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Georgia Elizabeth May
University of Nebraska Medical Center

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THE ROLE OF POTASSIUM IN REFRACTORY ALKALOSIS

IN POST-SURGICAL PATIENTS

Georgia Elizabeth May

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INTRODUCTION

It is the purpose of this paper to draw added attention to an electrolyte abnormality commonly seen in surgical patients, namely, an alkalosis characterized by:

    a. elevation of the serum bicarbonate
    b. diminution of the serum potassium
    c. diminution of the serum chloride with normal or increased output of chloride in the urine in spite of low serum values.

Any surgical patient subject to excessive electrolyte deficiencies, regardless of etiology, may be a candidate for this metabolic abnormality.

Recent investigations have drawn particular attention to the importance of the potassium ion in electrolyte balance, and more specifically, its role in alkalosis. Since the low potassium syndrome is so often observed in surgical patients, this paper is written for an analysis of the great accumulation of literature on this subject. To obtain this purpose, current articles and medical journals were reviewed.

NORMAL POTASSIUM METABOLISM

Potassium is the chief basic ion (cation) of the cells, its concentration being variously estimated between 140-160 milliequivalents per liter of cell water. Sodium is the chief cation in the extracellular spaces, and normally potassium exists here in a concentration of only 4.0-5.5 milliequivalents per liter (roughly 16-21 milligrams per cent). The total potassium content of the adult body is about 4000 milliequivalents (160 grams) of which only 70 milliequivalents is in the extracellular fluids.[1] These figures provide a ratio of approximately 59:1 and accent the extremely high concentration of this cation within the cell as compared with its concentration in the extracellular fluid. Between the two compartments, there must be maintained ionic, osmolar, and acid-base equilibria.

There has been no adequate explanation of how and why the tissue cells acquire and maintain so much higher a concentration of potassium than that of the serum or interstitial fluid, but there is normally an equilibrium maintained between the low extracellular concentration and the high cellular concentration. This equilibrium is unstable in opposition to osmotic forces which tend to equalize the concentrations. Hoffman[1] believes this unstable equilibrium is being maintained by the oxidative energy of the cells, thus in conditions of cellular anoxia, potassium would go out of the cells into the extracellular fluids. This phenomenon might thus account for the rise in serum potassium concentration with exercise and in agonal states; it would also explain the progressive transfer of red cell potassium to plasma in stored blood.

Weller,[2] however, states that the equilibrium in the body between

the cellular potassium and the extracellular potassium is actually the resultant of a constant dynamic interchange of potassium between the two compartments. In his experiments, by using radioactive potassium as a tracer, it was demonstrated that the potassium of the red blood cell is constantly being exchanged with the potassium of the plasma, and that all of the red blood cell potassium is exchangeable. The red blood cell exchanges potassium at a relatively slow rate (1.6% per hour), but cells of other tissues have been shown to exchange their potassium with greater rapidity. Radioactive potassium requires fifteen hours before reaching equilibrium with cellular potassium.[1]

Potassium enters the cells when certain structures are being formed. Since glycogen is deposited with about 0.36 millimols of potassium per gram of glycogen,[3] a rough calculation of this factor can be made. In muscle, about 3 millimols of potassium is found for each gram of nitrogen.[3] Although nitrogen can be stored, at least for short periods, without potassium, nitrogen storage eventually demands increases in intracellular potassium. (There is some evidence that testesterone produces accumulation of body protein that may lead to a low serum potassium concentration.

In order for potassium to pass from the plasma, where it exists in a low concentration, into the cell, where it is present in a high concentration, energy must be expended. There is considerable evidence that this energy is derived from the metabolism of glucose, showing that the metabolism of the two are closely related. Human erythrocytes utilize one millimol of glucose for each millimol of potassium that enters the cells and lose potassium if their supply of glucose is exhausted.[2] Apparently this is due at first to an increase in the amount of potassium

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leaving the cell, however, later the amount of potassium entering the cell becomes reduced.

Conversely, potassium is also necessary for the cellular metabolism of glucose, being specifically required for some enzymatically controlled reaction in the carbohydrate cycle. If insulin is present, not only does more potassium move into the muscle cells, but also more glucose is utilized by the cells. Probably the metabolism of glucose provides energy by supplying high energy phosphate bonds to a reaction which directly controls the transfer of potassium.

By means of this energy transfer mechanism, potassium metabolism may be related to those series of chemical reactions involving acetylcholine metabolism. Permeability of nerve membranes to ions is increased by the action of acetylcholine. Human erythrocytes, when incubated in the presence of high concentration of choline esterase inhibitors, lose potassium. The inhibition of the formation of acetylcholine is also possibly related to cellular potassium metabolism. The potassium ion concentration is also of importance in controlling the rates of formation and breakdown of acetylcholine. It is possible not only that the cellular potassium ion concentration may control the rates of these reactions, but also that these reactions may control the cellular potassium ion concentration.

Any apparent interference with this chain of reaction at one or more of the following three points causes alterations in cellular potassium metabolism:

        1--glucose metabolism
        2--acetylcholine formation
        3--acetylcholine breakdown

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The concentration of potassium in the extracellular compartment is clearly the result of how much of this element comes in and how much goes out. Potassium can enter the extracellular compartment in two ways-- either by way of the gut (absorption of ingested potassium), or by emerging from the cells. This ion can leave the extracellular space by entering the cells or by excretion in the urine (only in severe diarrhea are significant amounts of potassium lost in stools). Deficiencies may also occur by loss of gastric juice, such as occurs in excessive vomiting or prolonged gastric suction since gastric juice contains potassium in concentration two-five fold greater than the plasma concentration. Howard[4] and Carey have found this true in patients with and without free hydrochloric acid.

The source of potassium is chiefly dietary and the averabe adult ingests 70-100 milliequivalents (2.7 Gm. to 4 Gm.) daily. Normally almost all ingested potassium is absorbed,[5] and after a meal rich in potassium the serum potassium level rises slightly but soon returns to normal for in the healthy adult none of this potassium intake is stored[1] but instead is excreted in the urine. Rarely more than 10% of dietary potassium is found in the stools.[5]

Darrow and his co-workers[6] confirmed previous evidence that there exists a reciprocal relationship between sodium and potassium in muscles, that is, whenever muscle potassium was lowered, there was a corresponding increase in the sodium content. They also found in their rats that whenever a decrease in muscle potassium of more than 10% was present, there was invariably a significant lowering of the concentration of potassium in the serum. Analysis of the serum and muscles of rats have also shown that, under certain circumstances, the concentration of bicarbonate in

serum varies directly with intracellular sodium and inversely with muscle potassium. (Since cell membranes are considered permeable to sodium and potassium, high bicarbonate in serum must either facilitate the transfer of potassium out of cells or increase entrance of sodium). They pointed out that in their experimental animals there existed a high degree of correlation between the concentration of bicarbonate and chloride in the serum, and the muscle content of sodium and potassium. High serum bicarbonate and low serum chloride invariably accompanied low muscle potassium and high muscle sodium whether the latter state had been induced by low potassium diet, desoxycorticosterone, or administration of sodium salts. It was emphasized by Darrow and co-workers that these predictable relationships were found to apply only after biological equilibrium had been reached, a term implying that renal function was being normally carried out.

Earle et al[7] reported in their studies that in general there was a reciprocal relation between sodium and potassium balance as the potassium intake was varied; this suggests that sodium moves into the cells as they are depleted of potassium. As the cells are repleted with potassium on a high intake, the sodium moves out into the extracellular fluid and subsequently is excreted by the kidney. The converse, however, does not appear to hold. Potassium balance is not affected by sodium intake even though considerable sodium depletion may be present. This is not surprising in view of the chiefly extracellular position of sodium and the relatively unimportant contribution of potassium to the total osmotic pattern of the extracellular compartment. Chloride balance appeared to be related to the sum of the sodium and potassium balance in that chloride was retained when base was retained and vice versa.

Laboratory tests are probably of greater aid to the surgeon in the preoperative preparation of the patient than in any other circumstance. If the patient has been vomiting or has been on a low oral intake for several days, there may be a deficiency in electrolytes including, particularly, sodium, chloride, and potassium. Fortunately, tests for these electrolytes are accurate when performed correctly. No major operation should be performed on any patient with vomiting or decreased oral intake without first obtaining data on the plasma level of these ions. It must be emphasized that the determination of sodium chloride as a single test is misleading; an accurate estimation of true values can be obtained only by a test for each ion individually.

It is clear that changes in the acid-base equilibrium involve alterations in the intracellular as well as extracellular fluids. In general, the normal reaction of the blood cannot be maintained without a suitable relation between the body contents of sodium, potassium, chloride, and water. (Although other factors such as the buffers and the balance of phosphate are involved, the body content of sodium, potassium, chloride, and water describes the main features for many purposes). If the circulatory and renal functions are adequate, some sort of adjustment will be achieved, particularly if sufficient water is available. However, at present, it is not possible to define the relation between the acid-base equilibrium and tissue composition when multiple disturbances involving body water, sodium, potassium and chloride occur. It is certain that the serum bicarbonate concentration does not predict the intracellular composition under these conditions. However, a deficit of one of the ions, sodium, potassium, or chloride will tend to reach an adjustment if sufficient water and the other ions are available and the circulatory and renal functions permit adequate renal excretion.

ROLE OF THE KIDNEY IN MAINTAINING POTASSIUM
CONCENTRATION OF THE BODY FLUIDS

The regulation of body potassium through renal function is just beginning to receive the attention it deserves. The kidney is the principal means of potassium excretion in the normal adult, although small amounts may be excreted in the sweat and feces. As has been mentioned, normally less than 10% of ingested potassium is found in the stools and a considerably lesser amount in the sweat. Thus, since little or no ingested potassium is normally stored and since more than 90% is excreted by the kidneys, balance is maintained in the normal adult by the simple functions of renal filtration and of renal reabsorption. Data on ability of the kidney to conserve potassium is meager, but isolated observations lead one to assume that the normal kidney can produce urine which contains potassium at no greater concentration than that of the serum.

In the normal adult economy almost the same quantity of potassium is excreted in the urine as has been ingested.[4] In most types of renal insufficiency, as long as urinary volume is maintained, the capacity to excrete potassium remains adequate to cover the requirements, and clinically significant deviations from the normal concentration of potassium in the serum do not occur unless unusually heavy loads are thrown on the mechanism such as administration of potassium salts.

