

Original Article

## Potential benefits of potassium deposition with periodic fluid redistribution using periodic head down tilt during diminished muscular activity

**Yuri F. Federenko\***, Pavel L. Merkov, Yuri N. Yaroshenko,  
**Sergei K. Denogratov**, Kyrill P. Charapakhin  
and Nikolai H. Neofitov

Institute of Hypokinetic Physiology,  
Athens, Greece

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### Abstract

**Objective :** Fluid redistribution (FR) is an important cornerstone in treating diseases. Findings of FR with periodic head down tilt (PHDT) had sparked renewed interest in treating electrolyte disturbances. Therefore this study aimed to determine the potential benefits of potassium (K<sup>+</sup>) deposition with periodic FR by PHDT during diminished muscular activity (hypokinesia; HK).

**Methods :** Studies were conducted on 40-male volunteers. They were equally divided into 4-groups: active control subjects (ACS), hypokinetic subjects (HKS), periodic fluid redistribution control subjects (PFRCS) and periodic fluid redistribution hypokinetic subjects (PFRHS).

**Results :** Muscle K<sup>+</sup> increased (p<0.05) and plasma K<sup>+</sup> level and K<sup>+</sup> losses decreased (p<0.05) in the PFRHS group compared to the HKS group. By contrast in the HKS group muscle K<sup>+</sup> reduced (p<0.05) and plasma K<sup>+</sup> level and K<sup>+</sup> losses increased (p<0.05) compared to pre-experimental period levels and the values of the other groups. In the PFRCS group the muscle K<sup>+</sup>, plasma K<sup>+</sup> concentration and K<sup>+</sup> losses were affected much less than in the PFRHS group.

**Conclusion :** The current study shows that periodic-applied fluid volume addition into the body's regional areas by PHDT increases muscle K<sup>+</sup> content and decrease K<sup>+</sup> losses suggesting potential benefits of K<sup>+</sup> deposition during diminished muscular activity.

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### Introduction

Diminished muscular activity (Hypokinesia; HK) is defined as a condition of physical inactivity beyond

that associated with daily functioning and deconditioning of the skeletomuscular system, cardiovascular system, kidneys and renal system and other organs and systems and vessels of the lower extremities. Diminished muscular activity leads to the energy catabolism, body weight loss and reduction of energy production, oxidative phosphorylation (OP), mitochondrial density and adenosine triphosphate (ATP) synthesis (1-3). Diminished muscular activity affects muscle mass, blood volume and tissue oxygen supply. Deposition

**\*Corresponding author :**

Yuri F. Federenko, Institute of Hypokinetic Physiology,  
Odos Eptapirgou 4, GR-162 32 Athens, Greece  
Tel.: 302107628676  
Email: yfederenko@gmail.com

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of such electrolytes as potassium, sodium, magnesium, phosphate and calcium is affected (4-12). To counteract consequences of diminished muscular activity different preventive measures have been used with little success (13-18).

With diminished muscular activity blood and other body fluids tend to pool into the lower part of the body. Fluid volume shifting into the legs eventually leads to fluid volume deficiency within the circulatory system. Diminished muscular activity is associated with retention of large fluid volume in the lower part of the body than what is the norm for the lower extremities resulting in lower blood volume and diminished filling with blood of central vascular bed (19). Because of fluid shifting into the lower extremities more fluid volume migrates into the pelvic region and the lower half part of the body. Fluid volume that can fit into venous system of the lower part of the body may determine the severity of changes in the delivery of fluid volume to the upper part of body and thus extracellular and interstitial fluid volume. Periodic fluid redistribution (PFR) induced by periodic head down tilt (PHDT) may be important in regulating electrolytes (20).

The PHDT is not analogous to the head-down tilt (HDT) (in humans) and hindlimb suspension (in rats) which are used to simulate weightlessness. Although these situations share a significant increase in thoracic fluid volume there are other factors specific to PHDT. The biochemical and physiological reactions occur progressively during PHDT and not acutely as in the HDT. With PHDT the biochemical and physiological reactions are under different control from that of HDT. The primary mechanisms which drive fluid volume into the body's regional areas with PHDT are different from the mechanisms which shift fluid volume to the upper part of the body with HDT, as are many other features specific to PHDT [20]. By contrast to the HDT, with the PHDT fluid volume is intravascular and intracellular and therefore does contribute to vascular volume. To differentiate fluid redistribution (FR) with PHDT from other types of FR as with the HDT and hindlimb suspension, water immersion, bed rest, weightlessness, postoperative and/ or postural manipulations is required specific knowledge of biochemical and physiological reactions.

