaneously, a large number of sodium ions moves inward. The membrane is now depolarized, that is, there is a reversal of polarization on the membrane such that the outer surface is now negatively charged. This wave of depolarization, called a nerve impulse, is propagated along the nerve cell. Repolarization follows depolarization, thus restoring the cell to its original resting state. This electrolyte change causes the nerve to conduct electrical impulses to the muscle and causes that muscle to contract (Stroot et al. 1977; Guyton 1976).

#### Potassium Regulation

The primary regulator of potassium balance is the kidneys. Therefore, the major loss of potassium from the body is through the urine. Even though the human body has an efficient mechanism for conserving sodium, it has no such mechanism for conserving potassium.

The kidneys do not conserve potassium. Even in times of need the kidneys continue to excrete potassium. Approximately 2.9 mEq of potassium per gram of protein is lost with the excretion of nitrogen waste products through the kidneys. This averages about 40 mEq of potassium for each liter of urine output. Nitrogen waste products are the result of cellular metabolism and occur regardless of other loss mechanisms. This continued loss of potassium can quickly result in a deficit or hypokalemic state (Stroot et al. 1977; Metheney and Snively 1979).

There are two main methods by which the kidneys attempt to regulate potassium balance. The first has to do with the selective permeability of the cell membrane in which potassium and hydrogen ions compete for exchange with sodium ions in the renal tubules (Stroot et al. 1977). The major portion of filtered potassium is reabsorbed in the proximal tubule of the kidney. Simultaneously, the distal tubule cell of the kidneys maintains a high intracellular potassium concentration by virtue of the sodium potassium pump. The net excretion of potassium is determined by: 1) the rate of active uptake across the peritubular membrane; and 2) the difference between passive movement into the lumen down an electrochemical potential gradient and active reabsorption across the luminal cell membrane (Netter 1973).

The second method involves the secretion of aldosterone. Aldosterone is a mineralcorticoid secreted by the adrenal cortex in response to a decreased level of sodium or an increased blood level of

potassium (Jensen 1976). Its main physiological effects are on the distal tubule. Basically, aldosterone causes the kidneys to retain sodium which results in an increased water retention. In exchange for the sodium retention the body excretes potassium. This is particularly significant with the release of adrenal hormones in a stress situation, when potassium is lost while sodium and water are retained in order to maintain adequate blood volume (Stroot et al. 1977).

### Hypokalemia

Hypokalemia is defined as a decrease in the concentration of serum potassium (Berk et al. 1976). For purposes of this study hypokalemia will be defined as a serum potassium level less than 4.0 mEq/L. This level is chosen because in clinical practice potassium replacement is continued until the patient reaches a level of at least 4.0 mEq/L. And also because the administration of digoxin, a cardiotonic drug that has both positive inotropic and negative chronotropic action, is withheld until a level of 4.0 mEq/L is obtained.

### Postulated Mechanisms of Potassium Loss and Hypokalemia

#### Intracellular Movements

Investigators have suggested that one of the immediate, though transient, causes of serum hypokalemia in the first few hours postoperatively can be attributed to a redistribution of the intravascular potassium to the intracellular compartment (Roe 1973; Adroque et al. 1971; Abe et al. 1977). In part, factors which have contributed to this

inward ionic movement of potassium are due to changes in acid base equilibrium and the stress response.

Marcial et al. (1969) in a study of 50 patients undergoing a variety of cardiectomy procedures found that respiratory alkalosis due to both anesthetic hyperventilation and excitement of the patient immediately before the operation were important factors in the diminishment of serum potassium levels. The physiologic reasoning supporting this observation is based on the reciprocal relationship between potassium and the hydrogen ion across cell membranes. Infused potassium rapidly enters the intracellular space combining with cellular anions and displacing hydrogen ions which diffuse out into the extracellular space. Infused potassium thus produces hyperkalemic acidosis. The reverse occurs when the plasma potassium is low (Ayres et al. 1974).

Primary alterations in hydrogen ion concentration produce the same reciprocal change in potassium. Potassium leaves the extracellular fluid and diffuses into the cell when intracellular hydrogen ion concentration is low. Thus alkalosis leads to hypokalemia, and hypokalemia leads to alkalosis (Ayres et al. 1974). The final result of the entire process is an extracellular depletion of potassium.

The trauma of surgery evokes a physiological stress response in the surgical patient. As part of this response the hypothalamus activates the sympathetic nervous system to secrete norepinephrine, which has two effects. First, it aids alpha and beta cells in the islets of Langerhans to increase glucagon and decrease insulin output,

respectively. Secondly, it causes the adrenal medulla to secrete epinephrine which potentiates the effects of norepinephrine on insulin and glucagon. Simultaneous with these interactions the pituitary portal system carries a releasing factor to the pituitary gland where it releases ACTH. This causes the adrenal gland to secrete cortisol, which enhances the effects of the anti insulin stress hormones (Kaminski 1976). In effect insulin is antagonized and is unable to move potassium into the cells, thus upsetting part of the mechanism responsible for maintaining normal extracellular potassium equilibrium.

Abe et al. (1977) in a study of 18 open heart surgical patients showed that the stress response in these patients was a time limited phenomenon. Specifically, blood insulin rose slightly in the early stages of bypass, decreased during bypass, began to increase from partial bypass, and increased after the end of bypass.

