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Rubidium and Potassium **MASTER** **Concentrations In** **Human Erythrocytes, Plasma** **and Urine**

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RUBIDIUM AND POTASSIUM CONCENTRATIONS (COO-119-238) O. LEW WOOD, AUGUST 1968

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RUBIDIUM AND POTASSIUM CONCENTRATIONS
IN HUMAN ERYTHROCYTES, PLASMA AND URINE

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LIST OF SYMBOLS

ARR	-	Adjusted Retention Ratio
Cd	-	Cadmium
Cl	-	Chlorine
cm	-	Centimeter
Cs	-	Cesium
Cu	-	Copper
d	-	Day
$X^{T_{\frac{1}{2}}}$	-	Equivalent Biological Half-Time for Element X
ft	-	Foot
g	-	Gram
gK	-	Grams of Potassium
h	-	Hour
I	-	Iodine
IR	-	Increase Ratio
kg	-	Kilogram
Pb	-	Lead
l	-	Liter
μ	-	Microgram
mA	-	Milliampere
mg	-	Milligram
ml	-	Milliliter
nm	-	Nanometer
O	-	Oxygen
K	-	Potassium
$\frac{\Delta K}{\Delta t}$	-	Potassium Excretion Rate
RR	-	Retention Ratio
Rb	-	Rubidium
Na	-	Sodium
V	-	Volt
y	-	Year
Zn	-	Zinc

ABSTRACT

The naturally occurring rubidium and potassium concentrations were measured in human plasma, erythrocytes and urine for normal, diseased and pregnant Utah subjects. The mean plasma Rb concentration in the normal adult subjects was 0.16 microgram/ml (γ /ml) with a standard deviation (SD) of ± 0.028 γ /ml and the mean K concentration was 160 γ /ml (± 16.1 γ /ml SD). The mean erythrocyte Rb concentration in the normal adult subjects was 4.18 γ /ml (± 0.623 γ /ml SD) and the mean K concentration was 3840 γ /ml (± 142 γ /ml SD). The mean urine Rb concentration in the normal adult subjects was 1.52 γ /ml (± 0.549 γ /ml SD) and the mean K concentration was 1910 γ /ml (± 581 γ /ml SD). The Rb and K concentrations in the pregnant and diseased subjects did not vary significantly from the normal means. The mean estimated Rb dietary intake rate for the normal adult subjects was 2.16 mg/d (± 0.747 mg/d SD) and the estimated mean rate for K was 2.46 g/d (± 0.740 g/d SD).

The Adjusted Retention Ratio (ARR), a ratio of concentration ratios, was defined as

$$ARR = \frac{\left(\frac{Rb}{K}\right)_{\text{Erythrocytes}}}{\left(\frac{Rb}{K}\right)_{\text{Excreta}}}$$

The mean ARR for the normal adult subjects was 1.19 (± 0.106 SD). A mean ARR > 1 indicates that Rb is preferentially retained in the erythrocyte compared to K when normalized for

dietary intake. A subject with Duchenne muscular dystrophy had an ARR of 0.995 (± 0.0694 SD). The estimated Rb whole-body burden in a normal 37 y old, 82 kg, 178 cm tall male was 0.28 g as calculated from ^{83}Rb tracer measurements and the urine output rate of naturally occurring Rb. The Rb whole-body burden for a 15 y old, 69 kg, 140 cm tall male with Duchenne muscular dystrophy was 0.064 g.

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1.0 INTRODUCTION

1.1 Rubidium and Potassium

Rubidium and potassium are both alkali metals belonging to the Group I elements of the periodic table. Members of this group in order are: lithium, sodium, potassium, rubidium, cesium and francium.

Naturally occurring potassium is present as three isotopes: stable ^{39}K with an abundance of 93.10 percent, radioactive ^{40}K with an abundance of 0.0118 percent and stable ^{41}K with an abundance of 6.88 percent (Goldman and Roesser, 1966). Artificially produced ^{42}K is used for short-term biological tracer studies as its short physical half-time of 12.4 hours limits more extensive studies.

Naturally occurring rubidium is present as two isotopes: stable ^{85}Rb with an abundance of 72.15 percent and radioactive ^{87}Rb with an abundance of 27.85 percent (Goldman and Roesser, 1966). Two artificial radioisotopes of Rb used for biological tracer studies are ^{83}Rb with a physical half-time of 83 days and ^{86}Rb with a physical half-time of 18.7 days. Thus, the radioisotopes of Rb allow for long-term biological investigations.

The similarity of physiochemical properties of rubidium and potassium suggests that radioactive rubidium can be used as an analog of potassium in studies of metabolism. Ringer (1882) discovered that Rb ions produce an effect similar to K ions on the heart ventricle of a frog. Zwaardemaker (1920)

confirmed Ringer's work by again demonstrating that Rb could replace K in maintaining *in vitro* heart action in Ringer's mixture. However, Zwaardemaker erroneously attributed the physiological action of K and Rb to the slight radioactivity in their naturally occurring compounds. Loeb (1920) showed that Cs as well as Rb could replace K required for the development of fertilized sea urchin eggs to swimming blastulae.

Mitchell, Wilson and Stanton (1921) demonstrated that CsCl and RbCl were absorbed by active muscle perfused by potassium-free Ringer solution. Inactive muscle did not absorb the Cs and Rb. Rats given synthetic diets in which Cs or Rb replaced the K died within 10 to 17 days with characteristic symptoms including tetanic spasms. The results of their experiments showed that although Cs and Rb were physiologically similar to K, they were not perfect analogs.

Sheldon and Ramage (1931) analyzed a large number of human tissues for various elements and found Rb to be present in many organs, particularly in cardiac and striated muscle.

Interest in the physiological similarity of Cs, K and Rb continued with Brown and Feldberg (1936), and Mann, Tennenbaum and Quastel (1939) showing that Rb and to a lesser extent Cs have effects similar to K on the liberation of acetylcholine from perfused brain tissue. Histological

studies by Follis (1943) of rats on a low K diet supplemented by either Cs or Rb showed that myocardial and renal necroses appeared in the low K rats whereas the addition of Rb prevented necroses and the addition of Cs reduced necroses. Tracer experiments by Greenberg, *et al.* (1943) demonstrated that Rb behaved similarly to K in penetrating the blood-cerebrospinal fluid barrier.

Bertrand and Bertrand (1951) measured the Rb content of human blood and found rubidium in both the plasma and erythrocytes. Solomon (1952) reported on the transport of K and Rb across the human erythrocyte membrane. Love and Burch (1952) found that the calculated rate of exchange of K between plasma and erythrocytes using either ^{42}K or ^{86}Rb as an *in vitro* tracer was the same by their procedure. However, they stated that, "The results suggest that Rb^{86} ... may be useful under some circumstances as a tracer for potassium, at least from a qualitative point of view. Pertinent data should be validated with K^{42} whenever possible". Burch, Threefoot and Ray (1955) later studied the applicability of ^{86}Rb as a tracer in normal humans and humans with congestive heart failure. Although ^{86}Rb did not trace the K precisely, the method provided valuable generalizations on K metabolism.

Ansell and Zimmermann (1954) proposed the use of stable rubidium for measurement of total exchangeable body potassium. The calculation of total exchangeable potassium in dogs using stable rubidium was within the range of values obtained with

radioactive potassium. Tyor and Eldridge (1956) investigated the simultaneous metabolism of ^{86}Rb to ^{42}K in humans. They found that ^{86}Rb to ^{42}K ratios in plasma, leukocytes and erythrocytes were the same as the injected ^{86}Rb to ^{42}K ratio whereas the urine ratio was depressed. They attributed this decreased urine ratio to a slower excretion of ^{86}Rb .

Kahn (1962) investigated further the transfer of ^{42}K and ^{86}Rb into human erythrocytes. Kahn discovered two phases of Rb entry into erythrocytes: a rapid phase not requiring active transport which occurred within five minutes and slower phase requiring active transport and continuing for at least four hours. In both phases the sites involved have a higher affinity for Rb than for K with Rb being favored by a factor of approximately 1.55 in the active transport phase. Kahn states that, "For quantitative comparisons, Rb is not a satisfactory substitute for K".

Yamagata, *et al.* (1966) described *in vivo* experiments using ^{132}Cs , ^{42}K and ^{86}Rb in a human subject. They also measured naturally occurring K and Rb levels in human blood. They found that the K and Rb partitioned similarly between the erythrocytes and plasma with approximately 95 percent of the K and 98 percent of the Rb in the erythrocytes.

Several investigators have demonstrated that while Rb is very similar to K in its metabolism by humans, there are important differences that make quantitative comparisons

between the two elements invalid in many instances. With the exception of Ansell and Zimmerman (1954) and Yamagata, *et al.* (1966), the experiments were done with radioactive tracers and the results extrapolated to the naturally occurring elements. The studies were not done under equilibrium conditions. Thus, this investigation fulfills the need for the investigation of the *in vivo* metabolism of naturally occurring K and Rb in human erythrocytes under equilibrium conditions.

The objectives of this investigation are:

- a) To determine the plasma concentration of naturally occurring rubidium and potassium in normal Utah adult humans,
- b) To determine the erythrocyte concentration of naturally occurring rubidium and potassium in normal Utah adult humans,
- c) To determine the urine concentration of naturally occurring rubidium and potassium in normal Utah adult humans,
- d) To determine the plasma and erythrocyte concentrations of naturally occurring rubidium and potassium in diseased and pregnant Utah humans,
- e) To determine the dietary intake of naturally occurring rubidium and potassium in normal Utah adult humans,
- f) To compare Rb kinetics and K kinetics of the naturally occurring elements in normal Utah adult

humans by utilizing erythrocyte and urine concentrations,

g) To determine the Rb whole-body burden in a normal adult Utah male and in a dystrophic Utah male.

1.2 Atomic Absorption Spectrophotometry

Atomic absorption spectrophotometry is a recently developed technique whereby it is possible to measure minute quantities of trace elements in physical and biological samples (Robinson, 1966). Atomic absorption spectrophotometry augments other techniques of trace element analysis such as spectrophotometry, fluorometry, emission spectroscopy, x-ray emission spectrography, mass spectrometry and nuclear activation analysis (Morrison, 1965).

Atomic absorption spectrophotometry involves the absorption of monochromatic radiant energy by ground-state atoms to produce excited atoms. The amount of radiant energy absorbed by the ground-state atoms is measured and correlated to the number of atoms present in the sample. An atomic absorption spectrophotometer is comprised of a light source, a flame atomizer to produce ground-state atoms from the sample, a monochromator and a detector.

