A Comparison of the Distribution of Potassium and Exchangeable Rubidium in the Organs of the Dog, Using Rubidium$^{86}$

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From determinations of radioactivity and potassium content at intervals after the injection of Rb$^{86}$, it was inferred that most organs of the dog contained exchangeable rubidium in a concentration paralleling but exceeding that of potassium, as compared with their relative concentrations in the plasma. A "lag phenomenon" resulting in higher rubidium specific activity in the myocardium than plasma was present. Analysis indicated that this was dependent on the relationship of myocardial rubidium exchange rate and the rate of decline of plasma rubidium specific activity. In experiments requiring prolonged observation, Rb$^{86}$ (half life, 19.5 days) is a useful tracer of potassium.

Potassium$^{42}$ enters the myocardium from the blood stream at a more rapid rate than in most other organs.$^{1}$ A study of this process of transfer of K$^{42}$ in normal and diseased hearts might produce data of importance concerning the dynamics of myocardial circulation and potassium metabolism because this rapid rate must be dependent upon the rate of delivery of isotope by the coronary blood, the permeability of capillaries and cell membranes, and/or the rate of mixing in extracellular fluid and cellular contents. The use of K$^{42}$ (half life 12.4 hours) for such studies is not entirely satisfactory because it entails the injection of biologically significant amounts of carrier potassium and the duration of observations is limited to one or two days.

The element rubidium has biologic properties similar to those of potassium, and it is widely distributed in animal tissues, including those of man.$^{2}$ Its isotope, Rb$^{86}$, has a half life of 19.5 days. Rubidium will replace potassium in maintaining the beat of an isolated heart,$^{3}$ and is similar to potassium in many other respects,$^{4-9}$ including the kinetics of its exchange across the red cell membrane.$^{10}$ Since important differences between potassium and rubidium have been noted,$^{8}$ however, the present series of experiments was performed to determine the relative distribution of rubidium and potassium in the organs of the dog, prior to the use of Rb$^{86}$ in cardiac experiments on dogs and man. Data were obtained which allowed the qualitative comparison of the rates of transfer of Rb$^{86}$ for various organs with those of K$^{42}$ as reported by others. The "lag phenomenon" (lag in the fall of organ radioactivity after equal specific activity with the plasma has been reached) was found to be prominent in the myocardium, indicating that future study of the heart must be planned in accordance with this finding.

Materials and Methods

Rb$^{86}$ was obtained as the carbonate from the Oak Ridge National Laboratories and neutralized with hydrochloric acid before use. A long-lived radio-contaminant in past shipments, tentatively identified as Cs$^{134}$, was not detected in the decay curves during these experiments. However, the cells of the body might in some instances sharply distinguish between

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cesium and rubidium, concentrating the cesium in some site. Recounts of the specimens after decay of the Rb86 revealed only insignificant amounts of long-lived radioelements in the two instances tested, and it is not likely that Cs134 contamination was present in sufficient quantity to invalidate the observations and data presented for Rb86.

The usual dose injected was 50 microcuries (2 ¥ 107 cpm) per kilogram body weight, containing an estimated 5 to 50 mg of rubidium as carrier. This is a significant amount of rubidium, equal to from 2 to 30 times the total extracellular rubidium if the plasma rubidium levels of dog and man are comparable.11 Therefore, tracer conditions for rubidium were not attained. However, if the exchanging rubidium entered the potassium pool, the quantity of carrier used would have had no detectable effect in producing mass movement of rubidium into cells, because the amount of rubidium injected was small compared with the potassium content of the plasma. This was true for red cells studied in vitro,12 but does not necessarily apply to these experiments in dogs. The Rb86 was diluted with 0.15 M NaCl solution and injected into a vein of the foreleg or the femoral vein, and once in the femoral artery. In most instances the injection was complete within 10 seconds, but three times the injection was intentionally slowed to require up to 15 minutes.

The dogs were mongrel strays, housed and fed an adequate diet for two or more months. All experiments were terminated, after the intravenous injection of 75 mg of heparin, by opening the chest under pentobarbital anesthesia and clamping the great vessels at the base of the heart. This required less than one minute. In several experiments the chest was opened trans-sternally prior to injection of the tracer in order to make special cardiac studies. Respiration was maintained by supplying oxygen through an endotracheal tube at an intermittent positive pressure of 15 cm. of water. Isotope data on the heart and lungs of these dogs were not included in the general analysis.

