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USE OF THE POWER FUNCTION IN CALCULATIONS INVOLVING THE METABOLISM OF RADIOACTIVE BONE-SEEKERS

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Human Studies Project

To calculate quantities pertaining to or derived from the biological retention patterns of radioactive isotopes, it is desirable to have direct measurements of retention over the entire period of interest. However, in the case of radioelements which show an affinity for bone, it is well known that the period during which retention is biologically important is usually very long and may considerably exceed the lifespan of man. The consequent paucity of data covering such extended periods of time requires that current predictions of retention and related quantities depend upon extrapolations based upon data taken over relatively short intervals.

Earlier attempts at such extrapolations were based upon the assumption that the retentions of bone-seeking radioelements decreased as first-order exponentials. Thus a derived constant, the "biological half-life," is often used as a fundamental parameter of such retention phenomena-- especially in calculations of permissible body burdens and permissible daily intakes of radioactive isotopes (1,2).

Over the past several years evidence has accumulated to show that the concept of an exponential decrease in retention is altogether untenable when applied to bone-seekers. More specifically, these data show that the <u>overall</u> retention patterns of many bone-seeking elements, when administered as soluble compounds readily accessible to circulating fluids, may be described in the terms of the power function. This has been well documented for the alkaline earths-- calcium (3), strontium (3,4,5,6,7), radium (3,8,9,10,11), and, by analogy, barium-- in laboratory animals. In addition, Norris <u>et al</u>. (9) have shown that all the available

1169158

data from studies of radium metabolism in humans over a period of 25 years after administration are amenable to mathematical treatment by this method. Stehney and Lucas (12) used the power function to describe the increase in radium burden of human subjects at the natural level of dietary intake.

Brues and Stroud (13) found in mice that retention of C^{14}, given as $NaHC^{14}O_3$, followed a power function over a period of 10 months. More recently, Langham has presented data to show that the retention and excretion of plutonium-239 by man over a period of 5 years may also be described in this manner (14). Similarly, Bernard and Strumness (15) have found it applicable to the description of uranium retention by humans.

Although it is probable that the retention patterns of certain other bone-seeking elements may be described by the power function, the available data are somewhat fragmentary and usually do not extend over sufficient periods of time to be conclusive.

In this paper (16) it is proposed first, to appraise the value of the power function as an empirical description of the retention phenomenon, and second, to explore some of the consequences implied from its use in the mathematical treatment of retention.

General Concept of the Power Function

The members of the special class of hyperbolic functions having the mathematical form

$$y = x^a \qquad (1)$$

are generally referred to as power functions, and plot as straight lines

1169159

on log-log paper. The applicability of this form to the description of the metabolism of bone-seeking elements is entirely empirical and of little value in the elucidation of the mechanisms involved. However, its ability to describe the retention patterns of many elements in simple mathematical fashion over extended periods of time outweighs, at least in part, the disadvantage of its empirical nature.

The mineral phase of bone undergoes several physico-chemical reactions (17) in addition to those processes attendant upon growth and maintenance of the skeleton. As a first approach to a comprehensive mechanistic analysis all these reactions may be considered as first-order. Recent attempts at such mechanistic analyses, using analog computer methods, have utilized the sum of five or more first-order exponential terms as a model (18,19).

It can be demonstrated, using graphical methods, that a sum of inter-related first-order exponential terms can often be closely approximated by a power function over a large portion of the interval of quantitative significance. For example, Way and Wigner (20) described the radioactive decay of mixed fission products by this method. The goodness with which a power function approximates a sum of exponentials is determined by the number of component terms and the distribution of the values of the coefficients and exponents of these terms. Where only a very few exponential terms exist, the approximation of their sum by a power function may be fortuitous, since restrictions on the distribution of values of coefficients and exponents become severe.

1169160

In the preferred model, a sum of first-order exponentials, retention may be formally represented as

$$R_t = \sum_{i=1}^{n} \alpha_i e^{-\beta_i t} \qquad \beta_i \geq 0 \qquad (2)$$

where R_t is retention at time t following a single administration of the bone-seeking radioelement, and α_i and β_i are constants. It is tentatively hypothesized that, in normal members of a given species, the values of β_i and the number of terms, n, are independent of age. The age variable in retention is then to be found in the values of the coefficients, α_i.