Advantages of atomic absorption spectrophotometry include a high sensitivity of less than a part-per-million for many elements, few interferences, simplicity and relatively

low cost.

Disadvantages include a limited application to less than half the elements, the use of flame atomizers which means samples must be in a liquid form, the preclusion of simultaneous multielement analysis by the limited capability of commercially available equipment and the destructive testing of the sample.

An atomic absorption spectrophotometer was used in this study to measure the rubidium concentration in human plasma, erythrocyte and urine samples. The percentual concentration limit (PCL) for rubidium, which was the concentration required to give a one percent absorption, was approximately 0.02 γ /ml.

1.3 Whole-Body Counting

Whole-body counting of humans is a useful technique for the study of the *in vivo* metabolism of radioactive trace elements either by measuring naturally occurring body burdens or by administering suitable tracers. Present whole-body counters utilize scintillation spectrometry to measure primary photons from gamma emitters or bremsstrahlung from internally absorbed beta radiation (Lloyd, Mays and Atherton, 1963).

Since 1949 the number of whole-body counters has increased dramatically which illustrates the importance of this technique (Mehl and Rundo, 1963). Applications of whole-body counting include the study of fallout radioactivity

in humans, the studies required to develop radiation protection programs and clinical studies in medicine (Roesch, 1965).

The Radiobiology Division of the University of Utah College of Medicine has had a whole-body counter operating since 1957 (International Atomic Energy Agency, 1964). These whole-body counting techniques were developed in conjunction with an internal radioactive emitter research project with pure-bred beagles.

In addition, extensive studies have been made of the ^{137}Cs and ^{40}K levels in humans. Calibration of the whole-body counter involves giving known levels of ^{132}Cs and ^{42}K to humans and counting them (Lloyd, 1964).

The University of Utah whole-body counter was used during this investigation to measure the *in vivo* levels of ^{40}K and ^{83}Rb in humans. The ^{40}K levels in urine and feces and the ^{83}Rb levels were also measured.

2.0 EXPERIMENTAL PROCEDURE

2.1 Preparation of Blood and Urine Samples

At least three blood samples and three urine samples were provided at approximately one week intervals by each of six healthy adult human males and six healthy adult human females. In addition, single blood samples were obtained from several other individuals to aid in establishing normal values for Rb concentration in plasma and erythrocytes. Blood and urine samples were also obtained from pregnant and diseased individuals.

A flow diagram illustrating the preparation and analysis of the blood samples appears in Figure 1. A similar flow diagram for urine appears in Figure 2.

EDTA was used as an anticoagulant for 20 ml blood samples drawn by venipuncture. Experiments demonstrated that the chelating effect of EDTA did not influence the assay for Rb. Two samples of blood were drawn from donors, one sample with EDTA and one sample with no anticoagulant. The sample without an anticoagulant was defibrinated by gently swirling it in a flask with glass beads. The fibrin clot was removed and the sample was then processed in the same manner as the sample with EDTA. Analyses of both samples gave the same results for Rb concentration, within experimental limits. The procedure of using EDTA was adopted for the study because it was a simpler process.

An aliquot of the freshly drawn blood was taken for

FIGURE 1.

FLOW DIAGRAM FOR BLOOD SAMPLE ANALYSIS

FIGURE 2. FLOW DIAGRAM FOR URINE SAMPLE ANALYSIS

hematocrit determination and RBC count. An International Micro-Capillary Centrifuge Model MB, International Equipment Co., Boston, Mass., was used for microhematocrit measurements. RBC counts were done with a Coulter Counter Model A, Coulter Electronics, Inc., Hialeah, Florida.

The freshly drawn blood was centrifuged at 2200 g for 20 minutes and the plasma immediately decanted with a Pasteur pipette. An aliquot of the plasma was taken for K measurement with a Coleman Flame Photometer Model 21 and a Coleman Spectrophotometer Model 6C, Coleman Instruments Corp., Maywood, Illinois. The rest of the plasma was diluted in saline to give a Na concentration of 10^4 γ /ml. This dilution was analyzed for Rb with a Perkin-Elmer Atomic Absorption Spectrophotometer Model 303, Perkin-Elmer Corp., Norwalk, Conn.

The packed erythrocytes were reconstituted in normal saline approximately on an equal volume basis. This procedure resulted in some trapped plasma with the erythrocytes. However, the K and Rb concentrations were approximately 25 times greater in the erythrocytes than in the plasma. The low concentration in the plasma coupled with the small volume of trapped plasma resulted in negligible error in the erythrocyte assay. Washing the erythrocytes could have leached ions from the erythrocytes and removed adsorbed ions resulting in erroneously low values when measured. An aliquot of the reconstituted erythrocytes was

taken for microhematocrit determination and RBC count. The reconstituted erythrocytes were lysed and diluted 1:10 in saline to give an approximate Na concentration of 10^4 γ /ml. This was accomplished by adding 2.0 ml of the reconstituted erythrocytes to 8.2 ml of deionized water and then adding 9.8 ml of saline with a Na concentration of 2.0×10^4 γ /ml. If the saline was added before the deionized water, the erythrocytes crenated and later plugged the aspirator of the atomic absorption unit. An aliquot of the dilution was assayed for K by flame photometry and the rest of the dilution was assayed for Rb by atomic absorption spectrophotometry.

Subjects of the experiment collected urine for the time required to fill a 3.5 l container. An aliquot of the urine sample was diluted 1:10 with deionized water and assayed for K by flame photometry. Another aliquot of the urine sample was diluted 1:2 in saline to give a Na concentration of 10^4 γ /ml and assayed for Rb by atomic absorption spectrophotometry.

Throughout the experimental procedure care was taken to avoid contamination of the samples. Numerous checks showed no Rb and K contamination in the samples.

2.2 Assay for K by Flame Photometry

Assay for K in the erythrocyte, plasma and urine samples was relatively straightforward. All measurements were done with a Coleman Flame Photometer Model 21 and a Coleman

Spectrophotometer Model 6C, Coleman Instruments Corp., Maywood, Illinois. Experiments indicated that the K assay was somewhat influenced by the Na concentration in the samples with higher Na concentrations causing higher K readings. Thus, the plasma and urine samples were measured with K standards containing 3300 γ /ml Na and the erythrocytes were measured with K standards having 10^4 γ /ml Na.

The K concentration in the erythrocytes was also measured by atomic absorption spectrophotometry and found to be in agreement with flame photometry values. Urine K was also determined by measuring ^{40}K in three samples. These values were in reasonable agreement with those obtained by flame photometry. Flame photometry was used for K assay in the general study because it was a simpler technique.

2.3 Assay for Rb by Atomic Absorption Spectrophotometry

Assay for Rb in the erythrocyte, urine and plasma samples by atomic absorption spectrophotometry was much more difficult than the K assay, primarily because the concentration of Rb was approximately 10^{-3} that of the K. Indeed, the plasma Rb concentration was in the range of published values of the percentual concentration limit (PCL) (Robinson, 1966). The PCL is that concentration limit which gives an absorption of one percent. Through careful procedures the Rb PCL was reduced five-fold in this study to a value of approximately 0.02 γ /ml.

Initial experiments were performed to determine possible ionization interference of Rb caused by the flame atomizer of the atomic absorption unit (Janauer, Smith and Mangan, 1967). The alkali metals have low ionization potentials with 5.12 V for Na, 4.32 V for K and 4.16 V for Rb as the first ionization potential (Weast, 1967). The energy from the flame is sufficient to ionize a significant number of Rb atoms. This ionization interference reduces the ground state atom population and decreases the sensitivity of the atomic absorption unit because there are less ground state atoms to absorb the light.

The ionization interference of the Rb was overcome by adding Na to the samples. The Na as well as the Rb was ionized by the flame. However, since the ionization potential of Na was higher than that of Rb, the excess electrons attached to the Rb ions which increased the number of ground state Rb atoms.

The enhancement of the Rb sensitivity by the addition of Na is shown in Figure 3. Varying concentrations of Na were added to two Rb concentrations of 0.10 γ /ml and 10.0 γ /ml. The absorption (sensitivity) for Rb increased with increasing Na concentration until a plateau occurred. There were insufficient electrons provided by the Na until plateau concentration for Na was attained. At concentrations greater than those required to reach the plateau the excess electrons had no effect on the Rb sensitivity.

FIGURE 3.

ENHANCEMENT OF Rb BY Na

because the ionized Rb atoms were already saturated with electrons. Very high concentrations of salt reduced the sensitivity because of the large amount of energy required to decompose the salt from the flame.

A Na concentration of 10^4 γ /ml was chosen as a working concentration for the diluted samples to be analyzed. The Rb concentration in the diluted samples varied from approximately 0.10 γ /ml to 1.3 γ /ml. Thus, a Na concentration of 10^4 γ /ml was sufficient to insure that the working point was far enough onto the plateau so that minor variations in Na concentration away from 10^4 γ /ml would not influence the Rb sensitivity.

After elimination of the ionization interference for Rb by the addition of Na, several experiments were conducted with erythrocyte, plasma and urine samples to determine the possible matrix effects of compounds contained in the samples. If compounds present in the samples either enhanced or diminished the Rb signal, then comparison with Rb standards prepared with H_2O would give erroneous results.

The method of additions was used to determine these possible matrix effects. The method of additions is commonly used in analytical chemistry and involves the addition in various concentrations of the element of interest to the sample. Figures 4 and 5 illustrate the method of additions for Rb applied to human erythrocytes, plasma

FIGURE 4. METHOD OF ADDITIONS FOR ERYTHROCYTES & PLASMA

FIGURE 5. METHOD OF ADDITIONS FOR URINE

and urine. The abscissa coordinates to the right of the origin represent the amount of Rb added to the samples and to the standards prepared in H_2O with a Na concentration of 10^4 γ/ml . The abscissa coordinates to the left of the origin represent the amount of Rb in the samples as determined by a linear extrapolation of the sample plot. The point of intersection of the extrapolation with the abscissa gives the Rb concentration in the sample provided that there is no matrix effect. If the Rb concentration by extrapolation is the same as the Rb concentration determined by comparison with the standards, then the matrix effect does not exist.

In Figure 4 the erythrocyte Rb concentration by additions is 0.14 γ/ml and by comparison with standards it is 0.15 γ/ml . Also in Figure 4 the additions method for plasma gives 0.12 γ/ml and standards comparison gives 0.125 γ/ml . The urine shown in Figure 5 has a concentration of 0.36 γ/ml by additions and a concentration of 0.37 γ/ml by comparison with standards. Thus, there is negligible matrix effect in the erythrocyte, plasma and urine samples. Accordingly, the Rb concentration was determined by comparison with standards.

