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Diagnosis and treatment of potassium intoxication

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THE DIAGNOSIS AND TREATMENT OF POTASSIUM INTOXICATION

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INTRODUCTION

Under the direction of George W. Loomis, M. D. at the University of Nebraska Medical Center, several medical students (M.O., L.S., R.B.) have been fortunate in having the opportunity to participate in the treatment of patients with renal disease and exogenous poisons by the use of the artifical kidney. During this experience many different problems in renal disease presented themselves. Among these, diagnosis and treatment of potassium intoxication appeared to me to be especially interesting.

The purpose of this paper is to present to the reader,

(1) The physiology of the potassium ion in the human body and the effects of other electrolytes on it.

(2) A method of detecting impending intoxication with this ion by use of the electrocardiograph.

(3) Various methods of it's treatment and

(4) Three case summaries in which this problem was treated.

PHYSIOLOGY OF THE POTASSIUM ION

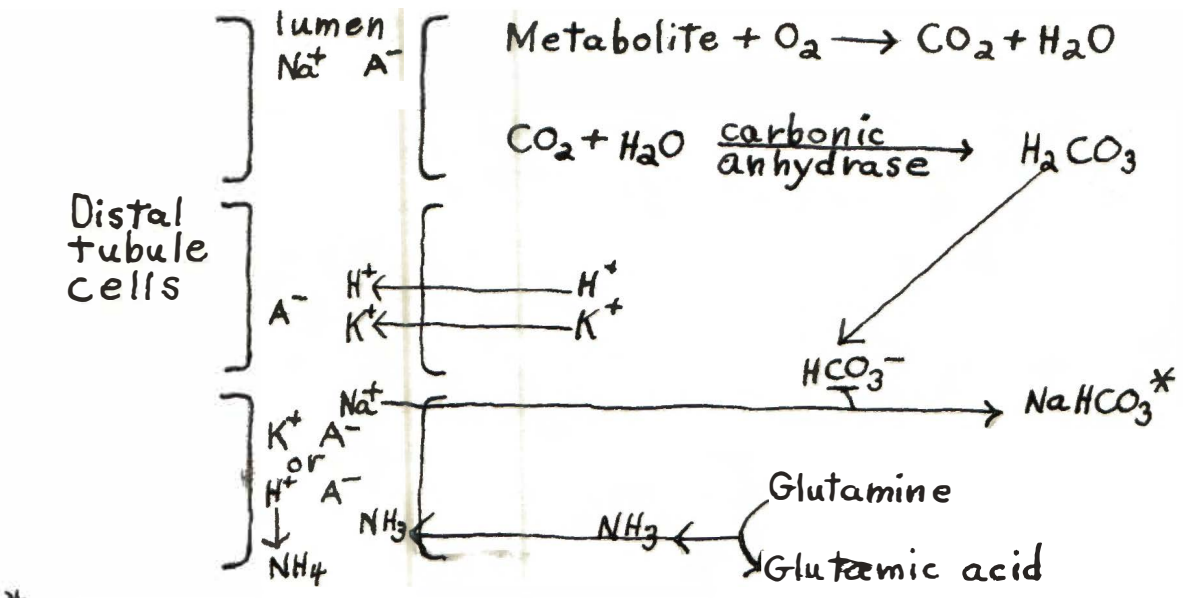
In low concentrations of serum potassium nervous tissue is hyperactive and in higher concentrations it is hypoactive, these effects being particularly important in relation to nerve synapsis or to myoneural junctions. Under normal conditions, its effects resemble those of parasympathetic stimulation and are usually inhibited by calcium. (ie. neuromuscular excitability.) (1)

The potassium ion in extracellular fluid is necessary for normal cardiac function. In the absence of potassium, the heart will stop in systole, and in high concentrations the heart will stop diastole. This latter is due to the direct depressant effect of the ion on the myocardium. Potassium effects both the impulse conduction and muscle contractility. In the absence of potassium, the heart will not respond to vagal stimulation. This fact is related to the role of potassium in transmission of nerve impulse.