PFR is defined as periodic fluid shifting into the regional areas of the body beyond that of daily FR. PFR is reprogramming skeletomuscular system and cardiovascular system and kidneys and urinary system and vessels of the lower half part of the body and other organs and systems. PFR contributes to the aerobic respiration, hypervolemia and tissue perfusion and decreases blood and interstitial fluid pressure. In addition chronic PFR is a factor of anabolism induction, adenosine triphosphate (ATP) synthesis, mitochondria density, oxidative phosphorylation (OP), glycogen production, tissue oxygen supplies, aerobic metabolism and cell mass preservation.

Unpublished data accumulated over 20 years have shown that chronic PFR has the potential to increase longevity by 30% to 40% in human population. Unpublished studies done over many years have shown that PFR may prevent myocardial infarctions and stroke, restore insufficiency of kidney and heart, widening of coronary arteries, and increase the left ventricular volume, cardiac output, number of capillaries, cell mass, muscle mass, bone mass and repair damaged tissues. PFR may lower interstitial fluid pressure in different diseases as in solid malignancies and inflammation as osteoarthritis that may increase the access to nutrients, oxygen and drugs.

With periodic shifting of blood and other body fluids toward the head the brain does not interpret its elevation of blood supply as excess fluid volume but rather as simple FR. In response to this misperception, brain does not signal kidneys and other organs to lower blood volume and other body fluids. The systems tend to adapt to PHDT while fluid volume expands due to periodic fluid shifting to the head and baroreceptors do not stretched and do not interpret this as an excess fluid volume, and do not stimulating the body to urinate so that excess fluid is eliminated. This process slows electrolyte losses contributing to more tissue electrolytes. Thus, PHDT that moves fluid away from the lower part of the body into regional areas of the body may be one solution for maintaining blood volume, tissues oxygen supply and regulating electrolyte deposition (20).

Fluid redistribution with PHDT had shown that it may improve electrolyte regulation when it is used over long period of time and at least 8 hrs per day (20). Therefore to determine the potential benefits of K<sup>+</sup> deposition with periodic addition of fluid volume into the regional areas of the body over long time and at least 8 hrs per day using PHDT we measured muscle K<sup>+</sup> content, plasma K<sup>+</sup> concentration and K<sup>+</sup> losses in health subjects during diminished muscular activity.

## Materials and methods

The studies have conformed to the principles of the Declaration of Helsinki and the procedures were reviewed and approved by the Institutional Review Board. Subjects gave informed consent to take part in the study after a verbal and written explanation of risks and methods involved were given. Among the subjects were no medical problems and none of the subjects were under any drug therapy which could have interfered with potassium metabolism. From the study were not drop-outs. Financial incentives relative to average monthly earnings were used to encourage compliance with the protocol of the study. Forty physically healthy male subjects 24.2±6.3 years of age were chosen as subjects. All subjects were run average distances of 10.5±1.6 km.day<sup>-1</sup> at a speed of 10.5±1.3 km.h<sup>-1</sup> for three to five years. Subjects had a body weight of 75.5±8.0 kg and peak oxygen uptake of 47.2±7.0 mL. kg<sup>-1</sup>. min<sup>-1</sup>. In pre-experimental period of 390-days subjects were run average distances of 10.4±1.4 km.day<sup>-1</sup> at a speed of 10.6±1.3 km.h<sup>-1</sup>.

Assignment of subjects into four groups was done randomly and randomization was prepared by someone independent from the recruitment procedures and treatment of periodic redistribution of fluid volume and a concealed method was used.