A Perkin-Elmer Model 303 Atomic Absorption Spectrophotometer was used for the Rb assays, Perkin-Elmer Corp., Norwalk, Conn. An Osram Rb discharge lamp model 303-6006 was used as the light source, available from Perkin-Elmer

Corp. Air and acetylene were used for the flame with a setting of 9.0 each on the flow meters. A Bowling burner was used to prevent clogging by the biological samples. Source current to the lamp was 500 mA. The wavelength setting was 390 nm. The range setting was for visible with the slit set at 5. The meter response was set at 2 and the filter was in position. The scale expansion was 10 for the erythrocyte and plasma samples and 5 for the urine samples.

2.4 Whole-Body Counting for Rb and K

The whole-body counting facilities of the Radio-biology Laboratory were used to measure ^{83}Rb and ^{40}K . The inside of the counting room was approximately $8 \times 8 \times 12$ ft³ and was constructed from 12 inch steel lined with 1/8 inch thick Pb, 1/32 inch thick Cd and 1/32 inch thick Cu. Two Harshaw Tl doped NaI scintillation crystals, 4 inches high by 8 inches in diameter, were used as the detectors, Harshaw Chemical Company, Cleveland, Ohio. A Radiation Instrument Development Laboratory 400 Channel Analyzer Model 34-12B was coupled to the crystals, Radiation Instrument Development Laboratory, Division of Chicago Nuclear Corp., Chicago, Illinois. The whole-body positioner was constructed of stainless steel and polyethylene.

These facilities were used to measure the naturally occurring body burden of ^{40}K . Tracer studies using $^{83}\text{RbCl}$ taken orally were also performed (Mays and Lloyd, 1968).

3.0 RESULTS AND DISCUSSION

3.1 Rb and K Concentration in Plasma

Values for Rb and K concentration in plasma from normal Utah humans appear in Table I. The average Rb concentration for nine normal Utah adult males was $0.18 \text{ } \mu\text{Ci/ml}$ with a standard deviation of $\pm 0.019 \text{ } \mu\text{Ci/ml}$. The average value for the male K concentration was $170 \pm 8.29 \text{ } \mu\text{Ci/ml}$. The average Rb concentration for 12 normal Utah adult females was $0.15 \pm 0.023 \text{ } \mu\text{Ci/ml}$ and the average K concentration was $151 \pm 15.9 \text{ } \mu\text{Ci/ml}$. The average concentration for both males and females was $0.16 \pm 0.028 \text{ } \mu\text{Ci/ml}$ for Rb and $160 \pm 16.1 \text{ } \mu\text{Ci/ml}$ for K. Thus, the average K to Rb ratio in plasma for normal Utah adult humans was 1000:1.

The results for the plasma Rb concentration were in fairly good agreement with values reported by Lang (1965) and Yamagata and Iwashima (1966) and in poor agreement with values given by Bertrand and Bertrand (1951). Bertrand and Bertrand, employing spectrophotometry, listed a value for plasma Rb of $2.0 \text{ } \mu\text{Ci/ml}$ for one of their subjects. Yamagata and Iwashima, using neutron activation analysis, indicated a Rb concentration of $0.12 \text{ } \mu\text{Ci/ml}$ for one subject and less than $0.079 \text{ } \mu\text{Ci/ml}$ for three other subjects, assuming a hematocrit of 0.45. Lang reported an average serum Rb concentration of $0.217 \text{ } \mu\text{Ci/ml}$ for 52 subjects as determined by flame spectrophotometry.

The average K concentration for males and females was

TABLE I
Rb AND K CONCENTRATION IN PLASMA
FROM NORMAL UTAH HUMANS

NORMAL MALES

SUBJECT	AGE (y)	NO. OF MEAS.*	Rb CONC. (γ /ml)	STD. DEV. (γ /ml)*	K CONC. (γ /ml)	STD. DEV. (γ /ml)*
GL	24	3	0.17	$\pm 0.021 (\pm 12\%)$	180	$\pm 4.73 (\pm 2.63\%)$
GT	26	3	0.19	$\pm 0.012 (\pm 6.3\%)$	172	$\pm 3.79 (\pm 2.20\%)$
BJ	29	1	0.20	$\pm 0.028 (\pm 14\%)$	157	$\pm 9.92 (\pm 6.32\%)$
VD	30	3	0.17	$\pm 0.025 (\pm 15\%)$	170	$\pm 17.6 (\pm 10.4\%)$
LW	31	13	0.16	$\pm 0.035 (\pm 22\%)$	161	$\pm 15.1 (\pm 9.38\%)$
WW	32	4	0.18	$\pm 0.032 (\pm 18\%)$	181	$\pm 7.70 (\pm 4.25\%)$
CM	37	5	0.20	$\pm 0.019 (\pm 9.5\%)$	167	$\pm 15.1 (\pm 9.04\%)$
VD	48	1	0.16	$\pm 0.022 (\pm 14\%)$	168	$\pm 10.6 (\pm 6.32\%)$
NS	50	1	0.21	$\pm 0.029 (\pm 14\%)$	178	$\pm 11.2 (\pm 6.32\%)$
AVERAGE - MALES			0.18	$\pm 0.019 (\pm 11\%)$	170	$\pm 8.29 (\pm 4.88\%)$

NORMAL FEMALES

SUBJECT	AGE (y)	NO. OF MEAS.*	Rb CONC. (γ /ml)	STD. DEV. (γ /ml)*	K CONC. (γ /ml)	STD. DEV. (γ /ml)*
LC	22	1	0.18	$\pm 0.031 (\pm 17\%)$	151	$\pm 8.52 (\pm 5.64\%)$
JL	24	3	0.13	$\pm 0.035 (\pm 27\%)$	167	$\pm 4.16 (\pm 2.49\%)$
MM	24	1	0.13	$\pm 0.022 (\pm 17\%)$	145	$\pm 8.18 (\pm 5.64\%)$
JM	25	3	0.13	$\pm 0.012 (\pm 9.2\%)$	144	$\pm 3.06 (\pm 2.13\%)$
OD	26	1	0.15	$\pm 0.026 (\pm 17\%)$	156	$\pm 8.80 (\pm 5.64\%)$
VJ	26	3	0.12	$\pm 0.010 (\pm 8.3\%)$	154	$\pm 8.73 (\pm 5.67\%)$
CA	27	1	0.20	$\pm 0.034 (\pm 17\%)$	184	$\pm 10.4 (\pm 5.64\%)$
ID	28	3	0.15	$\pm 0.015 (\pm 10\%)$	152	$\pm 16.7 (\pm 11.0\%)$
YW	30	3	0.15	$\pm 0.045 (\pm 30\%)$	145	$\pm 11.4 (\pm 7.86\%)$
EW	31	3	0.14	$\pm 0.023 (\pm 16\%)$	160	$\pm 7.51 (\pm 4.69\%)$
PN	34	1	0.13	$\pm 0.022 (\pm 17\%)$	118	$\pm 6.66 (\pm 5.64\%)$
NH	65	1	0.14	$\pm 0.024 (\pm 17\%)$	141	$\pm 7.95 (\pm 5.64\%)$
AVERAGE - FEMALES			0.15	$\pm 0.023 (\pm 15\%)$	151	$\pm 15.9 (\pm 10.5\%)$

AVERAGE FOR
MALES AND FEMALES 0.16 $\pm 0.028 (\pm 18\%)$ 160 $\pm 16.1 (\pm 10.1\%)$

*The average standard deviation is assumed for single measurements. Multiple measurements were made at approximately one week intervals.

in excellent agreement with the value of 160.9 γ /ml reported by Fawcett and Wynn (1956). The average plasma concentration for both Rb and K in the normal males was slightly elevated compared to the concentrations in the normal females.

Table II lists the Rb and K concentration in plasma from diseased and pregnant Utah humans. There were no significant deviations from normal values. The average Rb concentration for four pregnant females was 0.14 ± 0.030 γ /ml compared to 0.15 ± 0.023 γ /ml for the normal group.

Table III gives variations in the plasma Rb and K concentrations over a period of several weeks in the same Utah adult male. Note the large variability in Rb concentration and the much smaller variability in K concentration. The Rb concentration varied from 0.09 γ /ml to 0.20 γ /ml and the K concentration varied from 139 γ /ml to 188 γ /ml. The Rb variation was due to biological factors as the Rb assay instrumentation error was measured at less than ± 3 percent. The K variation was also due to biological factors as there was a comparable instrumentation error. The variability of the dietary rate of intake of Rb is probably the main cause of plasma Rb variability. Lang (1965) also noted a large fluctuation in human serum Rb concentration over a period of three to four days.

3.2 Rb and K Concentration in Erythrocytes

Values for Rb and K concentration in erythrocytes

TABLE II

Rb AND K CONCENTRATION IN PLASMA
FROM PREGNANT AND DISEASED UTAH HUMANS

SUB.	SEX	AGE (y)	CLIN. COND.	Rb CONC. (γ /ml)	STD. DEV. (γ /ml) *	K CONC. (γ /ml)	STD. DEV. (γ /ml) *
DH	M	15	Duch. Dyst.	0.17	$\pm 0.024 (\pm 14\%)$	160	$\pm 10.1 (\pm 6.32\%)$
TA	M	26	Met. Ca of Lung	0.13	$\pm 0.018 (\pm 14\%)$	168	$\pm 10.6 (\pm 6.32\%)$
SM	M	50	Anemia	0.20	$\pm 0.028 (\pm 14\%)$	172	$\pm 10.9 (\pm 6.32\%)$
MC	F	56	Arth.	0.13	$\pm 0.022 (\pm 17\%)$	159	$\pm 8.97 (\pm 5.64\%)$
RB	F	20	Preg.	0.17	$\pm 0.029 (\pm 17\%)$	154	$\pm 8.69 (\pm 5.64\%)$
PP	F	22	Preg.	0.10	$\pm 0.017 (\pm 17\%)$	149	$\pm 8.40 (\pm 5.64\%)$
DA	F	22	Preg.	0.13	$\pm 0.022 (\pm 17\%)$	174	$\pm 9.81 (\pm 5.64\%)$
JM**	F	23	Preg.	0.15	$\pm 0.0082 (\pm 5.4\%)$	163	$\pm 6.63 (\pm 4.07\%)$

AVERAGE FOR
PREGNANT FEMALES 0.14 $\pm 0.030 (\pm 21.4\%)$ 160 $\pm 11.0 (\pm 6.88\%)$

*The average standard deviation is assumed for single measurements.

**Four measurements were made at approximately one week intervals for subject JM. Single measurements were made for all other subjects.