As potassium is lost from the muscle cell, as in prolonged muscle stimulation, the contraction of the muscle decreases in strength. Potassium also excites muscle contractions. Local application of the ion to the surface of an isolated muscle fiber can effect a critical depolorization and initiate an impulse. (2) (3)

Potassium is maintained within the cell, while sodium is found mainly in extracellular fluids. Potassium is transmitted across the cellular membranes in states of dehydration, catobolic states, crushing injuries, etc. These will cause an increase in potassium concentration in the plasma, which is normally handled by the kidney in the following manner: Potassium is removed from plasma by glomerular filtration and, like sodium and chloride, undergoes extensive (over 90%) reabsorption in the tubules. However, unlike sodium and chloride, it is also excreted into the tubular lumen by the cells of the distal portion of the renal tubules. This active process, which apparently competes with hydrogen ions in the sodium exchange mechanism, is perhaps the phase of potassium excretion which is influenced by adenocortical hormones (enhancing potassium excretion). (4)

As mentioned above, potassium participates in the hydrogen ion, sodium ion exchange in the distal tubules of the kidney. Potassium ion in the renal tubule cells is exchanged for sodium ion in the tubular lumen, Figure 1.



*To alkaline base reserve

Serum potassium may be elevated in an untreated case of renal failure. Hyperkalemia in such cases is due to inadequate renal excretion of excessive amounts of potassium passing from cells to extracellular fluid, in part because of progressive dehydration, and in part protein malnutrition and excessive protein catobolism. These cell losses are aggravated by fever. (6) (8)

If the cells of the renal tubules are destroyed by renal disease or renal disease only, specifically lower nephron necrosis, then they are unable to excrete potassium as illustrated in Figure 1., and symptoms of potassium intoxication supervene.

DIAGNOSIS OF POTASSIUM INTOXICATION AND INFLUENCE OF OTHER IONS ON ITS DETECTION

The only chemical abnormality that is likely to cause death in the first week of uremia is potassium intoxication. Usually the normal serium potassium does not excede 5.5 millequivalents per liter. Normal daily catobolism of cells provides the plasma with a small quanity of potassium that is readily excreted. This amount of potassium can be handled by an anuric patient for many days; even several weeks, without accumulation of significant quantities in the plasma. However, the basic condition that originally produced the renal insufficiency is often characterized by excessive loss of potassium from cells.

Devitalized tissue, whether permanently destroyed or temporarily embarrassed by trauma, infection, chemical or physical agents, or hypoxia, give up potassium to the plasma.

The first and most important evidence of toxicity is seen in the cardiac picture. The electrocardiogram is used to show this evidence. The electrocardiogram is, in fact, an accurate gauge of the plasma level of potassium in man when there are no abnormalities except hyperpotassemia.(7) The first sign of hyperkalemia is usually tenting of the T waves, which may also be enlarged and broadened. There is a shortening of the S-T segment and with higher concentrations there is widening of the Q.R.S. and P. waves. With still higher levels, auricular

standsill and bizarre appearing ventricular complexes are seen. Finally, there is a sine wave and this may degenerate to no electrical deflection on the electrocardiogram.

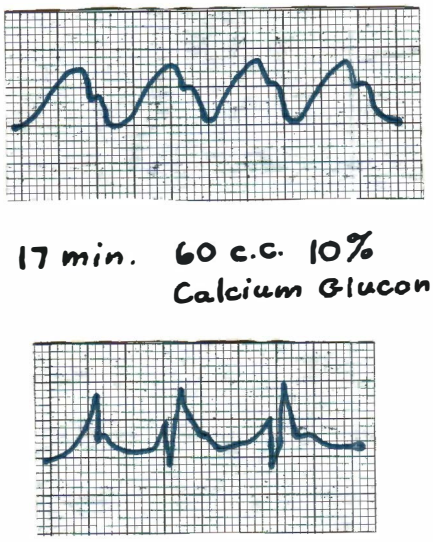
There may be superimposed factors effecting the pattern of potassium intoxication. Discrepancies stem from the rarity with which pure hyperkalemia occurs. In the oliguric patient, substances that normally would be excreted in the urine are retained within the body, and some of these substances effect the behavior of potassium.

The retention of inorganic phosphate although not itself harmful, is associated with a fall in the level of plasma calcium during oliguria. A deficit of plasma calcium is of cardinal importance during oliguria because calcium is a specific antagonist of potassium, and hyperpotassemia and hypocalcemia occur at the same time. As the plasma potassium level rises, the degree of toxicity recorded by the electrocardiograph is consistent with it only if the plasm calcium is maintained; otherwise, the electrocardiogram abnormality - - and the threat to the patient's life - - are greatly increased. Replacement of the calcium deficit produces a striking improvement in the electrocardiogram, which then is reverted to that degree of abnormality characteristic of the plasma potassium level. Short of hemodialysis, the only effective way to maintain a normal calcium in plasma that is high in phosphate is by

continuous intravenous infusion of calcium, because of its very transient effect with a single injection.