Group 1 : Ten subjects were run average distances of 10.5±1.5 km.day<sup>-1</sup> for 364-days. They were assigned to the active control subjects (ACS) group. Group 2 : Ten subjects walked average distances of 3.6±0.5 km.day<sup>-1</sup> for 364-days. They were assigned to the hypokinetic subjects (HKS) group. Group 3: Ten healthy subjects were run average distances of

10.5±1.8 km.day<sup>-1</sup> and were subjected to a -8 to -12 degrees of PHDT for 8 to 10 hrs per day for 364 days. They were assigned to the periodic fluid redistribution control subjects (PFRCS) group. Group 4: Ten healthy subjects walked average distances of 3.6±0.8 km.day<sup>-1</sup> and were subjected to a -8 to -12 degrees of PHDT for 8 to 10 hrs per day for 364 days. They were assigned to the periodic fluid redistribution hypokinetic subjects (PFRHS) group.

### Protocol

The investigation consisted of a 390-day pre-experimental period and a 364-day experimental period. Diets were served as a 7-day menu rotation. The meals were all prepared under standard conditions in a research kitchen. Mean daily energy consumption of the metabolic diet was 3530 ± 558, 2915±307, 3580±578 and 3131±360 SD Kcal, and the mean daily consumption of K<sup>+</sup> was 84.3±1.4, 84.4±1.3, 84.2±1.7 and 84.2±1.5 SD mmol for the ACS, HKS, PFRCS and PFRHS groups, respectively. The subjects were housed in a facility in which the temperature, humidity, activities, and dietary intakes were monitored 24 hrs per day and 7 days per week.

### Simulation of diminished muscular activity

To simulate a certain level of hypokinesia the number of km walking per day was restricted to an average of 3.6±0.6 km.day<sup>-1</sup> and was monitored daily by an accelerometer. The activities allowed were those which approximated the normal routines of the hypokinetic individuals. Subjects were allowed to walk to the dining rooms, lavatories and different laboratories where the tests were given. Climbing stairs and other activities which required greater efforts were not allowed. Subjects were mobile and were not allowed outside the laboratory grounds so that the level of diminished muscular activity was remained relatively constant and easily monitoring.

### Simulation of periodic fluid redistribution with periodic head down tilt

For the simulation of PFR subjects were submitted to PHDT of -2 to -12 degrees for 8 to 10 hrs per day during the sleeping period in the pre-experimental period of 390 days and experimental period of 364 days. In pre-experimental period subjects were

progressively submitted to PFR by increasing the level of PHDT to -2, -4, -6, -8- and -12 degrees every 64 to 71 days. Then subjects were submitted to PHDT of -8 to -12 degrees for about 8 to 10 hours per day and for the rest pre-experimental period and actual experimental period. The selection of 390-days pre-experimental period and the submission of subjects every 64 to 71 days to the PHDT of -2, -4, -6, -8 and -12 degrees and their exposure to the PHDT of -8 to -12 degrees for 364 days period was established from a preliminary experimentation aiming to determine the adaptation of subjects to PHDT. The PHDT of -8 to -12 degrees was changed from time to time in order to conform to the subjects' requirements to that position at the time. Individual differences of biochemical and physiological reactions, that is, renal, hormonal, cardiovascular and metabolic reactions of the subjects as well as their clinical manifestations and sensitivity to PHDT were taken into account. The schedule of PHDT was alternated from time to time to conform to the adaptational reactions of subjects.

#### **Blood, urinary and fecal sample collection**

To accommodate inter-individual differences in bowel habits, urine and feces were analyzed daily and were pooled to form 6-days composites, while blood samples were assayed every 6-day during the pre-experimental and the experimental period. The 6-day (consecutive days) pooled samples were collected. Blood samples were collected with disposable polypropylene syringes. Following overnight fasting for about 8-9 hours, venous samples of blood were taken at rest and before any meals. Blood samples were drawn under the same conditions between 8.00 and 9.00 a.m., without a venous stasis and after the subjects had been sitting for about 30 min. The sample volume was 7 to 9 mL. To obtain plasma, blood samples were collected in heparinized ice-chilled tubes and were centrifuged immediately at  $10,000 \times g$  for 3 min at room temperature and separated using glass capillary pipettes which were washed in hydrochloric acid and deionized distilled water. Immediately after centrifugation plasma samples were frozen on dry ice and were stored at  $-20^{\circ}\text{C}$  until analyses were conducted for plasma  $\text{K}^+$ . Twenty four hour urine samples were stored at  $-4^{\circ}\text{C}$