The concentration of bicarbonate in serum is dependent on the amount of base (cations) available to form bicarbonate at the particular carbon-dioxide tension with the particular amounts of blood electrolyte. (The changes in base available to form bicarbonate in the body as a whole are

adequately defined by balance of sodium plus potassium minus chloride).
The base available to form bicarbonate is regulated by the kidneys. The
kidneys have the ability to control the acid-base equilibrium of the blood
by regulating the acidity of the urine.[8] This function demands adequate
circulation and sufficient water and electrolyte.

Several theories explain the control of acid-base balance by the
kidneys. According to one theory, an acid urine is produced by exchange
of hydrogen ions for other cations.[8] The same observations can be equally
well explained by the effect of removal of carbonate and bicarbonate on
the pH of the remaining constituents of the glomerular filtrate. The
kidneys form ammonium, which may be substituted for other cations, and
thereby save sodium and potassium, which would otherwise be necessary for
the excretion of large amounts of anions. This mechanism takes twelve
or more hours to come into full activity. The failure to reabsorb
bicarbonate from the glomerular filtrate explains the excretion of an
alkaline urine. It is noteworthy that formation of an alkaline urine
fails to occur when there is a considerable deficit of electrolyte.

Berliner and his co-workers have attempted to clarify the nature of[9]
the relationship between acidification of the urine and potassium excretion
and have indicated that there is competition between hydrogen and potassium
ions at some common point in their secretory pathway. The fact that
elimination of hydrogen ions secreted into the urine (by inhibition of
carbonic anhydrase) leads to the increased secretion of potassium by the
renal tubules is in accord with the concept that there is competition
between hydrogen and potassium ions for some component of the ion exchange
mechanism whereby sodium is reabsorbed in the distal tubules. For example,
in the presence of acidosis one would expect that a greater share of the

exchange would be given over to hydrogen ion secretion at the expense
of potassium secretion and retention of potassium might be expected.
When the changes in potassium are primary, exactly the converse effects would
be anticipated. In the presence of alkalosis of the body fluids, ex-
change of potassium for sodium rather than of hydrogen for sodium would be
favored.

It has been shown in balance experiments[9] that the administration of
potassium salts increases the potassium content of cells and it may be
presumed that the renal tubule cells participate in this process. When
potassium concentration in the renal tubule cells is elevated, the exchange
of potassium for sodium would be favored, that of hydrogen for sodium
suppressed and an alkaline urine would be produced. The loss of base
that excretion of an alkaline urine implies would lead to the production
of acidosis. On the other hand, when the body is depleted of potassium,
the normal balance between potassium and hydrogen ions is tipped in favor
of the latter and an acid urine isproduced despite the alkalosis which
results. Recognizing a competition between potassium and hydrogen ions,
these contingencies may reasonably be predicted and are in accord with
experimental and clinical observations.[9] Thus an excess of acid is
excreted when body potassium is depleted and a relative retention of
potassium occurs in the presence of acidosis. Evidence that such changes
in renal excretion actually occur can be adduced from the observations
that administration of potassium salts leads to the production of an
alkaline urine and acidosis of the body fluid while depletion of potassium
has been found to be associated with the production of an acid urine in the
face of marked increase in plasma pH and bicarbonate.

The kidneys can excrete more potassium than can be accounted for by the glomerular filtrate, and, though some potassium is always present in the urine, the concentration may be less than that of the plasma. It has been demonstrated that secretion of potassium ions by the renal tubules is required to account for the potassium excretion which may be induced by rapid rates of potassium administration by hypertonic solutions and that this secretory process is one of ion exchange, potassium ions within the cells of the distal tubule being exchanged for sodium ionsfrom the tubular lumen.[9] In experiments on dogs, Mudge et al have observed potassium[10] clearances greater than the simultaneously determined filtration rates, and interpreted as evidence that all of the potassium excreted in the urine cannot be accounted for by the filtration-reabsorption theory alone, but that tubular secretion of potassium also occurs. Excretion of potassium by the tubule cells is not solely dependent on theplasma potassium level, urine flow, or filtration rate.[7] Glomerular filtration rate, but not the other renal functions, seem to vary directly with the potassium intake.[7]

In normal subjects under usual conditions the amount of potassium excreted in the urine represents less than 15% of the amount filtered at the glomeruli, and rarely exceeds 20%. Most of the filtered potassium, therefore, is reabsorbed by the tubules.

Patients with nephritis and reduced glomerular filtration rates tend to excrete in the urine abnormally high percentage of filtered potassium. Such an excretion is essential if potassium balance and a normal potassium concentration in the body fluids are to be maintained in the presence of unchanged intake and reduced filtration rate. Under conditions of low potassium intake as much as 50% of the potassium filtered at the glomeruli has appeared in the urine (normal less than 20%).[7]

It has been shown recently that alkalosis per se can cause reduction in renal function which may require a number of months to return to normal.

It is not clear whether the salt-retaining hormone of the adrenal cortex increases the excretion of potassium by a direct effect on the renal tubules or whether potassium excretion is augmented indirectly when sodium excretion is decreased. All the final regulations of the kidneys are inadequate when circulation is impaired or renal disease develops.

In the production of a marked potassium deficiency in surgical patients, the importance of the continued renal excretion of potassium in the presence of hypopotassemia has been well emphasized by Tarail and Elkinton.[12] In their patients, the concentration of potassium was never lower in the urine than in the serum. Marks[31] found this to be true on observing ten surgical patients studied during a period of hypopotassemia. Apparently the renal tubules have a minimal rate of excretion of potassium and will not reabsorb potassium against a concentration gradient.[12] In fact, as has been previously pointed out, experiments have shown that the renal tubules may secrete potassium.[10] Thus, unlike sodium, potassium is excreted by the kidney during an existing deficiency; for this reason it can be seen that the clinician receives little help from the patient's body in the correction of a deficiency. Massive infusions of saline or glucose are important factors in potassium loss; sodium replaces potassium in this process, giving rise to edema. Losses may be large in dehydration because the kidney preferentially secretes potassium instead of sodium.[13] Potassium losses after major operations are large and are greatest during the first twenty-four hour period, partly because of the high nitrogen loss during this period.

From the foregoing discussions, it can be seen that both the kidney and cell mass play important roles in the normal homeostasis of extracellular potassium (the blood and tissue cells contributing potassium to maintain plasma concentration). But there are limits to the capacity of these homeostatic mechanisms, as will be seen later.

ABNORMAL POTASSIUM METABOLISM

HYPOKALIEMIA

It was formerly believed that the cell membranes were impermeable to sodium, potassium, and other electrolytes; however, ideas on this subject have been sharply modified in the last few years and have proved this postulate to be erroneous. This new knowledge has provided a physiologic background which enables the physician to better understanding of the clinical physiology of potassium and to better therapy of dehydration.

Actual serum potassium concentration is determined by a balance of all factors operating at the moment, the equilibrium between cellular and extracellular potassium constantly being interfered with by a number of events which serve temporarily to raise or lower unduly the concentration of serum potassium.[1] It has been previously pointed out that the transfer of potassium between the extracellular components is relatively rapid while its transfer through the cell membrane is slow as compared to the transfer of water. Moore[14] demonstrated this slow permeability of the cell membrane by the injection of radioactive potassium and found that a period of fifteen hours was required before radioactive potassium reached an equilibrium with cellular potassium. By comparison he found that when heavy water was injected an equilibrium with total body water was reached in two hours.

There are many factors which tend to decrease serum potassium levels. Those of greatest interest to the surgeon in post-operative patients are:

1. decreased potassium intake
2. increased extracellular fluid volume by potassium-free fluids
3. vomiting or diarrhea
4. alkalosis
5. increased renal excretion of potassium which may occur in diuresis, acidosis, or adrenal cortical hyperactivity.

There are other contributing factors, for it is highly probably that anesthesia and operative trauma, are, in part, responsible for the sustained high potassium output in patients. (On the other hand, decreased output of potassium and nitrogen in the older patients, especially true of elderly women, maybe indicative of decreased protein synthesis as a primary difficulty, and therefore poorer stores for the catabolism incident to fasting)[15]. Hemorrhage, shock, dehydration, and glycogenolysis are other contributing factors.

The most important of the several factors which interfere with cellular and extracellular potassium balance follow.

1. Starvation

It has been previously mentioned that following a meal rich in potassium, the serum potassium may rise slightly but none is stored and the serum level returns to normal as the ingested potassium is excreted by the kidneys[12]. In gastrointestinal disease potassium may be lost not only because of losses through vomiting and diarrhea but also because normal ingestion of potassium may be prevented. Meanwhile, the kidneys continue to excrete potassium in spite of reduced storage levels.

The production of potassium deficiency is dependent on greater output than intake. It should be understood that deficiency of potassium refers to greater loss of potassium than other cellular constituents. In the undernourished, starved, or debilitated patient, catabolism of the cells occurs, that is, the body "burns itself for fuel." If potassium and nitrogen are excreted in the proportions found in the cells, the remaining tissues may have essentially normal composition. This causes serious undernutrition but not deficiency of

potassium, however. Balance studies made preoperatively and post-
operatively on surgical patients by Randall and his coworkers[16] have
shown that the potassium losses were from two to three times higher
than would be anticipated by nitrogen loss, and therefore, this
potassium came from intact cells. Loss of potassium in excess of the
amount expected from loss of nitrogen is presumptive evidence of
intracellular potassium deficit, and has been observed during the
immediate postoperative period by several others.[17] Such losses may occur
from dietary deprivation. Also there seems to be a general correlation
between the severity of the operation and the magnitude of the
potassium loss.

Since the kidney and stools always contain potassium, diets low
in potassium result in deficiency of this ion. Most foods contain
adequate amounts of potassium, therefore, parenteral feeding is the
chief means of nutrition that is likely to cause deficiency in
patients.

This state of chronic intracellular potassium deficit is often
seen in surgical patients. A starved patient who has lost five killo-
grams of muscle tissue needs, among other things, about 600 milliequiva-
lents to rebuild it.[14] (But the concept that one can make him rebuild
this tissue simply by giving him the building blocks through an intra-
venous needle is in radical need of revision. This tissue will not
be rebuilt unless the endocrine stimulus for synthesis of tissue is
present).

Cellular breakdown which occurs in starvation, trauma, and disease
results in the release of potassium from the destroyed cells. This
release often occurs at a rate greater than that at which it can be

removed by excretion or by transfer to other cells, in which case

hyperpotassemia results.[18] For every gram of nitrogen broken down

in such conditions, about 2.4 grams of potassium is released.