Specimens of approximately 1 Cm. were obtained from the organs listed in table 1 and placed in weighing bottles. Care was exercised to avoid contamination with blood or fluids from other organs, and excess blood was removed by blotting with gauze moistened in 0.30 M sucrose solution. Specimens were weighed to the nearest milligram, and the tissue transferred to 30 ml digestion flasks.

Digestion was accomplished by adding 2 ml of concentrated HNO3 to the specimens and allowing them to stand overnight. After heating until clear, the excess of nitrates was driven off by adding formic acid according to the method described by Sheppard and Martin.13 The content of the flasks was then filtered and transferred quantitatively into 10 or 25 ml volumetric flasks, washing with distilled water.

Radioactivity of this fluid was measured with a thin mica end-window Geiger-Muller tube, using methods previously described.14 When known quantities of Rb86 were added to specimens of heart muscle prior to digestion, 97.8 per cent was recovered in the digest. Although a precipitate sometimes formed in the diluted digestion fluid, it contained insignificant amounts of Rb86.

For potassium determination, a portion of the digest was further diluted until the potassium concentration was between 0.1 and 1.5 mEq per liter and the sodium concentration between 0.10 and 0.75 mEq per liter. Sodium and potassium were determined on the same aliquot of diluted digest by means of a modified Beckman model DU flame photometer. Correction for excitation of potassium by sodium was made empirically, based on the observed excitation in known solutions. Sodium concentration was too high to be determined with the same dilution of the digest necessary for potassium analysis of the femur, cartilage, skin, tendon, bile, and gall bladder. In these instances, the exciting effect of potassium on sodium estimations was negligible, so that sodium was measured on a separate dilution and the appropriate correction for potassium made. Compensation for the exciting effect of sodium on the potassium estimation in plasma and cerebrospinal fluid was provided by adding sodium, 7 mEq per liter, to the potassium standards. Recovery of known quantities of potassium added to solutions of digested bone averaged 95 per cent. Reproducibility of potassium determination in a series of aliquots of a specimen of homogenized heart muscle was 1.2 per cent (coefficient of variation), and the average recovery of added potassium was 100.3 per cent.

**Method of Analysis**

The time course of the Rb86 content of the organs was obtained from analysis of samples collected at the time of sacrifice of the dogs, which ranged from seven minutes to seven days after injection of the tracer. All calculations of radioactivity were reduced to a dose of 20,000,000 cpm per kilogram body weight. Because it was not possible to obtain chemical measurements of rubidium in the plasma or organs, it was impossible to estimate exchangeable rubidium content in absolute terms. This study, therefore, was limited to defining the comparative distribution of rubidium and potassium. The ratio between Rb86 cpm and milliequivalents of potassium in the plasma was compared with the same ratio in each organ. If these ratios were identical, then rubidium was concentrated in the organ in the
same relative amounts as was potassium. For convenience, this relative concentration was converted to a percentage by expressing the ratio of Rb$^{86}$ cpm per milliequivalent of potassium for each organ as a percentage of the ratio in the same dog's arterial plasma. In the recording of results, all organ specimens were considered to be samples of single homogeneous compartments which communicated directly with the plasma and in which the tracer was distributed homogeneously. Since each organ consisted of a mixture of cells of different types, in contact with the plasma indirectly by way of the interstitial fluid, this method of treatment is greatly oversimplified. However, it was necessary because in the analyses for radioactivity and potassium no distinction was possible between that contained in the cells and that in the extracellular fluid of the specimen. Since nonexchanging rubidium cannot be detected with Rb$^{86}$, reference to rubidium in an organ in this report should be understood to refer to the detectable exchangeable rubidium. According to the concept of tracers, the entry of Rb$^{86}$ into the organ was due primarily to a process of exchange of the rubidium naturally present in the organ with that in the plasma, and not to a mass movement of the injected rubidium out of the plasma. Furthermore, no consideration was made of any change in the relative rubidium concentration of organs that might occur during the course of an experiment, for differences in relative concentrations in different dogs, or for changes in the rate of rubidium exchange by organs. These simplifications were necessary to obtain an approximate calculation of the relative rubidium concentration in the organs, but they could not have reflected the true state of affairs precisely. The relative rubidium content of the plasma and any organ can be measured by isotope methods only at a time when the Rb$^{86}$ to nontracer rubidium ratio (the specific activity of rubidium) is the same in both. Since rubidium was not measured chemically, this equality of rubidium specific activities could be recognized only by inference, based on certain theoretic considerations which may be outlined as follows.