Once the calcium deficit is replaced, the electrocardiogram reflects the plasma level of potassium rather accurately, although still other factors, less apparent in these patient's have been shown to be influential. (5) (7)

Figure 2 shows electrocardiographic changes with correction of serum calcium levels with no appreciable change in potassium levels in the serum.



K^+	Ca^{++}	P
mEq/ℓ.	mgm / 100 c.c.	
9.2	6.5	15.5
>10	12.2	17.0

VARIOUS METHODS OF TREATING POTASSIUM INTOXICATION

It has been shown above that transient improvement of electrocardiograph tracing follow the administration of calcium gluconate, and that these are sustained with constant intravenous infusion. Also, if the serum calcium level is maintained near normal levels, then electrocardiograph changes more nearly reflect serum potassium levels.

Sodium is another ion that should be used in the practical management of potassium intoxication. Sodium and potassium are inversely related in the plasma of the oliguric patient; raising the plasma sodium concentration causes a fall in plasma potassium concentration and modifies the electrocardiograph effects of potassium intoxication. An alkaline salt of sodium is preferred, however, because the retention of organic acids regularly produce acidosis in these patients. It is presumed that raising the plasma sodium concentration forces potassium back into cells. The improvement in the electrocardiogram that followed a rise in plasma sodium level and a fall in the plasma potassium level was sometimes greater than would be expected from the lower level of potassium. This suggests that sodium, in addition to depressing the plasma concentration of potassium, may also have some antagonistic effect

similar to that of calcium.(7) (8)

The use of molar sodium lactate in 12 cases of hyperkalemia was reported by Bellet and Wasserman:(9) "The hyperpotassemia in the 12 cases was of an advanced grade often associated with a secondary uremia, with a concomitant shock - like state and characteristic electrocardiographic changes of advanced potassium intoxication. The serum potassium ranged from 6.4 to 10.7 MEq./l. Molar sodium lactate had a prompt and salutary effect not only on the electrocardiograph but also on the circulatory changes. The clinical picture in almost all cases was vastly improved. The ultimate outcome of the patients was primarily determined by the extent and reversibility of the renal damage."

In these 12 cases they did not encounter a single instance in which molar sodium lactate failed to improve or to reverse entirely the electrocardiographic changes due to potassium poisoning. Generally the clinical and electrocardiograph evidence of improvement appeared within 2 to 30 minutes following the infusion of molar sodium lactate.

While most efficaceous in acute potassium intoxication, the solution was also used for insidiously developing hyperpostassemia and acidosis. This group of patients is of particular importance since in them we have been able to prevent

cardiac arrest as a cause of death with sodium lactate.

After treating with molar sodium lactate, the electrocardiograph shows improvement with (1) narrowing of QRS complexes, (2) less peaked T waves, and (3) return of AV conduction with a R-P time shortening.(8) (9)

The Q-T segment may show prolongation, which suggests coexistent hypercalcemia. After treatment with about 100 mEq of molar sodium lactate the electrocardiograph show almost no signs of potassium intoxication.

The mechanisms of action of molar sodium lactate in increasing cardiac rhythmicity is still under investigation. The following were originially postulated: (a) The production of alkolosis increased the irritability of the myocardium. (b) The increase in sodium raised the height of the action potential, (c) The lactate provided additional fuel for the heart, and (d) A vagolytic effect increased the cardiac rate. Recently it has been suggested that one of the major factors involved is a decrease in potassium in the extracellular fluid, which is accomplished by expansion of the intracellular space and movement of potassium ions intracellularly. A more favorable sodium: Potassium ratio is probably an additional factor. The effects on rhythmicity, while due chiefly to a variation in extracellular potassium, may be influenced indirectly by other electrolytes; e. g., sodium calcium and to a lesser degree,

magnesium.(9) (10)

The plasma potassium level may also be reduced by the infusion of a hypertonic dextrose solution. It's metabolism, which can be hastened with exogenous insulin, removes potassium and phosphate from plasma. While calcium anatagonizes the effect of potassium without changing the quanity present in the plasma, and sodium forces potassium into cells by some physio-chemical means, glucose carries potassium into cells by a more active process. As glycogen is formed, potassium, as well as phosphate, is incorporated into the carbohydrate complex; this is an effective, although a slow method of controlling potassium intoxication.