Chronic intracellular potassium deficit on the basis of

starvation seldom coexists with a low plasma **potassium** concentration.

Most patients suffering from slow starvation maintain a normal extra-

cellular concentration of intracellular electrolytes despite the fact

(at least at the outset) the loss of potassium exceeds the loss of

nitrogen.[14]

2. INFUSION OF POTASSIUM-FREE FLUIDS

The malnutrition of the surgical patient may be aggravated by

infusion of potassium-free fluids in the treatment of dehydration.

This results in a rapid lowering of serum potassium concentration by:[19]

 1. the dilution of the extracellular fluid
 2. the transfer of water from cells to the extracellular
   fluid in an attempt to lower the osmotic pressure
   of the latter
 3. the increased renal excretion of potassium accompanying
   the excretion of urine.

Stewart and Rourke[20] proved that prolonged therapy with daily infusions

of glucose and saline produce potassium deficits. Gamble[21] showed in

a patient with daily urine potassium excretion of approximately 60

milliequivalents per 24 hours, when 20 Gm sodium chloride were given

daily, the urine excretion of potassium rose to approximately

90 milliequivalents per 24 hours and promptly fell to 40 milliequivalents

per 24 hours when sodium chloride was once again withheld. When ammonium

chloride was ingested, the urinary excretion of potassium rose to

130 milliequivalents per 24 hours. Thus to preserve the normal total

ionic concentration, removal of intracellular electrolyte occurred. In

order to keep the total milliosmols around 310 to 315 milliosmols per

liter, potassium necessarily leaves when sodium is added.

Changes in intracellular potassium may occur without detectable changes in intracellular sodium, although there is usually a reciprocal relationship between intracellular sodium and potassium. Under abnormal conditions as much as one-half of the intracellular potassium may be replaced by about two-thirds of the equivalent amount of sodium.[8]

It will be seen that deficit of chloride and deficit of potassium tend to produce the same changes in both extracellular and intracellular fluids. At biologic equilibrium, a deficit of one of these ions tends to lead to deficit of the other.

The hypothesis that the excretion rate of a substance is ordinarily proportional to load is untenable in the case of surgical patients.[22] The normal kidney is able to concentrate sodium chloride taken orally to the extent of 0.29 to -.33 milliequivalents per milliliter. In spite of heavy salt loads, no patient approximates this value.

The concentration of potassium in serum may decrease fairly rapidly owing to factors not involving the external balance. When this occurs, the decrease in serum concentration may be attributed to increase in extracellular volume, to increase in organic constituents of the cells that are accompanied by higher amounts of cellular potassium, and to alteration in the activities and the structures of cells that lead to increase in cellular potassium. In the first place, expansion of extracellular volume is most rapid and important when a decrease in extracellular water and electrolyte is restored by solutions containing sodium and sodium bicarbonate. If extracellular volume is expanded from 0.15 to 0.25 liters per kilogram,[3] the resulting concentration of potassium in serum will be six-tenths of the initial concentration if the changes are entirely dependent on the increase

in extracellular fluid. Normally, the intracellular fluid limits
the fluctuation in extracellular concentration of potassium because
potassium enters the cells when extracellular concentration rises or
potassium leaves the cells when extracellular concentration diminishes.
The state of intracellular potassium limits this reaction, particularly
when there are deficits of potassium in the cells.

Coller and his co-workers[22] published data to show that urine
excretion of potassium was greater in patients infused with isotonic
saline solution than in those receiving hypotonic solution. Gamble
and Wallace[24] measured the amounts of sodium and potassium excreted
in the urine with an intake of 1,200 cc fluid and 100 Gm glucose and
found that when 4.5 Gm of salt were added to this intake, the urinary
potassium excretion was greatly increased.

As a result of increased salt load and increased hypertonicity of
the extracellular compartment, osmotic relationships can only be
maintained by a shift of water from intracellular to extracellular
space. Coller and his coworkers[22] concluded from their observations of
intravenous administration of isotonic salt solutions postoperatively
that the injection of "isotonic NaCl" was attended by an average
retention of 53% of the sodium, 46% of the chloride, and 19% of the water
thirth hours after the operation. Such retentions of salt indicate
a withdrawal of several liters of fluid from the intracellular compart-
ment in order to maintain isotonicity. (However, the infusion of
hypotonic solutions resulted in the average retention of 27% of sodium,
32% of chloride, and 39% of water during the same postoperative period.
Extra water is thereby provided for excretory function of skin and
lungs, and the intracellular compartment is not involved. They thus

advocate that in the post-operative care of the surgical patient, hypotonic solution of 0.45%sodium chloride, or better, 0.38% sodium chloride plus 0.11% sodium bicarbonate solution should replace the "isotonic" solution commonly in use. Also, the administration of sodium chloride solution facilitates the excretion of potassium by the kidneys.[8]

The infusion of these solutions are of consequence also, because a primary change in one physiologic variable, such as the sodium content of the body, is attended by secondary changes in other physiologic variables; consequently, the restitution of the primary variable to "normal" content does not insure the return to normal of the secondary variables upon which ultimate recovery may rest.[22] Therefore, it is obvious that the infusion of sodium salts alone will not satisfy the physiologic demands of the organism after reconstitution of the extracellular salt water volume, and the administration of potassium salts should be considered as an integral part of the treatment. Another factor of importance is the depressed renal function following operation and trauma, and therefore, solutions of 0.9% sodium chloride or 5% glucose are not universally applicable repair solutions. Therefore, the solutions employed in the correction of fluid disequilibrium states should be constituted as to effect the correction without depending on the kidneys.

3. VOMITING, SUCTION, DIARRHEA, etc.

More recent reports have served to emphasize the fact that any surgical patient subject to excessive electrolyte deficits, either by vomiting, prolonged gastric suction, Miller-Abbott tube suction, or intestinal fistula may be a candidate for the metabolic abnormality of

an alkalosis characterized by a low serum potassium, a high serum bicarbonate, a low serum chloride, and normal or increased output of urine chloride.

Although metabolic alkalosis may be produced by relative excess of sodium, it usually results from relative deficit of chloride. The commonest cause is loss of gastric juice by vomiting or suction drainage. Furthermore, potassium concentration is normally high in gastric secretions and may at times be as high as 40 milliequivalents per liter, although usually is approximately 22 milliequivalents per litter (80-90 mg%). Thus in vomiting, gastric suction, or severe diarrhea, large quantities may be lost with the enteric contents.

Potassium concentration in intestinal juices is usually 8-10 milliequivalents per liter.[16] Normally almost all of the potassium in gastric and intestinal secretions is absorbed back into the blood. Losses of gastro-intestinal fluids undoubtedly contribute to deficits of electrolytes other than sodium and chloride. Prolonged or severe losses of such fluids, however, would be required to cause significant potassium deficit, since various intestinal secretions are relatively low in potassium content.[17] In many patients studied by Elkel et al[17] with this syndrome, loss of gastro-intestinal secretions was either absent or insignificant, indicating that such losses are not essential to the development of the syndrome.

The work of Darrow and his co-workers[6] h as given biochemical foundation to the observations seen in this condition. They noted that loss of the ion from within the cell resulted in an attempt by the body to maintain intracellular isotonicity by migration of the sodium

ion into the cell from the extracellular space. When this change has occurred, as a result of excessive potassium loss, equilibrium between the intra-and extra-cellular structure is maintained by a rise in serum bicarbonate. Rise in the serum bicarbonate results in the preferenterial excretion of the chloride ion by the kidney in an effort to maintain isotonicity of the extracellular fluid. Thus, the lowered serum chloride concentration is, at leas t in part, a compensatory measure and not a primary deficiency of this ion.[25] Added evidence of this fact is seen in observation that the urine contains normal or increased amounts of chloride in spite of lowered serum chloride levels. With these changes in mind, it is quite apparent that this condition cannot be corrected by sodium chloride administration alone.

As a result of vomiting and loss of gastric juice, animals do not show a deficit of potassium unless abundant water is available.[10] Apparently, some vomiting patients will not get sufficient water to permit the renal adjustment to loss of chloride; others get enough water to lead to losses of potassium as well as chloride.

Differential intracellular potassium deficit accurately describes the situation so commonly seen in surgical practice in which electrolyte and water loss from cells outstrips the loss of nitrogen and matrix. A differenterial (disproportionately large) loss of potassium is therefore observed relative to cell proteins and structure. A normal plasma potassium concentration is the rule. Patients with intestinal obstruction, peritonitis, advanced stages of cancer, biliary disease, and vomiting show this differential loss of potassium with regularity.[14] Theprovision of potassium to such patients acquires an

importance wholly apart from the provision of nitrogen and these patients constitute the only true example of acute potassium deficiency seen in surgical practice.

Of importance in these conditions is the rate of water depletion. A condition seen often in surgical cases in which there is moderate rapidity of water depletion is that of pyloric obstruction or high intestinal obstruction in which there is a predominant extracellular loss occurring over the course of two to seven days. Here the loss of water takes place at a rate which calls on compensation largely across the fast membrane (capillary) because it is proceeding at a rate more rapid than cellular water aan be collected in replacement. [14] The result is a negative sodium balance which far outstrips potassium and nitrogen losses and which may go on to a fatal outcome with high hematocrit and low plasma volume indicating that the loss is out-stripping compensation across the fast membrane. The loss of potassium in such cases is of importance, and it almost always exceeds the loss of nitrogen (suggesting that the cell mass is capable of some dehydratin and loss of electrolytes before its protoplasmic structure breaks down) yet the potassium loss is quantitatively small as compared to the loss of sodium.

4. METABOLIC ALKALOSIS

Closely allied with hypokaliemia is the problem of refractory alkalosis. Metabolic alkalosis is produced by primary increase in the sodium available to form bicarbonate in the serum and usually results from relative deficit of chloride rather than relative excess of sodium. If sufficient water is available to permit renal adjustment

potassium will tend to be lost from the cells and sodium will partially replace the intracellular deficit of potassium. Recently Darrow and his associates[6] found that when intracellular potassium is depleted and the intracellular sodium is increased, biologic equilibrium is achieved only by a high serum bicarbonate, which in turn increases output of urine chloride. Thus it is quite fallacious to push the administration of chloride in an attempt to overcome the hypochloremia and alkalosis of this type, as the kidney is already doing its best to excrete chloride because of a high serum bicarbonat. Obviously, the rational therapy would be designed to increase the intracellular potassium and decrease the intracellular sodium which would allow the serum bicarbonate to fall to normal and make room for the serum chloride to rise to normal.