TABLE III

VARIABILITY OF Rb AND K CONCENTRATION
IN PLASMA FROM NORMAL UTAH HUMAN MALE

Subject - LW Age 31

DATE	Rb CONC. (γ /ml)	K CONC. (γ /ml)
1-10-68	0.20	188
1-16-68	0.20	188
1-25-68	0.16	172
2-2-68	0.14	154
2-15-68	0.12	162
2-23-68	0.19	172
2-23-68	0.17	155
2-23-68	0.17	157
2-29-68	0.14	160
2-29-68	0.15	139
3-21-68	0.11	151
3-28-68	0.09	145
4-17-68	0.18	152
AVERAGE AND STANDARD DEVIATION	0.16 $\pm$ 0.035 ($\pm$ 22%)	161 $\pm$ 15.1 ($\pm$ 9.38%)

from normal Utah humans appear in Table IV. The average concentration for nine normal Utah males was 4.28 ± 0.745 γ /ml for Rb and 3780 ± 142 γ /ml for K. For 12 normal Utah females the average concentration for Rb was 4.10 ± 0.535 γ /ml and for K it was 3880 ± 134 γ /ml. The average concentration for both males and females was 4.18 ± 0.623 γ /ml for Rb and 3840 ± 142 γ /ml for K. These values for both normal adult Utah males and females gave an erythrocyte K to Rb ratio of 919:1 compared to a plasma ratio of 1000:1.

Yamagata and Iwashima (1966) indicated a Rb concentration of 4.54 γ /ml for one of their subjects and concentrations between 3.66 γ /ml and 4.22 γ /ml for three other subjects, assuming a hematocrit of 0.45. Bertrand and Bertrand (1951) listed an erythrocyte Rb concentration of 5.32 γ /ml for one of their subjects. Thus, the erythrocyte Rb concentrations determined in this study were in good agreement with the above results.

The average erythrocyte K concentration in normal Utah males and females of 3840 γ /ml was in good agreement with the value of 3720 γ /ml reported by Hald (1946).

Note the small variability for a given individual of both the erythrocyte Rb and K concentrations. The average standard deviation for normal males was ± 2.34 percent for the Rb concentration and ± 2.37 percent for the K concentration. For normal females it was ± 3.60 percent for Rb and ± 2.88 percent for K. These standard deviations were

TABLE IV

Rb AND K CONCENTRATION IN ERYTHROCYTES
FROM NORMAL UTAH HUMANS

NORMAL MALES

SUB.	AGE (y)	NO. OF MEAS.*	Rb CONC. (γ /ml)	STD. DEV. (γ /ml)*	K CONC. (γ /ml)	STD. DEV. (γ /ml)*
GL	24	3	4.04	$\pm 0.0346 (\pm 0.856\%)$	3700	$\pm 183 (\pm 4.95\%)$
GT	26	3	3.75	$\pm 0.0962 (\pm 2.57\%)$	3840	$\pm 30.6 (\pm 0.797\%)$
BJ	29	1	5.51	$\pm 0.129 (\pm 2.34\%)$	3910	$\pm 92.7 (\pm 2.37\%)$
VD	30	3	3.83	$\pm 0.135 (\pm 3.52\%)$	3820	$\pm 64.3 (\pm 1.68\%)$
LW**	31	13	3.16	$\pm 0.0892 (\pm 2.82\%)$	3720	$\pm 82.9 (\pm 2.23\%)$
WW	32	4	4.26	$\pm 0.110 (\pm 2.58\%)$	3690	$\pm 118 (\pm 3.20\%)$
CM	37	5	5.16	$\pm 0.0886 (\pm 1.72\%)$	3690	$\pm 50.0 (\pm 1.36\%)$
VD	48	1	4.00	$\pm 0.0936 (\pm 2.34\%)$	3610	$\pm 85.6 (\pm 2.37\%)$
NS	50	1	4.81	$\pm 0.113 (\pm 2.34\%)$	4070	$\pm 96.5 (\pm 2.37\%)$
AVERAGE MALES			4.28	$\pm 0.745 (\pm 17.4\%)$	3780	$\pm 142 (\pm 3.76\%)$

NORMAL FEMALES

SUB.	AGE (y)	NO. OF MEAS.*	Rb CONC. (γ /ml)	STD. DEV. (γ /ml)	K CONC. (γ /ml)	STD. DEV. (γ /ml)
LC	22	1	4.00	$\pm 0.144 (\pm 3.60\%)$	3870	$\pm 111 (\pm 2.88\%)$
JL	24	3	3.95	$\pm 0.010 (\pm 0.253\%)$	3980	$\pm 185 (\pm 4.65\%)$
MM	24	1	4.00	$\pm 0.144 (\pm 3.60\%)$	3780	$\pm 109 (\pm 2.88\%)$
JM	25	3	3.52	$\pm 0.145 (\pm 4.12\%)$	3730	$\pm 175 (\pm 4.69\%)$
OD	26	1	4.66	$\pm 0.168 (\pm 3.60\%)$	4150	$\pm 120 (\pm 2.88\%)$
VJ	26	3	4.28	$\pm 0.141 (\pm 3.29\%)$	4020	$\pm 56.9 (\pm 1.42\%)$
CA	27	1	4.94	$\pm 0.178 (\pm 3.60\%)$	3790	$\pm 109 (\pm 2.88\%)$
ID	28	3	4.41	$\pm 0.150 (\pm 3.40\%)$	3980	$\pm 108 (\pm 2.71\%)$
YW	30	3	3.72	$\pm 0.300 (\pm 8.06\%)$	3810	$\pm 70.0 (\pm 1.84\%)$
EW	31	3	3.53	$\pm 0.0875 (\pm 2.48\%)$	3840	$\pm 76.4 (\pm 1.99\%)$
PN	34	1	4.86	$\pm 0.175 (\pm 3.60\%)$	3910	$\pm 113 (\pm 2.88\%)$
NH	65	1	3.34	$\pm 0.120 (\pm 3.60\%)$	3690	$\pm 106 (\pm 2.88\%)$
AVERAGE FEMALES			4.10	$\pm 0.535 (\pm 13.0\%)$	3880	$\pm 134 (\pm 3.45\%)$

AVERAGE FOR MALES

AND FEMALES 4.18 $\pm 0.623 (\pm 14.9\%)$ 3840 $\pm 142 (\pm 3.70\%)$

*The average standard deviation is assumed for single measurements. Multiple measurements were made at approximately one week intervals.

**There are nine measurements for the K concentration in subject LW.

experimentally determined and included instrumentation error. Thus, the intracellular concentration in a given individual represented by the erythrocytes is much more stable than the extracellular concentration represented by the plasma, especially so for the Rb. This stability demonstrates that intracellular concentrations of Rb and K are very important criteria in studying Rb kinetics and K kinetics of the naturally occurring elements.

However, when the erythrocyte Rb and K variability is compared between different normal humans, an important difference is observed. The standard deviation for erythrocyte K concentration in normal males as a whole was ± 3.76 percent and for normal females as a whole was ± 3.45 percent. Corresponding values for the erythrocyte Rb concentration were ± 17.4 percent and ± 13.0 percent.

The erythrocyte maintains homeostasis much better for K concentration than for Rb concentration. The erythrocyte Rb concentration is, therefore, likely a good reflection of whole-body Rb while the K concentration is obviously a poor reflection of whole-body K. The extremely small abundance of Rb compared to K in the erythrocyte is undoubtedly a factor in the failure of a feedback mechanism to maintain good homeostasis for Rb concentration.

Thus, dietary intake of Rb influences the long-term Rb erythrocyte concentration much more than dietary intake of K influences the K concentration. The two normal males

with highest Rb intake as determined by urine Rb excretion also had the highest erythrocyte Rb concentration and the normal male with the lowest Rb excretion had the lowest Rb concentration. (See Table IX). The K intake also influences the Rb erythrocyte concentration with high K intake tending to reduce the Rb absorption and reduce the intracellular concentration. The situation for the normal females is not apparent. Other anomalies in the normal females are discussed later. (See 3.4). Since the dietary intake of Rb and K influences the erythrocyte Rb concentration, it is important that the intakes be determined so that they can be used as normalization factors. This was done by measuring urine Rb and K excretion, assuming steady-state conditions exist and assuming the same partitioning factors for excretion in the urine and feces for all subjects. (The partitioning factors for Rb and K were different).

Table V further illustrates the stability of erythrocyte Rb and K concentration for a period of several weeks in the same normal adult Utah human male. The standard deviation for the Rb concentration was ± 2.82 percent and for the K concentration it was ± 2.23 percent.

Table VI gives the erythrocyte Rb and K concentrations for pregnant and diseased Utah humans. As with the plasma concentrations for these individuals, there were no significant deviations in the erythrocyte Rb and K concentrations

TABLE V

VARIABILITY OF Rb AND K CONCENTRATION
IN ERYTHROCYTES FROM NORMAL UTAH HUMAN MALE

Subject - LW Age 31

DATE	Rb CONC. (γ /ml)	K CONC. (γ /ml)
1-10-68	3.26	
1-16-68	3.16	
1-25-68	3.33	
2-2-68	3.11	
2-15-68	3.15	3640
2-23-68	3.27	3750
2-23-68	3.21	3590
2-23-68	3.16	3680
2-29-68	3.07	3700
2-29-68	3.17	3790
3-21-68	3.02	3690
3-28-68	3.12	3710
4-17-68	3.06	3890
AVERAGE AND STANDARD DEVIATION		
	3.16 $\pm$ 0.0892($\pm$ 2.82%)	3720 $\pm$ 82.9($\pm$ 2.23%)

TABLE VI

Rb AND K CONCENTRATION IN ERYTHROCYTES
FROM PREGNANT AND DISEASED UTAH HUMANS

SUB.	SEX	AGE (y)	CLIN. COND.	Rb CONC. (γ /ml)	STD. DEV. (γ /ml)*	K CONC. (γ /ml)	STD. DEV. (γ /ml)*
DH	M	15	Duch. Dyst.	4.23	$\pm 0.0990 (\pm 2.34\%)$	3570	$\pm 84.6 (\pm 2.37\%)$
TA	M	26	Met. Ca of Lung	4.55	$\pm 0.106 (\pm 2.34\%)$	3790	$\pm 89.8 (\pm 2.37\%)$
SM	M	50	Anemia	4.70	$\pm 0.110 (\pm 2.34\%)$	4210	$\pm 99.8 (\pm 2.37\%)$
MC	F	56	Arth.	4.36	$\pm 0.157 (\pm 3.60\%)$	4030	$\pm 116 (\pm 2.88\%)$
RB	F	20	Preg.	5.33	$\pm 0.192 (\pm 3.60\%)$	3810	$\pm 110 (\pm 2.88\%)$
PP	F	22	Preg.	3.70	$\pm 0.133 (\pm 3.60\%)$	3760	$\pm 108 (\pm 2.88\%)$
DA	F	22	Preg.	3.58	$\pm 0.129 (\pm 3.60\%)$	3880	$\pm 112 (\pm 2.88\%)$
JM**	F	23	Preg.	3.55	$\pm 0.0881 (\pm 2.48\%)$	3570	$\pm 67.0 (\pm 1.88\%)$

AVERAGE FOR
PREGNANT FEMALES 4.04 $\pm 0.862 (\pm 21.3\%)$ 3760 $\pm 133 (\pm 3.54\%)$

*The average standard deviation is assumed for single measurements.