After injection of the isotope at zero time, the Rb$^{86}$ content of any organ rises until the specific activity of the rubidium within that organ becomes equal to that of the plasma. The speed with which equality of specific activities is reached is dependent upon the rate of rubidium exchange between organ and plasma, and also on the speed with which the specific activity of plasma rubidium falls, due to passage of Rb$^{86}$ into other organs and to its excretion from the body. This equality of rubidium specific activities may be reached at a time when the Rb$^{86}$/potassium ratio of the organ is higher or lower than the corresponding ratio in the plasma, because organs concentrate rubidium to a greater or lesser extent than they do potassium, relative to the plasma. Once equal specific activities of rubidium have been attained, there is a net flow of Rb$^{86}$ out of the organ, because the plasma rubidium specific activity continues to fall. Therefore, the time at which an organ reaches its maximal Rb$^{86}$ content corresponds to the time at which the specific activity of its rubidium is equal to that of the plasma, and to the first time at which relative rubidium content can be gauged. This time is difficult or impossible to determine experimentally, because a large number of observations would be required and these would be affected by differences between animals. Therefore, estimations of rubidium content must be made by analysis of the behavior of Rb$^{86}$ after the maximal organ content has been reached, and its radioactivity is decreasing. A difficulty arises owing to the fact that the specific activity of the exchanging rubidium of the organs during this period is always higher than that of the extracellular fluid. The amount of this difference or "lag" is dependent on the relationship of the rate of rubidium exchange by the organ to the rate of decline of plasma rubidium specific activity. This influence which the rubidium turnover rate of any organ has on its Rb$^{86}$ content must be analyzed in detail, since the tracer concentration in an organ cannot be used to estimate the nontracer content or concentration except when the specific activity of the rubidium within the organ is essentially equal to that
of the plasma. Using such an analysis, it may
be possible to distinguish between the Rb\(^{86}\)
which is present in an organ at any given time
because of this "lag phenomenon" and that
which is present because of equilibration with
nontracer rubidium, if one can rule out the
presence of the former. For the formulations
of this analysis we are indebted to Prof. J. A.
Cronvich of the Tulane University Depart-
ment of Electrical Engineering.

After the intravenous injection of Rb\(^{86}\), the
time course of the decay of plasma radioactivity
can be represented by the sum of a series of
exponential functions. Assuming no significant
net flow of rubidium out of the plasma, this
expression also describes the changes in specific
activity of rubidium in the plasma. For the
purpose of illustration, one of these exponential
rates of declining rubidium specific activity
can be represented by:

\[ A_t = A_0 e^{-bt} \]

where: \( A_t \) is the plasma specific activity at
any time, \( t \); \( A_0 \) is the plasma specific activity
when \( t = 0 \); \( b \) is the fractional rate of change
of plasma specific activity.

\[ \ln \frac{A_0}{A_t} = \frac{dA_t}{dt} = -\frac{d}{dt} \ln A_t. \]

If \( S \) is the specific activity of a compartment
(exchange) with the plasma at a constant
rate, and \( K \) is that rate, expressed as the
fraction of the rubidium content of the com-
partment which enters or leaves per unit time, then:

\[ \frac{dS}{dt} = -K(S - A). \]

Solving for \( S \) yields the expression:

\[ S = \frac{KA_0}{K - b} \left( e^{-bt} - e^{-Kt} \right). \]