The fact that insulin secretion was inhibited despite high blood sugar levels during bypass could be caused by an increase of adrenalin (epinephrine) secretion by the stress of bypass, low body temperature, and insufficient circulation in the abdominal viscera during bypass. Insulin secretion increased after bypass, and this is presumed to be closely related to potassium movement into the cells (Abe et al. 1977).

#### Extracellular Translocation

Extracellular potassium losses are those losses which can be measured in the renal excretion, or from the secretions of the stomach

and gastrointestinal tract. In open heart surgical patients the extracellular loss of potassium can be attributed to a combination of factors.

According to Guyton (1976) approximately 65 percent of the potassium is absorbed in the proximal tubules and another 25 percent is absorbed in the loops of henle, so that by the time the tubular fluid reaches the distal tubules, the total quantity of potassium delivery to the distal tubules each minute is less than 10 percent of that in the original glomerular filtrate. This is true under normal physiological conditions. However, it has already been stated that the surgical procedure produces a "stress response," and thus alters the normal physiological response.

The normal mechanisms which regulate potassium ion concentration, that is, the aldosterone feedback mechanism and extracellular fluid potassium levels, are temporarily diminished in their functional ability. In clinical studies this recovery period lasted from three to five hours (Marcial et al. 1969; Madal et al. 1969; and Yokoyama et al. 1972).

During the time that the normal mechanisms for potassium reabsorption are not functioning to their full capacity, potassium is lost by way of passive excretion. According to Jensen (1976) most of the potassium found in the urine is added to the tubular fluid by the process of passive secretion as the urine moves through the distal convoluted tubules and collecting ducts. The net quantity of

potassium that is secreted into the urine in these parts of the distal nephron is determined principally by the transtubular potential as well as the intracellular potassium concentration. Again, this refers to a fully functioning homeostatic system, which is not the case in the immediate postoperative period of the cardiac surgical patient.

#### Review of Clinical Studies on Potassium Replacement

Clinical studies in medicine that document the correlation between open heart surgery and the loss of extracellular potassium (Marcial et al. 1969; Vasko, DeWall and Riley 1973; Abe et al. 1977; Adroque et al. 1971) did not offer criteria, protocol or suggestions for the intravenous replacement of the potassium ion after the operative procedure.

A review of the nursing literature offered a plethora of clinical signs and symptoms which indicated that cardiac surgical patients have a low serum potassium, but like the medical studies, no guidelines or rationale for maintaining potassium equilibrium in postoperative open heart surgery patients was offered.

Nowhere in the literature were specific methodologies found that proposed how to correct potassium depletion, or even what the rationale for replacement was per se. Kettlewell et al. (1970) state that in view of the large postoperative loss of potassium it is suggested that potassium supplements at this stage should be larger than those generally given. And Abe et al. (1977) concluded, to prevent

hypokalemia following bypass, it is recommended to add KCl in the perfusate of the heart lung machine, and to give intravenous drip of KCl immediately after bypass. These suggestions are made but no exact parameters are established.

To summarize, this chapter has presented basic physiological mechanisms involved in potassium metabolism as well as mechanisms operational and etiological of hypokalemia, a pathophysiological state of potassium imbalance. Identification of the postoperative pattern of potassium imbalance in coronary artery bypass patients is the primary focus of this study.

## CHAPTER 3

### DESIGN AND METHODOLOGY

#### Introduction

In order to answer the research question posed in this study, what is the temporal pattern of serum potassium fluctuation in the coronary artery bypass patients during the immediate four hour post-operative period, a longitudinal descriptive design was used. This design was chosen because it offered the best way of obtaining complete and accurate information for the problem that was being studied. This chapter presents the population and sample, criteria for sample selection, human rights protection, methods of procedure followed for data collection, and techniques followed in potassium analysis, reliability and validity, as well as the statistical analysis of the data and the limitations of the study.

#### Population and Sample

The population for this study was drawn from a group of in-patients who were admitted to the Cardiothoracic Unit (CTU) of a hospital in an urban area of the southwestern part of the United States.

Ten subjects, eight men and two women, were chosen as a convenience purposive sample from a group of patients who were scheduled for open heart surgery.

### Criteria for Selection

The criteria for subject selection were as follows:

1. All subjects had to read and understand written and spoken English.
2. All subjects had to be a good surgical risk as determined by consultation with the Cardiothoracic Surgeon.
3. All subjects had to be undergoing some type of direct cardiomy procedure such as coronary artery bypass, valve replacement or aneurysmectomy.
4. Subjects who had any known chronic underlying metabolic disease were excluded from the study as were subjects who had previous open heart surgery.

### Protection of Human Rights

The human rights of all subjects were protected by the National Institutes of Health guidelines as well as the written policies of the University of Arizona College of Nursing and the Arizona Health Sciences Center Ethical Review Committee's "Human Subjects Committee Manual of Procedures" (1977). Prior to admission to the study all cardiac surgery patients were invited to participate. Those who volunteered to do so signed a witnessed consent form which explained to them the risks associated with the study. Data were coded to protect each subject's privacy; analysis was done via computer using the coded data.

## Methods of Procedure

### Kinds of Data Collected

The data collected from all subjects was of two types. First, demographic data which included: age, sex, surgical procedure and pump time was collected. In addition, a 3 ml sample of arterial blood was drawn from an indwelling arterial catheter initially upon the subjects arrival into the cardiothoracic unit from the operating room, and every hour thereafter for four consecutive hours. The total amount of blood obtained from each subject was 15 ml.