**Four measurements were made for subject JM at approximately one week intervals. Single measurements were made for all other subjects.

from normal values. The average erythrocyte Rb concentration for four pregnant females was 4.04 ± 0.862 γ /ml compared with 4.10 ± 0.535 γ /ml for the normal group. The average erythrocyte K concentration for the pregnant group was 3760 ± 133 γ /ml compared with 3840 ± 142 γ /ml for the normal group.

3.3 Rb and K Concentration and Output in Urine

The Rb and K concentration in urine from Utah humans is given in Table VII. The average Rb concentration for normal males was 1.56 ± 0.567 γ /ml and the average K concentration was 1920 ± 557 γ /ml. For normal females the Rb and K concentrations were 1.48 ± 0.583 γ /ml and 1890 ± 685 γ /ml, respectively. The average values for both the normal males and females were 1.52 ± 0.549 γ /ml for Rb and 1910 ± 581 γ /ml for K. The ratio of urine K concentration to Rb concentration in the normal males and females was 1260:1 compared to 1000:1 for plasma and 919:1 for erythrocytes. Table VII also gives urine Rb and K concentrations for a gravid subject and a subject with Duchenne muscular dystrophy. These concentrations do not vary significantly from the normal values.

There was a large variability of urine Rb and K concentration in a given individual over a period of several weeks as well as a large variability between different individuals. These variabilities are due to: a) differences in dietary intake of Rb and K, and b) differences in the rate of urine production. Thus, short-term urine collections give

TABLE VII

Rb AND K CONCENTRATION IN
URINE FROM UTAH HUMANS

NORMAL MALES

SUBJECT	AGE (y)	NO. OF MEAS.	Rb CONC. (γ /ml)	STD. DEV. (γ /ml)	K CONC. (γ /ml)	STD. DEV. (γ /ml)
GL	24	3	1.39	$\pm 0.121 (\pm 8.71\%)$	1780	$\pm 120 (\pm 6.74\%)$
GT	26	3	1.86	$\pm 0.268 (\pm 14.4\%)$	2400	$\pm 531 (\pm 22.1\%)$
VD	30	3	1.08	$\pm 0.376 (\pm 34.8\%)$	1400	$\pm 421 (\pm 30.1\%)$
LW	31	4	0.840	$\pm 0.317 (\pm 37.7\%)$	1340	$\pm 420 (\pm 31.3\%)$
WW	32	4	2.39	$\pm 0.470 (\pm 19.7\%)$	2750	$\pm 752 (\pm 27.3\%)$
CM	37	4	1.78	$\pm 0.0424 (\pm 2.38\%)$	1840	$\pm 86.4 (\pm 4.70\%)$
AVERAGE MALES			1.56	$\pm 0.567 (\pm 36.3\%)$	1920	$\pm 557 (\pm 29.0\%)$

NORMAL FEMALES

SUBJECT	AGE (y)	NO. OF MEAS.	Rb CONC. (γ /ml)	STD. DEV. (γ /ml)	K CONC. (γ /ml)	STD. DEV. (γ /ml)
JL	24	3	1.43	$\pm 0.322 (\pm 22.5\%)$	1960	$\pm 305 (\pm 15.6\%)$
JM	25	3	1.48	$\pm 0.239 (\pm 16.1\%)$	1690	$\pm 253 (\pm 15.0\%)$
VJ	26	3	1.53	$\pm 0.0897 (\pm 5.86\%)$	2010	$\pm 106 (\pm 5.27\%)$
ID	28	3	1.14	$\pm 0.329 (\pm 28.9\%)$	1450	$\pm 442 (\pm 30.5\%)$
YW	30	3	0.776	$\pm 0.196 (\pm 25.3\%)$	1170	$\pm 315 (\pm 26.9\%)$
EW	31	3	2.52	$\pm 0.183 (\pm 7.26\%)$	3070	$\pm 228 (\pm 7.42\%)$
AVERAGE FEMALES			1.48	$\pm 0.583 (\pm 39.4\%)$	1890	$\pm 658 (\pm 34.8\%)$

AVERAGE FOR
MALES AND FEMALES 1.52 $\pm 0.549 (\pm 36.1\%)$ 1910 $\pm 581 (\pm 30.4\%)$

PREGNANT AND DYSTROPHIC SUBJECTS

SUBJECT	AGE (y)	NO. OF MEAS.*	Rb CONC. (γ /ml)	STD. DEV. (γ /ml)*	K CONC. (γ /ml)	STD. DEV. (γ /ml)*
DH (Male-Duchenne Dystrophy)	15	1	2.28	$\pm 0.447 (\pm 19.6\%)$	2330	$\pm 475 (\pm 20.4\%)$
JM (Pregnant)	23	3	1.75	$\pm 0.0742 (\pm 4.24\%)$	2350	$\pm 220 (\pm 9.36\%)$

*The average standard deviation is assumed for single measurements. The multiple measurements were made at approximately one week intervals.

unreliable results. Collections should be over at least a 24 hour period. Table VIII gives insight into these variabilities. In Table VIII the Rb and K concentration and output rate in urine from two normal Utah males are given. The slower rates of urine production resulted in higher concentrations of Rb and K and vice versa. This inverse relationship tends to stabilize Rb and K output in a given individual. Note the large individual variability in Rb and K concentrations and the relatively small variability in the output rates.

Table IX lists the Rb and K output rates in urine from Utah humans. For the normal males the Rb output rate was 1950 ± 588 γ/d and the K output rate was 2.40 ± 0.462 g/d. The output rate for the normal females was 1380 ± 444 γ/d for Rb and 1.82 ± 0.687 g/d for K. The average for the normal males and females was 1670 ± 578 γ/d for Rb and 2.11 ± 0.635 g/d for K.

The average output rates for the normal males were higher than those of the normal females as was expected. The output rates for the male with Duchenne muscular dystrophy were considerably lower than those for the normal males as this subject was confined to a wheelchair and had a reduced dietary requirement. The output rates for the pregnant female were higher than those of the average normal female.

Table X gives the K to Rb ratios in the urine and also the estimated dietary intake rate of Rb and K based on estimated partitioning factors for urinary and fecal excretion.

TABLE VIII

Rb AND K CONCENTRATION AND OUTPUT RATE IN URINE
FROM TWO NORMAL UTAH HUMAN MALES

Subject - LW Age 31

DATE	COLL. TIME (h)	COLL. VOL. (l)	Rb CONC. (γ /ml)	Rb OUT. (γ /d)	K CONC. (γ /ml)	K OUT. (g/d)
2-15-68	81.5	7.00	0.626	1290	1050	2.17
2-23-68	17.3	0.830	1.31	1510	1960	2.26
2-29-68	48.5	3.45	0.736	1260	1130	1.93
3-21-68	48.0	3.50	0.688	1200	1210	2.12
AVERAGE			0.840	1320	1340	2.12
STANDARD DEVIATION			± 0.317	± 134	± 420	± 0.140
			($\pm 37.7\%$)	($\pm 10.2\%$)	($\pm 31.3\%$)	($\pm 6.60\%$)

Subject - WW Age 32

DATE	COLL. TIME (h)	COLL. VOL. (l)	Rb CONC. (γ /ml)	Rb OUT. (γ /d)	K CONC. (γ /ml)	K OUT. (g/d)
2-21-68	63.0	3.50	2.36	3150	2480	3.31
2-28-68	96.0	3.50	3.04	2660	3830	3.35
3-6-68	61.5	3.50	1.92	2620	2090	2.86
3-13-68	65.5	3.50	2.25	2890	2600	3.33
AVERAGE			2.39	2830	2750	3.21
STANDARD DEVIATION			± 0.470	± 242	± 752	± 0.239
			($\pm 19.7\%$)	($\pm 8.55\%$)	($\pm 27.3\%$)	($\pm 7.45\%$)

TABLE IX

Rb AND K OUTPUT RATE IN URINE
FROM UTAH HUMANS

NORMAL MALES

SUBJECT	AGE (y)	NO. OF MEAS.*	Rb OUT. (γ /d)	STD. DEV. (γ /d)	K OUT. (g/d)	STD. DEV. (g/d)
GL	24	3	1540	± 166 ($\pm 10.8\%$)	1.97	± 0.238 ($\pm 12.1\%$)
GT	26	3	1970	± 33.9 ($\pm 1.72\%$)	2.52	± 0.285 ($\pm 11.3\%$)
VD	30	3	1580	± 271 ($\pm 17.2\%$)	2.06	± 0.385 ($\pm 18.7\%$)
LW	31	4	1320	± 134 ($\pm 10.2\%$)	2.12	± 0.140 ($\pm 6.60\%$)
WW	32	4	2830	± 242 ($\pm 8.55\%$)	3.21	± 0.239 ($\pm 7.45\%$)
CM	37	4	2450	± 177 ($\pm 7.22\%$)	2.53	± 0.141 ($\pm 5.57\%$)
AVERAGE - MALES			1950	± 588 ($\pm 30.2\%$)	2.40	± 0.462 ($\pm 19.3\%$)

NORMAL FEMALES

SUBJECT	AGE (y)	NO. OF MEAS.*	Rb OUT. (γ /d)	STD. DEV. (γ /d)	K OUT. (g/d)	STD. DEV. (g/d)
JL	24	3	927	± 141 ($\pm 15.2\%$)	1.27	± 0.137 ($\pm 10.8\%$)
JM	25	3	1070	± 122 ($\pm 11.4\%$)	1.22	± 0.105 ($\pm 8.61\%$)
VJ	26	3	1340	± 40.6 ($\pm 3.03\%$)	1.78	± 0.0649 ($\pm 3.65\%$)
ID	28	3	1100	± 103 ($\pm 9.36\%$)	1.38	± 0.147 ($\pm 10.7\%$)
YW	30	3	1950	± 347 ($\pm 17.8\%$)	2.93	± 0.593 ($\pm 20.2\%$)
EW	31	3	1910	± 196 ($\pm 10.3\%$)	2.34	± 0.294 ($\pm 12.6\%$)
AVERAGE - FEMALES			1380	± 444 ($\pm 32.2\%$)	1.82	± 0.687 ($\pm 37.7\%$)

AVERAGE FOR
MALES AND FEMALES 1670 ± 578 ($\pm 34.6\%$) 2.11 ± 0.635 ($\pm 30.1\%$)

PREGNANT AND DYSTROPHIC SUBJECTS

SUBJECT	AGE (y)	NO. OF MEAS.*	Rb OUT. (γ /d)	STD. DEV. (γ /d)*	K OUT. (g/d)	STD. DEV. (g/d)*
DH (Male-Duchenne Dystrophy)	15	1	1210	± 112 ($\pm 9.28\%$)	1.24	± 0.128 ($\pm 10.3\%$)
JM (Pregnant)	23	3	1670	± 220 ($\pm 13.2\%$)	2.26	± 0.417 ($\pm 18.5\%$)

*The average standard deviation is assumed for single measurements. Multiple measurements were made at approximately one week intervals.