The loss of potassium from the kidneys or the gastrointestinal tract is accompanied by loss of chloride which has come from the extracellular compartment. This unbalanced loss of extracellular anions (the chlorides) is compensated for by a rise in the extracellular metabolic bicarbonate anions with a resulting alkalosis.

The co-existence of intracellular potassium deficit and metabolic alkalosis has been demonstrated both experimentally and clinically by Darrow and his co-workers[17], who have observed that in rats made potassium deficient by several means, an excellent correlation exists between the degree of alkalosis and the lowering of muscle potassium content. An increase of muscle sodium coincident with the potassium loss was also observed. It has been shown that the alkalosis and potassium deficit in such rats can be accounted for by a diuresis of potassium and frequently of chloride, and a retention of sodium relative to chloride. Simultaneous expansion of the radiosodium

space and recuction of the chloride content have also been demonstrated in these animals.

The development of metabolic alkalosis and of intracellular potassium loss and sodium gain was considered by Darrow[6] et al to be the result of a biologic equilibrium that is attained in the presence of normal renal function when there is loss of a single ion such as potassium or chloride. Interference with renal function by severe infection or urinary tract obstruction or loss of multiple ions in intestinal fluids might be expected to prevent attainment of this equilibrium.

The chemical signs of an intracellular potassium deficit are:

1. a persistently high carbon-dioxide combining capadty
2. a high blood urea (or NPN)
3. a low chloride concentration in plasma.

If the attempt is made to correct the high carbon-dioxide combining power and the "hypochloremia" by further administration of sodium chloride, the deficit of potassium tends to be aggravated regardless of whether the sodium chloride is retained or excreted, and the chloride concentration of plasma remains low and the carbon-dioxide combining power high. Evans[26] has remarked that if an alkalosis with a carbon dioxide volume above 60% persists in patients with vomiting, or after adequate hydration and sodium chloride therapy, a potassium deficiency should be suspected. It is now likewise appreciated that hypochloremic alkalosis is an indication of potassium deficiency. Elevation of NPN with no kidney damage may be due to chloride and potassium depletion presumably unless the patient is severely dehydrated.[13]

Intracellular sodium may reach levels several times the normal

value and several times the equivalent of the bicarbonate in extracellular fluids. This relationship is important, first because alkalosis will tend to persist if potassium cannot be replaced and second, because deficit of potassium will tend to lead to alkalosis if it is not restored.

5. ANOXIA, DEHYDRATION, SHOCK, HEMORRHAGE, GLYCOLYSIS

In the past decade, potassium has been shown to move out of the cell in shock[27], dehydration[18], hemorrhage[28], anoxia[3], and glycolysis[3] or failure of carbohydrate metabolism[3]. In these conditions, potassium is released from the cells. Possibly this transfer of potassium from the cells to the extracellular fluids and the accompanying urinary excretion is, in part dependent on the increased activity of the adrenal cortex in response to "stress."

If shock is present, deficiency of potassium in the cells may occur with normal or high concentration in serum. During peripheral circulatory failure (shock), there are disturbances in renal function. The rate of glomerular filtration decreases and the concentration of NPN increases. Alteration in renal circulation during shock seriously interferes with renal regulation of electrolyte concentration. Furthermore, accompanying local changes in the tissues, potassium leaves the cells and is replaced by somewhat less than equivalent amounts of sodium. This produces metabolic acidosis and leads to high concentration of potassium in the serum. As long as urine is excreted, a high serum potassium leads to urinary excretion of this ion causing cellular deficits leading to replacement of potassium by sodium in the cells[29].

A similar exchange of potassium for sodium in the cells occurs

in anoxia and explains the rise in concentration of potassium in serum in peripheral vascular failure. High concentration of serum potassium is frequently found in diarrhea and diabetic coma before treatment is initiated despite the fact that the intracellular fluids are deficient in this ion. This sort of reaction leading to urinary excretion of potassium explains in part the loss of this ion in diarrhea, diabetic acidosis, and other conditions. However, the chief interest is the fact that internal shifts of sodium as well as loss of sodium from the body act together to produce acidosis. Reversal of this process must occur during recovery, including recovery from shock.

In dehydration, the slow rate of water loss involved from water deprivation alone occurs in such a way that water transfer across both the fast and slow membranes can keep up with the externally imposed conditions. The water loss is approximately prorated through the plasma, extracellular fluid and cellular water. Negative balances of sodium are followed later by loss of potassium and nitrogen approximately equivalent to body composition, although nitrogen loss may lag slightly behind potassium loss.[14]

6. ADRENOCORTICAL HYPERFUNCTION

Evidence has been presented that adrenal hyperfunction resulting from surgical trauma leads to potassium deficiency.[11] The clinical and electrolyte disturbances seen in the syndrome resemble those in some cases of Cushing's syndrome. Metabolic alkalosis and potassium deficit have been produced frequently in human beings by the injection of ACTH and Cortisone and there is a striking resemblance between

other metabolic changes seen postoperatively and those associated with adrenal hyperfunction. However, evidence that increased excretion of potassium by the kidney from injection of desoxycorticosterone acetate, Cortisone and ACTH (or conditions leading to activation of the adrenal gland by ACTH) occurs regularly in conditions thought to be dependent on the "alarm reaction" has not been obtained.[3]

Lowered muscle potassium, increased muscle sodium, and the metabolic alkalosis have been produced in rats by administration of desoxycorticosterone acetate either alone or with a potassium deficient diet.[6] Reductionof circulating eosionphils is taken as evidence of increased adrenocorticoid secretion. Increased ketosteroid and "S" hormone (sugar hormone responsible for gluconeogenesis) excreted in the urine also is indicativeof increased adrenocortical function. Post operative glycosuria and hyperglycemia offer further evidence of adrenocortical hyperfunction.

Eliel and co-workers[17] believe that surgical trauma causes increased production of ACTH by the pituitary body which stimulates the adrenal cortex to secrete one or more hormones ("alarm reaction"). This reaction probably results in renal loss of potassium and loss or retention of chloride but with retention of sodium relative to chloride and development of metabolic alkalosis if there is inadequate provision of potassium. These statements imply that the events described are very likely to occur after any type of tissue injury-- namely, surgical or accidental trauma, myocardial infarction, acute infections, radiation, nitrogen mustard therapy, etc.

There is evidence[3] that adrenocortical steroids alter the

distribution of water between intracellular and extracellular fluid. Desoxycorticosterone increases extracellular volume and adrenocortical extracts increase intracellular volume. Since these compounds also alter the ion transport, the effect on the concentration in extracellular fluids is modified by internal shifts of ions and renal secretion. Since intracellular volume is at least twice the volume of extracellular fluid, a decrease in extracellular potassium produces but a small change in intracellular concentration unless the transfer is confined to a small part of intracellular fluid. On the other hand a small increase in intracellular concentration will produce a significant decrease in extracellular concentration.

Desoxycorticosterone acetate not only enables the kidneys to reabsorb sodium and chloride from the glomerular filtrate but also increases the rate of excretion of potassium.[8] This may lead to deficit of potassium, particularly if large amounts of sodium chloride are given. The deficits of potassium may lead to low concentration of chloride and potassium in the serum and to high concentration of serum bicarbonate and serum sodium when renal adjustment to deficit of potassium is attained in the presence of abundant sodium chloride. Certain adrenocortical tumors have a similar effect. The deficiency of potassium, especially when large amounts of sodium chloride are given, probably explains some of the instances of cardiac failure noted in patients receiving desoxycorticosterone acetate. Paralysis due to deficiency of potassium has been noted in animals receiving desoxycorticosterone acetate.

7. ABNORMALITIES OF KIDNEY FUNCTION

During the immediate postoperativeperiod, potassium is
excreted in the urine in excess of that anticipated from the break-
down of protoplasm. Darrow[8] has pointed out that because the adjust-
ment of the kidney to loads of water and salt is slow, a more rapid
method of adjustment is afforded by a shift of water from the intra-
cellular to the extracellular compartment. Furthermore, so-called
isotonic solution may not be necessarily isotonic when infused,
as the various compartments of body water possess considerable
variability in respect to content of normal electrolyte and water.
It is therefore felt that the chief factor in pronounced potassium
diuresis during the first six to eighteen hours of these studies is
the necessity of adjustment of the compartments of body water to
fluid given parenterally. Such adjustment is apparently accompanied
at the expense of the intracellular fluid.

Renal losses are exaggerated not only by diuresis but also by
acidosis and by excess adrenal cortical hormone supply.

8. GLYCOGENESIS

The process of glycogenesis carries potassium from extracel-
lular fluid into the cellular compartment in specialized glycogen-
containing tissues, such as muscles and liver. This transfer is
increased by glucose ingestion, insulin and epinephrine. The fall
in serum potassium is rapid although temporary; this change in serum
concentrationis not significant in normal persons. In potassium-
deficient patients and those with diabetic acidosis, the rapid
decrease in serum potassium already low in this electrolyte may

produce serious symptoms. This phenomenon is seen in a relatively
uncommon condition known as familial periodic paralysis in which
attacks are presumably initiated by low serum potassium;
attacks can be brought on by administering sugar, insulin, or
epinephrine.

It is important to the surgeon to remember that lowered serum
potassium always indicates potassium deficiency. On the other hand, the
converse statement is not true and potassium deficiency may be present
in spite of a normal serum concentration. This is explained by the
fact that severe losses of potassium produce tissue breakdown and the
release of potassium from these destroyed cells raises the reduced
extracellular potassium to normal levels.

Disturbances of potassium metabolism might then be sought
in diseased states which produce functional aberration in one or more
of these systems involved in homeostatic regulation, namely, renal
disease, nutritional disease, or abnormalities of cellular metabolism.

CLINICAL EVIDENCE OF HYPOKALIEMIA

The clinical recognition of potassium deficiency depends primarily on the knowledge of conditions under which potassium loss occurs. The prevalence of these conditions in surgical patients should be emphasized.

The signs and symptoms of this disorder, other than electrocardiographic changes, are not specific, for they may be found in many debilitating conditions. They constitute a number of complaints and findings which may be lightly passed off by the busy clinician if he is not aware of their possible significance. The more common symptoms are lassitude, drowsiness, weakness, and loss of appetite, associated with the findings of moderate adynamic ileus, oliguria, and hemoconcentration. The presence of any two of these symptoms or signs in a patient in whom one might anticipate substantial electrolyte loss, should lead one to suspect and investigate the possible presence of this condition.[25]

Clinically, potassium deficit can only be proved by demonstration of a greater reltive loss of potassium than nitrogen during the development of the condition or a greater relative retention of potassium than nitrogen during recovery. If body water and circulation are relatively normal, deificiency of potassium is likely to be accompanied by low concentration of potassium in serum. Under these sonditions, certain patients show paralysis of the skeletal muscle and abnormal function of the cardiac muscle.