If dextrose is to be used effectively by the intravenous route, it should be given continuously. Intermittent intra-venous injection of dextrose causes a sharp spike in blood sugar level followed by hypoglycemia. The hypoglycemic period has the double disadvantage of failure to remove potassium during that period and provocation of glycolysis with further release of potassium to the plasma.

On the basis of the above observations the following standard solution has been devised and found to be effective in controlling potassium intoxication for many days:

Calcium gluconate 10%	100 cc.
Sodium bicarbonate 7.5%	50 cc.
Dextrose 25% in water (containing 50 units of regular insulin)	400 cc.

Isotonic sodium chloride solution or 1/6 molar sodium lactate

Volume of output

This solution should be given intravenously, preferably through a catheter in a large vein, at constant rate of about 25 cc. an hour.(5) (7)

Ion-exchange resins are effective agents for withdrawal of potassium from the plasma into the intestine under certain circumstances. If, however, the patient is unable to take anything by mouth, and rectal instillation of resins attempted, there is likely to be formations of intractable concretions. A great deal of water may be necessary to remove these causing water absorption and overhydration. (7)

Artifical kidney dialysis is the most effective treatment known for removal of potassium, but dialysis for hyperpotassemia alone is in the experience of most investigaters, rarely indicated. Kolff,(11) in his earlier experience, would restrict use of the artifical kidney to patients with acute anuria with serum potassium levels of 7.0 mEq/l or more, CO_2 content 12 mEq or less, and blood urea nitroges (BUN) of 150 mg. per 100 cc. or

more. It is the combination of these toxins in the blood which make up the indications of dialysis. In the anuric patient, however, with a high serum potassium, it is common to find abnormalities of other serum components, so it would be rare to find a patient with an isolated high potassium.

Patients with high serum potassium levels should be dialyzed against a bath which contains lower amount of potassium than would be used if potassium intoxication did not exist. Normally the bath contains 5 mEq/l of potassium, where in potassium intoxication 1.8 to 3.7 mEq/l is probably advisible. By having lower concentrations of potassium in the bath the osmatic equalibrium between the serum and the bath would be in the direction of the bath, thus fascilitating extraction of potassium from the blood stream. (12) (14)

Acute potassium intoxication may be precipitated in patients who have borderline high serum potassium levels when the artifical kidney is used for the treatment of severe renal disease, especially at the onset of dialysis. Some of the reasons for this are, (1) use of 3 units of Bank blood in filling the dialyzing coils, which, because of storage, processing etc., contains a high serum potassium, and (2) citrated blood causes a lowering of the ionized calcium, which, as pointed out earlier, will potentiate any impending potassium intoxication.

Since calcium levels are important to keep in mind in patients

with high serum potassium levels, it is advisable to have a intravenous drip running which contains 10 cc. of 10% calcium gluconate in 500 ml of 5% glucose and water. (7) If any signs of tetany appear, such as a positive Trousseau's sign or Chvostek's sign, the calcium drip can be increased. Also, by the use of the intravenous drip calcium, the serum calcium levels in the patient are more stable and this make the electrocardiograph changes, which may occur in acute potassium intoxication, more meaningful; i.e., the electrocardiograph changes reflex the serum concentration more precisely.

