HYPOPOTASSEMIA *in Human Starvation and Gastric Resection*

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THE CLINICAL picture of potassium ion lack is widely recognized and discussed at the present time.[1,2] We believe there may be more effects of a potassium deficiency than have been described and that they may appear after months of deprivation. Before describing our observations, a brief discussion of the causes of this deficiency is presented.

It is agreed that a reduced food intake plus normal and abnormal losses of potassium in bodily secretions underlie most instances of this syndrome. Gastrointestinal disorders, including prolonged vomiting, diarrhea of infants, the sprue syndrome, and draining fistulas have been shown to cause large potassium ion losses;[3,4] with these there is often an associated poor intake. Lowered serum potassium levels are seen in the aforementioned disorders, as well as in diabetic acidosis, alkalosis of Cushing's disease or desoxycorticosterone intoxication, and in familial periodic paralysis. In addition to potassium deprivation and unusual loss, there is the constant urinary loss which is obligatory and may amount to 1.5 to 3 Gm. daily even during fasting.[1,5,6,8]

The usual symptoms of potassium lack are: listlessness, muscular weakness of the extremities, dyspnea and gasping respirations, abdominal distention, and ultimately paralysis of both skeletal and cardiac muscle.[2]

It seems inevitable that prolonged starvation alone should produce hypopotassemia. Amatuzio[7] found low serum potassium levels in cirrhotics who had had an inadequate food intake for 4 to 6 months. Danowski[3] mentions anorexia nervosa as another possible cause. Recently we have seen three patients who developed severe potassium deficiency entirely on the basis of starvation, or starvation with a poorly functioning gastric resection. Our patients presented several unusual features.

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CASE REPORTS

Case 1

The first case reported is that of a patient who voluntarily starved six months and lost 50 pounds; the resulting weakness and apparent psychotic state were associated with hypopotassemia. Correction of the low serum level paralleled her recovery.

Mrs. M. B., a 55-year-old white woman, entered the hospital on August 11, 1951, so weak and irrational that a history was necessarily obtained from her family and later verified by the patient. Because of fear of cancer, for six months prior to admission to the hospital she had eaten a diet consisting only of grapes and grape juice in order to avoid the many other types of food which she imagined were injurious. Although she felt that her peculiar diet had relieved this distress, she had lost 50 pounds of weight since the beginning of her deprivation, and her strength had gradually ebbed, so that for five weeks she had been bedridden.

The patient was a malnourished and dehydrated white woman with deeply pigmented skin, who weighed 95 pounds. She was weak and irrational. The blood pressure was 92/60 mm., pulse 92 and regular, and respirations 16 per minute. Examination of the head, mucous membranes, neck, and heart and lungs

were within normal limits. There was a midline abdominal scar but no other abnormalities. Fundus and adnexae were not palpable; there were black feces in the rectum. The skin was gray-brown over the entire body except the palms and soles; skin creases were darkened. The reflexes were hypoactive and the knee jerks and ankle jerks were absent. There was a questionable Babinski sign on the left. Muscle strength was generally diminished, more so on the left side.

The patient's course during her first weeks in the hospital was marked by weakness and variable mental aberrations. It should be emphasized that, because of her extreme weakness, she was unable to feed herself or even to turn herself in bed. Her mental symptoms took the forms of melancholia, hallucinations, and occasional euphoria. The initial clinical impression was that starvation was the most likely cause of her illness, but Addison's disease and carcinoma with cachexia were considered.

