dizing β-hydroxybutyrate. Furthermore, active exchange of the K^+ bound to the mitochondrial membrane fragments coupled to respiration has been demonstrated with K^{42} as a tracer. It is inhibited by cyanide or dinitrophenol, demonstrating that the binding of the potassium to the digitonin fragments is linked to electron transport and phosphorylation mechanisms. However, ATP cannot substitute for respiration in causing binding of radioactive K^+. Since the preparations have relatively insignificant capacity to bind Na^+ under any conditions, this active potassium-binding mechanism of the mitochondrial membrane appears to be selective.

These experiments demonstrate that the digitonin fragments may provide an important lead for investigation of the molecular mechanisms involved in active transport; further work on identification of the binding sites for K^+ is in progress.

Conclusion

Although the membrane fragments are still highly organized, they are considerably less complex than intact mitochondria and thus relatively free of extraneous side reactions not relevant to oxidative phosphorylation and of structural "compartmentation" of pools of intermediates. With the information gained on these preparations, still less organized portions of the complex enzymatic machinery may soon be dissociated and studied separately, toward the ultimate goal of demonstrating the mechanism of oxidative phosphorylation.

These investigations are being carried out with full appreciation of the eventuality that such classical approaches to reconstruction applied to the highly integrated and structure-dependent respiratory chain and its energy-coupling mechanisms may never succeed to the same extent or in the same way as they have for other metabolic cycles which occur by interaction of essentially soluble enzymes, because of a possible necessity for special polymolecular arrangements to direct protein-protein collisions. For this reason, the problem of electron transport and oxidative phosphorylation represents a great challenge in the large and relatively uncharted area of "solid-state" enzymology.

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Retention of Radioactive Bone-Seekers

Calculations based on the power function cast doubt on the present concept of biological half-times.

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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 cover the entire life span 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 *over-all* retention patterns of many bone-seeking elements, when administered as soluble

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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 (*3–7*), radium (*3*; *8–11*), and, by analogy, barium—in laboratory animals. In addition, Norris *et al.* (*9*) have shown that all the available 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 carbon-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 Struxness (*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 article (*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 by its use in the mathematical treatment of retention.

General Concept of the Power Function

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

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

are generally referred to as power functions, and plot as straight lines 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 physicochemical 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, by use of analog computer methods, have utilized the sum of five or more first-order exponential terms as a model (*18, 19*).

It can be demonstrated, by graphical methods, that a sum of interrelated 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 the restrictions on the distribution of values of coefficients and exponents become severe.

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

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

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 *approximate* relationship between Eq. 2 and a form of Eq. 1:

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

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

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

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 linear log-log transform of the retention function and consequently is always of *negative* sign. The quantity $e^{-\lambda t}$ is included to account for physical decay of the radionuclide, and λ is the appropriate decay constant. It is apparent that the value of $e^{-\lambda t}$ will be essentially 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.

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

From Eq. 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 Eq. 6 becomes

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

The quotient of Eqs. 5 and 6 gives the instantaneous coefficient of elimination (CE) which, when t is not too small, closely approximates the fraction of the retained burden being excreted per day as a function of time.

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

When radioactive decay may be neglected, its value varies inversely with time.

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 con-

tinuous exposure over any period of time. It is necessary, of course, to assume that the time course of retention resulting from any given dosage is not affected 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, $\overline{R}_t$, following continuous exposure is given by integrating the single dose retention function, Eq. 5.

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

When λ is very small, Eq. 9 is approximated by

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

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 over-all retention pattern may be described as follows:

$$\overline{R}_t = A\int_0^T (t-\tau)^b\, e^{-\lambda(t-\tau)}dt \qquad t \geqq T \quad (11)$$

$$= \frac{A}{\lambda^{b+1}}\{\Gamma_{(\lambda t)}\,(b+1) - \Gamma_{[\lambda(t-T)]}\,(b+1)\} \quad (12)$$

where τ is the integration variable.