### Blood Collection Protocol

The following procedure was adhered to for all blood collection. Once the patient was received into the CTU from the operating room, the baseline blood sample was drawn, with a 5 ml syringe, from an indwelling arterial line which had been started in the operating room suite. This sample was coded with the subjects identification letter and labeled  $T_0$ . (The range of time for collecting this initial sample was from six to 52 minutes). Blood collection was dependent on the length of time it took CTU nurses to attach: EKG electrodes, chest tubes to suction, set parameters on the ventilator and how long it took for the patient's vital signs to stabilize. For example, if a patient was hypotensive and experiencing arrhythmias upon arrival into the CTU, blood drawing had to be delayed until these parameters were controlled. Each hour thereafter, for four hours, a 3 ml sample

of blood was obtained from the arterial line. The samples were labeled  $T_1$ ,  $T_2$ ,  $T_3$ , and  $T_4$ . All but three of the fifty arterial blood samples were collected by the primary investigator.

#### Technique of Potassium Analysis

The arterial blood samples were allowed to clot; after the blood clotted the tube was reamed, and centrifuged at 2,900 rpm for ten minutes to separate the cells from the serum. The serum was transferred to plastic vials using a Pasteur pipet. The vials were coded, labeled as to time sequence, and placed in a freezer where they were maintained at a temperature of -10 to -15 degrees centigrade until potassium analysis.

Analysis of all serum samples was done in one six hour period on 2 October 1979 in order to control for intervening variables such as temperature, humidity and instrument performance. Serum potassium concentrations were measured by flame photometry using a Turner Flame Photometer (model 510). The reliability and validity of this instrument has been established for measuring sodium and potassium in both nonclinical and clinical investigations (Marcial et al. 1969; Adrogué et al. 1971).

#### Reliability

The reliability of the flame photometer was determined by checking the photometer against known standard concentrations of potassium and sodium, prepared from Turner stock solutions, by the

investigator, according to the manufacturer's instructions! Twice distilled (2X) water was used to prepare standards and samples in order to ensure identical solvent background. Sodium and potassium standards were prepared as follows (Turner Flame Photometer Operating Instruction Service Manual 1978):

1. One part of Lithium stock concentrate (Turner #510-022, 1500 mEq/L) was diluted to 100 parts with distilled water (1:100).
2. One part of the Flame Standard Serum (Turner #510-020, 140 mEq Na/L, and 5 mEq K/L) was diluted to 200 parts with the Lithium diluent prepared in step #1 (1:200).

These standards were used to calibrate the photometer. To determine the sensitivity of the photometer during the calibration procedure the following 1:200 dilutions were prepared and tested:

3. 0.5cc of the Flame Standard Serum (Turner #510-020, 140 mEq Na/L and 5 mEq K/L) was diluted to 100cc with the Lithium diluent prepared in step #1 (0.5cc:100cc).
4. 0.25cc of the Flame Standard Serum (Turner #510-020, 140 mEq Na/L and 5 mEq K/L) was diluted to 50cc with the Lithium diluent prepared in step #1 (0.25cc:50cc).
5. 0.125cc of the Flame Standard Serum (Turner #510-020, 140 mEq Na/L and 5 mEq K/L) was diluted to 25cc with the Lithium diluent prepared in step #1 (0.125cc:25cc).
6. 50 microliters of Flame Standard Serum (Turner #510-020 140 mEq Na/L and 5 mEq K/L) was diluted to 10cc with the Lithium diluent prepared in step #1 (50 $\mu$ l:10cc).

The reliability of the instrument was further determined by analyzing repeated samples from a single source of pooled human serum. The mean mEq/L serum potassium concentration of pooled human serum was 3.07. The mean percent relative error for the eight triplicate samples of pooled human serum was 4.30. This reliability data was within the limitations of the potassium assay. These data are shown in Appendix A.

The reliability and validity were further substantiated by having a sample of the same pooled human serum analyzed by an independent laboratory.

#### Validity

The procedure for analyzing all serum was as follows. Using an Eppendorf pipet, 50 microliters of serum were pipeted into a 15 ml plastic test tube which contained 10 ml of the Lithium diluent (1:200 dilution). Each sample was prepared in triplicate; prior to photometric analysis all samples were vortexed.

After every three samples the instrument was recalibrated, and because precision was maintained the calibration checks were advanced to six unknowns, and finally after every nine unknowns. This calibration check was more frequent than the initial check (after every five to ten unknowns and less frequently after fifteen minutes of operation) recommended by the manufacturer.

### Statistical Analysis of the Data

Statistical analysis of the data was done using descriptive statistics, and the paired t-test applied to specific intervals based on an examination of the plotted means, to determine whether significant changes in the potassium occurred between the time of sampling,  $T_0$  to  $T_4$ . An alpha level of .05 was selected, however the alpha slippage problem with this type of analysis is acknowledged.

### Limitations of Study

1. The sample size was small ( $n = 10$ ).
2. The pump time for the patients was not controlled and this may have affected potassium ion concentration.
3. The intraoperative fluid intake was not controlled and this may have altered the postoperative potassium ion concentration.
4. The intraoperative intravenous potassium replacement was not controlled and this may have altered the post operative potassium state.
5. Intravenous potassium postoperatively was not controlled and this may have altered the potassium level.