Repeated determinations of the CO_2 combining power during the first three days of her hospitalization consistently showed levels above 80 volumes per cent. (The county hospital laboratory colorimetric determinations were not accurate above 80 volumes per cent.) The nonprotein nitrogen was 37 mg. per 100 cc. and two blood sugars were 125 mg. per 100 cc. and 128 mg. per 100 cc. Urinalyses were normal. Hemoglobin was 10 Gm. per 100 cc. Wasserman and Kahn serologic tests were negative. Serum calcium, phosphorus and chlorides, bromsulphalein excretion, total proteins, A/G ratio, and spinal fluid tests were normal. Samples of hair, nails, and urine were negative for arsenic. Gastric analysis, ACTH-eosinophil test, and Kepler water tests were all within normal limits. Stools were negative for occult blood. Chest fluoroscopy and x-ray, skull x-ray, upper gastrointestinal series, and oral cholecystogram were all normal.

An electrocardiogram taken two days after admission showed depressed ST segments, low T waves, and prolonged QT intervals (Fig. 1). The blood pressure persisted at levels of 80–90 mm. systolic and 50–70 mm. diastolic.

Because of the patient's severe dehydration and malnutrition, she was first treated with intravenous fluids consisting chiefly of 5 per cent glucose in water and sodium chloride. Although she seemed slightly more alert following these hydration measures, her mental status and physical weakness remained abnormal. She had multiple complaints of a bizarre nature, including chills and sweating without a temperature variation, afternoon leg cramps, sudden losses of vision without opthalmologic evidence of disease, and marked emotional lability.

It was the opinion of the staff, and concurred in by the psychiatrist, that involutional melancholia was the most likely diagnosis, and that commitment to a mental institution for electroshock therapy was indicated. Neurological examination now revealed hypoactivity of tendon reflexes of the upper extremities with absent ankle and knee jerks, but with active ankle and patellar clonus. The Babinski sign was definitely present on the left. There was generalized muscular weakness and flaccidity. Inco-ordination was greater on the left side.

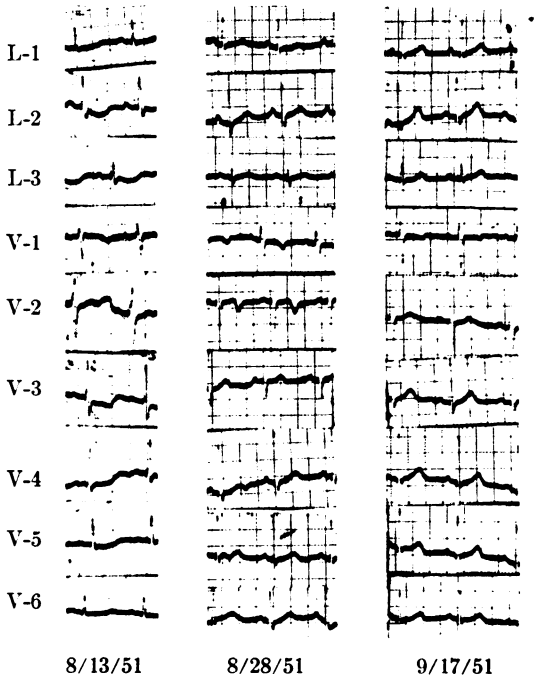

Fig. 1. M. B.

A serum potassium taken one day after admission was reported on August 15, 1951, as 12 mg. per 100 cc. (3.1 mEq./L.) in a hemolyzed specimen. The sodium was 354 mg. per 100 cc. (154 mEq./L.). In spite of this and the signs of low potassium on the electrocardiogram, only 1 liter of KCl (2 Gm.) was given. For the subsequent two weeks she gained in strength, but was still disoriented and confused, and had thick speech and very poor co-ordination. Although the electrocardiogram was now nearly normal, the serum potassium on September 5, 1951, was only 9.3 mg. per 100 cc. (2.4 mEq./L.) in a well-drawn serum. Intensive therapy with potassium was now decided upon.