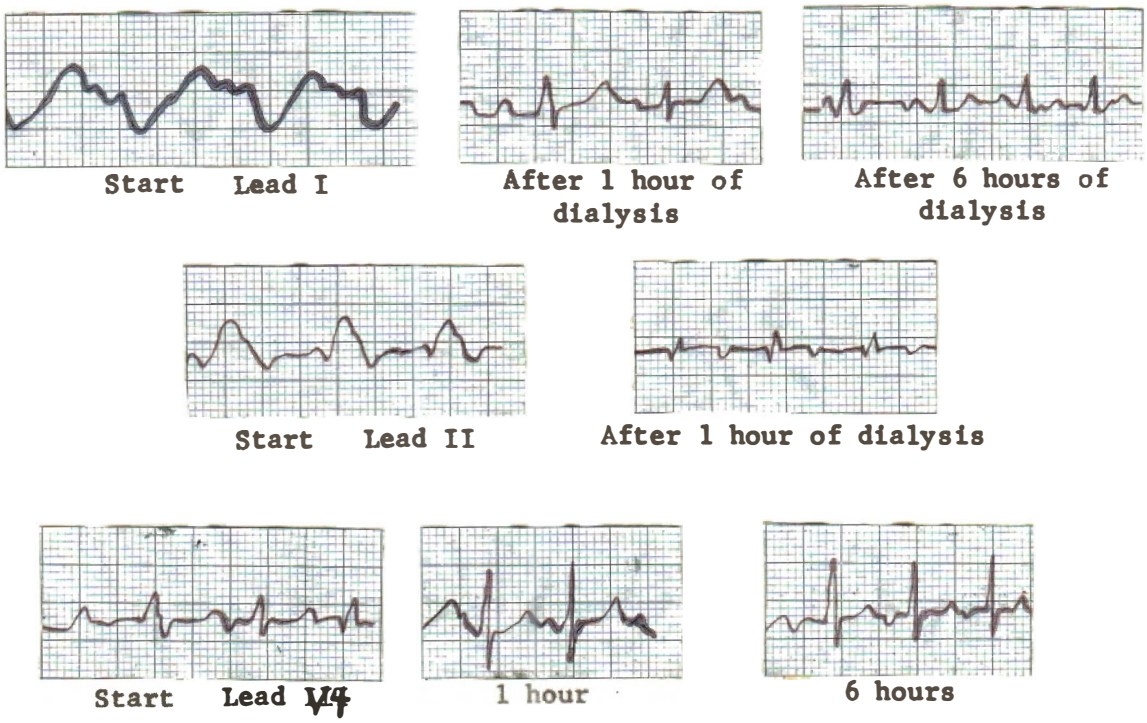
CASE REPORTS ON TREATMENT RENAL FAILURE WITH POTASSIUM INTOXICATION

(1) Kohn and Keley, (13) report a case of a 28 year old negro woman who entered the hospital because of anuria. Two weeks before entering she had fever, cough and generalized malaise. Oliguria occurred somewhat later, when severe electrolyte derangement was noted. Temperature was 99.6°F; pulse 100; respirations 20; blood pressure 105/65 mm of Hg. Many small blebs were seen over the lower limbs, and the abdomen was distended, somewhat tender, and tympanetic. Hemoglobin 11.5 mg. per cent, white count 17,000. Urinalysis showed acid reaction, specific gravity, 1.003; albumin 3 pluse; microscopic 50-60 red cells and 20-25 white cells per high power field. Marked potassium intoxication was evident in the electrocardiogram and this was treated by glucose and insulin intravenously at the time

of admission, followed by hemadialysis for six hours. The run was noteworthy only in the rapid improvement in the electrocardiogram shown in figure (3). No potassium was in the bath for the first hour.

Blood chemical changes were as follows: sodium, 117 to 130 mEq/l; potassium 8.3 to 4.7 mEq/l; calcium, 5.8 to 5.3 mEq/l; bicarbonate, 10 to 13 mEq/l; chloride, 87 to 94 mEq/l; non-protein nitrogen, 156 to 58 mg. per cent, creatinine, 14.9 to 7.7 mg. per cent. Diuresis began the day after dialysis, and the patient's further course was uneventful.

Figure (3)



Of the nineteen hemodialysis preformed at the Bishop Clarkson Memorial Hospital, Omaha, Nebraska, under the supervision of George W. Loomis, M. D., the following two case reports are presented to illustrate the diagnosis, treatment and complications in acute potassium intoxication.

(2) R. C. (First dialysis), a 13 year old white male presented with a diagnosis of acute glomerular nephritis with early potassium intoxication indicated by a 7.6 mEq/l serum potassium and electrocardiograph changes. Predialysis electrolyte studies revealed non-protein nitrogen, 296 mg%; CO_2 combine power, 17 mEq/l; chloride, 104 mEq/l; sodium, 138 mEq/l; potassium, 7.6 mEq/l; and creatinine 13.6 mg%. The hemoglobin was 12.2 mg. and the white blood count was 7900 per mm^3.

Dialysis started with the first bath containing only 2.5 mEq/l of potassium. The patient was previously given 56 mgm. of heparin and an addition 20 mgm. added to each of three blood bottles.

Shortly after dailysis started, the patient developed signs of acute potassium intoxication manifested by a feeling of numbness all over, with agitation and hypotension. The blood pressure at this time was 50/10. The acute potassium intoxication was alleviated by transfusing 250 cc. of 0.85% sodium chloride solution. The electrocardiogram reverted from idioventricular rhythm with wide bizarre Q.R.S. complexes to the pre-dialysis appearance of normal sinus rhythm with narrow peaked T waves.

This dialysis was complicated by a mechanical failure in which the bar holding the dialyzing coil in place broke off. This caused the coil to bulge up out of the confines of the container, bleeding the patient into it. Acute tachycardia and hypotension followed, but was corrected with transfusion of 200 cc. of whole blood.