The role of \( K \) in determining the relation-
ship of \( A \) and \( S \) is illustrated in figure 1. If the
specific activity of the rapidly exchanging
organ (\( S_1 \)) is expressed as a percentage of the
activity of the plasma existing at the same
time, it rises to approach asymptotically a con-
stant value greater than 100 per cent. In the
case of such compartments where the exchange
rate of the compartment is greater than the
rate of fall in plasma specific activity, and the
rates of decline in plasma and organ specific
activity have become essentially equal,

\[ \frac{-bA}{A} = -\frac{K(S - A)}{S} \]

or

\[ \frac{S}{A} = \frac{K}{K - b}. \]

Values for \( S \) as a per cent of \( A \), where \( K \) is
greater than \( b \) by varying amounts, are shown
in figure 2. In organs (\( S_2 \)) in which the frac-
tional rate of exchange of nontracer is less
than the fractional rate of decrease in plasma.
specific activity \((K < b)\), the specific activity has a constantly increasing percentile relationship to that of the plasma. These relationships can be confirmed by the use of models.\(^{14}\) In 1941, Fenn, Noonan, Mullins, and Haege\(^ {16}\) called attention to the possible importance of this “lag phenomenon” in isotope experiments. The following extension of these calculations to the particular experiments to be analyzed makes it possible to determine to what extent this “lag phenomenon” can influence the organ specific activity at any particular time during the seven day period of observations made in these experiments on the dog.

In figure 3, \(A\) represents the plasma specific activity analyzed by the method described by Geilhorn, Merrell, and Rankin.\(^ {16}\) It is represented by an expression with the general form:

\[
A_t = A_{a1} e^{-b_1 t} + A_{a2} e^{-b_2 t} + A_{a3} e^{-b_3 t} + \ldots + A_{an} e^{-b_n t} + A_{one} e^{-b_{one} t}
\]

where \(t\) is expressed in hours. The multiple rates of regression actually obtained in these experiments do not apply accurately to the first minutes of the curve where mixing is an important factor. They are the result of the averaging of the influence of the uptake of \(\text{Rb}^{86}\) by innumerable compartments at a continuous spectrum of rates; except that in the slowest rates, the effect of intake and output from the body as a whole is predominant. At any time \(t\), the specific activity of an organ \((S)\) exchanging with the plasma is given by an expression of the general form:

\[
S = \frac{K A_{a1} (e^{-b_1 t} - e^{-K t})}{K - b_1} + \frac{K A_{a2} (e^{-b_2 t} - e^{-K t})}{K - b_2} + \frac{K A_{a3} (e^{-b_3 t} - e^{-K t})}{K - b_3} + \ldots + \frac{K A_{an} (e^{-b_n t} - e^{-K t})}{K - b_n}.
\]

![Figure 2](image1.png)

**Fig. 2.** Graph in which specific activity of any organ \((S)\) as a per cent of that of the plasma \((A)\) is shown as a function of the ratio between organ exchange rate \((K)\) and the fractional rate of decline of plasma specific activity \((b)\). This relationship applies only where \(S\) and \(A\) are decreasing at the same fractional rate. See figure 1 lines A and S1.

![Figure 3](image2.png)

**Fig. 3.** Data for plasma \(\text{Rb}^{86}\) in a series of dogs. \(A\), multi-exponential decay curve fitted to data. Dotted lines \((S_1, S_2, S_3)\), expected time course of the rubidium specific activity in organs exchanging at varying rates \((K)\) with the plasma, if \(A\) represents plasma rubidium specific activity.
Since the value of $b$ decreases with time while $K$ remains constant, in those organs where $S$ has become equal to and then greater than $A$ the relationship between $S$ and $A$ varies with the values of $b$. After the plasma decay curve becomes essentially a single exponential, the amount of "lag" becomes constant and persistent, or steadily increases. The time at which the specific activity of the rubidium of an organ would be expected to become equal to that of the plasma is shown in figure 4, plotted as a function of the rubidium exchange rate of the organ ($K$). The maximal "lag" possible at any given time is shown in figure 5. Thus when the organ relative rubidium concentration has become stable and such calculations indicate the absence of significant "lag," organ Rb$^{86}$ content may be considered to reflect rubidium content accurately, within the limits imposed by the assumptions of the analysis.

