HYPERPOTASSEMIA AND BODY WATER DISTRIBUTION IN AN ANURIC CHILD

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New York

CONSERVATIVE management of anuria has in many instances prolonged life. This involves the correction of water and electrolyte deficits and the utilization of the protein-sparing effects of glucose to decrease the rate of tissue catabolism. These measures attempt to preserve the integrity of the body fluids, thus retarding the accumulation of toxic substances, i.e., potassium, and reducing the risk of water intoxication and possible pulmonary edema which often results from vigorous fluid, water administration in anuric patients.

Attempts to simulate renal excretion by peritoneal lavage, gastrointestinal irrigation, exsanguino-transfusion and the artificial kidney technic seek to maintain homeostasis until there is a return of renal function. Therapy directed at restoration to normal of body water and electrolyte requires knowledge of the normal distribution and of the factors influencing shifts of these substances between the extra- and intracellular compartments.

The following is a report of clinical observations and studies of body water distribution during the course of anuria with progressive hyperpotassemia in a 6 year old child.

CASE HISTORY

L. T., a 6 yr. old Negro female, was admitted to the Children's Medical Service, Bellevue Hospital, after anuria of 4 days' duration and vomiting and constipation of 6 days' duration.

Family history was not remarkable other than that the mother had been treated for syphilis 13 yr. previously. There was no known renal disease. Past history revealed that gestation and delivery were uncomplicated except for a repeat course of antiluetic therapy for the mother. Neonatal course, growth and development were normal. Immunizations included diphtheria, tetanus, pertussis and smallpox vaccination. Previous illnesses included rubella, rubella, epidemic parotitis, and varicella. Review of systems revealed frequent colds, 2 to 3 each winter lasting 2 to 3 wk., and occasional chronic cough with slight production of yellow sputum, but no known streptococcal infection. There were no previous genitourinary tract difficulties, hematuria, pyuria or oliguria prior to the present illness.

The patient had been well until 2 wk. prior to admission when she began to cough. Eight days prior to admission the onset of anorexia, malaise and fever occurred. The family physician diagnosed tonsillitis and cervical adenitis and prescribed rhubarb and soda and aspirin. Six days prior to admission, fever and anorexia continued, vomiting after meals and constipation were noted, and the child was more somnolent than usual. She urinated normally 7 days prior to admission.

Five days prior to admission she continued febrile and was examined at another hospital where sulfadiazine was prescribed. The amount ingested by the patient is not known, but it is thought to be small because the medication was vomited more often than retained. Symptoms continued as before. Three days prior to admission, the patient was said to have passed a small amount of smoky urine.
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which was not seen by the mother. This is the last known voided specimen. Vomiting, headache, periumbilical pain, malaise and anorexia continued until admission.

Anuria was essentially of 7 days' duration, except for the possible small specimen 3 days prior to admission. No history could be elicited of ingestion of toxic substances other than the few doses of sulfadiazine.

Physical examination revealed a well-developed, well-nourished alert cooperative 6 yr. old female Negro child who did not appear acutely ill. The rectal temperature was 36.7° C, respiratory rate 26/min., pulse rate 68/min., blood pressure 125/88 mm.Hg and wt. 26.5 kg. The breath had a uremic odor, but the face was not puffy. The pharynx was minimally injected. The lungs were clear to percussion and auscultation and the heart sounds were of good quality. A soft medium-pitched blowing systolic murmur was heard over the entire precordium, maximal at the fourth intercostal space at the left sternal border. There was moderate costovertebral angle tenderness bilaterally but no abdominal masses or peripheral edema were observed. Otherwise the physical examination was normal.