## CHAPTER 4

### DATA ANALYSIS

This chapter consists of the arithmetical and statistical analysis of the data of this study as well as a graphic display of measured serum potassium levels in the ten subjects from  $T_0$  to  $T_4$ .

#### Age Range and Surgical Procedure

The age range for this sample ( $n = 10$ ) was 35 to 67, with a mean age of 55.2 years. Nine subjects were scheduled for coronary artery bypass with a range of one to four bypasses performed. Three of the nine subjects (F, G, I) had an additional cardiomy procedure, specifically; subjects G and I had left ventricular aneurysmectomies and subject F had a mitral valve replacement. These data are shown in Table 1.

Table 2 shows the temporal data comparing the subject's arrival time in the Cardiothoracic Unit with the time the initial blood specimen was obtained. The range of time for collecting this initial sample was from 06 to 52 minutes. The mean collection time for this initial specimen was 21.8 minutes of the time the patient was received into the CTU from the operating room. The reasons for this time variation were explained in Chapter 3.

Table 1. Characteristics of Sample: Sex, Age in Years, and Surgical Procedure

Subject	Sex	Age	Procedure
A	M	67	CAB x 3*
B	F	67	CAB x 3
C	M	56	CAB x 2
D	M	57	CAB x 4
E	M	63	CAB x 3
F	M	44	CAB x 1 and MVR#
G	F	45	CAB x 1 and LVA+
H	M	61	CAB x 3
I	M	35	CAB x 1 and LVA
J	M	57	MVR

\*Coronary artery bypass followed by number of bypasses

#Mitral Valve Replacement

+Left Ventricular Aneurysmectomy

Table 2. Arrival Time in the Cardiothoracic Unit (CTU), Time First Blood Specimen Obtained, and Lapsed Time in Minutes

Subject	Arrival Time in CTU	First Specimen obtained	Lapsed Time
A	1225p	1237p	12
B	545p	610p	25
C	600p	614p	14
D	1203p	1218p	15
E	130p	155p	25
F	730p	756p	26
G	1130a	1136a	06
H	1135a	1155a	20
I	1208p	100p	52
J	1212p	1235p	23

### Results

Serum potassium concentrations for seven of the 10 subjects (A, B, C, D, F, I, J) showed a marked decrease from  $T_0$  to  $T_4$ , with the decrement beginning at  $T_1$ , continuing to  $T_2$ , and continuing through  $T_3$  (see Table 3). Three subjects (E, G, H) did not follow the overall pattern of serum potassium decrease from  $T_1$  to  $T_3$ . Rather, serum concentrations increased from  $T_1$  in these three subjects with each showing a variant pattern. These patterns are shown in Table 3 and graphically displayed in Figure 1.

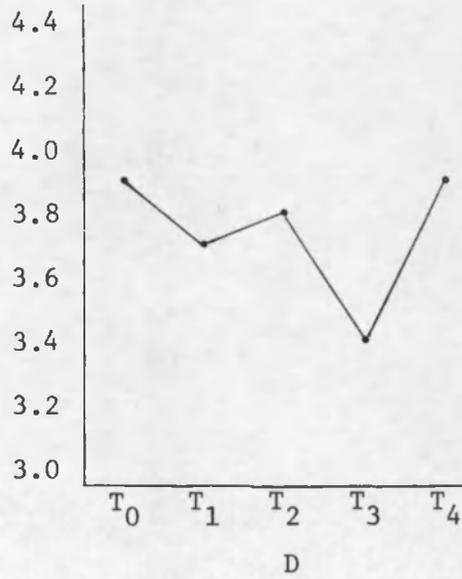
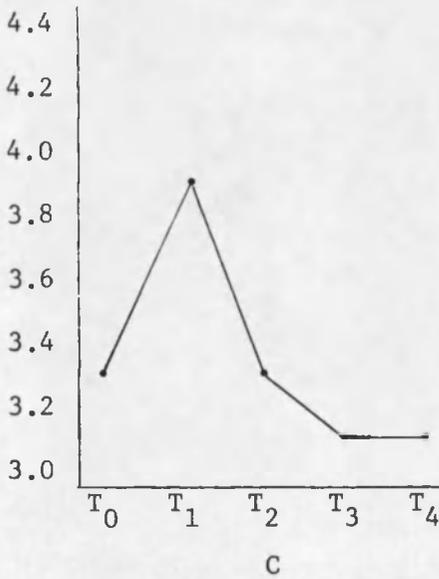
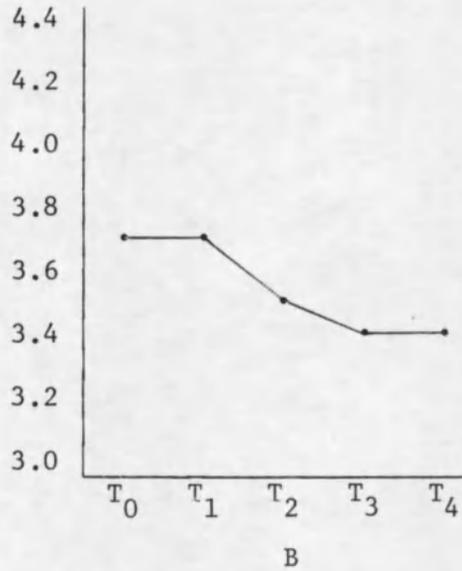
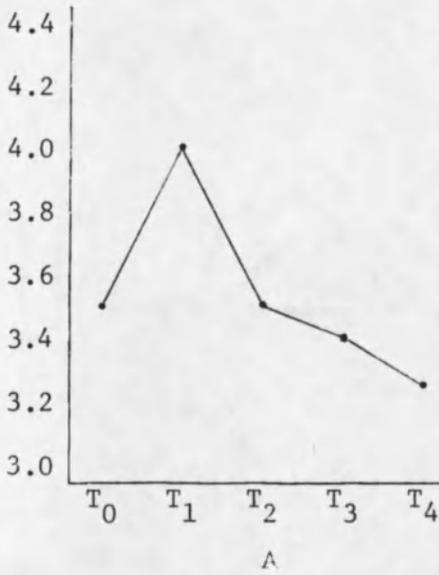
For all 10 subjects a mean increase in serum potassium levels occurred from  $T_0$  to  $T_1$  (a mean increase of 0.2 mEq/L), followed by a decrease from  $T_1$  to  $T_3$  (a mean decrease of 0.2 mEq/L). No change in mean potassium concentration occurred from  $T_3$  to  $T_4$  for  $n = 10$ . These data are shown in Figure 2.