However, detailed knowledge of the retention process is required before this model can be used satisfactorily as a basis for calculation and description. Therefore, experimental observations that a power function will ordinarily describe retention of bone-seeking elements are taken as the basis for the following <u>approximate</u> relationship between equation 2 and a form of equation 1

$$R_t = \sum_{i=1}^{n} \alpha_i e^{-\beta_i t} \cong At^b \qquad -1 < b < 0 \qquad (3)$$

This restriction on b is made since only over this range of values is the function of biological interest.

Mathematical Description Following a Single Dose

If q units of a soluble, bone-seeking radioactive element are administered instantaneously, the description of retention afforded by the power function is

$$R_t^* = Aqt^b e^{-\lambda t} \qquad t \geq 1 \qquad (4)$$

1169161

where R_t^* is retention at t units of time (days) after administration, A is a constant equal to the fraction of q retained when t is equal to 1, and b is a constant equal to the slope of the retention line and consequently always of negative sign. The quantity $e^{-\lambda t}$ is included to account for physical decay of the radio-nuclide and λ is the appropriate decay constant. It is apparent that the value of $e^{-\lambda t}$ will essentially be unity when the half-life of the nuclide is much larger than the period of observation. Equation 4 may be converted to describe retention in terms of a fraction of the administered dosage by dividing by q. Hereafter R_t ($R_t = R_t^*/q$) will be expressed in these terms.

$$R_t = At^b e^{-\lambda t} \qquad t \geq 1 \qquad (5)$$

From equation 5, the basic equation of retention, the concomitant instantaneous rate of excretion is obtained by differentiating (21).

$$dR_t/dt = At^{b-1}e^{-\lambda t}(b-\lambda t) \qquad (6)$$

In instances where radioactive decay is not significant, λ may be assumed to have a value of zero and equation 6 becomes

$$dR_t/dt = bAt^{b-1} \qquad (7)$$

The quotient of equations 5 and 6 gives the coefficient of elimination, (CE), which is the fraction of the retained burden being excreted per unit interval of time as a function of time; when radioactive decay may be neglected, its value varies inversely with time.

$$(CE) = \frac{dR_t/dt}{R_t} = \frac{b-\lambda t}{t} \qquad (8)$$

1169162

Description of Multiple or Continuous Administration

The description of retention following a single dosage may be immediately extended to describe retention resulting from multiple administrations or continuous exposure over any period of time. It is, of course, necessary to assume that the time course of retention resulting from any given dosage is unaffected by previous dosages.

In the case of multiple administrations of dissimilar quantities, or of similar quantities given at long or dissimilar intervals, estimates of retained amounts (and related quantities) must be derived by summation of individual items over the appropriate time intervals. However, when repeated administrations of similar magnitude are given at reasonably short and constant intervals, the resulting retention picture can be closely approximated by assuming that the total dosage was given continuously during the total time of administration (9). This description of retention, $\bar{R}_t$, following continuous exposure is given by integrating the single dose retention function, equation 5.

$$\bar{R}_t = A\int_0^t e^{-\lambda t}\, t^b\, dt = \frac{A}{\lambda^{b+1}}\, \Gamma_{(\lambda t)}\,(b+1) \qquad (9)$$

When λ is very small, equation 9 is approximated by

$$\bar{R}_t = \frac{A}{b+1}\, t^{b+1} \qquad (10)$$

Equation 9 has the form of the incomplete gamma function and may be evaluated directly by reference to compiled tables (22,23).

Similarly, for instances in which a period of continuous exposure to radioactive bone-seekers is terminated, if T is the time during which exposure persisted, and t is the total time of observation, the

1169163

overall retention pattern may be described as follows:

$$\bar{R}_t = A\int_0^T (t - \tau)^b e^{-\lambda(t - \tau)} d\tau \qquad t \geq T \qquad (11)$$

$$= \frac{A}{\lambda^{b+1}} \left\{ \Gamma(\lambda t)(b + 1) - \Gamma[\lambda(t-T)](b + 1) \right\} \qquad (12)$$

where τ is the integration variable.