until needed for  $\text{K}^+$  analysis. To ensure complete twenty four hour urine collections the creatinine loss was measured by a colorimetric method using Jaffe's reaction. Feces were collected in plastic bags, weighed and stored at  $-20^{\circ}\text{C}$  for  $\text{K}^+$  analysis. Fecal samples were dried-ashed in a muffle furnace at  $600^{\circ}\text{C}$  overnight. Ashed samples were dissolved in 5% nitric acid. To ensure complete feces recovery polyethylene glycol was used as a marker.

#### **Muscle preparations, potassium extraction and analysis**

Muscle biopsies were performed by a percutaneous needle technique (21) under local anesthesia. Specimens were taken from the lateral portion of the quadriceps femoris muscle, 13–20 cm proximal to the knee. The muscle (mean weight 14.6 mg) was placed on a piece of quartz glass and with nonmetal tweezers carefully dissected free from all visible fat and connective tissue. Traces of blood were wiped off by rolling the specimens on the piece of quartz glass. Muscle was then placed on a platinum hook and dried in an oven at  $110^{\circ}\text{C}$  to constant weight, extracted in 1 mL of petroleum ether for 2 h and dried to constant weight and fat-free dry solids (FFDS) weight was calculated. The potassium extracted from muscle by treatment with 250  $\mu\text{L}$  2.5 M  $\text{HNO}_3$  for twenty-four hour. From each sample, 100  $\mu\text{L}$  of supernatant was diluted to 10 mL with 0.25%  $\text{SrCl}_2$  and analysis of potassium in muscle was performed by using a Flame Emission Spectrophotometer on a Perkin-Elmer 320 Model, Perkin-Elmer Corp., Norwalk, CT. The results obtained on muscle potassium content were calculated in  $\text{mmol}/100 \text{g}^{-1}$  FFDS.

#### **Potassium measurements**

Samples were analyzed in duplicate and appropriate standards were used for the measurements: The muscle  $\text{K}^+$  content, plasma  $\text{K}^+$  level and  $\text{K}^+$  loss in feces and urine was measured by a Flame Emission Spectrophotometer of a Perkin-Elmer 320 Model, Perkin-Elmer Corp., Norwalk, CT.

#### **Data analyses**

A 2-way interaction [treatment (4 levels) by days (6

levels)] analysis of variance (ANOVA) was used to determine whether PFR can affect muscle K<sup>+</sup> deposition during HK. The ANOVAs with repeated measures of 2-way interaction (treatment/days, pre-experimental/experimental levels, hypokinetic/periodic fluid redistribution hypokinetic groups, hypokinetic/control groups) was used. The ANOVAs for each time point measurements were used. The level of significance was set at  $p < 0.05$ . The results obtained were reported as mean $\pm$ SD (Standard Deviation).

## Results

At the initial stages of the investigation the volunteers who were subjected to PHDT manifested analogous reactions as those in the HDT position. This is a consistent reaction to PHDT which is characterized as adaptational in nature. Then the PFRHS and the PFRCS groups exhibited some signs and symptoms typical to PHDT (Table I). However, as the duration with the treatment of PFR increased and the subjects were adapted to PHDT all signs and symptoms disappeared and by the end of the study none of the subjects were complained of any signs and symptoms. The subjects who were treated with PFR failed that were much better off physically than before the treatment and that they have gained energy and strength and therefore they have decided to continue the treatment with PFR after completion of the study.

During the pre-experimental period, muscle K<sup>+</sup> content, plasma K<sup>+</sup> concentration and urinary and fecal K<sup>+</sup> losses were remained relatively stable in the HKS group and the ACS group (Table 1). Initially

TABLE I: Initial reactions of healthy subjects to chronic periodic head down tilt.