The decrease in serum potassium levels between:  $T_0$  and  $T_4$ ,  $T_0$  and  $T_1$ , and  $T_1$  and  $T_3$  was not significant at the .05 level. These data are shown in Table 4.

Table 3. \*Mean Levels of Serum Potassium (mEq/L), at T<sub>0</sub>, T<sub>1</sub>, T<sub>2</sub>, T<sub>3</sub> and T<sub>4</sub> for all 10 Subjects

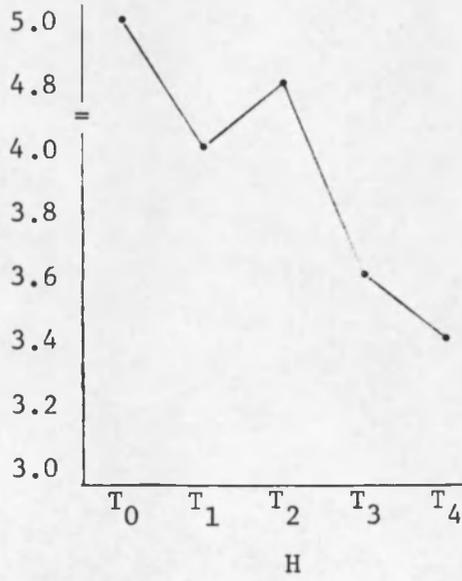
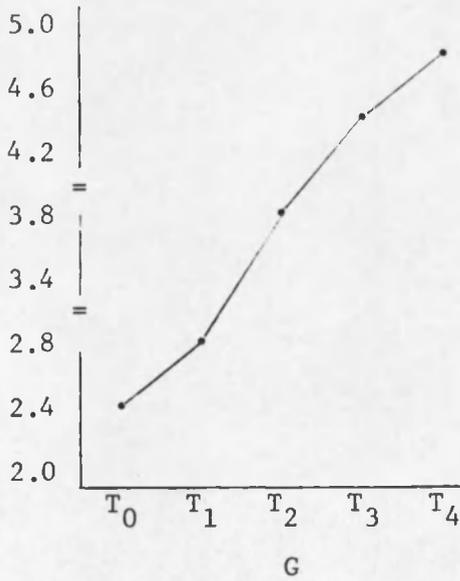
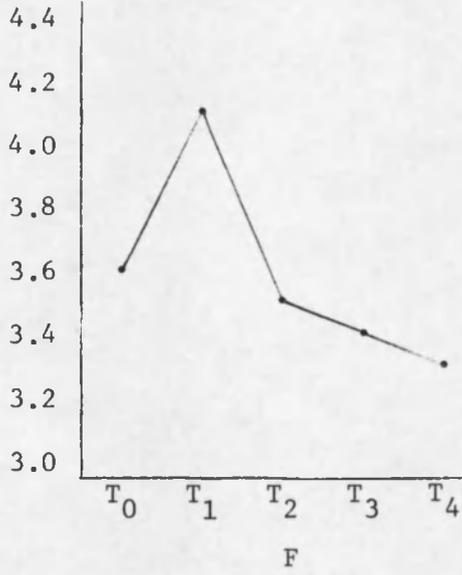
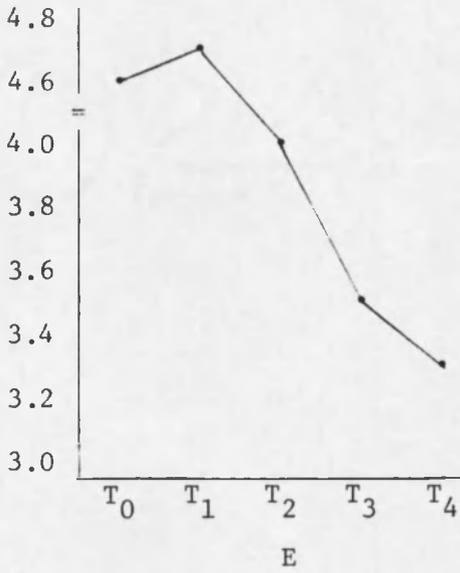
Subject	T <sub>0</sub>	T <sub>1</sub>	T <sub>2</sub>	T <sub>3</sub>	T <sub>4</sub>
A	3.5	4.0	3.5	3.4	3.3
B	3.7	3.7	3.5	3.4	3.4
C	3.3	3.9	3.3	3.1	3.1
D	3.9	3.7	3.8	3.4	3.9
E	4.6	4.7	4.0	3.5	3.3
F	3.6	4.1	3.5	3.4	3.3
G	2.4	2.8	3.8	4.5	4.7
H	5.0	4.0	4.8	3.6	3.4
I	4.0	4.0	3.4	3.7	3.5
J	<u>3.8</u>	<u>3.8</u>	<u>4.2</u>	<u>4.5</u>	<u>4.0</u>
Total Mean:	3.7	3.8	3.7	3.5	3.5
Standard deviation:	0.748	0.499	0.438	0.390	0.485