The signs and symptoms, in order of frequency, as observed by Eliel and associates[17] were abdominal distention and cramps, lethargy, apathy, depression, anorexia, nausea or vomiting, and muscular weakness.

Less frequently seen were confusion, disorientation, delirium or
hallucinosis, nervousness, irritability and apprehension, ielus (with
x-ray evidence), muscle twitching or tetany, and edema (except for a
fall in serum protein concentration there was no obvious clinical explana-
tion for its appearance). Irregular pulse and shallow respirations
were rare. Administration of potassium chloride was followed, with few
exceptions, by prompt and sometimes striking improvement in mental
attitude, muscular strength, appetite, bowel function and cardiac
rhythm, along with disappearance of the edema.

The symptoms and signs as summarized by Darrow[8] and co-workers
are as follows:

1. weakness and hypotonia of the skeletal muscles progressing
   to frank paralysis (usually the paralysis of the arms and
   legs appears first and that of the respiratory muscles
   later).

2. dyspnea with gasping respirations in which the accessory
   respiratory muscles are involved.

3. cyanosis which is chiefly respiratory in origin, but may
   be in part cardiac.

4. abdominal distention which seems to be dependent on atonia
   of the smooth muscle.

5. nausea and vomiting.

6. cardiac enlargement with the appearance of systolic murmurs.

7. increased pulse pressure with Corrigan pulse.

8. elevated venous pressure and signs of cardiac failure.

The paralysis of the diaphragm and abdominal muscles and the functional
disturbances of the myocardium accounted for the major clinical signs
and symptoms. These signs and symptoms were abolished by the restoration
of the serum potassium concentration to its normal level.

It is indeed unfortunate that there is no consistency in the

symptomatology of potassium deficiency; in fact, there is no single symptom which can be considered strongly indicative of the condition. The two most dependable mechanisms of confirming the condition are EKG tracings and serum potassium determinations. Alkalosis is fairly constant but obviously may be caused by many other conditions. Many clinicians agree[13] that any patient who has had a major operation and at least three full days of gastro-intestinal decompression, is likely to have a potassium deficiency. Complaints of the patients may run from inability to sleep to irrationality. There is, however, one consistent feature about the symptoms, namely, that they disappear rapidly after the patient begins to eat and reatin food; likewise, the serum potassium level reverts to normal rapidly after eating is resumed.

Physiological Aspects of the Clinical Manifestations

Of the three principal ions, sodium, chloride, or potassium, only potassium seems to alter cellular functions owing to specific ion effects. Although it has long been known that potassium plays certain essential roles in neuromuscular physiology, only recently has the clinical significance of alteration of the potassium ion been realized.

Peripheral, as well as cardiac, neuromuscular mechanisms are disturbed as the result of abnormal concentration of potassium. Curiously enough, the neurologic manifestations are much the same whether the potassium be high or low.[4] Sensory disturbances are minimum, usually with complaints of only mild paresthesias of the extremities. Motor phenomena are striking--first weakness and then flaccid paralysis of the

extremities, sometimes of the ascending or Landry's type. The trunk and cranial nerves are rarely involved, but weakness of the respiratory muscles results in a shallow, definitely regular, rapid pattern which is distinctive. These paralyses are apparently dependent on the effect of low serum potassium on the myoneural junction. However, these peripheral neuromuscular defects are late manifestations of hyper- or hypo-kaliemia, and are always preceded by EKG changes. Conversely, in recovery from the dysfunction of hypokaliemia, the EKG shows reversion to normal soon after return of the serum potassium to normal, whereas the paralytic phenomena pass far more slowly and, indeed, may persist for several hours.[4]

In rats subjected to pronounced potassium deficiency, dilated intestines developed and no stools were passed. Without therapy these rats would die as if they had paralytic ileus. The evidences of intestinal paralysis were relieved by potassium.

Deep tendon reflexes were usually hypoactive in patients observed by Earle,[7] however they were variable and showed no particular relation- ship to potassium intake or plasma levels. Periods of potassium deple- tion were characterized by three findings which may be attributed to involvement of the autonomic nervous system.[7] Thus, when low potassium intake was instituted, troublesome constipation, bladder atony, and prolongation of the P-R interval in the EKG developed. These abnormalities regressed promptly on administration of potassium.

ELECTROCARDIOGRAPHIC DISTURBANCES ACCOMPANYING HYPOKALIEMIA

In hypopotassemia, the electrocardiograph reveals a typical tracing, although the changes parallel only approximately the changes in serum potassium concentration. While not absolutely specific, reversal of the EKG changes accompanying restoration of the concentration of potassium in serum indicates that they are related to serum potassium concentration. The changes which have been attributed to abnormal serum potassium are illustrated diagrammatically in the following figure:[8]

serum K mM/L		inverted T; depressed ST; prolonged QT
low		low wide T; long QT; low voltage
normal (3.5-6)		normal
high [7]		elevated T
		long PR; wide QRS; low ST
		absent P
		absent P
[10]		biphasic
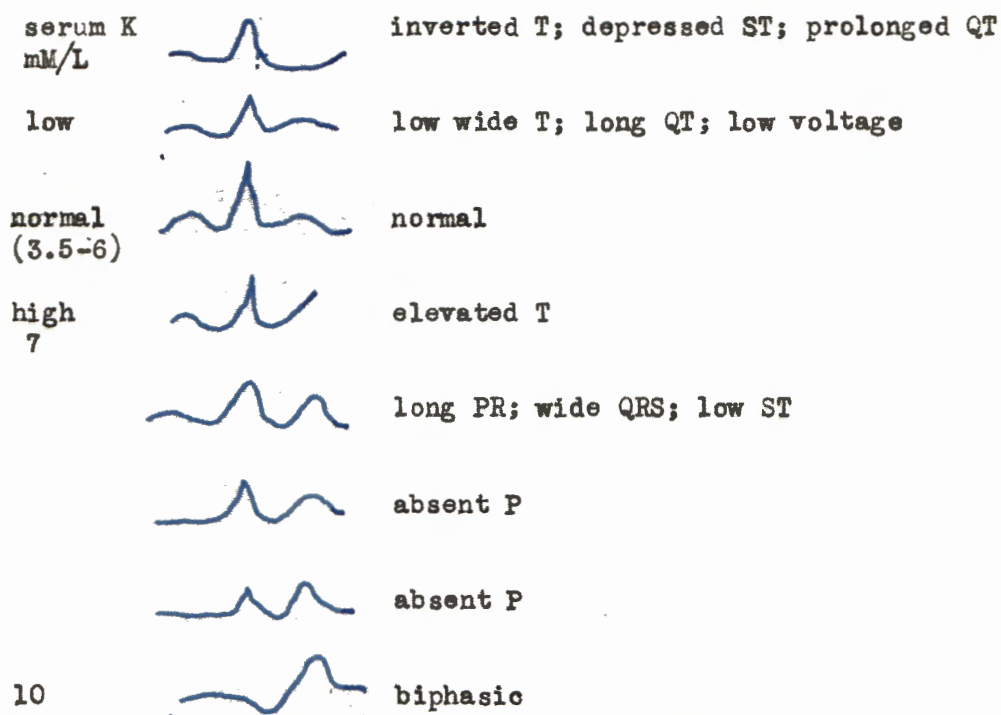
The following changes accompanying low concentration of potassium in serum should be noticed:

1. slightly prolonged Q-T interval
2. decreased height and inversion of the T waves
3. rounded and prolonged T waves
4. depression of the S-T segment
5. possible inversion of the P waves, extrasystoles, and auriculo-ventricular block.

prolonged Q-T

low T wave

sagged S-T segment

depressed S-T

As the serum potassium is lowered, prolongation of the Q-T interval is the first change seen in the EKG. The second change is lowering or inversion of the T waves, and in the third stage the S-T segments sag. In the final stage the take-off of the S-T segment is depressed and there is a slow staircase-like rise to a low late T wave. This final stage is seen with potassium levels in the range of 1.5 mEq per liter or lower. Marks[4] found that the precordial leads CF_2, CF_3, and CF_4[31] are of particular value in detecting early changes.

Thompson[32] showed direct correlation between the height of the T waves and the level of serum potassium; therefore, if one sees a low T wave on the EKG, the possibility of hypokaliemia should be considered. The height of the T waves has been found also to be influenced by the pH and the partial pressure of carbon-dioxide as well as the concentration of potassium in the serum.[8]

The low broad T wave of hypokaliemia is primarily responsible for the prolongation of the Q-T interval, while in hypocalcemia, the T wave is normal and the lengthened S-T segment produces the change. Digitalis and myocardial disease influence the Q-T interval and these factors should be considered in interpreting this measure. Studies by Eliel[17] have shown that in some patients lowered amplitude of the T waves was coincident with the development of alkalosis and hypochloremia, but preceding a fall in serum potassium, thus indicating that the EKG

may in certain cases be a better index of tissue potassium deficit than the serum potassium level. This would fit observations that there may be considerable tissue losses of potassium without depletion of extracellular potassium. The almost invariably lowered amplitude of T waves that occur in cases reported suggest that this change may be used in the diagnosis of potassium deficit, particularly if serum potassium levels are not readily attainable. Confirmatory evidence can usually be found in the presence of elevated serum pH and serum carbon dioxide content, and hypochloremia. As has been mentioned, the presence of myocardial lesions or the administration of digitalis will obscure EKG changes from potassium deficit.

    Earle,[7] however, reports that normal EKG was observed at times in the presence of moderate hypokaliemia. He concluded also that abnormalities in the cardiac electrical potentials occurred <u>only</u> in the presence of hypokaliemia and their extent from day to day bore no close relation to the level of plasma potassium.

    The potassium ion is necessary for normal cardiac function. In the absence of potassium, heart block will ensue and the heart will stop beating in systole (if the concentration of potassium is too high, the heart will once again fail, but in diastole due to a direct depressant action of the ion on the myocardium).[33] The action of potassium on the heart is two-fold, affecting both the impulse conduction and the muscle contractility. Therefore, potassium depletion affects the heart in two ways:[7]

    1. An effect on the muscle cell indicated by the prolongation, flattening and broadening of the T wave.
    2. A neurogenic effect indicated by readily reversible increased

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vagal tone. These effects could be separated by releasing vagal control, as with atropine. Atropine was found to have no effect on the T waves and S-T segment abnormalities] thus the A-V block appears to be an effect of potassium depletion on relative vagal control.