In addition to her diet containing approximately 5 Gm. of potassium, 800 cc. orange juice per day and 6 Gm. of potassium chloride were given by mouth every day. She received this for one week beginning Sept. 6, 1951, with remarkable subjective and objective improvement. Repeated neurological examination now showed a slight hyperactivity of all tendon reflexes, absent patellar clonus, absent abdominal reflexes, absent right but present left ankle clonus, and positive Babinski and Hoffman signs on the left side. Sensory modalities were not impaired. There still remained a general motor weakness, more marked in the left arm and the right thigh and leg. Co-ordination, by the finger to nose and heel-knee-toe tests, was impaired, more noticeably on the left side. By this time the blood pressure had gradually risen to a level of 150/100 mm. Hg.

Oral potassium was then discontinued and replaced with a one-week course of 6 Gm. KCl intravenously per day. Clinically, improvement was approximately the same as by the oral route; neurological findings were not significantly altered except for an increase in muscle strength proportionately equal to that noted during oral potassium therapy. The serum potassium taken 5 days after discontinuance of all but a general diet, revealed a level of 12.8 mg. per 100 cc. (3.3 mEq./L.); the 24-hour urine potassium output was 180 mg. per 100 cc. (47 mEq./L.) or 2.48 Gm. per 24 hours. (The normal urinary excretion of potassium is about 2 to 4 Gm. per 24 hours.)*

On the basis of clinical improvement and laboratory reports, the patient on Sept. 23, 1951, was again put on a course of oral potassium chloride in the amount of 6 Gm. per day. Both objective and subjective improvement were rapid. Electrocardiograms taken during and after potassium therapy had reverted to normal. Neurological findings became entirely normal, although slight right leg and left arm paresis persisted.

The patient had become physically able and mentally alert and was discharged from the hospital on 9 Gm. of potassium chloride daily. However, after approximately one month of this high potassium intake, the serum potassium on Oct. 15, 1951, was still only 13.8 mg. per 100 cc. (3.5 mEq./L.), and the 24-hour urine potassium was 132 mg. per 100 cc. (34 mEq./L.) or a total of 2.11 Gm. (54.4 mEq.) per day. Oral potassium was discontinued at this time. On Nov. 30, 1951, the serum level was still low, 12.9 mg. per 100 cc. (3.3 mEq./L.).

When she was last seen on Jan. 1, 1952, Mrs. M. B. had taken no extra-dietary potassium for approximately two and a half months. There had been no recurrence of symptoms. Physical examination was identical to her last hospital visit except for weight gain to 145 pounds. Her serum potassium had risen to a normal of 15.8 mg. per 100 cc. (4.1 mEq./L.).

The trace of a left hemiparesis and right leg weakness suggests that a number of cerebral focal lesions could produce these widespread central nervous system changes. However, no clearcut onset of any such accident or accidents can be elicited. This patient's almost complete recovery now emphasizes a more diffuse nervous system injury.

Case 2

Mrs. K. I., a 42-year-old woman who weighed 90 pounds and was very weak, also

* The Tisdall chemical technique as modified by Jacob and Hoffman was used in all potassium determinations. *J. Biol. Chem.* 93: 685, 1931; *Ibid.* 120: 57, 1937.

had a low serum potassium one and one half years following a gastric resection. She was first seen in May, 1952, complaining of pain in the left upper quadrant of her abdomen. She had had abdominal pains of many kinds for about 17 years. A diagnosis of duodenal ulcer had been made two years before and in October of 1951 a gastric resection was performed. Since that time she had gradually lost weight and although her burning epigastric discomfort had disappeared she had right and left upper quadrant cramping, intermittent distress, fullness, and nausea. This was always worse after eating and better after vomiting.

Physical examination showed an emaciated woman with a slightly tan skin. She weighed $90^1/_4$ pounds. The only abnormality other than emotional lability was a definite ataxia in the left arm during the finger-to-nose test. She was left-handed.