Hgb. 11 gm./100 cc. (Sahli), RBC 4.3 million/ccmm., and WBC 15.5 thousand/ccmm. with a normal differential. Catheterization of the bladder yielded a few cc. of yellow urine, pH 5.5, albumin negative. The sediment contained a few white blood cells but no crystals or other formed elements. Initial blood chemical analyses showed: blood NPN 193 mg./100 cc., blood sulfadiazine concentration 0.89 mg./100 cc., serum CO2 combining power 12.5 mEq./l., serum sodium 133 mEq./l., plasma potassium 7 mEq./l. (table 1).

The patient remained afebrile and in good general condition over the 1st 24 hr. Occasional vomiting persisted. In view of the history of sulfadiazine ingestion and the finding of sulfonamide in the blood, bilateral ureteral alkaline washouts were done under light ether anesthesia. No urine was obtained from either ureter. The irrigation fluid revealed no sulfonamide crystals nor could any be detected by chemical analysis. Ureteral catheters remained in situ for 18 hr., after which they were removed and a Foley catheter placed in the bladder. During the 1st 24 hr. minimal intravenous fluids were given (300 cc. of 5% glucose and 50 cc. of 10% inulin, 50 cc. 25% mannitol, 34.5 cc. 99.8% deuterium oxide and 30 cc. water) . Feedings of glucose solution were vomited.

Her condition appeared to be good on the third hospital day. Fluids tolerated by mouth included 470 cc. orange juice, 120 cc. water and 70 cc. of 5% sodium bicarbonate. No intravenous fluids were given. Blood pressure was normal. Tissue turgor was good although muscle tone was poor. A fluid wave in the abdomen was noted. Weight remained stationary.

TABLE 1

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Blood NPN mg/100 cc.</th>
<th>Serum CO2 Combining Power mEq/l.</th>
<th>Serum Na mEq/l.</th>
<th>Plasma K mEq/l.</th>
<th>Blood Sulfadiazine mg/100 cc.</th>
<th>Serum Ca mg/100 cc.</th>
<th>Serum P mg/100 cc.</th>
<th>Serum T.P. em. 100 cc.</th>
<th>A/G</th>
<th>Body Wt. kg</th>
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<tr>
<td>6/10</td>
<td>10 a.m.</td>
<td>193</td>
<td>12.5</td>
<td>111</td>
<td>133</td>
<td>7.0</td>
<td>0.89</td>
<td>8.57</td>
<td>4.62</td>
<td>26.5</td>
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<tr>
<td>6/11</td>
<td>10 a.m.</td>
<td>12.5</td>
<td>87</td>
<td>129</td>
<td>7.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>26.5</td>
<td></td>
</tr>
<tr>
<td>6/11</td>
<td>6 p.m.</td>
<td>91</td>
<td>140</td>
<td>8.0</td>
<td>5.7</td>
<td>5.6</td>
<td></td>
<td></td>
<td></td>
<td>25.9</td>
<td></td>
</tr>
<tr>
<td>6/12</td>
<td>6 a.m.</td>
<td>76</td>
<td>139</td>
<td>9.4</td>
<td>6.2</td>
<td>4.9</td>
<td></td>
<td></td>
<td></td>
<td>27.0</td>
<td></td>
</tr>
<tr>
<td>6/12</td>
<td>5 p.m.</td>
<td>90</td>
<td>139</td>
<td>9.5</td>
<td>10.4</td>
<td>4.9</td>
<td></td>
<td></td>
<td></td>
<td>27.0</td>
<td></td>
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<tr>
<td>6/13</td>
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<td>292</td>
<td>13.8</td>
<td>85</td>
<td>139</td>
<td>9.5</td>
<td>9.95</td>
<td>10.4</td>
<td>4.9</td>
<td>27.0</td>
<td></td>
</tr>
<tr>
<td>6/14</td>
<td>4 a.m.</td>
<td>284</td>
<td>79</td>
<td>130</td>
<td>10.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>27.0</td>
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* From the chemistry laboratory of The Children's Medical Service.
On the fourth hospital day the blood pressure was normal, respirations were slightly labored, but the lungs remained clear. The patient was more lethargic. Slight puffiness about the eyes and definite pitting edema of the lower extremities were evident. Skin turgor was fair. The blood NPN concentration was markedly elevated and the plasma potassium concentrations of blood samples drawn on previous days were observed to be at subtoxic levels (Table 1). Fluid intake was limited to 610 cc. of orange juice with added sodium bicarbonate. The ECG now showed minimal evidence of potassium intoxication, widening of the QRS complex, depression of the ST segment, elevated T waves and relative shortening of the Q-T interval (Fig. 1C). At 10:55 p.m., the patient was noted to have a slow irregular pulse at a rate of 50/min. ECG revealed marked potassium intoxication as evidenced by the ventricular rhythm with widened QRS, apparent auricular paralysis and the appearance of an even higher T wave (Fig. 1D). Ten cubic centimeters of 5% calcium gluconate were given intravenously with a transient increase in the heart rate and a return to a regular rhythm.