Puffiness in the face
Tachycardia
Arrhythmias
Loud heart sounds
Tinnitus in the left and more in the right ear
Feeling of fullness (pressure) or stiffness in the left ear and more in the right ear
Deep vein symptoms in the left and more in the right leg
Pain in the left and more in the right foot
Pain in the upper and the lower parts of the body
Pain in the calcaneal tendon region (Achilles) in the left and more in the right leg
Pain in the left and more in the right forearm
Cold sensation in the left and more in the right hand

in the PFRHS group and the PFRCS group muscle K<sup>+</sup> content decreased and plasma K<sup>+</sup> level and K<sup>+</sup> losses in urine and feces increased; however as the duration with the PFR treatment increased muscle K<sup>+</sup> content increased and plasma K<sup>+</sup> concentration and K<sup>+</sup> losses in urine and feces decreased (Table

TABLE II: Potassium in Urine and Feces, Plasma Potassium and Muscle Potassium Measured in the Control and the Hypokinetic Groups and the Periodic Fluid Redistribution Control and the Hypokinetic Groups During the Pre-experimental and the Experimental Period.

Experimental period in days	Potassium			
	Urine mmol/days	Feces mmol/days	Plasma mmol/L	Muscle mmol/100g <sup>1</sup> FFDS
Active control subjects (ACS), n=10				
Average values				
Pre-experimental	74.0 $\pm$ 12.0	20.0 $\pm$ 2.3	4.18 $\pm$ 0.04	34.18 $\pm$ 4.40
60th	73.1 $\pm$ 11.3	19.5 $\pm$ 2.4	4.17 $\pm$ 0.05	34.28 $\pm$ 3.35
120th	74.0 $\pm$ 12.4	19.7 $\pm$ 2.2	4.18 $\pm$ 0.03	34.42 $\pm$ 5.41
180th	73.5 $\pm$ 10.5	19.8 $\pm$ 2.4	4.17 $\pm$ 0.04	34.51 $\pm$ 4.37
240th	73.1 $\pm$ 11.4	19.3 $\pm$ 2.3	4.18 $\pm$ 0.03	34.67 $\pm$ 5.44
300th	72.3 $\pm$ 10.3	18.7 $\pm$ 2.5	4.17 $\pm$ 0.04	34.75 $\pm$ 4.50
364th	73.1 $\pm$ 11.5	19.5 $\pm$ 2.2	4.18 $\pm$ 0.05	34.86 $\pm$ 5.43
Hypokinetic subjects (HKS), n=10				
Average values				
Pre-experimental	73.5 $\pm$ 12.4	19.8 $\pm$ 3.4	4.18 $\pm$ 0.04	34.17 $\pm$ 3.43
60th	91.5 $\pm$ 10.6 <sup>†</sup>	25.0 $\pm$ 3.3 <sup>††</sup>	4.50 $\pm$ 0.05 <sup>††</sup>	31.11 $\pm$ 4.32 <sup>††</sup>
120th	90.6 $\pm$ 12.3 <sup>††</sup>	24.3 $\pm$ 4.0 <sup>††</sup>	4.47 $\pm$ 0.02 <sup>††</sup>	31.20 $\pm$ 3.40 <sup>††</sup>
180th	95.7 $\pm$ 10.6 <sup>††</sup>	26.2 $\pm$ 5.0 <sup>††</sup>	4.55 $\pm$ 0.03 <sup>††</sup>	30.41 $\pm$ 5.51 <sup>††</sup>
240th	93.3 $\pm$ 12.4 <sup>††</sup>	25.0 $\pm$ 4.3 <sup>††</sup>	4.51 $\pm$ 0.02 <sup>††</sup>	30.58 $\pm$ 4.45 <sup>††</sup>
300th	106.5 $\pm$ 11.5 <sup>††</sup>	30.1 $\pm$ 5.0 <sup>††</sup>	4.81 $\pm$ 0.04 <sup>††</sup>	28.13 $\pm$ 5.30 <sup>††</sup>
364th	111.0 $\pm$ 12.4 <sup>††</sup>	29.7 $\pm$ 4.6 <sup>††</sup>	4.77 $\pm$ 0.03 <sup>††</sup>	28.18 $\pm$ 4.41 <sup>††</sup>
Periodic fluid redistribution control subjects (PFRCS), n=10				
Average values				
Pre-experimental	78.0 $\pm$ 10.2	21.1 $\pm$ 2.0	4.30 $\pm$ 0.01	33.75 $\pm$ 3.50
60th	76.0 $\pm$ 12.0	20.5 $\pm$ 2.2	4.23 $\pm$ 0.02	34.40 $\pm$ 3.50
120th	77.8 $\pm$ 10.5	20.8 $\pm$ 3.3	4.25 $\pm$ 0.03	34.37 $\pm$ 5.32
180th	74.3 $\pm$ 11.0	19.2 $\pm$ 4.4	4.15 $\pm$ 0.04	34.81 $\pm$ 3.46
240th	75.6 $\pm$ 10.6	19.7 $\pm$ 3.7	4.17 $\pm$ 0.01	34.67 $\pm$ 3.50
300th	72.5 $\pm$ 13.5	19.0 $\pm$ 5.0	4.15 $\pm$ 0.05	35.43 $\pm$ 3.48
364th	73.3 $\pm$ 12.4	19.1 $\pm$ 5.6	4.17 $\pm$ 0.04	35.34 $\pm$ 5.55
Periodic fluid redistribution hypokinetic subjects (PFRHS), n=10				
Average values				
Pre-experimental	77.7 $\pm$ 12.4	20.8 $\pm$ 2.4	4.27 $\pm$ 0.03	33.80 $\pm$ 4.43
60th	67.7 $\pm$ 10.6 <sup>+</sup>	18.0 $\pm$ 4.4 <sup>+</sup>	4.17 $\pm$ 0.04 <sup>+</sup>	34.31 $\pm$ 5.32 <sup>+</sup>
120th	68.0 $\pm$ 11.3 <sup>+</sup>	18.3 $\pm$ 3.3 <sup>+</sup>	4.18 $\pm$ 0.05 <sup>+</sup>	34.25 $\pm$ 4.40 <sup>+</sup>
180th	66.7 $\pm$ 12.4 <sup>+</sup>	17.0 $\pm$ 5.0 <sup>+</sup>	4.13 $\pm$ 0.03 <sup>+</sup>	34.93 $\pm$ 5.52 <sup>+</sup>
240th	67.0 $\pm$ 11.3 <sup>+</sup>	17.5 $\pm$ 5.5 <sup>+</sup>	4.16 $\pm$ 0.05 <sup>+</sup>	34.87 $\pm$ 4.36 <sup>+</sup>
300th	63.5 $\pm$ 12.0 <sup>+</sup>	16.3 $\pm$ 4.6 <sup>+</sup>	4.03 $\pm$ 0.04 <sup>+</sup>	36.07 $\pm$ 5.46 <sup>+</sup>
364th	64.0 $\pm$ 10.6 <sup>+</sup>	16.7 $\pm$ 4.4 <sup>+</sup>	4.06 $\pm$ 0.03 <sup>+</sup>	36.01 $\pm$ 4.41 <sup>+</sup>