TABLE X

K TO Rb RATIOS IN URINE AND ESTIMATED
DIETARY INTAKE RATE OF Rb AND K IN UTAH HUMANS

NORMAL MALES

SUB.	AGE (y)	NO. OF MEAS.*	K/Rb RATIO	STD. DEV.	Rb		K	
					IN.** (mg/d)	STD. DEV.	IN.** (g/d)	STD. DEV.
GL	24	3	1280	±2.05%	2.00	±10.8%	2.32	±12.1%
GT	26	3	1270	±8.41%	2.56	±1.72%	2.96	±11.3%
VD	30	3	1310	±6.53%	2.05	±17.2%	2.42	±18.7%
LW	31	4	1630	±6.97%	1.71	±10.2%	2.49	±6.60%
WW	32	4	1130	±7.81%	3.68	±8.55%	3.78	±7.45%
CM†	37	4	1030	±2.44%	3.18	±7.22%	2.75	±5.57%
AVERAGE-MALES			1280	±15.9%	2.53	±30.2%	2.79	±19.4%

NORMAL FEMALES

SUB.	AGE (y)	NO. OF MEAS.*	K/Rb RATIO	STD. DEV.	Rb		K	
					IN.** (mg/d)	STD. DEV.	IN.** (g/d)	STD. DEV.
JL	24	3	1380	±9.16%	1.20	±15.2%	1.49	±10.8%
JM	25	3	1140	±6.71%	1.39	±11.4%	1.44	±8.61%
VJ	26	3	1320	±2.33%	1.74	±3.03%	2.09	±3.65%
ID	28	3	1260	±2.94%	1.43	±9.36%	1.62	±10.7%
YW	30	3	1450	±2.33%	2.53	±17.8%	3.45	±20.2%
EW	31	3	1220	±2.69%	2.48	±10.3%	2.75	±12.6%
AVERAGE-FEMALES			1300	±8.62%	1.80	±32.3%	2.14	±37.7%

AVERAGE FOR MALES

AND FEMALES 1290 ±12.2% 2.16 ±34.6% 2.46 ±30.1%

PREGNANT AND DYSTROPHIC SUBJECTS

SUB.	AGE (y)	NO. OF MEAS.*	K/Rb RATIO	STD. DEV.*	Rb		K	
					IN.** (mg/d)	STD. DEV.*	IN.** (g/d)	STD. DEV.*
DH††	15	1	1020	±5.70%	1.64	±9.28%	1.38	±10.3%
(Male-Duchenne Dystrophy)								
JM	23	3	1340	±5.06%	2.17	±13.2%	2.66	±18.5%
(Pregnant)								

*The average standard deviation is assumed for single measurements. Multiple measurements were made at approximately one week intervals.

**Based on the assumption that 77 percent of the Rb is excreted in the urine and 85 percent of the K is excreted in the urine.

†Based on measurements for 77 percent of Rb and 92 percent of K excreted in urine for subject CM.

††Based on measurements for 74 percent of Rb and 90 percent of K excreted in urine for subject DH.

The K/Rb ratios were computed by calculating the K/Rb ratio in each urine sample from a given individual and taking the average of these ratios. In a given individual the K/Rb ratio was fairly constant as shown by the relatively small standard deviation.

However, there was a much larger variability when the ratios were compared against different individuals. This larger variability is caused by two factors: a) dietary differences in the kinds of food eaten and b) individual differences in the partitioning of Rb and of K between the urine and the feces. Tanaka, *et al.* (1966) reported that in Japanese food, pork and cows milk have five to 10 times as much Rb compared to K as do fish meats and vegetables. A preference for high Rb foods would markedly change the Rb/K intake ratios.

Pendleton, *et al.* (1965) indicated that 85 percent of the ^{40}K was excreted in the feces in three Utah adult male individuals with a range for the urine of from 79 percent to 91 percent. Yamagata, *et al.* (1966) using ^{86}Rb and ^{42}K tracers reported that 68 percent of the ^{86}Rb was excreted in the urine and 75 percent of the ^{42}K was also excreted in the urine. The extremes for ^{86}Rb were 66 percent and 72 percent and the extremes for ^{42}K were 61 percent and 82 percent. Fujita, *et al.* (1964) as reported by Yamagata, *et al.*, gave a urinary excretion for K of 80 percent (range 79-81 percent).

Ray, Threefoot and Burch (1955) gave a urinary excretion value for ^{86}Rb of 77 percent. Over a period of seven months in subject CM reported in this study, the urinary excretion of ^{83}Rb was 77 percent and the urinary excretion of ^{40}K was 92 percent (Mays and Lloyd, 1968).

Thus, there was some variability in the percentage of Rb and K excreted in the urine of different subjects. The variability in partitioning, however, is of secondary importance compared to the dietary variability in causing a large difference in urinary K/Rb ratios between different individuals.

In Table X the Rb intake rate was calculated from the urinary output rate assuming 77 percent was excreted in the urine except for subject DH who had a measured value of 74 percent (Mays and Lloyd, 1968). The K intake rate was calculated from the urinary output rate assuming 85 percent was excreted in the urine except for subject CM (92 percent) and subject DH (90 percent) (Mays and Lloyd, 1968). The values of 77 percent for Rb and 85 percent for K were assumed in this study because these represented the best present estimates for average values for Utah adult humans.

The average calculated Rb intake rate for normal Utah adult human males was $2.53 \text{ mg/d} \pm 30.2\%$ for Rb and $2.79 \text{ g/d} \pm 19.4\%$ for K. For the normal females the Rb intake rate was $1.80 \text{ mg/d} \pm 32.3\%$ and the K intake rate was $2.14 \text{ g/d} \pm 37.7\%$. The average for the normal males and females was 2.16 mg/d

$\pm 34.6\%$ for Rb and $2.46 \text{ g/d} \pm 30.1\%$ for K. Yamagata (1962) gave a daily intake for Rb of 1.26 mg for urban adults and 1.65 mg for rural adults. Yamagata's values for the K intake were 1.231 g for the urban adults and 1.638 g for the rural adults. These values were for Japanese with a standard man mass of 56 kg .

The average dietary intake of the Japanese humans should be somewhat less than the average intake of Utah humans because of the smaller size of the Japanese. The smaller size alone, however, is not sufficient to explain completely the lower intake rates of Rb and K in the Japanese subjects compared to the Utah subjects. Note the higher intake for Rb and K in the rural Japanese compared to urban Japanese. The rural Japanese are presumably more active than their urban counterparts and, hence, have a greater dietary intake. Could it be that the Utah subjects are more industrious than the Japanese or, as is more likely, are they more gluttonous? Also, a lower concentration per unit calorie of Rb and K in Japanese food could cause a lower average intake.

3.4 Comparison of Rb Kinetics and K Kinetics

The metabolism of Rb and K in humans is shown in Figure 6. After ingestion of Rb and K, these metabolites are absorbed into the plasma through the gut. Equilibrium is maintained, under steady state conditions, between the plasma and other blood elements and between the plasma and other

FIGURE 6. METABOLISM OF Rb AND K IN HUMANS.

body tissues. The Rb and K are eliminated from the body through the urine and feces. Losses through perspiration are negligible under normal conditions. As discussed in Section 3.3, it is assumed that an average of 77 percent of the excreted Rb and 85 percent of the excreted K is in the urine.

The data on the Rb concentration in erythrocytes given in Section 3.2 and the data on the Rb and K output rate in urine shown in Section 3.3 suggest that the erythrocyte Rb concentration varies directly with the urine Rb output and inversely with the urine K output. Kahn (1962) showed that the *in vitro* absorption of Rb by erythrocytes varied inversely with the extracellular K concentration and vice versa. The Rb and K compete for entry into the erythrocyte. The *in vivo* plasma concentration of Rb, however, is not sufficient to affect the *in vivo* erythrocyte absorption of K.

A mathematical formulation of the above relationships for equilibrium *in vivo* conditions is stated as:

$$(1) \quad (Rb)_{\text{Erythrocytes}} \propto \left(\frac{Rb}{K}\right)_{\text{Urine}}.$$

In Section 3.2 the data show that the erythrocyte K concentration can be regarded as a constant between different normal individuals. Thus, relationship (1) can be reformulated as:

$$(2) \quad \left(\frac{Rb}{K}\right)_{\text{Erythrocytes}} \propto \left(\frac{Rb}{K}\right)_{\text{Urine}},$$

since a proportional relationship remains after dividing one side by a constant. The erythrocyte Rb is divided by the

erythrocyte K to make the Retention Ratio, defined in equation 3, representative of the relative affinity of the erythrocyte for Rb and K. Formalizing the above relationship into an equation results in

$$(3) \quad \left(\frac{Rb}{K}\right)_{\text{Erythrocytes}} = RR \left(\frac{Rb}{K}\right)_{\text{Urine}},$$

where RR is defined as the Retention Ratio.

The Retention Ratio then can be calculated from the Rb/K ratio in the erythrocytes divided by the Rb/K ratio in urine,

$$(4) \quad RR = \frac{\left(\frac{Rb}{K}\right)_{\text{Erythrocytes}}}{\left(\frac{Rb}{K}\right)_{\text{Urine}}}$$

The Retention Ratio is similar to the Increase Ratio of Pendleton, *et al.* (1965).

Note that the Retention Ratio does not give the true physiological retention, adjusted for dietary intake, of Rb compared to K in the erythrocytes because an average of 77 percent of the Rb is excreted in the urine while 85 percent of the K goes into the urine. If the partitioning of the two elements between the urine and feces were identical, then the Retention Ratio would be a true comparison of the metabolism of the two elements. However, the Retention Ratio is directly proportional to the true ratio and is slightly larger.