The serum potassium at this time was 11.9 mg. per 100 cc. (3 mEq./L.). For three months she continued to wax and wane, showing weight gain of a pound or two on a special feeding program and tincture of belladonna. In August 1952 she began to have more distress and was discouraged and extremely weak. The serum potassium was 12.9 mg. per 100 cc. (3.3 mEq./L.) and the electrocardiogram was normal. She was admitted to the hospital and given parenteral and oral potassium and restarted on a feeding program and tincture of belladonna. Since that time she has gained six pounds in weight, immeasurably in strength, and has returned to work. A serum potassium on Nov. 12, 1952, was 4.4 mEq./L. or 17.2 mg. per 100 cc. The left arm ataxia was gone.

Case 3

Mrs. H. J. was a woman with a weight loss of 30 pounds following a gastric resection three years before; return of low potassium levels to normal accompanied return of muscle strength and co-ordination.

She was admitted to the hospital on July 25, 1952, with a chief complaint of cramping, intermittent upper abdominal distress, and nausea. Such attacks had been present since she had had a gastric resection in 1949. She had not had vomiting or diarrhea, but had gradually eliminated one food after another from her dietary intake. She was weak, weighed only 100 pounds, and had a skin pigmentation which was brown and dappled in appearance. She also looked sallow. Her speech showed hesitancy, dysarthria, with a nasal quality, and she had great difficulty in keeping the trend of the conversation. Her vision was poor because of blurring.

There were many fine inspiratory rales throughout both lung fields. The heart rate was 80 per minute and forceful in beat, but there were no murmurs. The blood pressure was 98/68 mm. The abdomen was tympanitic and quiet; the liver was palpable in the right upper quadrant 7 cm. below the right costal margin in the right midclavicular line. It was not tender. Examination of the rectum and pelvis was normal. Reflexes were absent in all extremities. Vibratory sense was normal. There was moderate pretibial edema.

Clinical impression was that of starvation and a malfunctioning gastric resection. The serum potassium was 11.9 mg. per 100 cc. (3.3 mEq./L.), red blood cell count was 2,530,000/cu.mm., hemoglobin was 8.5 Gm. per 100 cc., and white blood cell count and differential were normal. Total serum proteins were 5 Gm. per 100 cc., and the serum bilirubin was 1.9 mg. per 100 cc. The electrocardiogram showed an increase in the interventricular conduction time and depressed T waves in limb leads 1 and 2 and in precordial leads 1, 2, 3, 4, 5, and 6 (Fig. 2).

She was treated with intravenous potassium and supportive fluids and put on a high calorie diet with frequent feedings, and therapeutic doses of vitamin B complex. The day after admission a chest x-ray showed evidence of pulmonary edema. Later, upper gastrointestinal, gallbladder, and barium enema x-rays were normal. Gastric analysis showed achlorhydria to histamine. She improved steadily in strength, her chest cleared on the third day, and by the tenth day her chest was clear to x-ray; the heart was smaller in size, and the electrocardiogram had significantly improved. She went home on the twelfth day after ad-

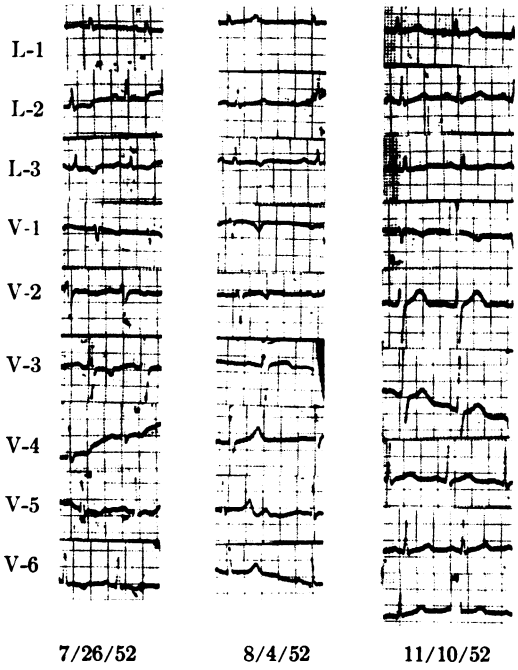

Fig. 2. H. J.

mission, and continued to gain in weight and strength.