FFDS (Fat Free Dry Solids). All values were expressed as mean $\pm$ SD.

<sup>†</sup> $P < 0.05$  significant differences between the pre-experimental and experimental period values.

<sup>††</sup> $P < 0.05$  significant differences between the control and the hypokinetic groups of subjects.

<sup>+</sup> $P < 0.05$  significant differences between the hypokinetic and the periodic fluid redistribution hypokinetic groups of subjects.

I). With the treatment of PFR  $K^+$  is being taken up for deposition and is being used by the body which in turn protected the net muscle  $K^+$  content and  $K^+$  losses.

In the experimental period muscle  $K^+$  content increased ( $p < 0.05$ ) and plasma  $K^+$  concentration and  $K^+$  losses of urine and feces decreased ( $p < 0.05$ ) in the PFRHS group compared to the HKS group (Table I). In the PFRHS group with  $K^+$  repleted muscle, plasma  $K^+$  concentration and  $K^+$  losses in urine and feces decreased. In the HKS group muscle  $K^+$  content decreased ( $p < 0.05$ ) and plasma  $K^+$  concentration and  $K^+$  losses in urine and feces increased ( $p < 0.05$ ) compared to the pre-experimental period levels and the values of the other groups (Table I). In the HKS group with  $K^+$  depleted muscle, plasma  $K^+$  concentration and  $K^+$  losses of urine and feces increased. In the ACS group muscle  $K^+$  content, plasma  $K^+$  concentration and  $K^+$  losses in urine and feces did not change compared to their pre-experimental values (Table I). The  $K^+$  deposition parameters in the PFRCS group were benefited much less than in the PFRHS group (Table I).