When λ is assumed to be zero in equation 12

$$\bar{R}_t = \frac{A}{b+1} \quad t^{b+1} - (t-T)^{b+1} \qquad (13)$$

Discussion

Because of the simplicity of its mathematical form and the ease with which its characterizing constants can be estimated, the power function offers some rather unique advantages for calculation of quantities related to the retentions of bone-seeking radio-elements. Other, less empirical methods have so far proven to be either so over-simplified as to be incapable of properly representing the available data, or too complex mathematically for ready exploitation. The question as to whether the constants of the power function, measured in comparable individuals, are expected to vary markedly, has already been answered to some extent. Norris et al. (9), Hursh (10), and Floyd et al. (11) independently measured these values for radium injected into adult dogs and agreed within very narrow limits.

This approach represents a substantial improvement over presently employed concepts which somewhat ambiguously employ the term "fixed" to indicate that rate of excretion has reached a low value. A more

quantitative description is supplied by the coefficient of elimination, which is a direct measure of the lability of skeletal deposits. When far removed in time from administration its values do not change rapidly and hence have been used to calculate quantities, erroneously called "biological half times." It should be emphasized that the term "biological half time" is meaningless in the context of the power function. If some similar quantity is desirable, the term "apparent biological half time" ($T_{1/2\ app.}$) could be used with the understanding that its value is directly proportional to time after administration. Thus, from equation 8, for $\lambda = 0$,

$$T_{\frac{1}{2}app.} = - \frac{0.693}{\frac{dR_t/dt}{R_t}}$$

$$= - \frac{0.693\ t}{b} \qquad (14)$$

If it is assumed that the actual retention function follows equation 2, then ultimately the retention data should depart markedly from the power function description and tend to follow a pattern determined by the exponential term of longest half life. However, the available data in humans appears to show that this point of flexure of the retention line is not reached within 25 years in the case of radium (9) nor within 5 years in the case of plutonium (14). This continuing adherence to the power function line is indicative of a failure of the bone-seeking element to attain a steady state in bone within the times mentioned. This may simply reflect biochemical reactions proceeding at very slow rates-- which approach those commonly associated with solid

1169165

state diffusion. However, if diffusion itself is the rate-limiting factor for excretion of the radioelement, the skeletal mineral may simultaneously exist in a condition of overall equilibrium. This is an interesting speculation since the diffusion model, which can be thought of as comprised of a large number of closely related exponential terms, will inevitably be described by a power function. On the other hand, there may be progressive changes in the chemical or physiological status of the skeleton with time. In the latter case no equilibrium condition would be reached.

The above line of reasoning provides a basis for estimation of the maximum error involved in extrapolating the power function retention line beyond the point where data are available. Retention following a single dosage will be considered. The maximum possible rate of decrease in retention following the last measure of retention, R_{t_x}, is described by assuming that a steady state has been attained at t_x. Then the $T_{1/2\ app.}$ calculated at t_x may be taken as the decay constant of the nth, or last, exponential term, and retention henceforth will be described as $R_t = R_{t_x} e^{-\left(-\frac{.693\ t_x}{b}\right)(t - t_x)}$. For the other extreme case, the minimum possible change in retention following t_x, is represented by the assumption that retention is constant, or essentially so, following t_x. The maximum error of extrapolation now becomes

$$E_{max.} = R_{t_x} - R_{t_x} e^{-\left(-\frac{.693\ t_x}{b}\right)(t - t_x)} + \hat{\sigma} \qquad (15)$$

where $\hat{\sigma}$ is the error associated with the individual measurements.

1169166

Most of the work from which power function constants have been derived has been done using adult subjects. It should not be assumed that constants measured in the adult animal can be applied to the young, growing individual. The well known fact that retention of bone-seeking elements is highest in young, growing animals guarantees some systematic changes in the power function constants as a function of rate of formation of bone.