It appears that potassium administration to the depleted subject is rapidly distributed to the heart, as judged by the rapid changes in the T wave of the EKG.[7] This is followed by redistribution of potassium to other tissues as evidenced by the gradual but steady increase in muscle strength over the subsequent forty-eight hour period of observation. In contrast, the height of the T waves of the EKG repeatedly reflected the acute changes in plasma potassium level following each administration of potassium, but this effect was transient so that the T waves had returned almost to the control value at a time when muscle strength was showing continuous improvement.

It is of interest to mention the experimental results that have been obtained on rats placed on potassium deficient diets. Several investigators have demonstrated in rats kept on a diet extremely deficient in potassium the development of focak necrosis throughout the myocardium with ultimate replacement of this heart muscle by connective tissue. Orent-Keiles and McCollum[34] report post mortem analysis of greatly reduced potassium content of the heart, skeletal muscle and kidney with necrosis and scarring of the heart muscle fibers, as well as necrosis of renal epithelium with tubular dilatation. Low serum potassium, low muscle potassium and myocardial necroses have been produced by poisoning with desoxycorticosterone, presumably in large part as the result of the potassium diuresis effected by this steroid.[35]

The occurrence of ectopic rhythms (ventricular premature beats and nodal rhythm) with potassium deficit has not previously been

emphasized. Bigeminal rhythm has been produced in a patient with familial periodic paralysis by the administration of a large quantity of glucose, with a subsequent fall in serum potassium concentration.[36]

Often, surgical patients with a hypokaliemia at the onset may develop hyperpotassemia from various causes to be enumerated later. Thus, it is appropriate to mention briefly EKG changes in hyper-potassemia. The sequence[8] of changes with increased concentration of serum potassium is:

1. appearance of peaked T waves
2. increased duration of QRS
3. increased duration of P-R interval leading to auricular standstill
4. Biphasic curve with progressive delay in ventricular conduction
5. total arrhythmia progressing to cardiac arrest.

Hyperkaliemia arises almost exclusively when renal excretion is greatly diminished because of renal disease or oliguria accompanying shock and dehydration. The increase in extracellular potassium may come from food or potassium-containing salts administered either orally or parenterally, from the release of potassium from the cells caused by the catabolism of cellular structures, or the release of cellular potassium which accompanies anoxia or other disturbances in cellular metabolism. It is difficult, if not impossible, to produce potassium intoxication by the oral administration of potassium salts to patients with normal kidneys and circulation. However, too rapid parenteral administration of potassium salts may produce hyperkaliemia. Heart block develops at concentration of ten millimoles or more of potassium per liter of serum,[8] but other minor evidences of cardiac disturbance may develop at concentrations as low as seven millimoles per liter.

The use of the EKG as a guide to judicious potassium repletion has been emphasized, particularly if determination of serum potassium levels are not readily available. Return of flattened T waves and low S-T segments to normal indicates adequate therapy, whereas the appearance of high, spiked T waves is the first indication of potassium toxicity.

The chief symptoms characteristic of potassium deficiency such as paralysis of skeletal muscle, EKG changes, intestinal distention, and paralytic ileus are related to the low concentration of potassium in the serum. However, myocardial necrosis probably is caused by disturbances in concentration in the cells.

All the EKG abnormalities, except those due to infarct, disappear on the administration of potassium chloride. The rate of disappearance in general parallels the restoration of the serum potassium level and may occur within twenty-four hours in some instances.[17]

OTHER CLINICAL SIGNS

Edema:

Generalized edema, pulmonary edema, enlargement of the liver, and myocardial failure are frequent in hypokaliemic states,[3] and these symptoms improve with potassium therapy or when food is taken. In addition, some patients show edema associated with low serum albumin. The injection of plasma proteins and amino acids fails to restore the serum protein but improvement follows potassium therapy. The beneficial effect is so striking that one gets the impression that the production of serum albumin is more adequate in tissues with normal potassium. However, the effect is probably indirect through improvement in

appetite and nutrition.

The sodium retention demonstrated by the space determination
and balance studies probably account for the water retention (edema)
and at least some of the hypoproteinemia observed in many cases.[17] Pro-
vision of potassium results in a diuresis of sodium and water, dis-
appearance of edema and rise in serum protein. Disruption of the
operative wound and evisceration occurred in two patients reported by
Eliel[17] after potassium deficit had developed. This suggests that
potassium deficit or resulting edema of the suture line, or both, may
interfere with wound healing. The edema, a symptom of postoperative
salt intolerance, may result not so much from the retention of water
with salt as from the shifting of water from the intracellular to the
extracellular space to maintain osmotic relationships. It is unknown
how much dehydration the cells can undergo before function breaks
down and ceases. The brain cells are especially sensitive to change
and the disorientation so often seen in cases of salt intolerance may
be a symptom of this fluid shift.

Jaundice:

Nelson[33] reported a patient with refractory alkalosis and low serum
potassium who developed jaundice. Liver function studies failed to
corroborate the possibility that the jaundice might be due to hepatitis
from the use of plasma or blood in the post-operative treatment of the
patient. The clinical course with the rapid diminution in the intensity
of the jaundice commensurate with restoration of the fluid and electrolyte
pattern to normal, together with the unusual association of results of
the liver function tests, lead one to believe that the jaundice was

probably due to malnutrition and electrolyte imbalance rather than anything more specific such as infectious hepatitis or homologous serum hepatitis.

Although it has been only during the past few years that the importance of potassium deficiency has been appreciated, it is now well established that it alone may occasionally result in death. Much more often, its influence, added to that of two or three other complications, may be responsible for the death of the patient. Respiratory paralysis, myocardial lesions (loss of striation, focal necrosis, leukocytic infiltration), frequent ventricular premature beats suggest that ventricular fibrillation may eventually result if the deficit is not corrected. Ileus resulting from potassium deficit may be a factor in post-operative death by contributing to fluid and electrolyte depletion and to malnutrition. A patient already critically ill may be brought to a needless operation for relief of obstruction with dire consequences. Prompt and adequate administration of potassium can easily prevent death from any of these complications.

SURGICAL CONDITIONS CHARACTERIZED BY

HYPOKALIEMIA

Because dehydration is such a common problem to the surgeon, usually necessitating parenteral fluid therapy for long periods, the management of problems of water and electrolyte balance is of major importance in surgery. It is now obvious that potassium balance is an integral part in the electrolyte balance and that management should include judicious potassium therapy for the surgical patient.

The clinical recognition of potassium deficiency depends primarily on the knowledge of conditions under which potassium loss occurs. The pathogenesis and prevalence of these conditions in surgical patients have been previously reviewed in this paper, however, it does not seem superfluous to briefly reiterate the surgical conditions causing hypokaliemia and resulting alkalosis. Typical cases on surgical wards are those in which potassium is gradually drained from the body stores, with progressive weakness of the patient due to :

> 1. prolonged Wangensteen drainage of the upper
>   gastro-intestinal tract
>
> 2. administration of potassium deficient intravenous
>   fluids
>
> 3. good urinary output resulting in urinary losses of
>   potassium.

The main causes of the low potassium syndrome in surgical patients are:

> 1. Potassium deprivation:
>   Adults on a normal intake who are abruptly deprived
>   of potassium will continue to excrete potassium
>   in the urine in excess of that expected from the
>   nitrogen balance. This loss may amount to about
>   20-50 mEq. on the first day and gradually decrease
>   thereafter. [17]

2. **Water and sodium chloride intake:**
   Large infusions of glucose or a large intake of
   sodium chloride either parenterally or orally will
   induce losses of intracellular potassium. Sodium
   chloride appears to cause substantially larger losses
   than glucose in water. Elevations in the concentration
   in serum produced by injection of sodium chloride
   release potassium from the cells and cause increased
   excretion. Some patients with renal insufficiency
   are unable to conserve potassium. This tendency is
   probably aggravated by large intakes of sodium chloride.

3. **Losses of gastro-intestinal secretions:**
   Metabolic alkalosis produced by excess withdrawal and
   inadequate replacement of chlorides from the stomach
   results in a potassium deficit, Prolonged duodenal
   drainage after operation provides the condition for
   development of alkalosis with potassium deficiency.
   The removal of the gastric fluid depletes the body
   of more chloride than sodium and produces alkalosis.
   The administration of sodium chloride facilitates
   the excretion of potassium by the kidneys. While
   sodium chloride is usually administered in sufficient
   amounts to replace extracellular electrolyte, the
   development of potassium deficiency alters the renal
   function so that metabolic alkalosis persists. The
   alkalosis probably develops because of a chloride
   deficit, but it persists because of a deficiency of
   potassium.

   High intestinal obstruction and the loss of fluids
   through catheters introduced into the upper intestinal
   tract after operative procedures produce alkalosis
   because the amount of gastric fluid removed is greater
   than the amount of the intestinal juices. Abnormal
   losses of water and electrolyte from the gastro-intest-
   inal tract may also occur as a result of vomiting,
   escape of gastro-intestinal fluids through fistulas,
   and diarrhea.

   The stools in diarrhea vary widely in composition.
   In some patients the concentration of eledtrolytes
   is so small that little decrease in body electrolytes
   developes despite the loss of large volumes of water
   in the stools. In other patients the stools contain
   so much water and electrolyte that the tissues are
   rapidly depleted of both water and electrolytes.
   Practically all types of diarrhea tend to produce
   greater relative losses of sodium and potassium than
   of chloride. The result is a type of metabolic
   acidosis in which changes in the composition of
   intracellular fluids play an important role.

However, recent experiments indicate that diarrhea in which the stools contain more chloride than sodium develops in rats subjected to potassium deficiency. Similar developments in adults may occur suggesting that a change in intestinal absorption leading to stools containing more chloride than sodium may result when pronounced deficit of potassium develops.

4. Malnutrition and debilitation:
Cellular breakdown occurring in these states results in the release of potassium from the destroyed cells. Howard and Carey have emphasized the possible role of prior malnutrition with potassium depletion in the development of operative potassium deficiency.

5. Adrenocortical hyperfunction:
Surgical trauma introduces the "alarm reaction" with resulting increased urinary secretion of potassium made available from body stores. The development of adrenal hyperfunction following surgical trauma is well established.

