The Effect of Age on the Turnover Rate of Potassium in the Rat

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Abstract. The turnover rate of potassium in the rat with special reference to age of the animal was investigated by means of tracer study and balance study. Tracer study revealed that the older animals have a longer biological half-life and higher body retention for intraperitoneally dosed $^{42}$K than the younger animals. Balance study was done by determining the body burden and daily intake of stable potassium for rats of various ages by using atomic absorption spectrometry. The turnover rate of potassium was calculated from these data on the assumption that the body is practically a single compartment for potassium kinetics. For the calculation the changes of body burden and daily intake of potassium versus age were expressed by a Gompertz function and an exponential function, respectively. The result was nearly the same as that of tracer study. The age trend of these results are in good agreement with those obtained for radioesium in the previous investigations. It is therefore reasonably assumed that the turnover rate of radioesium is closely related to that of potassium.

Since potassium is understood to be one of the most important elements for living organisms, attention and interest of many investigators have been paid to the behaviour of potassium in the organism. Microscopical behaviour of potassium in the organism, for instance the mechanisms of the transport of potassium across various biological membranes, has been extensively studied in these few decades. On the other hand macroscopical behaviour of the element, for instance whole-body retention and biological half-life of potassium, is of great interest not only from the physiological but from radiotoxicological point of view although only limited information is available in this field.

In the study of radioesium, which is one of the most dangerous radionuclides for its long physical half-life and easy entry into human body, it has been accepted practice to assume a similarity of the metabolism of cesium to that of potassium [3]. The observation that supplemental potassium can reduce the retention of ingested radioesium by mature and suckling rats is an evidence that supports this assumption [2], [10]. Our previous studies revealed that radioesium retention is a function of age, with increased retention time with increased age, except the special feature of the long retention time during the period from birth to weaning [1, 5, 6]. These studies suggest that the whole-body retention of potassium may also depend on age of the animal. Since little information is available on potassium turnover as a function of age it was the objective of the present investigation to collect data on the age dependency of whole-body retention of potassium by means of the tracer study using radioactive potassium and the balance study by determining body burden and daily intake of stable potassium.
Materials and Methods

Wistar strain rat (Wistar/Ms) of various ages bred and supplied by the animal and plant supply section of our institute was used as an experimental animal. Two methods of the experiment, tracer study and balance study, were performed using same rats in same period.

Tracer study

Non fasted groups of 28, 45, 75, 128, and 188 days of age, each containing 5 rats, were intraperitoneally administered $^{42}$K. The dosing solution given each rat contained 0.5$\mu$Ci of $^{42}$KCl (specific activity: about 100 mCi/g K) in 0.2 ml of distilled water. The radioactivity of potassium in each rat was determined by counting the living animal in a liquid scintillation detector for a small animal (Armac Model 446, Packard Instrument Co.) immediately after administration and once daily for three days. Each rat was kept in an individual metabolism cage (Natsume Seisakusho Co.) and was given powdered diet made from commercial rat diet (Furabashi Farm Co.) and tap water ad libitum. The powdered diet makes the determination of the daily diet intake easier. The rat was acclimatized to the metabolism cage for a few days prior to the time of $^{42}$K administration. The measured whole-body counts were corrected for radioactive decay using a phantom but not corrected for variation in self-absorption of radiation due to the growth of whole-body mass during the short experimental period.

Since the physical half-life of $^{42}$K is rather short to determine the exact retention curve, another tracer study was carried out using $^{43}$K which has longer physical half-life, 22.4 hours, than $^{42}$K. Rats of various ages were intraperitoneally given $^{43}$KCl, which was supplied from The Institute of Physical and Chemical Research, and the radioactivity of $^{43}$K in the rat was counted for 6 days. Rats were housed as groups and were kept in wire mesh bottomed cages. In all groups one or two rats were not given radioactivity and remained with the dosed rat in order to quantitate the extent of surface contamination of $^{43}$K. To correct for such cross contamination the counts of rats not given $^{43}$K were subtracted from those of rats given $^{43}$K.