**RESULTS**

In table 1 the results of determinations of potassium content of the organs examined are summarized. The time at which maximal Rb$^{86}$ content was reached in the various organs is also listed. When these values are used in conjunction with figure 4, an estimate of the fractional rubidium turnover rate of the organs can be obtained. Unfortunately, these estimates of the time of maximal Rb$^{86}$ content are subject to considerable error, due in large part to the small number of observations. This was especially true in the case of the organs which reached maximal content after four hours, and therefore had a long period during which their Rb$^{86}$ content was almost constant and near its maximum (See figure 3, line $S_0$). The values listed in table 1 for the relative rubidium concentration of the organs are much more reliable. They are based on the average of determinations at one, three, and seven days (two observations) after injection. When an organ did not reach maximal Rb$^{86}$ content by one day, this value was omitted. Figure 5 indicates that between one and seven days.

![Figure 4](image_url)

**Fig. 4.** Curve showing predicted time at which organs with varying exchange rates reach equal specific activity with plasma.

![Figure 5](image_url)

**Fig. 5.** Curves showing predicted maximal "lag" of organ specific activity at any time in dogs given Rb$^{86}$. Amount of "lag" equals quantity by which organ rubidium specific activity exceeds 100 per cent of simultaneous arterial plasma. Maximum represented by solid line joining peaks of dotted lines. Dotted lines, predicted rubidium specific activities of individual organs exchanging at different rates with the plasma.
Table 1.—Summary of Potassium Concentration and Relative Rubidium Concentration in Organs of 18 Dogs Injected with Rb\textsuperscript{86}. Relative Rubidium Concentration Obtained from the Average of the Ratios of Organ Rb\textsuperscript{86} cpm/K mEq. to Simultaneous Arterial Plasma Rb\textsuperscript{86} cpm/K mEq. at one, three, and seven days after the Injection. Approximate Time at which Each Organ Reached Maximal Rb\textsuperscript{86} Content also Given.