When λ is assumed to be zero in Eq. 12

$$\overline{R}_t = \frac{A}{b+1}\,[t^{b+1} - (t-T)^{b+1}] \quad (13)$$

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 radioelements. Other, less empirical, methods have so far proved to be either so oversimplified as to be incapable of properly representing the available data or too complex mathematically for ready exploitation. The question 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 the 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* ($T_{1/2\ \text{app.}}$) could be used with the understanding that its value is directly proportional to time after administration. Thus, from Eq. 8, for $\lambda = 0$,

$$T_{1/2\,\text{app.}} = -\frac{0.693}{\dfrac{dR_t/dt}{R_t}} = -0.693\ t/b \quad (14)$$

If it is assumed that the actual retention function follows Eq. 2, then ultimately the retention data should depart markedly from the power function description and follow a pattern determined by the exponential term of longest half-life. However, the available data in humans appear to show that this point of flexure of the retention line is not reached within 25 years in the case of radium (*9*) or 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 isotope to attain a steady state in bone within the times mentioned. This may simply reflect biochemical reactions proceeding at very slow rates—rates which approach those commonly associated with solid-state diffusion. However, if diffusion (or reactions with similarly slow rates) is the rate-limiting factor for excretion of the radioelement, the bulk skeletal mineral *may* simultaneously exist in a condition of *over-all* 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, an equilibrium condition would not necessarily 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 $T_{1/2\ \text{app.}}$ calculated at t_x may be taken as the half time of the nth, or last, exponential term, and retention henceforth will be described as

$$R_t = R_{t_x} e^{-(-b/t_x)(t-t_x)}$$

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

$$E_{\max.} = R_{t_x} - R_{t_x} e^{-(-b/t_x)(t-t_x)} + \hat{\sigma} \quad (15)$$

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

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, an 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 the rate of total excretion is described by the derivative of retention, the slope of excretion curves must always be less than -1.0 and 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 of b for urinary and fecal elimination differ. For urinary excretion the slope is greater than -1.0. This is interpreted by us 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 1 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 Eq. 10 agrees with a more precise estimation of the integrated retention pattern is illustrated in Fig. 1, using constants ($A = 0.54$; $b = -0.52$) which have been found to be 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 Fig. 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, Eq. 10 will somewhat overestimate retention following continuous administration (although never by more than the quantity administered during 1 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 (*24*) representing retention following a single dose is

$$R_t = \frac{(t+\gamma)^b e^{-\lambda t}}{\gamma^b}$$
$$t \geqq 0; -1 < b < 0; 0 < \gamma \quad (16)$$

where γ is a constant. This form approaches Eq. 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 determine accu-