Some hypotension persisted throughout the remainder of the dialysis, but was held in check with 500 cc. of blood transfused within 2½ hours.

The patient was given cedilanid, o.8 mg. intravenously, to improve cardiac output. Sodium phenobarbital, grains one was given for twitching and restlessness. Fifty mg. of heparin was given after 2½ hours of dialysis because of the Lee-White clotting time was down to 14 minutes.

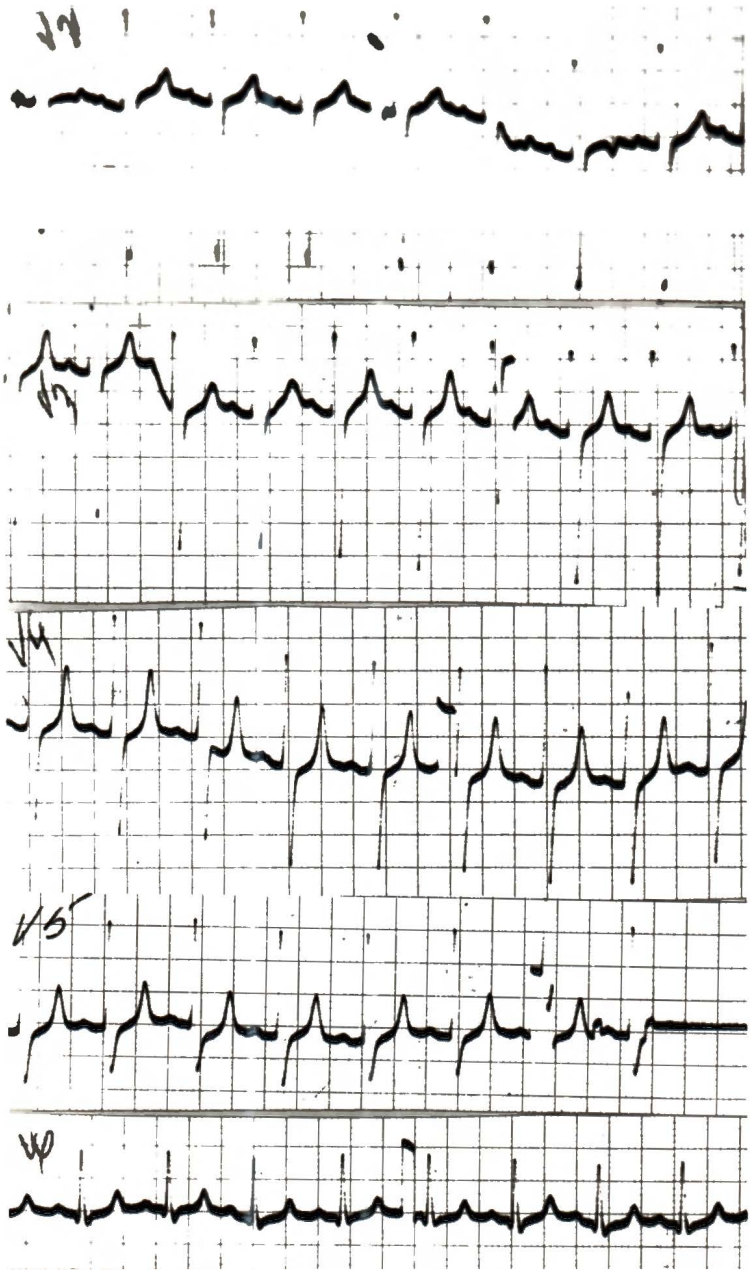
Dialysis was terminated after 2 hours and 45 minutes. The time was cut short because of mechanical difficulties. The day following dialysis, the patient was much better clinically, showing less edema, nausea and vomiting. The patient seemed more alert and was well oriented. Chemically, little improvement was seen. The non-protein nitrogen was 272 mg.% and the potassium was 8.1 mEq/l (probably an error).

This patient was redialyzed three days later because of progressive uremia and borderline potassium intoxication, dispite the administration of potassium absorbing resins and intravenous hypertonic glucose.