Balance study

During the period of the tracer study the body weight of the experimental animal and the amount of daily consumption of powdered diet were determined once daily. After the tracer study (on the fourth day post $^{43}$K administration) all rats were sacrificed with ether. The whole-body was dried at 110°C in an air bath for 48 hours and ashed at 500°C for 24 hours in an electric muffle furnace. The sample in the crucible was dissolved with a small amount of concentrated hydrochloric acid and diluted with distilled water. Potassium content was then determined by using an atomic absorption spectrometer (Perkin Elmer Model 405). The sample preparation and the potassium determination for powdered diet were carried out in the same manner. The turnover rate and the biological half-life of potassium were calculated from the body potassium content and the daily potassium intake on the assumption that the body is practically a single compartment for the potassium kinetics.

Results

Tracer study

The whole-body retention of $^{42}$K given intraperitoneally as single dose in rats of various ages is shown in Fig. 1 with each point representing the average of five animals together with its standard deviation. It is clearly recognized in the figure that the excretion rate of $^{42}$K from 28 days old rats is the greatest in all groups and the older animals have a longer biological half-life and higher body retention for $^{42}$K than the younger animals. Because of the

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (days)</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Body weight (g)</td>
<td>Body K (mg)</td>
<td>K concentration (B/A)</td>
<td>Daily intake of K (mg)</td>
</tr>
<tr>
<td>A</td>
<td>32</td>
<td>64</td>
<td>170</td>
<td>266</td>
<td>99</td>
</tr>
<tr>
<td>B</td>
<td>49</td>
<td>147</td>
<td>372</td>
<td>253</td>
<td>162</td>
</tr>
<tr>
<td>C</td>
<td>79</td>
<td>268</td>
<td>634</td>
<td>237</td>
<td>180</td>
</tr>
<tr>
<td>D</td>
<td>133</td>
<td>358</td>
<td>832</td>
<td>232</td>
<td>196</td>
</tr>
<tr>
<td>E</td>
<td>192</td>
<td>402</td>
<td>887</td>
<td>221</td>
<td>197</td>
</tr>
</tbody>
</table>
Fig. 1. Whole-body retention of $^{42}$K following intraperitoneal administration to 28, 45, 75, 128 and 188 days old rats

![Diagram showing whole-body retention over days with different symbols for each group.]

Remarks.

<table>
<thead>
<tr>
<th>Group</th>
<th>Age at $^{42}$K administration</th>
<th>Retention equation (% of dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>●</td>
<td>28 days old</td>
<td>$R = 100 \exp (\frac{-0.474}{t})$</td>
</tr>
<tr>
<td>○</td>
<td>45 days old</td>
<td>$R = 100 \exp (\frac{-0.397}{t})$</td>
</tr>
<tr>
<td>◦</td>
<td>75 days old</td>
<td>$R = 100 \exp (\frac{-0.270}{t})$</td>
</tr>
<tr>
<td>×</td>
<td>128 days old</td>
<td>$R = 100 \exp (\frac{-0.239}{t})$</td>
</tr>
<tr>
<td>△</td>
<td>188 days old</td>
<td>$R = 100 \exp (\frac{-0.229}{t})$</td>
</tr>
</tbody>
</table>

$t$ is in days.

Each point represents the mean and the standard deviation of five rats. The retention equation was fitted to the data by least squares method.

rapid decay of $^{42}$K (physical half-life: 12.5 hours) which necessitated the short experimental period it is very difficult to determine whether the retention curves should be expressed by a single or as the sum of two or more exponential functions; therefore, a single function has been assumed. Equations fitted to the present data by least squares method were also shown in the figure. The turnover rate constant (day$^{-1}$) of $^{42}$K was 0.47, 0.40, 0.28, 0.24, 0.23 for the 28, 45, 75, 128, 188 days old rat at time of dosing, respectively.

The result of the tracer study with $^{42}$K was shown in Fig. 2. In this case retention curves of $^{48}$K in rats of various ages can be clearly expressed by a single compartment exponential function. Correlation coefficients of the retention equations to the present data were nearly unity.

Balance study

The result of the balance study is shown in Table 1. Columns A and B in the table show the body weight (g) and stable potassium content (mg) in the whole-body of the rat determined by atomic absorption spectrometry, respectively. Column C shows the concentration of potassium in the rat
Fig. 2. Whole-body retention of $^{45}$K following intraperitoneal administration to rats of various ages

![Graph showing retention over time]

Fig. 3. Change of the body burden and the daily intake of potassium versus age of the rat

![Graph showing body burden and daily intake]

Remarks.