<table>
<thead>
<tr>
<th>Organ or Fluid</th>
<th>No. Observations</th>
<th>Potassium mEq./Kg. or L. Mean</th>
<th>Range</th>
<th>Relative Rubidium Concentr.</th>
<th>Time of Max. Rb\textsuperscript{86} Concentr.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal gland</td>
<td>10</td>
<td>68.0</td>
<td>57.8–79.5</td>
<td>133</td>
<td>&lt;45 min.</td>
</tr>
<tr>
<td>Aorta</td>
<td>7</td>
<td>43.4</td>
<td>38.6–47.0</td>
<td>174</td>
<td>45 min–4(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Artery, carotid</td>
<td>5</td>
<td>30.9</td>
<td>25.4–37.0</td>
<td>163</td>
<td>&lt;4(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Artery, pulmonary</td>
<td>6</td>
<td>39.9</td>
<td>31.7–47.0</td>
<td>165</td>
<td>30 min–4(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Bladder, urinary</td>
<td>8</td>
<td>73.4</td>
<td>55.2–84.7</td>
<td>158*</td>
<td>1 day–3 days</td>
</tr>
<tr>
<td>Bone, femur</td>
<td>7</td>
<td>8.2</td>
<td>6.3–10.0</td>
<td>56</td>
<td>30 min–1 hr.</td>
</tr>
<tr>
<td>Brain</td>
<td>7</td>
<td>87.4</td>
<td>79.7–92.7</td>
<td>55*</td>
<td>&gt;7 days</td>
</tr>
<tr>
<td>Cartilage, costal</td>
<td>4</td>
<td>24.3</td>
<td>20.4–28.9</td>
<td>106</td>
<td>&lt;1 day</td>
</tr>
<tr>
<td>Cartilage, ear</td>
<td>5</td>
<td>18.7</td>
<td>17.5–20.3</td>
<td>145*</td>
<td>&lt;3 days</td>
</tr>
<tr>
<td>Cerebrospinal fluid</td>
<td>7</td>
<td>8.7</td>
<td>4.5–15.0</td>
<td>55*</td>
<td>1 day–3 days</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>9</td>
<td>91.0</td>
<td>83.8–101</td>
<td>109</td>
<td>45 min–1 day</td>
</tr>
<tr>
<td>Esophagus</td>
<td>6</td>
<td>60.8</td>
<td>55.6–64.6</td>
<td>118</td>
<td>45 min–1 day</td>
</tr>
<tr>
<td>Esophagus, muscle coat</td>
<td>5</td>
<td>78.8</td>
<td>72.9–86.6</td>
<td>102</td>
<td>4(\frac{1}{2}) hr–1 day</td>
</tr>
<tr>
<td>Gall bladder</td>
<td>7</td>
<td>26.3</td>
<td>15.5–39.8</td>
<td>134</td>
<td>45 min–4(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Heart, av. ventricle\textsuperscript{1}</td>
<td>18</td>
<td>78.5</td>
<td>70.9–87.3</td>
<td>147</td>
<td>45 min–4(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Intestine, small</td>
<td>7</td>
<td>91.9</td>
<td>78.9–104</td>
<td>142</td>
<td>45 min–4(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Intestine, large</td>
<td>7</td>
<td>72.3</td>
<td>61.1–81.3</td>
<td>134</td>
<td>45 min–4(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Kidney</td>
<td>10</td>
<td>60.5</td>
<td>47.7–69.5</td>
<td>133</td>
<td>30 min–1(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Liver</td>
<td>13</td>
<td>76.6</td>
<td>67.3–84.3</td>
<td>191</td>
<td>45 min–1(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Lung</td>
<td>17</td>
<td>58.3</td>
<td>48.0–66.2</td>
<td>148</td>
<td>45 min–1(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Muscle, av. skeletal\textsuperscript{1}</td>
<td>13</td>
<td>92.5</td>
<td>72.5–103</td>
<td>108</td>
<td>4(\frac{3}{4}) hr–1 day</td>
</tr>
<tr>
<td>Nerve, vagus</td>
<td>7</td>
<td>22.2</td>
<td>18.3–26.0</td>
<td>131</td>
<td>30 min–1(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Pancreas</td>
<td>7</td>
<td>98.7</td>
<td>88.5–107</td>
<td>102</td>
<td>45 min–1(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Plasma, arterial</td>
<td>18</td>
<td>3.3</td>
<td>3.2–5.1</td>
<td>148</td>
<td>45 min–1(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Skin</td>
<td>7</td>
<td>20.9</td>
<td>17.0–25.7</td>
<td>130</td>
<td>45 min–1(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Spleen</td>
<td>9</td>
<td>102</td>
<td>96.4–109</td>
<td>152</td>
<td>45 min–1(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Stomach</td>
<td>6</td>
<td>64.0</td>
<td>48.6–83.3</td>
<td>152</td>
<td>45 min–1(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Stomach, muscle coat</td>
<td>5</td>
<td>76.1</td>
<td>50.7–98.5</td>
<td>150</td>
<td>&lt;4(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Thyroid</td>
<td>11</td>
<td>50.5</td>
<td>42.8–61.2</td>
<td>160</td>
<td>&lt;30 min.</td>
</tr>
<tr>
<td>Tendon, Achilles</td>
<td>7</td>
<td>8.2</td>
<td>6.3–10.6</td>
<td>102</td>
<td>45 min–4(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Testis</td>
<td>6</td>
<td>90.0</td>
<td>77.2–105</td>
<td>136*</td>
<td>1 day–3 days</td>
</tr>
<tr>
<td>Urine</td>
<td>6</td>
<td>145</td>
<td>64.5–160</td>
<td>66</td>
<td>45 min–1(\frac{1}{2}) hr.</td>
</tr>
<tr>
<td>Vena cava, abdominal</td>
<td>7</td>
<td>19.4</td>
<td>11.7–26.3</td>
<td>141</td>
<td>30 min–1(\frac{1}{2}) hr.</td>
</tr>
</tbody>
</table>

\* Average of values at three and seven days only.
† Average of four specimens from the left ventricle, three from the right ventricle, and one from the ventricular septum.
‡ Average of specimens from the leg, shoulder girdle, scalp, and neck.