The value of the constant, A, must reflect the distribution of the administered isotope in the various compartments available to it. In other words, given a fixed number of compartments, a larger value of A must indicate that relatively more of the administered element exists in compartments of longer half-life. Thus as values of A approach unity the corresponding values of b must approach zero. The correlation between the values of A and b is imposed by the system of biological mechanisms that influence retention. In light of present knowledge it seems impracticable to examine this point further.

In practice, there has not been reported, in single dose studies, a single instance in which b has fallen outside the limits of 0 to -1.0. The great majority of the values have been between 0 to -0.6. Since rate of total excretion is described by the derivative of retention, the slope of excretion curves must always be less than -1.0 and are ordinarily greater than -1.6. In instances where the materials excreted in urine and feces are derived from a common source in the body, it follows that the slopes of the lines representing their rates will be identical. Langham (14) has shown, in the case of plutonium in man, that the values

1169167

of b for urinary and fecal elimination differ. For urinary excretion the slope is greater than -1.0 which is interpreted by the present authors as being due to slow conversion of the chemical form of plutonium in the body. Langham described this changing ratio between urinary and fecal elimination by a power function and utilized it as another method of determining time since exposure.

The power function for $b < 0$ increases without bound as t approaches zero. Therefore it cannot be used to describe retention between the time of administration ($t = 0$) and some minimum value of t-- usually taken as one day.

It is apparent that the integrated retention function must suffer in the same fashion from this inadequate description at the earliest times. The extent to which equation 10 agrees with a more precise estimation of the integrated retention pattern is illustrated in Figure 1, using constants ($A = 0.54$, $b = -0.52$) which have been found applicable to the metabolism of radium by adult humans. It is necessary that the log-log line representing retention following a single dose depart from its straight line course and become asymptotic to a retention of unity at some small fraction of a day. When such a retention course is approximated, as in Figure 1, an improved estimation of retention following continuous administration may be obtained by graphical integration. One will note that retentions following either a single or continuous administration are now described by curves which, on log-log paper, resemble hyperbolas with the asymptotes being the total administered quantity and the power function line. Thus equation 10 will somewhat

1169168

overestimate retention following continuous administration (although never by more than the quantity administered during one day) by an amount which varies with time of observation and the value of b.

With slight modifications the power function can be made to conform to the physical requirement that retention must be unity when $t = 0$. The modified form representing retention following a single dose is

$$R_t = \frac{(t+\gamma)^b e^{-\lambda t}}{\gamma^b} \qquad t \geq 0,\ -1 < b < 0,\ 0 < \gamma \qquad (16)$$

where γ is a constant. This form approaches equation 5 asymptotically as t increases and satisfies the requirements discussed in the preceding paragraph. It can readily be integrated and differentiated and offers advantages in description-- especially over time intervals close to administration.

The estimation of γ requires data for sufficiently large t to accurately determine b. If recording times of the retention values are assumed to be error-free and the number of measurements at each time point is equal, the weighted least squares procedure (24) on the log transforms of the variables will yield efficient estimates of both the constants and their associated errors. The appropriate weighting factor for each transformed retention value is the retention value itself corrected for radioactive decay. Using this method it can be shown that γ is most readily evaluated from the relationship $A = 1/\gamma^b$, where A is the one day intercept of the power function line. When a suitable portion of the t values are not large enough to suitably define the power function asymptote, estimates of the constants may sometimes be

1169169

determined by using equation 16 directly and employing the general method of fitting non-linear equations (25). The estimation procedure, in this case, requires extensive computation.

All the arguments and the power function constants presented herein are derived from studies in which the bone-seeking isotopes were immediately available to the circulating body fluids-- as by intravenous injection. When such is not the case, it is necessary to introduce appropriate correction factors-- as for example, in intestinal absorption which, as a rule, is not quantitative. Marinelli et al. (26) have demonstrated that radium sulfate inhaled into the human lung does not go readily into solution. This situation was analyzed, using the power function method, as essentially an instance of continuous systemic administration due to the continuing solubilization of the material.