It was considered desirable to attempt to reduce the plasma potassium concentration by the technic of exsanguino-transfusion since no other means of effecting dialysis was available. After a biologic test transfusion for compatibility with 50 cc. of blood, the procedure was started. However, the ECG revealed extreme potassium intoxication (Fig. 1E) and the patient died about 1 hr. after the
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Exsanguino-transfusion was started. The patient was alert and cooperative until the last few hours. No autopsy was performed. The clinical diagnosis was acute renal failure, etiology unknown.

METHODS OF STUDY

Total body water was measured by the in vivo dilution of deuterium oxide (heavy water). The volume of extracellular water was measured by the in vivo dilution of inulin. The volume of intracellular water was then obtained by subtracting the inulin volume of distribution from the deuterium oxide volume of distribution. Plasma volume was measured with T 1824.

On the second hospital day, 101.7 cc. of a solution of 5% inulin and 12.5% mannitol were injected intravenously with a constant infusion at a rate of 3.39 cc./min. This was followed 9 hr. later by an intravenous injection of 34.5 cc. of deuterium oxide from a calibrated syringe. Before the injection, a control blood sample was obtained for determination of the plasma blank concentration,

TABLE 2

<table>
<thead>
<tr>
<th>Accepted Normal Values</th>
<th>Total Body Water</th>
<th>% of Body Weight</th>
<th>Extracellular Water</th>
<th>% of Body Weight</th>
<th>Intracellular Water</th>
<th>% of Body Weight</th>
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<tr>
<th>Experimental Values</th>
<th>Deuterium Oxide Space (D₂O)</th>
<th>Inulin Space</th>
<th>Deuterium Oxide Space minus Inulin Space</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>L</td>
<td>% Body Wt.</td>
<td>L</td>
</tr>
<tr>
<td>June 12, 1949</td>
<td>18.2</td>
<td>69</td>
<td>9.0</td>
</tr>
<tr>
<td>6:46 a.m.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>June 14, 1949</td>
<td>21.1</td>
<td>78</td>
<td>12.7</td>
</tr>
<tr>
<td>4:00 a.m.</td>
<td></td>
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B., for subtraction from subsequent plasma concentrations of inulin and mannitol. The volume of distribution of inulin and mannitol was calculated as the total amount injected (in mg.) divided by the concentration in plasma water (in mg./cc.). The deuterium space was calculated as the amount of deuterium oxide injected divided by the concentration of deuterium oxide in plasma water corrected for the natural occurrence of deuterium (0.02 atoms %).

Samples of blood were drawn at 1 to 12 hr. intervals until the patient's death. On 2 occasions the T 1824 space was measured from a single sample drawn 10 min. after injection and read against a control plasma blank drawn just before the dye was injected.