After injection of the tracer, the "lag" in organ specific activity could account for less than 10 per cent of organ Rb\textsuperscript{86} content, and in rapidly exchanging organs "lag" would be negligible. Therefore values for relative rubidium concentration during this period were not significantly influenced by the "lag phenomenon." This conclusion is, of course, dependent on the validity of the simplifying assumptions made above. Complete data on several organs are shown in figure 6.

Comment

The rate of Rb\textsuperscript{86} turnover was found to vary widely among the different organs studied, although quantitative analysis of these rates was
not considered to be justified. In addition to the heart, the organs requiring less than one and one-half hours to reach maximal Rb\textsuperscript{86} content were the lung, kidney, liver, bone, adrenal and thyroid glands. In the brain, activity equal to that of the plasma may not have been reached within seven days. The urinary bladder, and probably the cerebrospinal fluid and testis, required from one to three days. In the majority of the remaining organs, maximal Rb\textsuperscript{86} content had been reached by four and one-fourth hours. In skeletal muscle, the speed of equilibration undoubtedly is related to the amount or rate of exercise.\textsuperscript{17, 18} It should be remembered that all of the animals were caged, and those sacrificed at less than one hour were under anesthesia during the entire experiment.

The mean relative rubidium concentration (average of the ratios of organ Rb\textsuperscript{86}/K\textsuperscript{39} to plasma Rb\textsuperscript{86}/K\textsuperscript{39} \times 100 determined at one, three, and seven days after injection of Rb\textsuperscript{86}) in 28 of the 30 organs was greater than 100 per cent, with values varying from 191 per cent in the liver to 102 per cent in the muscle of the esophagus and in the Achilles tendon. The exceptions were the femur (56 per cent) and the brain (55 per cent). In the latter, maximal Rb\textsuperscript{86} concentration probably was not reached in seven days. Of the body fluids, the urine and spinal fluid had relative rubidium concentrations definitely less than the plasma. The bile, on the other hand, contained relatively more rubidium than the plasma (130 per cent), but much less than the liver from which it originated. Skeletal muscle, and muscle from the heart, diaphragm, and esophagus were nearly identical in relative rubidium content, averaging 108 per cent of the plasma concentration. However, the smooth muscle of the stomach was definitely higher (150 per cent). Any or all of these values may vary with the physiologic status of the animal, but no evidence to support this possibility is at present available.

The "lag phenomenon" was well documented by the ventricular muscle. Figure 6 shows an early rise of the myocardial relative rubidium concentration to 180 per cent, with a continuing high value at four and one-fourth

![Graph showing time courses of organ radioactivity](http://circres.ahajournals.org/)

**Fig. 6.** Graphs showing time courses of organ radioactivity for several organs of dogs given Rb\textsuperscript{86} intravenously. (a) Ratio of Rb\textsuperscript{86} cpm/mEq. K; (b) ratio plotted as a per cent of the simultaneous value in arterial plasma.
hours, and a return to the essentially final value of approximately 115 per cent within 24 hours. In three dogs, the Rb\(^{86}\) content of the coronary sinus blood became equal to or higher than that of the blood from the femoral artery in less than 45 minutes, indicating that the heart was discharging rather than taking up rubidium after this time. In one of these dogs, punch biopsies of the exposed heart showed that at the time when the heart stopped taking up Rb\(^{86}\), the Rb\(^{86}/K^{39}\) ratio of the heart and blood were nearly the same (fig. 7). This supports the concept that the ventricular value of 180 per cent was not due to continued gain in Rb\(^{86}\) after equal specific activity with the plasma had been reached, but rather to a “lag” in the loss of Rb\(^{86}\) from the myocardium. It is possible that net flow of injected nonradioactive rubidium into the myocardium played a role in this phenomenon, but the theoretic analysis indicates that “lags” could have occurred even in its absence. Despite apparently rapid rubidium turnover in the adrenal and thyroid glands and in the lungs, this type of curve was not obtained. This probably indicates that these organs did not approximate simple compartments in their behavior. A peak relative rubidium concentration of 275 per cent and a very high Rb\(^{86}\) content were observed at 45 minutes in the kidney. This may have been due to sequestration of Rb\(^{86}\) in the renal tubules or to an unusual renal hemodynamic state in this particular dog.