\*Data represent the mean triplicate measurements at each data point, T<sub>0</sub> - T<sub>4</sub>.



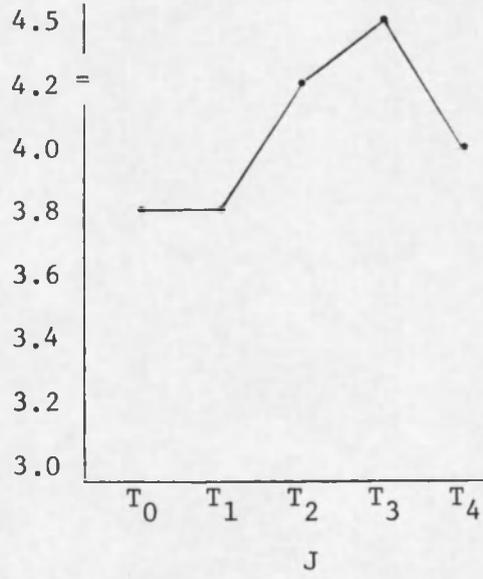
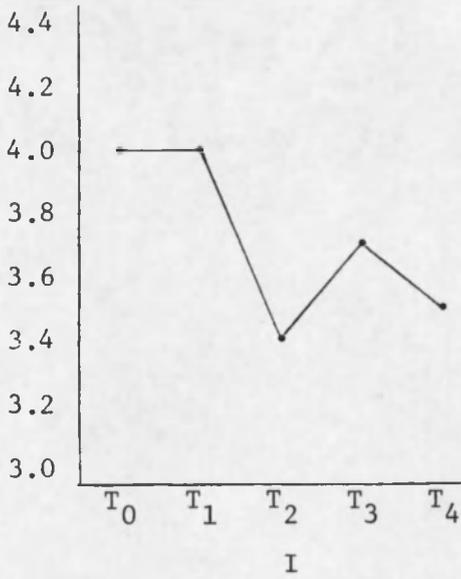
Subjects A through D

Figure 1. Graphic Display of the Mean Serum Potassium Levels (mEq/L) for Each of the Ten Subjects



Subjects E through H

Figure 1. Continued



Subjects I and J

Figure 1. Continued

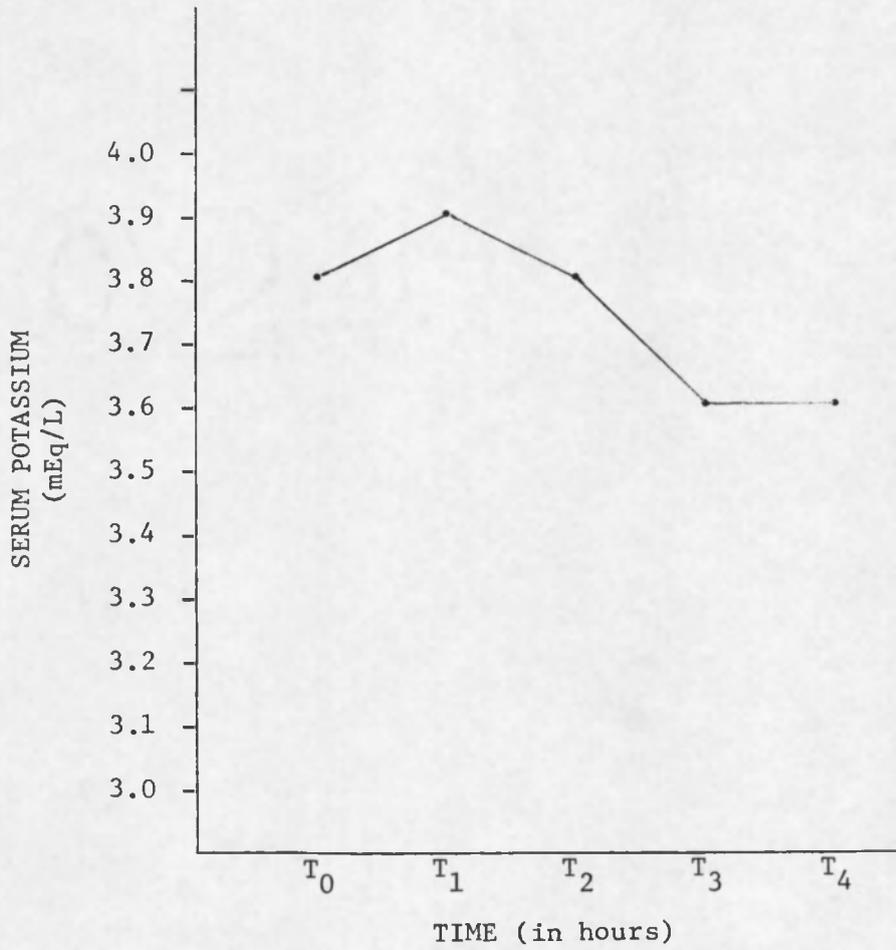


Figure 2. Graphic Display of Combined Mean Values of Serum Potassium for all Ten Subjects