Three months later, Oct. 29, 1952, her serum potassium was 4.4 mEq./L. and she had gained 15 pounds. The dysarthria, the hesitation in speech, forgetfulness, and the blurring of vision had all disappeared. The electrocardiogram taken on Nov. 10, 1952 was entirely normal.

Discussion

It seems clear that these are cases of hypopotassemia and that the body tissues suffered prolonged potassium lack. The presence of alkalosis in *Case 1* is corroboratory.[1] In this case, avidity of the tissues for potassium is shown by the sustained low serum levels of this ion and by the fact that there was no increased urinary potassium output in the face of large amounts of oral and parenteral potassium salts.[5]

Darrow[1] says, "Under abnormal conditions as much as one half of the intracellular potassium may be replaced by two thirds of the equivalent amount of sodium." The removal of intracellular sodium and the return of potassium to the cells is not a rapid process. According to Darrow,[1] "Deficits may be so large that they cannot be restored parenterally for 6 days because administration of more potassium does not restore all deficits more rapidly." Furthermore, Tarail[5] found only one of his hypopotassemia patients in positive potassium balance after treatment. The period of potassium feeding was too brief (8 days) in the others.

In our patients, generalized muscular weakness and hyporeflexia, although long lasting and slow to disappear, seem akin to what is seen in more acute deprivation. The mental slowness, dysarthria, emotional lability, and disorientation have been mentioned before in the literature on starvation.[9] Thiamine and niacin deficiencies are associated with well-recognized neurological changes. In *Case 1* clearing of the sensorium and return of muscle strength and reflexes coincided with potassium administration, but were not affected by two weeks of feeding alone. Extradietary vitamins were not used in *Case 1*. Thiamine, riboflavin, and niacin in therapeutic doses (at least 50 mg. thiamine, 25 mg. riboflavin, 200 mg. niacin, and vitamin C daily *per os* or intravenously) were given in *Cases 2* and *3*.

Perhaps the neurological abnormalities often observed during starvation are in part related to hypopotassemia. A prolonged mild deficiency of potassium seems as likely to produce damage to nerve tissues as an acute severe lack of the electrolyte. The usual treatment of starvation includes replacement by calories and vitamins and the effect of individual mineral replacements may be obscured. Certainly, more study of this point is clearly indicated.

Conclusions

Three cases of long-standing starvation and resultant potassium deficiency are presented. Potassium deficiency may be a frequent feature of starvation. Many signs of central nervous system damage were recorded and observed to disappear with treatment by food, vitamins, and potassium salts. A tremendous dose (261 Gm. or 3400 mEq.) of KCl in addition to a high potassium diet was given to one

patient over a period of one and half months.* Restoration of intracellular potassium may be slow in such cases. It is possible that many of the central nervous system changes in starvation are due to intracellular potassium deficit.

* 261 Gm. of KCl furnishes about 136 Gm. of potassium. During the $3^1/_2$ months of observation the daily urinary losses would equal between 2 and $2^1/_2$ Gm. per day or at least 225 Gm. of potassium all told. Therefore, extradietary potassium during this time was not sufficient to replace urinary losses and tissue reserves had to be built up from food.

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Resumen

Hipopotasemia en la inanición humana y en la resección gástrica

Se presentan tres casos de hiponutrición prolongada y de resultante hipopotasemia. La hipopotasemia puede ser un hecho frecuente en la inanición. Muchos signos de lesiones en el sistema nervioso central se han observado que han desaparecido al ser tratados con alimentación, vitaminas, y sales de potasio. Una dosis masiva (261 gms. o 3400 miliequivalentes) de KCl, sobreañadida a una dieta rica en potasio, se administró a un paciente durante un período de 1½ meses. La restauración del potasio intracelular puede ser lenta en tales casos. Es posible que muchos de los cambios que se observan en el sistema nervioso central durante la inanición sean debidos a un déficit de potasio intracelular.