Table XI lists the Retention Ratio and Adjusted Retention Ratio for Utah humans. The Adjusted Retention Ratio

TABLE XI

RETENTION RATIO AND ADJUSTED RETENTION
RATIO FOR UTAH HUMANS, COMPARISON OF Rb AND K.

NORMAL MALES

SUB.	AGE (y)	NO. OF MEAS.*	RETEN. RATIO	STD. DEV.	ADJ. RETEN. RATIO**	STD. DEV.
GL	24	3	1.40	$\pm 0.0757 (\pm 5.41\%)$	1.27	$\pm 0.0687 (\pm 5.41\%)$
GT	26	3	1.24	$\pm 0.109 (\pm 8.83\%)$	1.12	$\pm 0.0989 (\pm 8.83\%)$
VD	30	3	1.31	$\pm 0.0997 (\pm 7.61\%)$	1.19	$\pm 0.0906 (\pm 7.61\%)$
LW	31	4	1.38	$\pm 0.108 (\pm 7.85\%)$	1.25	$\pm 0.0981 (\pm 7.85\%)$
WW	32	4	1.31	$\pm 0.116 (\pm 8.83\%)$	1.19	$\pm 0.105 (\pm 8.83\%)$
CM†	37	4	1.44	$\pm 0.0472 (\pm 3.28\%)$	1.21	$\pm 0.0397 (\pm 3.28\%)$
AVERAGE-MALES			1.35	$\pm 0.0732 (\pm 5.42\%)$	1.21	$\pm 0.0531 (\pm 4.39\%)$

NORMAL FEMALES

SUB.	AGE (y)	NO. OF MEAS.*	RETEN. RATIO	STD. DEV.	ADJ. RETEN. RATIO**	STD. DEV.
JL	24	3	1.36	$\pm 0.140 (\pm 10.3\%)$	1.23	$\pm 0.127 (\pm 10.3\%)$
JM	25	3	1.08	$\pm 0.0989 (\pm 9.16\%)$	0.978	$\pm 0.0896 (\pm 9.16\%)$
VJ	26	3	1.40	$\pm 0.0764 (\pm 5.46\%)$	1.27	$\pm 0.0693 (\pm 5.46\%)$
ID	28	3	1.39	$\pm 0.0731 (\pm 5.26\%)$	1.26	$\pm 0.0623 (\pm 5.26\%)$
YW	30	3	1.46	$\pm 0.125 (\pm 8.59\%)$	1.32	$\pm 0.113 (\pm 8.59\%)$
EW	31	3	1.12	$\pm 0.0466 (\pm 4.16\%)$	1.01	$\pm 0.0420 (\pm 4.16\%)$
AVERAGE-FEMALES			1.30	$\pm 0.160 (\pm 12.3\%)$	1.18	$\pm 0.145 (\pm 12.3\%)$

AVERAGE FOR MALES

AND FEMALES 1.32 $\pm 0.121 (\pm 9.17\%)$ 1.19 $\pm 0.106 (\pm 8.91\%)$

PREGNANT AND DYSTROPHIC SUBJECTS

SUB.	AGE (y)	NO. OF MEAS.*	RETEN. RATIO	STD. DEV.*	ADJ. RETEN. RATIO**	STD. DEV.*
DH††	15	1	1.21	$\pm 0.0843 (\pm 6.97\%)$	0.995	$\pm 0.0694 (\pm 6.97\%)$
(Male-Duchenne Dystrophy)						
JM	23	3	1.33	$\pm 0.0790 (\pm 5.94\%)$	1.20	$\pm 0.0713 (\pm 5.94\%)$
(Pregnant)						

*The average standard deviation is assumed for single measurements. Multiple measurements were made at approximately one week intervals.

**Based on the assumption that 77 percent of Rb and 85 percent of K is excreted in urine.

†Based on measurements of 77 percent of Rb and 92 percent of K excreted in urine for subject CM for ARR.

††Based on measurements of 74 percent of Rb and 90 percent of K excreted in urine for subject DH for ARR.

represents the Retention Ratio corrected for the difference in the partitioning of Rb and K in the urine. The Adjusted Retention Ratio is defined under equilibrium conditions as

$$(5) \quad ARR = \frac{\left(\frac{Rb}{K}\right) \text{Erythrocytes}}{\left(\frac{Rb}{K}\right) \text{Excreta}}$$

or

$$(6) \quad ARR = \frac{\left(\frac{Rb}{K}\right) \text{Erythrocytes}}{\left(\frac{Rb}{K}\right) \text{Intake}}$$

The average Retention Ratio for normal adult Utah males was 1.35 ± 0.0732 and the average Adjusted Retention Ratio was 1.21 ± 0.0531 . For normal adult Utah females the average Retention Ratio was 1.30 ± 0.160 and the average Adjusted Retention Ratio was 1.18 ± 0.145 . The average Retention Ratio for both normal adult Utah males and females was 1.32 ± 0.121 and the average Adjusted Retention Ratio was 1.19 ± 0.106 . Note that the average Adjusted Retention Ratios were greater than unity. The Rb was more tenaciously retained in the erythrocytes than was the K. Kahn (1962) reported that the relative short-term *in vitro* affinity of ^{86}Rb for entry into human erythrocytes was 1.55 compared to ^{42}K . The ^{86}Rb and ^{42}K were present in equal concentrations in the extracellular incubating medium in Kahn's study.

The data for the Retention Ratio and the Adjusted Retention Ratio support the concept that these ratios should

be a constant for normal individuals. This concept is expressed in equations (4) and (5).

The range for the Adjusted Retention Ratio of the normal males was from 1.12 to 1.27 with a SD of ± 4.39 percent. The fundamental significance of this small range and standard deviation becomes apparent when the widely varying physiological conditions of the different subjects are considered. In Section 3.2 the average erythrocyte concentration in normal males in which repeated measurements were made was given as 4.28 γ/ml with a range of 3.16 γ/ml to 5.16 γ/ml . In Section 3.3 the average Rb concentration in the urine for the normal males was given as 1.56 γ/ml (range 0.840 γ/ml to 2.39 γ/ml) and the average K concentration was given as 1920 γ/ml (range 1340 γ/ml to 2750 γ/ml). There were large differences in the amounts of Rb and K excreted (ingested) and large differences in the ratios of excreted (ingested) Rb with respect to K.

Two of the normal female subjects, JM and EW had anomalously low Retention Ratios compared to the other normal females. It is not known why there was such a variance. Several factors may have contributed to this deviation: a) equilibrium may not have existed in these two subjects, but this is rather unlikely in view of the number of tests performed and the reproducibility of these tests, b) the assumed urine partitioning factors of 77 percent for Rb and 85 percent for K may be in error, but the range of variability

in metabolite partitioning in different subjects as measured by other investigators would indicate that partitioning variability is probably not sufficiently large to cause such a large variability in the Retention Ratio, c) there is a true physiological basis for the lower Retention Ratios in the normal females. Possibility c) is probably the basis for the variability.

All normal female subjects except VJ were married. All normal female subjects except YW and VJ were on birth control medication (JL and JM on C-Quens, EW on Ortho-Novum and ID on Norinyl). Urine collections were begun after cessation of menses. It is possible that there are variations in the Retention Ratio as a function of the menstrual cycle but there is not sufficient data in the present study to establish this.

Subject DH, who had Duchenne muscular dystrophy, had an Adjusted Retention Ratio of 0.995 ± 0.0694 compared with the average value for the normal males of 1.21 ± 0.0531 . The value for DH was more than three standard deviations below the value for normal males. Although DH was 15 years of age, the normal adult males probably served as a good control group because the plasma and erythrocyte Rb and K concentration values for DH correspond closely to the average normal adult male values. More investigation of the Retention Ratios in dystrophic subjects is required before the significance of the reduced Adjusted Retention Ratio in

subject DH can be established.

The Retention Ratio listed in Table XI for pregnant subject JM did not vary significantly from the average for the normal females.

Table XII lists the whole-body K, the K concentration (grams of potassium per kilogram of body mass) and the equivalent biological half-time for K. The equivalent biological half-time was computed from the equation,

$$(7) \quad K T_{\frac{1}{2}} = \frac{\ln 2 (K)_{\text{Whole-Body}}}{\left(\frac{\Delta K}{\Delta t}\right)_{\text{Excreta}}}$$

where $(K)_{\text{Whole-Body}}$ was the K whole-body burden and $\frac{\Delta K}{\Delta t}$ was the K output rate listed in Table X. The K whole-body burden was based on an approximate calibration of the whole-body counter and may be slightly revised at a later date. For more information on the equivalent biological half-time, see Lloyd, *et al.* (1966).

In Table XII the average K whole-body burden for the normal adult Utah males was 153 ± 19.3 g and the average K whole-body burden for the normal adult Utah females was 94.3 ± 5.99 g. The average for both the normal males and females was 124 ± 33.4 g. The average K concentration for the normal adult Utah males was 1.87 ± 0.0940 and for the normal adult Utah females it was 1.68 ± 0.194 while for the normal males and females it was 1.78 ± 0.176 . The average equivalent biological half-time for K for the normal adult Utah males was

TABLE XII

K WHOLE-BODY BURDEN, CONCENTRATION AND EQUIVALENT
BIOLOGICAL HALF-TIME IN UTAH HUMANS

NORMAL MALES

SUB.	AGE (y)	WT. (kg)	HT. (cm)	BODY BURDEN* (g)	K CONC.** (gK/kg)	HALF- TIME (d)
GL	24	92.1	181.2	183	1.99	54.7
GT	26	76.7	180.0	144	1.88	33.7
VD	30	68.8	172.3	134	1.95	38.4
LW	31	75.3	180.0	136	1.81	37.9
WW	32	97.0	189.0	168	1.73	30.8
CM	37	81.6	178.0	152	1.86	38.3
AVERAGE AND				153	1.87	39.0
STANDARD DEVIATION-MALES				±19.3	±0.0940	±8.29

NORMAL FEMALES

SUB.	AGE (y)	WT. (kg)	HT. (cm)	BODY BURDEN* (g)	K CONC.** (gK/kg)	HALF- TIME (d)
JL	24	56.0	163.7	99.0	1.77	46.0
JM	25	60.0	165.2	94.0	1.57	45.2
VJ	26	67.0	160.2	91.0	1.36	30.2
ID	28	45.1	162.2	85.0	1.88	36.4
YW	30	51.6	166.7	95.0	1.84	19.1
EW	31	61.0	170.5	102	1.67	25.7
AVERAGE AND STANDARD				94.3	1.68	33.8
DEVIATION-FEMALES				±5.99	±0.194	±10.8

AVERAGE FOR				124	1.78	36.4
MALES AND FEMALES						
STANDARD DEVIATION				±33.4	±0.176	±9.56

PREGNANT AND DYSTROPHIC SUBJECTS

SUB.	AGE (y)	WT. (kg)	HT. (cm)	BODY BURDEN* (g)	K CONC.** (gK/kg)	HALF- TIME (d)
DH	15	68.9	140.0	49.1	0.71	24.7
(Male-Duchenne Dystrophy)						
JM	23	52.2	167.0	83	1.59	21.6
(Pregnant)						

*The body burden is based on an approximate calibration for the whole-body counter and may be slightly modified at a later date.