Table 4. Comparison of Selected Serum Potassium Intervals Based on an Examination of the Plotted Means with the Paired t-values

Intervals	T-value
T <sub>0</sub> and T <sub>4</sub>	.58
T <sub>0</sub> and T <sub>1</sub>	-0.61
T <sub>1</sub> and T <sub>3</sub>	.83

Alpha level set at  $p = .05$ , with a significance level = 2.26

## CHAPTER 5

### DISCUSSION AND SUGGESTIONS FOR FUTURE STUDY

In this chapter the data presented in Chapter 4 will be discussed in relation to the theoretical framework and pertinent literature review.

Marcial et al. (1969) measured serum potassium changes in patients who submitted to open heart surgery with extracorporeal perfusion. These investigators measured serum potassium postoperatively and concluded that patients became hypokalemic for the first time three to four hours postoperatively and then, generally, serum potassium levels began to rise. The results of the present study (n = 10) show that potassium levels fluctuated postoperatively. Specifically, seven subjects (A, B, C, D, F, G, J) initially evinced a hypokalemic state, that is, a serum potassium level below 4.0 mEq/L was measured at  $T_0$ . Three subjects (E, H, I) showed variations in the opposite direction: I was normokalemic with a serum level of 4.0 mEq/L while E and H were hyperkalemic having values greater than 4.5 mEq/L, specifically 4.6 and 5.0 mEq/L respectively.

While seven of the ten subjects showed a marked decrease in mean serum potassium concentrations during the four hour period from  $T_0$  to  $T_4$  three subjects (E, G, H) did not follow this pattern. In the case of subject E this variation might be explained in relation to the

amount of time (109 minutes) spent on the cardiopulmonary bypass machine (pump). It is known that the stability of the cell wall is compromised when exposed to prolonged extracorporeal circulation. Specifically, the longer a patient is on the pump, the greater the possibility of red cell hemolysis and the more erroneous and suspect is the initial serum potassium level.

The variation in potassium levels for subjects G and H might be related to the pattern of potassium chloride replacement they received between  $T_0$  and  $T_4$ . These subjects received a total amount of exogenous potassium chloride replacement (between  $T_0$  and  $T_4$ ) of 52 and 25 mEq/L respectively (see Appendix B).

The initial rise in mean serum potassium level from  $T_0$  to  $T_1$  followed by a mean decrease of 0.2 mEq/L in seven of 10 subjects (from  $T_1$  to  $T_3$ ) is in accord with the data presented by Yokoyama and associates (1972) in which a 10 percent decrease in sodium, potassium and chloride were found at the end of cardiopulmonary bypass and was attributed to hemodilution perfusion. However, Yokoyama et al. (1972) acknowledged that factors such as pH changes, amount of total body potassium depletion from previous diuretic therapy, hormonal changes due to surgical stress, length of pump time, and the withdrawing of already fragile red blood cells through the small lumen of the arterial catheter may also be contributing to electrolyte decrement.

The findings of the present study of no change in serum potassium levels between  $T_3$  and  $T_4$  are similar to that of others (Marcial

et al. 1969, Mandal et al. 1969, and Yokoyama et al. 1972) who found that three hours after the operation serum potassium returned to the preoperative level.

An analysis of the fluctuations in serum potassium during the time periods:  $T_0$  and  $T_4$ ,  $T_0$  and  $T_1$ , and  $T_1$  and  $T_3$  were not statistically significant. However, it is difficult to tell if the nonsignificance occurs from an actual lack of difference or a small sample size. Thus the data will be presented from a descriptive viewpoint comparing the means. The reader needs to view the discussion cautiously due to limitations of the data. While the observed decrement in serum potassium found in this study was not statistically significant, it may have marked clinical significance to the open heart surgery patient. At present, there is insufficient data to indicate at what decremental level potassium begins to affect the activity of the cell, specifically the membrane bound sodium-potassium pump. In vitro experiments have shown that a high internal potassium concentration is necessary for protein synthesis. In hypokalemic states, however, the cell transports intracellular potassium to the extracellular space in order to maintain membrane excitability found in nerves and muscles. Thus, while the redistribution of potassium stores is meeting an immediate need of the body, that is, maintaining myocardial contractility, other vital processes associated with protein synthesis and cell integrity are in jeopardy. While it is not possible to measure either of these potassium mediated processes directly the clinical significance of maintaining

potassium equilibrium is recognized vital for maintenance of total body equilibrium.