## Discussion

Periodic fluid shifting into regional areas of the body is a powerful stimulus in the protection and /or increase of deposition of  $K^+$  as was shown by the significant differences between the PFRHS group and the other groups. With a long term PHDT and at least 8 hrs per day muscle  $K^+$  content increases and  $K^+$  losses decrease. Clearly PHDT had acted more as strong stimulus rather than as strong inhibitor as the HDT. The lower plasma  $K^+$  concentration suggests higher  $K^+$  deposition because plasma  $K^+$  level cannot decrease in  $K^+$  repleted muscle except if  $K^+$  is deposited. The decreased  $K^+$  losses show  $K^+$  regulation because  $K^+$  losses cannot decrease in  $K^+$  repleted muscle unless  $K^+$  is regulated. Moreover the decrease of  $K^+$  losses during PHDT suggest that periodic fluid shifting to the head is not sensed as an excessive fluid volume because electrolyte excretion cannot decrease with large fluid volume shifting upwards except if fluid migration to the head is sensed as simple FR. The higher muscle  $K^+$  content and the lower plasma  $K^+$  concentration

and  $K^+$  losses with PHDT and the lower muscle  $K^+$  content and the higher plasma  $K^+$  concentration and  $K^+$  losses without PHDT suggest that they are probably under different control. Evidently, PFR may improve and/or increase  $K^+$  deposition when it is used over long time and at least 8 hrs per day. Some studies (22-27) have shown that fluid volume expansion with daily intake of fluid and salt supplementation in small divided doses increases tissue electrolyte content and decrease electrolytes losses because chronic fluid volume expansion is not sensed as excessive fluid volume but rather as simple FR and the excretion mechanisms are not activated.

The control subjects with and without PFR treatment fail to show significant differences; this is because the PFRCS group was physically active which may have acted more as stressor rather than as stimulus to PFR. Physical activity may determine the ability of the body to adapt to fluid volume expansion because the higher physical activity the lower the adaptability of the body to fluid volume expansion (28-32). There fluid volume expansion, is neither intravascular nor intracellular fluid, and therefore does not contribute to vascular volume. Some studies (28-32) have shown that physical activity may not lead to more fluid volume and tissue electrolytes. Physical activity which moves fluid to the lower part of the body may determine the severity in the delivery of fluid to the upper part of the body and thus extracellular and interstitial fluid volume. Physical activity may affect PFR as was shown by minor changes in  $K^+$  deposition in the PFRCS group compared to the ACS group. Therefore one would not observe the significant  $K^+$  deposition improvements in the PFRCS group as was shown in the PFRHS group. Physical activity had played an important part in  $K^+$  deposition protection as was shown by no changes in muscle  $K^+$  content and  $K^+$  losses in the ACS group compared to the HKS group. It should be stated however that PFR even with physical activity is a powerful stimulus for the deposition of  $K^+$  provided that it is used over longer period than the time required without physical activity.

It is evident that periodic fluid shifting to the upper

part of the body over long period of time and at least 8 hrs per day increases muscle  $K^+$  content and decrease  $K^+$  losses. Because muscle  $K^+$  content increases as the treatment with PFR increases shows that the longer fluid is redistributed periodically the more  $K^+$  is deposited. This indicates a common conception that PFR over long period of time and at least 8 hrs per day is important for  $K^+$  deposition. This adds an important contribution to  $K^+$  deposition because people exhibit  $K^+$  depletion in response to the diminished muscular activity (4-12). Periodic fluid shifting from the lower to the upper part of the body with PHDT may be more of a stimulus than a stressor as with HDT. Moreover chronic PFR may improve body's ability to regulate fluid volume expansion and thus interstitial and extracellular fluid volume. Consequently PFR over long period of time and at least 8 hrs per day may affect  $K^+$  deposition and thus muscle  $K^+$  content and  $K^+$  losses. The mechanisms by which deposition of  $K^+$  increase in response to the PFR over long period of time and at least 8 hrs per day have not been established yet. However, the hypokinetic volunteers who were treated with PFR over long time may have experience a less labile and more responsive  $K^+$  deposition.