The power function may also be applied to the analysis of the situation in which a bone-seeking element is formed within the body as a result of radioactive decay of a parent element. Thus Gustafson et al. (27) concluded that the Ra^{223} arising from deposited Th^{227} behaved as if it were being continuously administered intravenously-- a finding in agreement with data reported by Van Dilla et al. (28).

Calculation of Permissible Levels

These formulations permit calculation, with greater accuracy than is otherwise possible, of the allowable daily absorption of radioactive bone-seekers into the blood stream (29). Given a value for the permissible body burden and the period of exposure, equation 9 can be used to determine the amount of isotope which, if absorbed daily, can be expected

1169170

to produce this burden by the end of the exposure period. This method has been discussed in detail by Healy (30).

Values for permissible daily intakes of Ra^{226}, Sr^{89}, Sr^{90}-Y^{90}, and Ca^{45} have been calculated using equations 9 and 10 and are presented in Table 1. (The final body burden is that proposed in 1955 for industrially exposed persons by the International Commission on Radiological Protection.(31)) The power function constants for Sr and Ca in humans are based on results of a survey of the literature by Marinelli (32) and were obtained from studies following intravenous administration to adults. The constants for Ra^{226} are taken from Morris et al. (9). The results are presented for two somewhat arbitrarily selected periods of intake, 30 years and 70 years which may be representative, respectively, of a working lifetime under industrial conditions and a lifespan under conditions of universal contamination. No effort has been made to break the figures down further into concentrations in air, water, and food, since the basic assumption requires only that the elements be freely accessible to body fluids, regardless of mode of intake. No consideration has been given to the more specialized situation which exists during the period of rapid skeletal growth in childhood and adolescence. Values calculated for the adult should be examined critically before they are applied to this segment of the population. The 70-year values in Table I, which include the period of childhood, were calculated on the basis of adult values and are incorrect to this extent.

1169171

Calculation of Radiation Dosage

The power function may also be used to calculate integrated radiation dosage from deposits of radioactive elements in bone. The mathematical considerations are essentially identical to those discussed with reference to retention. Since radiation dosage accumulates as the produce of concentration of the radioelement and time, the integrated dosage over t days, D_t, is

$$D_t = kf(R) \tag{17}$$

where k is the radiation dosage rate per day per microcurie in the skeleton (33). The quantity, f(R), in every case is the appropriate retention function integrated with respect to t over the period in question. It seems most reasonable to integrate over the entire period from zero time, since the inadequacies of the power function during the first day will not introduce appreciable error unless the total period of observation becomes quite short. In such a case, one should use equation 16 or, alternatively, integrate from 1 to t and add the best graphically determined estimate for the contribution from zero to 1 day. From equations 5 and 10 the appropriate values for f(R) are:

for single administration ($\lambda > 0$):

$$f(R) = \int_0^t Ae^{-\lambda t} t^b dt = \frac{A}{\lambda^{b+1}} \Gamma_{(\lambda t)} (b + 1) \tag{18}$$

for a single administration ($\lambda = o$):

$$f(R) = \int_0^t At^b dt = \frac{A}{b + 1} \; t^{b + 1} \tag{19}$$

1169172

for continuous administration ($\lambda = o$):

$$f(R) = \int_o^t \frac{A}{b+1} t^{b+1} dt = \frac{A}{(b+1)(b+2)} t^{b+2} \quad (20)$$

The f(R) for continuous administration with $\lambda > o$, equation 9, is not readily integrated and should be determined graphically.

Values for integrated radiation dosages from permissible quantities of Ra^{226}, Sr^{89}, Sr^{90}-Y^{90}, and Ca^{45} accumulated by continuous exposure have been calculated and included in Table I.