Inulin was determined by Harrison's modification of the method of Alving, Rubin, and Miller, mannitol by the method of Corcoran and Page and deuterium oxide was measured in the mass spectrometer.*

Equilibrium distribution of inulin was attained in this patient between 4 and 9 hr. after injection. At 6:46 a.m. on June 12, 1949, 14 hr. after the injection of deuterium oxide, simultaneous inulin and deuterium oxide spaces were 9.0 and 18.2 l., respectively, the difference being 9.2 l. (table 2). At 4:00 a.m., June 14, 1949, 45 hr. later and 2 hr. before death, repeat determinations revealed an

* The authors are indebted to Dr. Robert Jailer of the Sloan-Kettering Institute for the deuterium analysis with the mass spectrometer.
inulin space of 12.7 l. and a deuterium oxide space of 21.1 l., the difference being 8.4 l. The latter
deuterium oxide space is corrected for an assumed insensible water loss of 30 cc./kg. body weight/day.
The mannitol space was 10 l. at 6:46 a.m. on June 12, 1949, and 14.1 l. at 4:00 a.m. June 14, 1949.
The T 1824 space was 1,320 cc. at 7:00 p.m. on June 11, 1949, and 1,300 cc. when measured again
7 hr. before death at 8:05 p.m. on June 13, 1949. The hematocrit varied between 25.5 and 29.5 with
no consistent trend over the 4 day period of observation. Urine flow was less than 50 cc. throughout
the course.

**DISCUSSION**

Accepting the initial inulin space as a measure of the extracellular water volume, and
the initial deuterium oxide space as a measure of the total body water, the preceding
data demonstrate an abnormally increased extracellular fluid volume in the presence of a
normal total body water after a week of anuria (table 2).

Errors in the deuterium space arise from extrarenal losses of deuterium oxide and ex-
change of deuterium with available tissue hydrogen. The final deuterium oxide space has
been corrected for the estimated insensible water loss.*

Evidence that inulin is distributed in the extracellular space and, under normal circum-
stances, is not metabolized has been summarized elsewhere.18-20 The fact that the initial
mannitol space was greater than the inulin space probably is due to the metabolism of
mannitol rather than to inert penetration of tissue cells.21-23 Errors in the inulin space arise from possible cell penetration or metabolism after
prolonged retention of inulin in anuria. Berger and associates24 have evidence suggesting
that inulin is metabolized in the nephrectomized dog. However, if these sources of error
were insignificant, and the final inulin space measured the extracellular space, one would
be forced to postulate osmotic inactivation of cell electrolyte.

For these reasons, the authors hesitate to conclude that in this patient there occurred
the indicated final decrease in the intracellular fluid compartment, although the direction
of change of water from the intracellular compartment is consistent with (1) tissue
destruction (starvation) with release of intracellular water and electrolyte, (2) water
of oxidation and (3) osmotic attraction to the extracellular compartment as a result
of insensible water loss and administered sodium salts.

Fluid and electrolyte therapy in this case was directed toward maintenance of the
body weight and correction of the acidosis by administration of sodium bicarbonate and
water.1,2 Unfortunately, insufficient glucose was administered so that maximal retarda-
tion of tissue catabolism was not obtained as suggested by the rapidly increasing azotemia,
phosphatemia and hyperpotassemia (table 1). On the two days prior to her death, the
patient received 1,080 cc. of orange juice25 with added sodium bicarbonate and dextrose.
It was recognized subsequently that this amount of orange juice constituted an additional
burden of 47 mEq. potassium. Thus, in this patient a rapid rise in plasma potassium
concentration from 7.0 to 10.1 mEq./l. occurring over a four day period is in part
attributable to orally administered K present in orange juice. Peters26 has emphasized
recently that almost all food contains K and should be withheld in the management of
the anuric patient.

During the first 48 hours, when the plasma potassium concentration was 7.0 mEq./l.,
the ECG showed no evidence of potassium intoxication. Widening of the QRS and
early elevation of the T wave occurred when the plasma concentration was 9.4 mEq./l.