**The K concentration is the K body burden divided by body mass.

39.0 $\pm$ 8.29 d and for the normal adult Utah females it was 33.8 $\pm$ 10.8 d. For the normal males and females the average equivalent biological half-time was 36.4 $\pm$ 9.56 d.

Yamagata (1962) estimated the K equivalent biological half-time for the Japanese standard man (56 kg body mass) at 54 d which was somewhat higher than the values measured for the Utah subjects.

The equivalent biological half-time for K for pregnant subject JM was 21.6 d while the average for the normal females was 33.8 d. Normal females EW and YW also had short half-times. These three subjects had the highest output rates for K for the females as is shown in Table IX. The same relationship was noted in the normal males with the shortest equivalent biological half-times corresponding to the highest output rates and vice versa. This relationship demonstrates that the K whole-body burden is not directly proportional to the dietary intake of K.

The K concentration for dystrophic subject DH was 0.71 compared with a normal of 1.87 and his K equivalent biological half-time was 24.7 d compared with a normal of 39.0 d. Nagai, *et al.* (1966) reported an average K concentration of 1.23 and an average ^{86}Rb equivalent biological half-time of 27.2 d for seven Japanese subjects with Duchenne muscular dystrophy while average values for three control subjects were 1.85 and 54 d, respectively. In the present study dystrophic subject DH had an equivalent biological

half-time for ^{83}Rb of 27 d and the half-time for normal subject CM was 60 d (Mays and Lloyd, 1968). The preceding data lends support to the suggestion that an intracellular deficiency of K in the dystrophic muscle cells stems from a membrane defect resulting in abnormal permeability.

Vogel and Scott (1968) reported that the *in vitro* rate of active uptake of ^{86}Rb as well as the outward diffusion in erythrocytes was generally increased in patients with cancers. The exception was malignant lymphoma in which the rate of active uptake and outward diffusion was reduced below normal. The authors suggested that histamine and serotonin-like substances acted as cell membrane dialators. Addition of homochlorocyclizine to the blood (SA-97, $^+\text{N-p-chlorobenz-hydryl-N'-methyl-homo-piperazine-dihydrochloride}$, Abbott Laboratories), an antiserotonin and antihistamine drug, resulted in normal values for the cancer patient erythrocytes. In an earlier study Scott and Daniels (1963) noted the same results from the 5-hydroxytryptamine blocker, BOL (d-2-bromlysergic acid diethylamide). The drug, Hypertensin (Ciba), also was effective in producing normal values in erythrocytes from cancer patients. Little, if any effect on normal erythrocytes was noted.

The assumption that abnormal permeability of muscle cells in dystrophic subjects results in decreased body burdens of Rb and K leads to the suggestion of investigating

the action of antiserotonin and antihistamine drugs on the equivalent biological half-times and Retention Ratios in normal and dystrophic subjects. Arrest of the progression of dystrophy might be attained if normal equivalent biological half-times for K and Rb could be achieved in the dystrophic subjects.

Table XIII gives estimated whole-body burdens of Rb for subjects CM and DH.

TABLE XIII
EQUIVALENT Rb BIOLOGICAL HALF-TIME, OUTPUT
RATE AND ESTIMATED WHOLE-BODY BURDEN FOR
TWO UTAH MALE HUMANS

SUB.	AGE (y)	WT. (kg)	HT. (cm)	HALF- TIME (d)	OUT. RATE (mg/d)	BODY BURDEN (g)
CM (Normal)	37	81.6	178.0	60	3.18	0.28
DH (Duchenne Dystrophy)	15	68.9	140.0	27	1.64	0.064

The estimated whole-body burden for Rb was calculated from equation (7) where Rb values were substituted for K values. The equivalent biological half-times for Rb were determined by ^{83}Rb tracer studies. Yamagata (1962) estimated the Rb body burden for the standard man (70 kg) to be 0.36 g which was somewhat higher than subject CM who had a value of 0.28 g. The Rb body burden of dystrophic subject DH (0.064 g) was markedly reduced compared with normal subject CM. The

Rb body burden for subject CM may have been somewhat higher than the average normal Utah human because the dietary intake of Rb for CM was higher than average. However, the Rb body burden is also directly proportional to the equivalent biological half-time for which average values for normal Utah humans have not been established.

Note that the Rb body burden of subject DH is approximately one-fourth that of subject CM while the K body burden of subject DH is approximately one-third that of subject CM. From Table X the urinary K/Rb ratio for subject DH is 1020 while the same ratio for subject CM is 1030. The body burden of Rb in dystrophic subject DH is reduced relative to the body burden of K as indicated by comparison with the body burdens of normal subject CM. Both subjects have approximately the same dietary K/Rb intake ratios.

4.0 SUMMARY

This study discusses the *in vivo* metabolism of naturally occurring Rb and K under equilibrium conditions in normal, diseased and pregnant Utah humans. The Rb and K concentrations were measured in plasma, erythrocytes and urine. Atomic absorption spectrophotometry was used to measure the Rb concentrations and flame photometry was used to measure the K concentrations. The K whole-body burdens were calculated by measuring the ^{40}K whole-body burdens in a whole-body counter. Estimates of the dietary intake rates of Rb and K were made based on the output rates of Rb and K in the urine. The relative retention of Rb compared to K in the erythrocyte was determined by forming Retention Ratios and Adjusted Retention Ratios. The normal averages for these ratios were greater than unity which indicates that Rb in normal individuals is preferentially retained by the erythrocyte compared to K. Equivalent biological half-times for K were calculated based on K whole-body burdens and K excretion rates. Estimates for naturally occurring Rb body-burdens in an adult Utah male and a dystrophic Utah male were made based on equivalent biological half-times measured with ^{83}Rb tracers and based on Rb excretion rates.

The mean Rb concentration in the plasma for normal adult Utah human males was 0.18 γ/ml with a standard deviation of ± 0.019 γ/ml and for normal adult Utah human females it was 0.15 γ/ml (± 0.023 γ/ml SD). For the same two groups the

mean K plasma concentration was 170 γ /ml (± 8.29 γ /ml SD) and 151 γ /ml (± 15.9 γ /ml SD), respectively. There was a large variability in plasma Rb concentration with the variability in the K concentration being smaller. The main cause of the plasma Rb variability is probably the variability in the dietary rate of intake of Rb. Values of Rb and K plasma concentrations in the diseased and pregnant subjects did not differ significantly from normal values.

The mean erythrocyte Rb concentration in the normal adult Utah human males was 4.28 γ /ml (± 0.745 γ /ml SD) and in the normal adult Utah human females it was 4.10 γ /ml (± 0.535 γ /ml SD). The values for the diseased and pregnant subjects fell within the normal range for both Rb and K. There was small variability in the erythrocyte Rb concentration in a given individual over a period of several weeks and a large variability between different individuals. The mean erythrocyte K concentration was 3780 γ /ml (± 142 γ /ml SD) for the normal male group and 3880 γ /ml (± 134 γ /ml SD) for the normal female group.

For the normal adult Utah human males the mean urine Rb concentration was 1.56 γ /ml (± 0.567 γ /ml SD) and the mean urine K concentration was 1920 γ /ml (± 557 γ /ml SD). The corresponding values for the normal adult Utah human females were 1.48 γ /ml (± 0.583 γ /ml SD) for Rb and 1890 γ /ml (± 568 γ /ml SD) for K. There was a large variability of urine Rb and K concentrations in a given individual over a period of

several weeks as well as a large variability between different individuals. The primary cause of this variability was a difference in the rate of urine production with the concentration varying as an inverse function of the rate of production. A second cause was a varying dietary intake of Rb and K.

The estimated mean dietary intake rate of Rb for the normal adult Utah human males was 2.53 mg/d (± 0.765 mg/d SD) and for K it was 2.79 g/d (± 0.541 g/d SD). For the normal adult Utah human females the estimated mean dietary intake rate was 1.80 mg/d (± 0.580 mg/d SD) for Rb and 2.14 g/d (± 0.807 g/d SD) for K.

A Retention Ratio is defined as,

$$RR = \frac{\left(\frac{Rb}{K}\right) \text{ Erythrocytes.}}{\left(\frac{Rb}{K}\right) \text{ Urine}}$$

An Adjusted Retention Ratio is defined as,

$$ARR = \frac{\left(\frac{Rb}{K}\right) \text{ Erythrocytes.}}{\left(\frac{Rb}{K}\right) \text{ Excreta}}$$

The normal adult Utah human males had a mean Retention Ratio of 1.35 (± 0.0732 SD) and a mean Adjusted Retention Ratio of 1.21 (± 0.0531 SD). For the normal adult Utah human females the mean Retention Ratio was 1.30 (± 0.160 SD) and the mean Adjusted Retention Ratio was 1.18 (± 0.145 SD). Two of the normal females had anomalously low ratios. The average ratios for both the normal males and females were greater than

unity which indicates that the relative concentration of Rb in the erythrocyte was higher than that of K when normalized for dietary intake. The ratios for a pregnant subject were normal whereas for a male subject with Duchenne muscular dystrophy, the Retention Ratio was 1.21 (± 0.0843 SD) and the Adjusted Retention Ratio was 0.995 (± 0.0694 SD).

Equivalent biological half-times for K were calculated from whole-body burdens of K and from measured K excretion rates. The K whole-body burdens were based on an approximate calibration of the whole-body counter and may be slightly revised at a later date. The mean equivalent biological half-time for K for the normal adult Utah human males was 39.0 d (± 8.29 d SD), for the normal adult Utah human females it was 33.8 d (± 10.8 d SD), for a pregnant subject it was 24.7 d and for a male subject with Duchenne dystrophy it was 21.6 d.

Rb whole-body burdens for two subjects were calculated based on equivalent biological half-times determined with ^{83}Rb and based on measured Rb excretion rates. The Rb whole-body burden for a normal adult Utah human male was 0.28 g and for a dystrophic Utah human male it was 0.064 g.

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