In such calculations there is the major complication that bone-seeking elements, when administered over short periods of time relative to the lifespan, are rarely, if ever, found uniformly distributed in the skeleton. At this time there is no accurate basis for estimating the actual spectrum of concentrations and somewhat arbitrarily selected values must be included to compensate for this heterogeneity. However, in instances where intake of radioactive elements at a more or less constant rate has persisted for long periods up to the entire lifetime of the individual, it is apparent that the skeleton will be uniformly radioactive (34,35,36, 37), hence uniformly irradiated. Here the method of calculation gives accurate values.

It has been assumed that the radiations are completely absorbed by bone tissue. Since this may not always be the case, correction may sometimes be necessary to compensate for this loss. However, considerations of this nature are outside the scope of this discussion.

From the aspect of total radiation dosage, with respect to situations in which the permissible body burden will be found following some period

1169173

of time, t, there may exist considerable differences depending upon the mode of accumulation. This is best illustrated by comparing the two extreme cases: (1) a single administration of the bone-seeking element in such quantity that the tolerable body burden will remain after time, t, and (2) continuous administration at such a rate that the same body burden will occur at the same time, t. Since the final burdens are to be identical, equations 4 and 10 with $\lambda = o$ provide the following relationship:

$$qAt^b = \frac{CA}{b+1} t^{b+1}$$

$$\frac{q}{C} = \frac{t}{b+1} \qquad (21)$$

where C is the daily dosage, between the quantities given singly and on a continuous daily basis to bring about this condition. The relationship between the accumulated radiation dosages ($\lambda = o$) becomes:

$$\frac{D_t}{\bar{D}_t} = \frac{\frac{Aq}{b+1} t^{b+1}}{\frac{AC}{(b+1)(b+2)} t^{b+2}}$$

$$= \frac{q(b+2)}{Ct} \qquad (22)$$

or, substituting from equation 21 to impose the condition of equal final burden:

$$\frac{D_t}{\bar{D}_t} = \frac{b+2}{b+1} \qquad (23)$$

Thus, in the case of radium where b = -0.52, there is a safety factor of 3 in total integrated radiation dosage when the body burden is

1169174

achieved by daily increments. This is a minimum figure since this manner of exposure necessarily results in a more uniform concentration (i.e. smaller local concentration factors) than would be found following a single injection. Since concentration factors of at least 10 have been demonstrated for radium in the bone of humans who have received radium over short periods of time, it follows that total radiation dosage to parts of the skeleton may vary by at least a factor of 30, depending upon the mode of administration, with the same final body burden in either case.

Therefore, neither "permissible body burdens" nor resulting radiation damage can be considered to be independent of method of exposure. The large factors in integrated radiation dosage which appear when single dose and continuous exposure are compared, again point to the inadequacies of current procedures for assessing the hazards of bone-seeking radio-elements.

Conclusion and Summary

The power function has been found to provide a satisfactory empirical description of the retention of several radioactive isotopes which are preferentially deposited in skeletal tissue. The extent to which it may apply to bone-seeking elements in general is not yet known.

The ease of mathematical manipulation of the power retention function allows the derivation of several relationships which can be used to determine permissible daily intake or integrated radiation dosage, or to evaluate important factors relating to individuals who have already accumulated skeletal deposits.

1169175

The power function indicates clearly that, in its area of application, the concept of "biological half-times" is completely fallacious and may result in gross errors both actually and conceptually.

The method offers opportunities for more accurate and realistic approaches to the problems of poisoning by radioelements as well as in calculations of allowable daily intake levels and body concentrations of radioactive bone-seekers. It indicates that major differences in integrated radiation dosage may obtain depending upon the conditions of exposure and points out that "permissible body burdens" should be assessed in view of the manner in which the body burden is obtained.