<table>
<thead>
<tr>
<th>Group</th>
<th>Age at dosing (days)</th>
<th>Retention equation (% of dose)</th>
<th>Correlation coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>9</td>
<td>$100 \exp (-0.051 t)$</td>
<td>0.99</td>
</tr>
<tr>
<td>b</td>
<td>32</td>
<td>$100 \exp (-0.437 t)$</td>
<td>0.99</td>
</tr>
<tr>
<td>c</td>
<td>60</td>
<td>$100 \exp (-0.274 t)$</td>
<td>1.00</td>
</tr>
<tr>
<td>d</td>
<td>94</td>
<td>$100 \exp (-0.191 t)$</td>
<td>1.00</td>
</tr>
</tbody>
</table>

The constant of the retention equation was obtained by fitting it to the data by least squares method.

(mg potassium per g body weight) calculated from the values of Columns A and B. Column D shows the daily intake of potassium (mg/day) which was calculated from the measured amount of daily diet intake and the measured concentration of potassium in the diet (942 mg K/100 g diet).

In order to calculate the turnover rate of potassium in the rat from the body potassium content (Column B) and the daily potassium intake (Column D) it was assumed that the body is practically a single compartment for the potassium kinetics. The single compartment model is

\[ \frac{m(t)}{M(t)} \quad M(t) \quad \frac{m'(t)}{t} \]

where $M(t)$ is body burden of potassium in mg, $m(t)$ is daily intake of potassium in mg per unit time and $m'(t)$ is daily excretion of potassium in mg per unit time. As shown in the table $M(t)$, $m(t)$ and $m'(t)$ are the functions of age of the animal. The turnover rate of potassium in the body is

\[ \lambda(t) = \frac{m'(t)}{M(t)} \ \ \ \ \ \ \ (1) \]

Increase rate of body potassium can be described by

\[ \frac{dM}{dt} = m(t) - m'(t) \ \ \ \ \ \ (2) \]

From equations (1) and (2),

\[ \lambda(t) = \frac{dM}{dt} \ \ \ \ \ \ \ (3) \]

Functions for $M(t)$ and $m(t)$ were ob-
Fig. 4. Effect of age on the turnover rate of potassium in rats

![Graph showing the effect of age on the turnover rate of potassium in rats.]

Remarks.
- Solid line: data from the balance study.
- Point: data from the tracer study.

Obtained from the data in Columns B and D of the Table, respectively. The mathematical description of the increase of the body potassium with age of the animal was performed by applying a Gompertz function which is widely utilized for describing the growth rate for many organisms [9]. The equation is as the following,

\[ M(t) = M_0 \exp\{K[1 - \exp(-\alpha t)]\} \]  \ldots (4)

where \( M(t) \) is the body potassium at age \( t \); \( M_0 \) is the body potassium at birth; \( K \) and \( \alpha \) are random, uncorrelated parameters. \( M_0, K \) and \( \alpha \) were determined by fitting the equation (4) to the measured data by least squares method and the following solution was obtained.

\[ M(t) = 12.0 \exp\{4.3[1 - \exp(-0.084 \times (t - 3))]\} \]  \ldots \ldots \ldots (5)

where \( t \) is age in days. In the same way the daily intake of potassium with respect to age were fitted by an exponential function

\[ m(t) = 197 - 10 \times \exp\left(\frac{78 - t}{20}\right) \]  \ldots (6)

Fig. 3 illustrates the relevance of the Gompertz function and the exponential function as descriptive models of the body potassium and the daily potassium intake, respectively. Finally the turnover rate per day of potassium versus age in days of the animal was computed from equation (3), (5) and (6). The result of the balance study (solid line) is shown in Fig. 4 together with the result of the tracer study (points). This calculated result of the balance study is in a good agreement with that of the tracer study where it was obtained directly from the body retention curve.

**Discussion**

The age dependency of whole-body retention of potassium in rats was shown by two methods of experiment, tracer study and balance study. The present experiment deals with the rat older than weanlings. The tracer study on whole-body retention in suckling rats has been done and reported previously [3].