* The fact that the weight increment was less than the deuterium oxide space increment (table 1)
may be attributed to weighing errors and/or underestimation of the insensible water loss.
The onset of the terminal episode consisted of arrhythmia, bradycardia, absent P waves, premature ventricular contractions from varying foci of origin, widening of the QRS complex and marked elevation of the T waves. Ten cubic centimeters of 5% calcium gluconate was given intravenously with a transitory return to a regular rhythm and increase in the heart rate. Saline-lactate solutions in small amounts had no effect on the ECG. Progressive signs of potassium toxicity continued (Fig. 1C) until terminal disorganization of the ventricular complex was noted just preceding cardiac arrest. The continuous electrocardiographic changes and the high plasma potassium concentrations are sufficient evidence that the terminal episode was due to potassium intoxication.

Hoff, Smith, and Winkler17 have shown in dogs that death following nephrectomy or bilateral ureteral ligation results from potassium intoxication. Previously these authors described the serial changes in the ECG occurring with potassium intoxication in normal animals.28 They also noted that simultaneous administration of calcium diminished the effects of K on the cardiac conduction system although the usual toxic effects of K could be obtained at a higher plasma concentration of K.29

Normal humans rapidly adjust to the intake of potassium salts by increased renal excretion30–33 and uptake of K by the intracellular compartment.30,31 Even though patients with moderate to severe nephritis may excrete sufficient K daily to maintain a normal plasma concentration in the presence of tissue catabolism and moderate potassium intake, the principal limiting factor in the excretion of K probably is a reduction in the glomerular filtration rate.30,34,35 Certainly in anuria there is no other significant route of egress for K except for minimal skin and gastrointestinal losses. An increasing plasma potassium concentration with potassium intoxication is an ever present danger.30,37 Finch38 was able to ameliorate the symptoms of potassium intoxication with intravenous sodium salts; however, both patients succumbed shortly thereafter. He also treated one case with calcium gluconate intravenously with results comparable to those of the present investigators.

Recently Levene et al.39 described electrocardiographic changes associated with potassium intoxication in 16 cases, most of whom were anuric. They noted that the electrocardiographic manifestations of hyperpotassemia were potentiated by a diminished serum sodium. Reversal of the findings after administration of sodium salts occurred temporarily in a few cases. Many others have reported electrocardiographic changes of hyperpotassemia in patients with renal insufficiency.40,41

Treatment of hyperpotassemia may now be approached by use of an ion-exchange resin or by dialysis with the artificial kidney. With the latter technic, recently several groups have been able to lower the plasma potassium levels significantly.42–45 By proper adjustment of the dialysing medium this could be accomplished similarly by peritoneal lavage. While exsanguino-transfusion is the only alternative in the absence of facilities for the other methods, it is the least desirable, since it entails the hazards of a transfusion reaction and requires massive exchanges to significantly lower the plasma potassium concentration.

**Summary**

A patient with anuria in whom a rising plasma potassium concentration was associated with progressive signs of potassium intoxication exhibited a decrease in the intracellular compartment and increase of the extracellular compartment without significant change in plasma volume, while total body water remained essentially normal.
REFERENCES


**SPANISH ABSTRACT**

**Hiperpotassemia y Distribución del Agua del Cuerpo en un Niño Anurico**

Se reporta un caso de una niña de 7 años de edad con una insuficiencia renal aguda la cual desarrolló un aumento progresivo del potasio plasmático asociado con alteraciones electrocardiográficas. Esta hiperpotassemia fue atribuida en parte a la anuria, y en parte a la gran concentración del potasio contenido en el jugo de naranjas administrado. La distribución del agua del cuerpo fue estudiada usando la técnica del "deuterium oxide" in vivo, el agua extra-celular mediante el método de la inulina y el volumen del plasma fue determinado con el T 1824. Estos estudios revelaron que el volumen del plasma no se alteró y que el agua total del cuerpo fué esencialmente normal; sin embargo, se observó un aumento significante del compartimento extra-celular con una disminución del compartimento intra-celular.
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