1169176

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1169177

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1169178

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1169179

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33. In this case the most acceptable unit of dosage is the rad, which is defined as the dissipation of 100 ergs of energy per gram of tissue. The constants involved in this quantity are the disintegration rate per second per microcurie, 3.7×10^4; the number of seconds per day, 8.64×10^4; and the number of electron volts per erg, 6.24×10^{11}. In the case of radium-226, assuming 30 per cent retention of radon and its daughters in the skeleton, the total energy dissipated is 10.8×10^6 electron volts per disintegration. Thus the dose to the human skeleton (mass of 7000 grams) from 1 microcurie of radium becomes:

$$k = \frac{3.7 \times 10^4 \times 8.64 \times 10^4 \times 10.8 \times 10^6}{7 \times 10^3 \times 6.24 \times 10^{11} \times 10^2} = 0.079 \text{ rad}/\mu c \text{ day}$$

34. R. H. Hodges, et al. Strontium content of human bone. J. Biol. Chem. 185, 519 (1950).

1169180

Figure Legends

Figure 1. Illustration of the degree of applicability of the power function at early times after administration. The curved lines are required by physical considerations for a more accurate description at early times. These may be obtained using equation 16. The saw-tooth curve illustrates the similarity of retention between repeated doses of 1 unit per day $(R_t^* = A\sum_{i=1}^{n} q_i\ (t-t_i)^b)$ and continuous administration of the same amount.

1169181

$\frac{6.8}{2.2} \times \frac{10^{-4}}{10^{3}} \sim 3 \times 10^{-7}$

$\frac{1.02}{2.2} \times \frac{10^{-3}}{10^{3}} = 5 \times 10^{-7}$

Table 1

Calculated values of permissible daily intakes and associated skeletal radiation dosages for selected bone-seeking radioelements

	Radium-226	Strontium-89	Strontium-90-Yttrium-90	Calcium-45
Mean energy (ev/dis)*	10.8×10^{6} ‡	0.511×10^{6}	0.987×10^{6}	0.089×10^{6}
Rads per μc-day**	0.079	0.00374	0.00722	0.00065
Present permissible burden, μc†	0.1	2.0	1.0	14.0
A	.54 ††	.95 ‡‡	.95 ‡‡	1.0 ‡‡
b	-.52 ††	-.254 ‡‡	-.254 ‡‡	-.134 ‡‡
Over 70 years				
Daily dose to reach permissible level, μc/day	6.8×10^{-4}	0.066	7.53×10^{-4}	0.119
I Internal dose, μc-days	1723	51,000 §	18,140 §§	357,700 §
rads	136	190	131	232
Over 30 years				
Daily dose to reach permissible level, μc/day	1.02×10^{-3}	0.066	1.02×10^{-3}	0.119
Internal dose, μc-days	738	21,900 §	6964 §§	153,300 §
rads	58.3	80	50.3	99.6
Time to equilibrate body burden:				
days to 96% of asymptotic value	---	209	3.9×10^{4} (106.8 years)	653
days to 100% of asymptotic value	---	1239	2.318×10^{5} (635 years)	3570

*Values for β-emitters are taken as 0.35 E_{max}.

**Assuming uniform distribution in a skeletal mass of 7000 gm.

†Values taken from Recommendations of International Committee on Radiological Protection (31)

‡Assuming 30% retention of radon and its daughters.

††Norris (9).

‡‡Marinelli (32).

§ μc-Days for strontium-89 and calcium-45 assume a constant burden for the entire period.

§§ Integrated radiation dosage determined graphically.