Some studies (33-38) have shown that as a consequence of chronic fluid volume expansion by a daily intake of fluid and salt supplementation in small divide doses the brain does not interpret its expansion of blood supply as excessive fluid volume but rather as simple FR. In response to this misperception, the brain does not signal the kidneys and other organs to lower blood volume and other body fluids. The systems appear to adapt to the chronic fluid volume expansion and the baroreceptors do not stretch and do not interpret this as an excessive fluid volume and do not stimulate the kidney to urinate so that excess fluid volume is eliminated. The process contributes to the higher electrolyte deposition and lower electrolyte losses. Chronic fluid volume expansion may be one solution for more electrolyte deposition and less electrolyte losses (33-38).

The increased muscle  $K^+$  may be attributable to many factors and primarily to the intact cell mass (39). The fluid volume expansion increases mitochondria

density, adenosine triphosphate (ATP) synthesis, oxidative phosphorylation (OP), and aerobic metabolism. PFR expands blood volume and tissue oxygen supply which in turn restores or compensates cell structure and regulates or improves cell function. This increases cellular transport and decrease intracellular electrolytes and preserves and/or restores cell structure integrity contributing to stability of cellular contents thereby increasing cell holding capacity for electrolytes and improving electrolyte deposition.

The synthesis of ATP and OP are most susceptible to the blood supply and oxygen delivery to the tissues. Blood volume expansion and tissue oxygen delivery normalizes or compensates OP and ATP synthesis. As blood flow and oxygen tension within the cell increases, the synthesis of ATP and OP increases while during diminished muscular activity OP (40) and ATP synthesis (41) decreases. Increased mitochondria density and/or function are considered as the most likely culprit to explain the synthesis of OP and ATP. Blood volume expansion is a strong stimulus for the proliferation of mitochondria enzymes. Mitochondria density and cytochrome c, which are crucially important in aerobic energy production, increase when during the diminished muscular activity decrease (42). Mitochondria density depends on the duration and the intensity one can endure fluid volume expansion procedures and ability of the body to spare total glycogen. As the synthesis of OP and ATP increase, cell shifts into aerobic glycolysis which allows the synthesis of ATP from the breakdown of cellular glycogen. The production of new glycogen is stimulated and the glycogen depots are repleted when during diminished activity the glycogen stores are depleted (43). With blood volume expansion and tissue oxygen supplies aerobic metabolism of glycolysis becomes more efficient than the lower oxygen-dependent mitochondrial pathways and the cell function and morphology are preserved or restored thereby stimulating deposition of  $K^+$  contributing to more muscle  $K^+$  content and less  $K^+$  losses with PFR during diminished activity.

#### **Conclusion**

The PFR with PHDT is a powerful stimulus of

deposition of  $K^+$  as was shown by the differences between the PFRHS group and the other groups. The higher muscle  $K^+$  content shows utilization of  $K^+$  because muscle  $K^+$  content cannot increase with diminished muscular activity except if  $K^+$  is utilized. The lower plasma  $K^+$  level shows  $K^+$  deposition because plasma  $K^+$  level cannot decrease in  $K^+$  repleted muscle unless  $K^+$  is deposited. The lower  $K^+$  losses show  $K^+$  regulation because  $K^+$  losses cannot decrease with large fluid shifting upwards

except if  $K^+$  is regulated. It is evident that chronic PFR increases muscle  $K^+$  content and slow  $K^+$  losses suggesting potential benefits for  $K^+$  deposition. However, the underlying mechanism of  $K^+$  deposition with PFR using PHDT has not been established yet. In conclusion chronic PFR increases muscle  $K^+$  level and slow  $K^+$  losses apparently due to a more efficient  $K^+$  deposition. Further research of the potential benefits of PFR with PHDT on electrolyte deposition during diminished activity is in order.

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