An unexpected outcome of the serum collection, noted by the primary investigator over the four hour period, was related to an observable change in color of serum samples from  $T_0$  to  $T_4$ . That is, the initial serum sample ( $T_0$ ) was darker in color than the final sample ( $T_4$ ). There was a progressive diminishment of the dark color in the serial samples from  $T_0$  to  $T_4$  which suggests that all initial samples at  $T_0$  may have been hemolyzed, and if this was the situation, higher potassium concentrations may have been measured in vitro than actually existed in vivo in serum. This observation is consistent with the findings of Kettlewell et al. (1970) who suggested that potassium supplements the first three to four hours postoperatively should be larger than those generally given, presumably to compensate for the falsely high readings due to hemolysis from effects of both extracorporeal circulation and the aspiration technique used to obtain arterial specimens.

#### Suggestions of the Data

The data of this study suggests an emergent pattern of potassium fluctuation which reveals the following three characteristics:

1. Falsely high serum potassium readings at  $T_0$  due to release of intracellular potassium from hemolyzed cells during the first postoperative hour;

2. An attempt by the both to equilibrate the distribution of both intracellular and extracellular potassium from  $T_1$  to  $T_3$  with a resultant decrease in extracellular potassium at  $T_3$ ;
3. A return to preoperative potassium levels from  $T_3$  to  $T_4$ .

#### Implications

The major implications of this study are that postoperative open heart surgery patients who have some type of cardiectomy procedure requiring the use of extracorporeal circulation may need to be monitored more closely than they presently are with respect to changes in serum potassium levels during the immediate four hour postoperative period. The potassium replacement protocol used at the institution where the study was conducted consisted of a replacement of 2 mEq/L of exogenous potassium chloride for every 0.1 mEq/L that the serum potassium concentration was below 4.5 mEq/L. This replacement was done on a four hourly basis. As Table 3 shows, seven of 10 subjects (A, B, C, D, F, G, J) were initially hypokalemic at  $T_0$ , and by  $T_3$  another subject (H) was also hypokalemic for a total of eight of the 10 subjects. Figure 2 shows that the mean serum potassium concentration began to level out between  $T_3$  and  $T_4$ . This shows that the lowest decremental level occurs between  $T_0$  and  $T_3$ . This fluctuating pattern would suggest that temporal potassium replacement should coincide with the lowest serum potassium level if equilibrium is to be maintained.

The temporal aspects of exogenous potassium chloride replacement must also be tempered by the quantity of that replacement. If the

initial serum potassium value to  $T_0$  is indeed hemolyzed (for reasons cited earlier) then patients will be underreplaced with potassium at  $T_0$ . Underreplacement will prolong a return to a normokalemic state. Therefore, some correction factor must be derived that will compensate for this deficiency. The methodology used at the institution where the study was carried out does not allow for this factor.

The data of this study further imply that the frequency with which potassium chloride is replaced needs to be based on scientific data in order to provide optimum conditions for the maintenance of potassium equilibrium, since hypokalemia can produce generalized irritability in the myocardium which could lead to life threatening arrhythmias such as ventricular tachycardia and ventricular fibrillation or even death itself.

#### Suggestions for Future Studies

Suggestions for future study would include the following.

First, a replication of the study using a larger sample size to compensate for outliers.

Secondly, an experimental study in which one group receives potassium chloride replacement on an hourly basis, and the other group receives potassium chloride replacement according to established protocols (every four hourly replacement).

Thirdly, the use of a research design that would include an increased control over extraneous variables, such as:

1. cardiac parameters, frequency of PVC's, arrhythmia identification, and pressure problems;

2. water and electrolyte parameters including the assessment of hyper- and hypovolemic states to determine relative or absolute hemoconcentration or dilution;
3. evaluation of dose response to potassium chloride, using established potassium chloride replacement criteria.

Inclusion of the above parameters in a study with a larger sample would establish what criteria are needed by clinicians to: first, identify hypokalemia in its early stages; second, to provide clinicians with criteria to use to replace postoperative potassium chloride and to evaluate these criteria. Third, to anticipate and thus correct, clinical problems related to altered potassium metabolism that are at present being treated using empirical methodologies.

Fourthly, an experimental design using an animal model to determine the deposition of intracellular potassium in the immediate four hour postoperative period.

Fifthly, an experimental design to establish the dose response curve.

And finally, a descriptive study to determine the relationship between intravenous potassium intake and urinary potassium output.

APPENDIX A

COMPARISON OF THE MEAN VALUE OF SERUM SAMPLES USED TO  
 TEST THE ACCURACY OF THE FLAME PHOTOMETER WITH THE  
 DEVIATION FROM THE MEAN (DM) AND THE PERCENT  
 RELATIVE ERROR (%RE)

Sample	Potassium level (mEq/L)	DM	% RE
1	3.0	-.07	2.28
2	3.2	.13	4.23
3	3.1	.03	.98
4	3.2	.13	4.23
5	3.2	.13	4.23
6	3.0	-.07	2.28
7	3.2	.13	4.13
8	2.7	-.37	12.05
Mean	3.07		4.30

APPENDIX B

A COMPARISON OF THE AMOUNT OF POTASSIUM CHLORIDE  
 REPLACED FOR EACH SUBJECT BETWEEN  $T_0$  AND  $T_4$  WITH  
 THE AMOUNT OF TIME SPENT ON THE  
 CARDIOPULMONARY BYPASS PUMP (CBP)

Subject	Potassium Replaced (mEq/L)	Time on CBP (minutes)
A	10	76
B	12	70
C	10	46
D	20	93
E	0	109
F	8	107
G	52	56
H	25	73
I	0	47
J	8	91

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