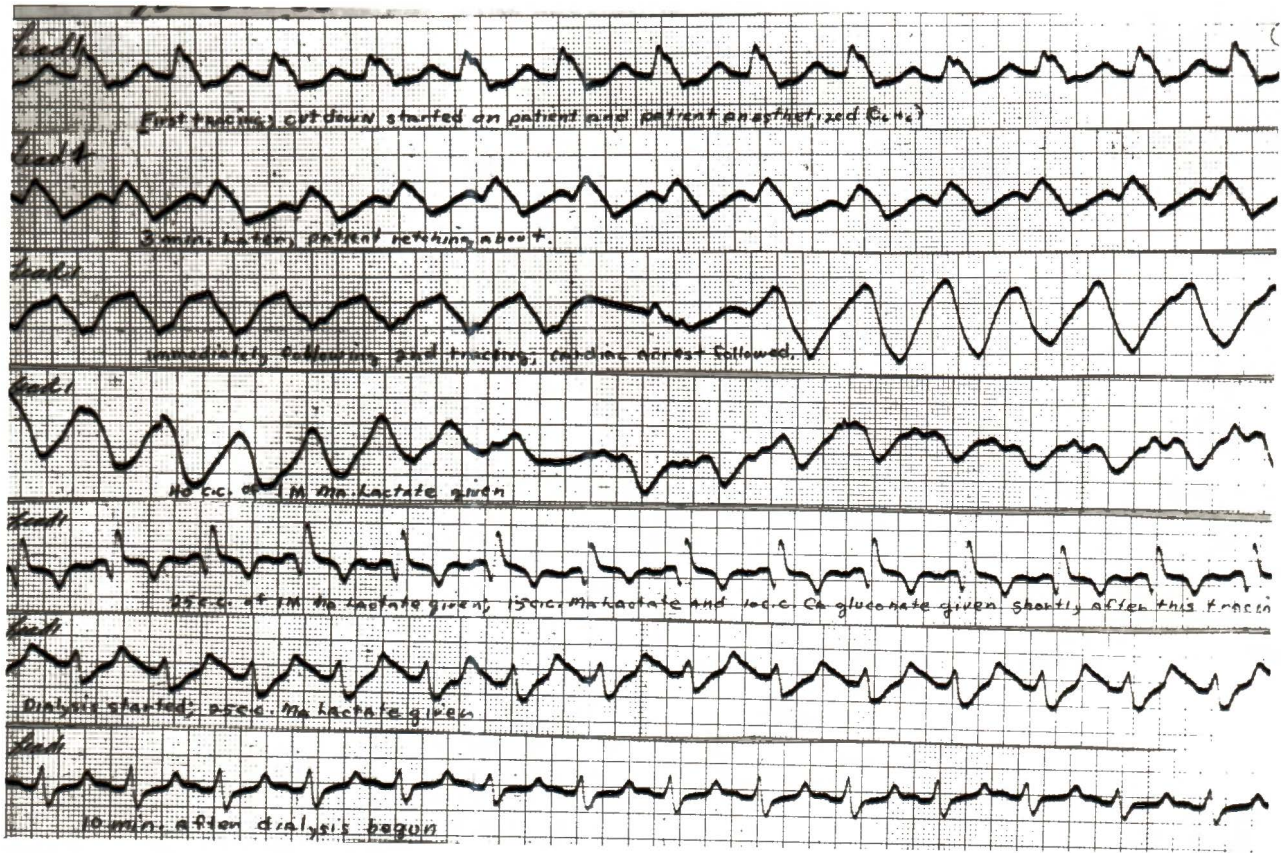
Electrolyte studies taken before the second dialysis on the patient reveal a non-protein nitrogen of 310 mg.%; potassium, 6.9 mEq/1; and a sodium of 132 mEq/1.

The patient was heperinized as usual, and dialysis started with a bath potassium of 3.75 - 4.0 mEq/1. The patient was given two grams of sodium phenobarbital and 50 mg. of demeral for sedation. Dialysis was uneventful for the first two hours, except for poor arterial flow through the coil, which was probably caused by arterial spasm which finally relented. Some hypotension was noted with change of the dialysing bath, which was probably due to expansion of the coil when the circulating pump was allowing the system to fill with the patient's blood. The blood pressure at this time was 92/70 and was raised to 108/90 with a 100 cc. blood transfusion. The bath potassium was maintained at 3.75 to 0.42 mEq/1 through the six hour of dialysis. Post-dialysis electrolyte studies showed a 158 mg% non-protein nitrogen and 5.1 mEq/1 serum potassium. The patient also was improved clinically but expired two weeks later, apparently from a irreversable kidney disease. An autopsy was preformed, at which time severe acute glomerular nephritis was found.