Difficulties in interpretation of results were encountered in the case of several organs. Insufficient data and scatter due to differences between dogs were contributing factors, but it should also be kept in mind that the organs need not have behaved as the single homogeneous, steadily exchanging compartments postulated. The kidney has been mentioned in this regard. In the skin and vagus nerve maximal Rb\(^{86}\) concentration was reached in less than four and one-fourth hours, but the apparent relative rubidium concentration continued to rise until the third day. This might have been due to the existence of fast and slowly exchanging portions of these tissues, a phenomenon which very well may have been present to a lesser extent in every tissue or cell.

Estimates of exchangeable potassium mass might be made using Rb\(^{86}\) as the tracer because of its convenience and the long period of observation which would be possible. If one assumes that the organs of man contain rubidium and potassium in the same concentrations as those of the dog, and that the rates of rubidium turnover in man are at least roughly similar to those in the dog, then, by using the values from Shohl\(^{19}\) for organ weight as per cent of total body weight, it is possible to estimate total body potassium and compare the result with the figure that should be obtained by isotope dilution methods, using Rb\(^{86}\). The calculated total potassium using the Rb\(^{86}\) values was estimated to be 115 per cent of the total potassium as measured by chemical determination. In actual practice, this measurement, when made by isotope dilution methods, would be subject to multiple sources of possible error,\(^{20}\) in addition to the error due to the use of Rb\(^{86}\) as the tracer.
GENERAL DISCUSSION

Rubidium was found to be present in all of the human tissues examined spectrographically by Sheldon and Ramage, with the exception of bone and serum. More recently, Bertand and Bertrand have shown rubidium to be present also in the plasma, the average normal value being 1.14 milligrams of rubidium per liter of plasma. This is approximately one-fifteenth of the rubidium concentration found in human muscle by Sheldon and Ramage, a ratio consistent with the findings in this series of dogs in which relative distribution was gauged from \( \text{Rb}^{86} \) content. In general, the absolute rubidium content of the various organs measured spectrographically was less than that which would be predicted from these isotope studies in dogs, using the plasma rubidium content of man, determined by Bertrand and Bertrand. However, Sheldon and Ramage emphasized that their results represented approximations. In addition, important differences between man and dog may exist.

The rate of gain of \( \text{Rb}^{86} \) and of \( \text{K}^{42} \) has been studied in the organs of several species of animals. Although quantitative comparison of the rates of gain of \( \text{Rb}^{86} \) and \( \text{K}^{42} \) cannot be made because of the differences in experimental procedure, it is clear from qualitative comparison of results that the same organs which exchange \( \text{K}^{42} \) rapidly also have a rapid turnover of \( \text{Rb}^{86} \), and similarly for organs in which exchange is slow or intermediate.

These experiments lend support to the idea that \( \text{Rb}^{86} \) can be used with profit in the study of myocardial potassium metabolism, since its concentration within the heart closely parallels that of potassium, and since the rate of uptake is very rapid, as is that of \( \text{K}^{42} \). A quantitative consideration of the “lag phenomenon” in these dogs shows that it is especially important in the heart, and that future work must be planned with this factor in mind.

SUMMARY

To test the possible usefulness of \( \text{Rb}^{86} \) as a tracer of potassium in studying the kinetics of myocardial electrolyte turnover, this isotope was administered to 18 dogs and the degree to which the heart and other organs concentrated exchangeable rubidium relative to the plasma was measured. Theoretic considerations involved in this determination are discussed, particularly the role of the “lag phenomenon” which results in organ \( \text{Rb}^{86}/\text{Rb}^{85} \) ratios that are higher than the simultaneous ratios for the plasma. These are especially important in the heart. It was found that the majority of organs, including the heart, concentrated exchangeable rubidium to a degree which paralleled their concentration of potassium. However, in most cases the organs contained more exchangeable rubidium relative to the plasma than they did potassium. The similarity of relative rubidium and potassium concentrations in most organs indicates that further exploration of the usefulness of \( \text{Rb}^{86} \) as a tracer of potassium is justified.

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A Comparison of the Distribution of Potassium and Exchangeable Rubidium in the Organs of the Dog, Using Rubidium

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