Although intravenous injection is preferable to intraperitoneal one for this kind of study, \(^{42}\)K was given to the experimental animal intraperitoneally in the present study because of the difficulty of intravenous injection into weanlings. The preliminary experiment showed that there was no significant difference of whole-body retention pattern between intravenous and intraperitoneal injection of \(^{42}\)K into adult rats. This fact may justify the adoption of intraperitoneal injection in the present experiment.

The result of the tracer study (Fig. 1) shows that the \(^{42}\)K given as a single dose was excreted exponentially. However, as stated before, the experimental period was not sufficiently long to determine whether the retention curve should be expressed by a single or as sum of two or more exponential functions because of the short physical half-life of \(^{42}\)K. In addition, the surface
contamination of animals due to $^{42}$K in the excreta also disturbed the analysis of whole-body retention curve. In order to check this possibility another tracer study was carried out using $^{42}$K. Using $^{42}$K for tracer, rats were housed in groups for the correction of the surface contamination, and the determination of body radioactivity was carried out for six consecutive days. The results of this experiment showed that the retention curve of $^{43}$K during the experimental period can be clearly described by a single exponential function. From this result the single exponential function is considered to be a good approximation to express the data of the present tracer study by $^{42}$K. However a few percent of the total body potassium is reported to be in non-easily exchangeable form [12]. This means that the whole-body retention curve might be expressed as sum of a few exponential functions if the body burden of radiopotassium could be followed for longer period.

The result of the balance study showed that the concentration of the body potassium decreases with age. Taking account of total body fat content shown by Spray and Widdowson [8], however, the potassium concentration expressed in potassium per unit mass of lean body is fairly same for present rats of various ages. Spray and Widdowson reported that the potassium concentration rises rapidly during the first 30 days after birth and then remains approximately constant. Present result of potassium concentration is in accord with this statement although the present values are lower than that obtained by them. It was assumed that the body is practically a single compartment for the potassium kinetics in the balance study. However it should be noted that the model is non-steady state because the size of the compartment $M$ increases with age of the animal. In the present model the turnover rate means a fraction of the potassium in the body transferred out of it per unit time. The turnover rate is therefore the function of body potassium ($M$) and the daily potassium excretion ($m'$). But the daily potassium intake was determined instead of daily potassium excretion because the former can be obtained with much more accuracy than the latter. As discussed before the single compartment model may be only an approximation but it is reasonably considered that this model is a good approximation because of the fact that 96%, at least, of the body potassium is reported to be in easily exchangeable form [11] besides the present result of the tracer study using $^{42}$K and $^{43}$K.

To describe the growth of the organisms many models, for instance the Gompertz equation [9], the cube root model [7], the logistic growth equation [4] and so forth, have been presented in numerous publications. In the present experiment the Gompertz equation was used because it allowed the best fit to the present data. To describe the change of the daily potassium intake versus age of the animal a modified exponential equation was used. This equation is considered to give a satisfactory approximation. As no or very few, if any, mathematical model about the change of the daily intake versus age has been reported, however, it seems that there might be a better model than the present equation to describe it but this problem remains to be solved.

Potassium is one of the essential element for living organisms and the body burden is kept fairly constant under a physiological control. The present tracer study and balance study indicated that the turnover rate of potassium in the rat decreases as a
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function of age. The present studies suggested that the rat body is a single compartment where potassium is in easily exchangeable form and that the turnover rate of potassium depends on the daily excretion or daily intake and daily increment of potassium body burden. The body burden and the daily intake of potassium versus age can be described by a Gompertz equation and a exponential equation, respectively. The fact that the younger animals consume more diet per unit body weight than older animals and so the younger animal has the greater relative excess of potassium explains the change of the turnover rate of potassium versus age of the rat in the present experiment.

Age trend of the turnover rate of potassium in rats obtained by the present study is in a good agreement with that of radiocesium obtained by the previous studies, where the turnover rate constant per day of $^{137}\text{Cs}$ was 0.29, 0.16 and 0.11 for rats of 30, 60 and 195 days of age, respectively [1, 5, 6]. Moreover, the result of the present study suggests that the turnover rate of radiocesium depends on that of potassium.

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References