6. Shock:
Disturbances of potassium metabolism are frequently encountered in shock whether traumatic, surgical, or of other etiology. In shock a hypopotassemia may be present from "an obligatory expansion of extracellular fluids owing to circulatory changes." On the other hand, oliguria is not an infrequent accompaniment of shock and in such patients the possibility of hyperpotassemia must be considered.

7. Polyuria:
The presence of polyuria in a patient should suggest the possibility of hypopotassemia. Potassium is excreted in the urine roughly in proportion to the amount of urine and in the presence of other factors disturbing normal potassium metabolism its loss may reach a clinically significant stage.

It should be recalled that in the post-operative course complicated by such events as urinary-tract infections, ureteral obstruction, peritonitis, pelvic abscess, evisceration, fecal fistula, etc., an associated alkalosis or hypochloremia (or both) may be absent. These complicating factors may account for the failure of alkalosis or hypochloremia to develop.

CASE PRESENTATION

The following case, as presented by Nelson and co-workers, is an excellent example of hypokaliemia in surgical patients. This case presents many interesting problems from the standpoints of fluid and electrolyte therapy, EKG changes, neuromuscular manifestations, jaundice, and operative findings.

History:

"Patient, age 30, following an uncomplicated delivery of a normal baby, began to vomit undigested food which temporarily subsided with administration of intravenous fluids and supportive measures; these symptoms recurred in three weeks with evidence of carpopedal spasm relieved by intravenous calcium. Past history of episodes of slight gaseous distention after meals and occasional vomiting spells since age of 12. No history of pain, hematemesis, or melana. Family history was noncontributory."

Physical examination:

Thin white woman, exhibiting all signs of frank tetany (which was relieved by intravenous administration of 20 cc 1% calcium gluconate); otherwise physical examination was negative.

Laboratory:

Urinalysis:	specific gravity:	1.035
	pH:	6
	albumin:	trace
	sugar:	4 plus (patient had received IV glucose)
	acetone:	negative
	diacetic:	negative
	rbc:	negative
	casts:	negative
	wbc:	occasional

Blood:	Hb:	9.5 Gm%
	wbc:	4900
	Differential:	
	polys: 50	
	lymph: 46	

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            monos:              2
        plasma cells:           2
    Blood type:                 A Rh positive
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Serum chemistries:

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    bicarbonate:            80 vol. %
    chloride:               94.0 mEq/liter
    protein:                 6.4 Gm %
    phosphorus:              2.0 mg.%
    calcium:                 8.4 mg.% (day following treatment for tetany)
    total bilirubin:         0.9 mg.%
       1 min. fraction:      0.4 mg.%
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X-ray:

> Marked gastric dilatation; enormously dilated duodenal cap
> (5-6 times normal size) and showing what appeared to be a
> complete obstruction between 1st and 2nd portions.

Gastric analysis: Positive for free acid.

EKG: 7th hospital day: Abnormal with negative T waves.
     42nd hospital day: 2nd degree heart block.
                          occasional supra-ventricular premature systoles.
                          depression of S-T segment.
                          low or negative T waves in all leads.

COURSE:

Complete obstruction preventing oral feedings and requiring aspiration
of foods already given. Gastric juice negative for bile.

4 blood transfusions over 10 day period raising Hb. to 16.6 Gm.

8th day: serum K 3.4 mEq/liter; serum Na 129 mEq/liter.
2 weeks of IV therapy averaging: 3-4 liters of 5% glucose daily
                                    15 Gm NaCl daily.
At this time alkalosis still persisted (serum bicarbonate between
33 and 36 mEq/liter).

Occasional bouts of tetany necessitating administration of calcium salts IV.

Testosterone: 25 mg. daily for 5 days to facilitate nitrogen deposition.

Fever, tachycardia, deep calf tenderness; diagnosis of thrombophlebitis
and put on 2 weeks course of dicumarol and heparin.
2 gastric juice analysis with triple histamine stimulation, both showing
no free acid in striking contrast to admission analysis.

Course progressively down-hill with increasing muscular weakness, lethargy, and unresponsiveness. On the 40th hospital day, the patient couldn't turn herself in bed because of profound weakness.

About this time, painless jaundice appeared. Serum bilirubin determination toatl of 5 mg%.

Irregular pulse, EKG showing presence of 2nd degree heart block. Patient appeared terminal.

Cephalin-cholesterol flocculation test: 2 plus;
thymol turbidity: 2.2 units
Bromsulfalein retention: 17% retention at 45 minutes
urine Ehrlich: 7.4 Ehrlich units.

It should be noted that the patient had received nothing but parenteral nourishment for approximately 50 days. The only potassium administered was that present in the blood and Amigen (18 mEq/liter).
    40th day: serum K 0.98 mEq/liter (normal 5 mEq/liter)
        serum Na 154 mEq/liter (normal 143 mEq/liter).

To correct this potassium deficit, potassium chloride was added daily to the intravenous fluids, with initial 3 Gm gradually increasing to 5Gm daily. Six days later the serum K was 1.1 mEq/liter. The dosage sehedule was increased to as much as 13 Gm administered in one day

It required 14 days of potassium administration to bring the serum K to normal level; a total of 1100 mEq potassium had been administered. During this period, the serum chloride rose from average of 90 mEq/liter to 110 mEq/liter. The serum bicarbonate fell to normal after being above normal for well over 6 weeks.

Other changes were noted with correction of the potassium deficiency:
   1. Chloride content of gastric juice (averaging 1-3 Gm/liter) rose sharply to 5-7 Gm/liter; gastric analysis once again revealed presence of free acid.

   2. Chloride content of urine--averaging 6-8 Gm/liter urine-- fell abruptly to more normal of 1-3 Gm/liter.

   3. Jaundice: completely disappeared; serum bilirubin was within normal limits; cephalin-flocculation negative 11 days later.

The urine excretion of sodium and potassium at the height of potassium deficit on the 40th postoperative day was:
    urine sodium: 78 mEq/liter (214 mg%) x 3.6 liters /24 hours equal 280.8 mEq /24 hours.

    urine potassium: 8.2 mEq/liter (33 mg%) x 3.6 liters of urine per 24 hours equal 29.5 mEq/24 hours.

Two weeks prior to surgery, further preoperative preparation consisted of 2500 cc of blood and 14 units (25 Gm each) of human salt poor serum

albumin. Average administration of parenteral fluid in addition
was 3-4 liters of glucose and/or Amigen per day plus the usual
saline therapy.

Surgery was performed on the 56th hospital day. At that time
laboratory findings were:

serum bicarbonate:	24.0 mEq/liter
chloride:	106.0 mEq/liter
potassium:	5.3 mEq/liter
sodium:	142.0 mEq/liter

Exploratory laparotomy showed duodenal-diaphragm.

The post-operative course was uneventful. The patient began oral
feedings on the 3rd post-operative day. She was discharged on
the 10th post-operative day.

DISCUSSION

The significant features in this case study are hypokaliemia,

alkalosis, EKG abnormalities associated with hypokaliemia, jaundice,

and complete duodenal-diaphragm.

Pathogenesis: The patient was administered potassium-free

fluids for more than 50 days, with the exception of small amounts

in Amigen and blood. In spite of a profound potassium deficit, the

kidneys were excreting approximately 1 Gm of potassium per day, as

determined at the peak of the potassium deficit. Although testosterone

causes a diminution in serum potassium, it is equivocal whether or

not the dosage (125 mg.) administered to this patient may have

had much effect in contributing to the potassium deficit. It has

been shown in previous discussion that prolonged therapy of daily

infusion of glucose and saline produces a potassium deficit. This

last factor, plus vomiting and gastric juice aspiration, undoubtedly

contributed much to the potassium deficiency in this patient.

The alkalosis, refractory until potassium deficits have been repleted, has been explained previously by the suggested theory that depletion of intracellular potassium results in increased intracellular sodium. Biologic equilibrium can then exist only when there is a high serum bicarbonate. The kidney must then excrete increased amounts of the chloride ion, and hypochloremia and alkalosis exist which will not yield until the underlying factors are corrected. Thus, when the intracellular potassium is increased and intracellular sodium is decreased, the serum bicarbonate falls to normal, thereby allowing the serum chloride to rise to normal. This was demonstrated in the above case where the urine contained tremendous amounts of chloride (6-8 Gm per liter) when the bicarbonate was elevated and the potassium was low. When the serum potassium was restored to normal levels, and presumably the intracellular deficit was corrected, the bicarbonate level fell, no longer obligating the kidney to excrete excess chloride, thus a more normal excretion of chloride was again found.

EKG Changes:

EKG findings, typical of those seen in hypopotassemia, were seen in this patient's EKG tracings. Depressed T waves, second degree heart block, occasional supraventricular premature systoles, and depression of the S-T segment were found. After three grams of potassium chloride were administered, the heart block was reduced to a first degree block and extrasystoles disappeared. Two days prior to surgery, the normal electrolyte pattern was restored and the EKG was then seen to be normal.

Jaundice:

Liver function studies failed to corroborate that the jaundice might be due to hepatitis from the use of plasma or blood. The rapid diminution in the intensity of the jaundice coincides with the restoration of the fluid and electrolyte pattern to normal. Thus the jaundice was probably due to malnutrition and electrolyte imbalance rather than anything more specific such as infectious hepatitis or homologous serum hepatitis.

Conclusions:

This case is an excellent example of the important chemical triad: alkalosis, hypochloremia, and hypokaliemia. This state has proved to be refractory to ordinary treatment of alkalosis until potassium deficit has been corrected.

TREATMENT

The intracellular electrolyte pattern, potassium-phosphate-sulfate-magnesium, is one not ordinarily provided parenterally by the solutions most commonly given. This complex is needed in order for any synthesis of tissue to take place, as are the other building blocks of protoplasm. It is a simple matter to provide these minerals orally, because animal and plant tissues contain these elements in large quantities. Parenteral provision, however, demands adequate understanding of the electrolyte balance of the body fluids. In general, the quantity and makeup of the intravenous infusions and the order of their administration should be designed to restore vital functions first, such as blood volume, oxygen-carrying power, blood pressure, renal circulation and normal pH, to be followed by correcting electrolyte deficits and enabling the patient to take fluids and nourishment orally as soon as possible.

The intsitution of potassium replacement should not be undertaken unless there is a good urine output, and rate of administration should be cautious, because of danger of toxic levels causing cardiac arrest. In fact, no progress of repair management is safe without frequent examinations, which include the clinical examination of the patient, determination of the urine volume, specific gravity and pH, as well as serum analysis for chloride, bicarbonate, sodium, and potassium.