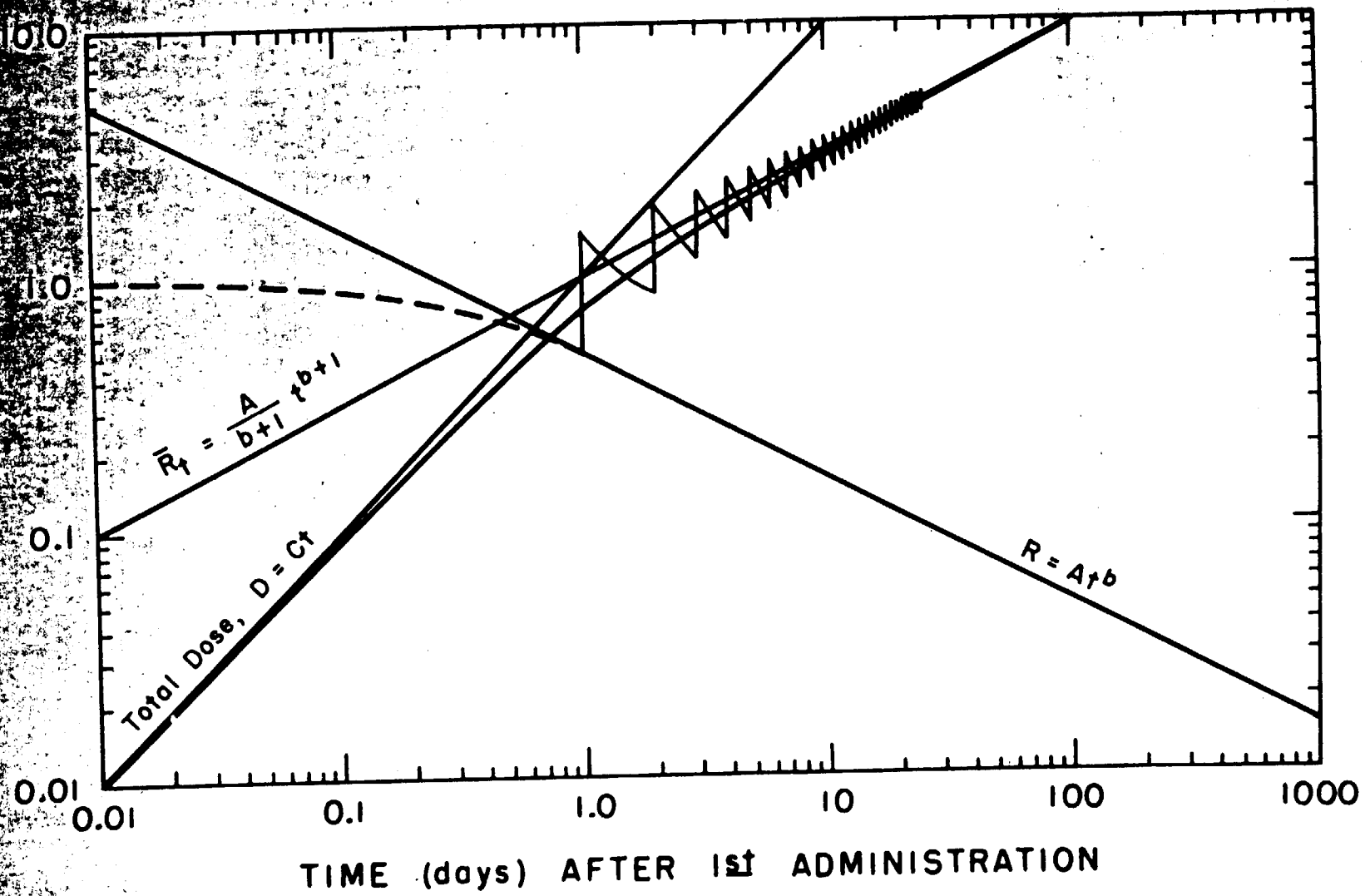
1169182

35. C. L. Comar, I. B. Whitney and F. W. Lengemann, Proc. Soc. Exp. Biol. Med. 88, 232-236 (1955).

36. N. S. MacDonald, R. E. Nusbaum, R. Stearns, F. Ezmirlian, C. McArthur and P. Spain, J. Biol. Chem. 188, 137-143 (1951).

37. G. V. Alexander, R. E. Nusbaum and N. S. MacDonald, J. Biol. Chem. 218, 911-919 (1956).

1169183


FRACTION OF TOTAL DOSE
10.0
1.0
0.1
0.01
0.01
0.1
1.0
10
100
1000
TIME (days) AFTER 1st ADMINISTRATION
$\bar{R}_t = \frac{A}{b+1} t^{b+1}$
Total Dose, D = Ct
R = At^b

1169111

$$\frac{A}{b+1} t^{b+1}$$

6.8×10^{-4} 70 yrs.

1×10^{-3} 30 yrs.

$$\frac{1 \times 10^{-3}}{2200} \sim 5 \times 10^{-7} \ \mu c/cm^3,$$

1169185