(3) H. D., a 5 year old white female presented with severe anuric acute renal failure, possibly bilateral renal cortical necrosis, or possibly tubular necrosis. The blood urea nitrogen was 190 mg%, potassium, 8.5 mEq/1. The electrocardiogram showed moderate potassium intoxication (peaked T waves). Figure (4).



Prior to the start of dialysis, the patient developed a spontaneous acute potassium intoxication, with degeneration of the electrocardiogram tracing to a sine wave. This was followed by a cardiac arrest, the chest was opened and a cardiac massage done. During this time that the heart was being massaged and had resumed beating, the patient was given 80 cc. of one molar sodium lactate in divided doses with 10 cc. of 10% calcium gluconate. Signs of potassium intoxication was slowly abolished with this treatment. Figure (5)



There was a slight return of potassium intoxication after dialysis was started, but promptly reverted to normal with the administration of an addiontal 25 cc. of one molar sodium lactate.

There was slight hypotension throughout the remainder of the dialysis but this was corrected by intermittent transfusions, ranging from 20-100 cc. each. The dialysis was discontinued after 4 hours, the serum potassium was down to 5.6 mEq/l and the blood urea nitrogen was 88 mEq/l.

A second dialysis of the patient was undertaken one week later because of progressive uremia despite a beginning urine output of up to 200 cc. /day. The patient was stuporous, vomiting and showed muscular twitching. Elecrolyte and other blood chemistry before the second dialysis were as follows: Blood urea nitrogen, 235 mg%; CO_2 combining power, 4.4 mEq/l; sodium, 118 mEq/l; potassium, 4.7 mEq/l; and the chloride, 77.6 mEq/l.

This dialysis was carried on for six hours, complicated only by slight hypotension. The post-dialysis blood studies showed a marked improvement. The blood urea nitrogen was 42 mg.%; CO_2 combining power, 18.7 mEq/l; sodium, 142 mEq/l and the potassium was 4.o mEq/l. The patient died one week later from inreversable renal disease.

DISCUSSION FOR CASE REPORTS

High serum potassium levels were lowered to normal levels in each of the three cases reported after one to two dailysis. Medical treatment of this disorder appears to be an important adjunct, especially during acute episodes of potassium intoxication. The most dramatic medical treatment was the use of molar sodium lactate during and after cardiac arrest, with almost complete return of a pre-dialysis electrocardiogram pattern.

The potassium was lowered to a normal level when the dialysis could be run for a full 6 hours without complications. The low concentrations of potassium in the baths throughout dialysis is thought to be an important factor in lowering the serum potassium.

Patients with irreversible kidney damage will maintain a normal potassium level after dialysis only for a short time, because of the catabolism of cells and the inability of the kidneys to excrete the potassium. This appeared to be true in the last 2 cases. Also it is speculated that bank blood may have an increase in serum potassium, which may add to the not too striking lowering of serum potassium after dialysis.

CONCLUSIONS

Potassium has been shown to be an important intracellular ion for normal nerve conduction; it is especially important for cardiac function. This ion in high concentration causes a

direct depressant action on the myocardium, effecting both impulse conduction and contractility.

In states of dehydration, injury, catabolism and increased adrenal steroid production, potassium is lost from the cell and is normally excreted by the kidneys. However, when there is kidney impairment, the kidneys are unable to excrete potassium, consequently, causing a rise in the serum levels of this ion.

The diagnosis of these state often can be made with accuracy by noting changes in the electrocardiogram tracings. This instrument is especially useful in helping control patients with severe renal impairment complicated by known high potassium levels. By inspecting a electrocardiogram, one may be able to avoid toxic levels of this ion, where as if laboratory analysis had to be relied upon the serum level could not be as closely observed.

Sodium and calcium ions seem to effect the electrocardiographic changes in potassium intoxication, so it is essential that these two ions be as near normal as possible.

There are various methods of treatment of this disorder, of which extra-corporal hemedialysis appears to be the most satisfactory. This method of treatment allows a complete balancing of all electrolytes and exogenous toxics which the damaged kidneys are unable to excrete. With reversible kidney disease, hemedialysis allows a longer lowering of serum potassium levels until the normal kidney function is resumed.

Medical treatment is important in acute potassium intoxication, molar sodium lactate appears to be most efficaceous in this situation. It is prompt in its action and is well sustained until more permanent correction can be instituted, such as hemadialysis.

Chronic high levels of this ion in the serum may be treated with hypertonic glucose and insulin or potassium absorbing resins with good results. Normal saline will also effect a lowering in serum potassium.

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