Since urinary potassium losses are greatest during the first few post-operative days, early provision of potassium is indicated in patients who cannot eat and who must be fed parenterally. It should, however, be withheld during the first twenty-four to forty-eight hours post-operatively and from patients who are extremely dehydrated and whose urinary output does not exceed 500 cc per day, or who demonstrate

nitrogen retention, unlessthe serum potassium is low. Question

arises as to whether it is necessary to give supplementary potassium

to all surgical patients maintained solely on intravenous fluids.

To this, one may comment that in the absence of exogenous potassium,

potassium deficiency will always develop in these patients and will not

be corrected unless potassium is supplied.

Daily parenteral administration of 50 mEq. after relatively atraumatic

procedures prevents potassium depletion in patients being maintained

on intravenous administration of fluid.[17] After more traumatic procedures

the daily requirements can usually be met by the provision of 80-100 mEq.

per liter.[17] This amount is ordinarily adequate for repair of deficits

also, since urinary losses tend to decline as the deficit grows.

Replacement of potassium losses in most gastro-intestinal fluids can be

estimated adequately on the basis of 10 mEq per liter of fluid lost.[17]

Two ampules of potassium chloride per liter providing a concentration

of 40 mEq. per liter are usually recommended, safely administered at

the rate of 80-100 drops per minute.

Potassium chloride is usually the salt of choice since chloride

and potassium deficiencies are likely to be associated with each other

and because this salt is readily sterilized and may be given intravenously,

subcutaneously, or orally. Oral administration is relatively safe, and,

if possible, is the route of choice. The normal adult ingests about four

grams of potassium or the equivalent of about eight grams potassium

chloride per day. This amount can be given divided into two to four

doses in twenty-four hours. The salt may be added to beverages or to

food.

The solution containing sodium chloride, sodium lactate, and potassium chloride developed by Darrow[36] (called "K-Lactate") contains sodium and chloride in the ratio of interstitial fluid together with an amount of potassium which is unlikely to raise the serum concentration of potassium to toxic levels when the solution is injected over a period of four or more hours in amounts which give appropriate amounts of sodium and chloride.[36] The composition of this solution is as follows:

	Gm/liter
NaCl	4
KCl	2.7
Na-lactate	6

The concentration of potassium is about ten times as great as that of serum. In order to avoid the danger of potassium intoxication, it should be injected, preferably subcutaneously, over a period of four or more hours for the dose appropriate for one day. The amount given in one day should seldom exceed 80 cc per kilogram of body weight.

The deficits of potassium are often so large that they cannot be restored parenterally in less than six days because of the dangers of more rapid parenteral administration of potassium and because administration of more potassium does not restore cellular deficits more rapidly. Potassium-lactate may be injected slowly into the veins or subcutaneously. If intravenous, one part of the solution should be diluted with two or three parts of 5% or 10% dextrose in water.

In the parenteral injection of potassium salts, the rate of administration must be slow enough not to lead to a temporary rise to toxic levels and the total dose must not be large enough to lead to a toxic extracellular concentration. Good urine output is necessary to prevent accumulation of administered potassium. Thus, in oliguria, it is wise

to refrain from intravenous therapy until normal urine output is again restored.

The use of Ringer's solution instead of isotonic sodium chloride solution for the initial injections will at least tend to prevent the dilution of extracellular potassium.[1] If more potassium has to be given intravenously, no more than two grams should be undertaken unless adequate laboratory facilities are available for quick potassium determinations.

It seems logical to assume that the best way to treat potassium deficiency in surgical patients is to prevent any marked degree of potassium depletion from occurring, wherever possible. Marks[31] and his associated surgical staff have prepared and used several types of potassium-containing solutions:

```
Solution I:   NaCl                        8.5 Gm
              KCl                         2.0 Gm
              Glucose                    50.0 Gm
              Distilled H2O  qs ad  1000.0 cc
```

Use 1 to 3 liters per day for treatment of medical alkalosis or for routine daily maintenance of patients on prolonged Wangensteen drainage of the upper gastro-intestinal tract.

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Solution II:  NaCl                        8.5 Gm
              KCl                         2.0 Gm
              NH4Cl                       8.5 Gm
              Distilled H2O  qs ad  1000.0 cc
```

Use 2 to 3 liters per day for treatment of severe alkalosis.

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Solution III: NaCl                        3.0 Gm
              NH4Cl                       4.5 Gm
              KCl                         2.0 Gm
              Distilled H2O  qs ad  1000.0 cc
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Use 1 to 2 liters per day for treatment of moderate alkalosis. This is especially useful in cardiac patients with alkalosis in whom one does not wish to replace an excess of sodium.

In cases of alkalosis with slightly low serum calcium values,

1 Gm of calcium gluconate may be added to one liter per day of the above solutions I, II, III.

Solution IV: NaCl   6.4 Gm
                    Na-lactate   5.6 Gm
                    KCl   2.0 Gm
                    Distilled H_2O qs ad 1000 .0 cc

Use 1 to 2 liters per day for moderate acidosis, especially in cases of diabetic acidosis in surgical patients.

Solution V: NaCl   4.25 Gm
                    KCl   6.0 Gm
                    Distilled H_2O qs ad 1000.0 cc

Use 1 to 2 liters per day for replacement of marked intra-cellular potassium deficiency. Given by clysis or IV.

It is important to realize that with solutions I, II, III, and IV, it is possible to supply the minimal daily requirement of potassium in an adult. However, they will not replace an already existing marked intracellular deficiency of potassium. Darrow[37] has estimated that 3.5 mEq. per kilogram per day of potassium can be safely administered in a period exceeding 4-8 hours.

It is safer to give large doses of potassium by the clysis route, as Darrow recommends, than by the intravenous route. For very large doses, the oral route is preferable whenever feasible. A solution containing equal parts of water and syrup of citric acid to disguise the bitter taste of potassium chloride can be used. This solution may be given to patients in various fluids, such as milk. Diarrhea may rarely develop following the administration of four grams of potassium chloride daily by the oral route.

The main precaution to be observed when giving parenteral potassium chloride solution is the maintenance of an adequate urinary output. An elevated blood urea nitrogen, per se, is not a contraindication to the

administration of potassium containing solutions. However, a daily
urinary output of over 750 cc when administering potassium solutions
is of extreme importance. Adrenal cortical insufficiency, hypocalcemia,
shock, severe dehydration with hemo-concentration, severe burns in acute
phase, and advanced renal insufficiency are contraindications until
first adequately treated, or unless a specific indication for potassium
can be demonstrated at the start of therapy. The effect of hyper-
potassemia on the heart is well appreciated and is to be guarded against
by the intelligent use of potassium solutions in a given patient.
Daily EKG and serum potassium levels should be taken if large doses of
potassium are being administered.

SUMMARY

A syndrome occurring in patients after operation is described along with presentation of a case history. This syndrome is characterized by :

1. clinical manifestations of apathy, lethargy, nervousness and irritability, muscular weakness, abdominal distention and occasional ileus, occasional confusion, disorientation, delirium, muscle twitching and tetany, EKG changes and occasional arrhythmias and edema;

2. chemical findings of hypopotassemia, metabolic alkalosis, hypochloremia, hypoproteinemia, and often increased NPN and hypophosphatemia;

3. a prompt reversal of the clinical and blood chemistry abnormalities upon administration of adequate amounts of potassium.

Attention is called to the recognition of an important chemical triad: alkalosis, hypochloremia, and hypokaliemia. This state has proved to be refractory to ordinary treatment of alkalosis until potassium replacement is carried out. The suggested theory for this mechanism is that when intracellular potassium is depleted and intracellular sodium is increased, biologic equilibrium exists only when there is a high serum bicarbonate. Because of high serum bicarbonate, the kidney excretes increased amounts of chloride ion, and hypochloremia and alkalosis exist which will not yield until the underlying factors are corrected. When the intracellular potassium is increased and intra-cellular sodium is decreased, the serum bicarbonate falls to normal thereby allowing the serum chloride to rise to normal.

Known factors in the pathogenesis of post-operative potassium loss are potassium deprivation, loss of gastro-intestinal secretions, large infusions of glucose or saline solution, dehydration and malnutrition, diarrhea, fistulas (especially biliary), diuresis or polyuria,

shock, hemorrhage, anoxia, and adrenal hyperfunction.

Prevention of the syndrome by provision of potassium early in the post-operative period is stressed. The various means of administering potassium and contraindications for its use are enumerated.

The institution of potassium replacement should not be undertaken unless there is a good urine output, and rate of administration should be cautious, because of danger of toxic levels causing cardiac arrest. Once potassium deficit has become severe, large doses are needed to restore this deficit. In patients with short-term illness who are able to maintain oral nutrition, enough potassium is obtained from food.

The hypokaliemic state in surgical patients is more common than heretofore realized. Potassium losses after major operations are large and are greatest during the first twenty-four hour period, partly because of the high nitrogen loss during this period. Recognition of hypokaliemia may be obtained through EKG and determination of the serum concentration of potassium, sodium, and chloride. Hypokeliemia is to be suspected in symmetrical peripheral motor palsies with little or no sensory changes. Potassium depletion should be suspected when, in the presence of normal kidney function, there is an unexplained high serum bicarbonate and low chloride concentration.

CONCLUSIONS

The low potassium syndrome may result from:

1. decreased intake or impaired absorption from the gastro-intestinal tract

2. increased loss from the body either in the urine or gastro-intestinal tract

3. an internal redistribution as in relation to carbohydrate metabolism (or in familial periodic paralysis).

Experimental evidence has shown that:

1. the kidneys fail to conserve potassium in the face of a potassium deficit

2. this potassium deficit is accentuated by coincident administration of sodium salts or glucose

3. the factors responsible for electrolyte imbalance with potassium loss appear to be in some degree under hormonal control, and that the adrenal cortical secretions play an important part in this mechanism

4. the reduction of cellular potassium below a certain point is dangerous, not only in causing muscular necroses, but that the serum potassium is also lowered with resulting non-specific clinical manifestations.

One may also conclude that:

1. patients with dehydration accompanied by deficits of potassium may be expected to develop alkalosis when they are treated solely with potassium-free fluids such as sodium and chloride

2. alkalosis may be expected to be relatively refractory to treatment with sodium chloride if a deficit of potassium persists

3. such refractory alkalosis can be corrected only by administering potassium salts, either orally or parenterally, to correct the deficiency

4. clinical manifestations disappear upon correction of the deficit of potassium.

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