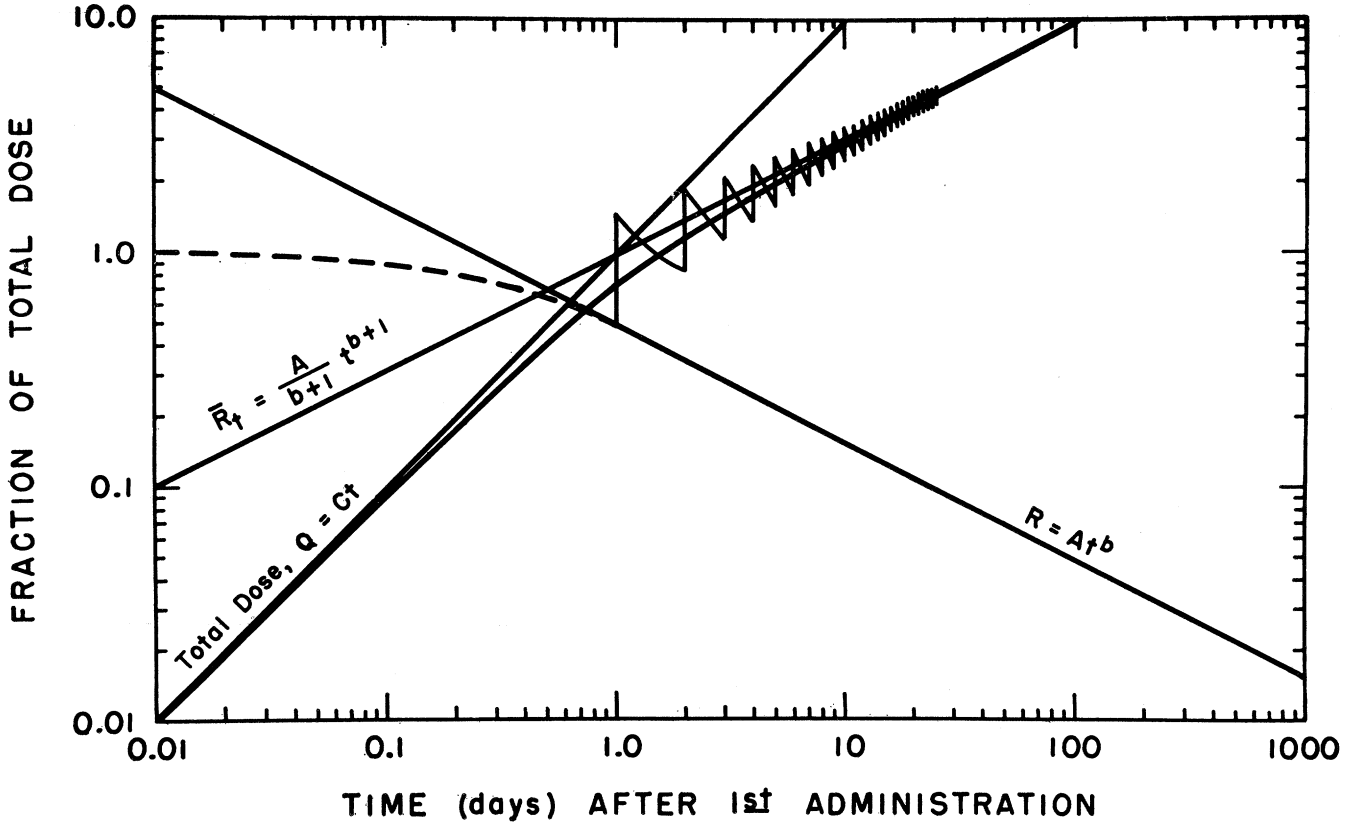

Fig. 1. Illustration of the degree of applicability of the power function at early times after administration. The curved lines are required by physical considerations for a more accurate description at early times. These may be obtained by use of Eq. 16. The saw-tooth curve illustrates the similarity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

Table 1. Calculated values of permissible quantities absorbed daily into the blood and associated skeletal radiation dosages for selected bone-seeking radioelements in humans.

Item	Radium-226	Strontium-89	Strontium-90–Yttrium-90	Calcium-45
Mean energy (electron volt/disintegration)*	10.8×10^6†	0.511×10^6	0.987×10^6	0.089×10^6
Rads per microcurie day‡	0.079	0.00374	0.00722	0.00065
Present permissible body burden for occupational exposure (μc)§	0.1	2.0	1.0	14.0
Power function constants				
A	0.54‖	0.95#	0.95#	1.0#
b	−0.52‖	−0.254#	−0.254#	−0.134#
Intake period: 70 years**				
Daily dose to reach permissible level (μc/day)	6.8×10^{-4}	0.066	7.53×10^{-4}	0.119
Internal dose				
Microcurie days	1723	51,000††	18,140‡‡	357,700‡‡
Rads	136	190	131	232
Intake period: 30 years**				
Daily dose to reach permissible level (μc/day)	1.02×10^{-3}	0.066	1.02×10^{-3}	0.119
Internal dose				
Microcurie 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	653
Days to 100% of asymptotic value		1239	2.318×10^5	3570

* Values for β-emitters are taken as 0.35 $E_{max.}$ † Assuming 30 percent retention of radon and its daughters. ‡ Assuming uniform distribution in a skeletal mass of 7000 g. § Values taken from the recommendations of the International Committee on Radiological Protection (*31*). ‖ Norris (*9*). # Marinelli (*32*) ** Calculations based on data for adults (see text). †† Microcurie days for Sr^{89} and Ca^{45} assume a constant burden for the entire period. ‡‡ Integrated radiation dosage determined graphically.

rately b. If recording times of the retention values are assumed to be error-free and if the number of measurements at each time point is equal, the weighted least squares procedure on the log transforms of the variables will yield efficient estimates of both the constants and their associated errors. The appropriate weighting factor (*24*) for each transformed retention value is the retention value itself corrected for radioactive decay. By using this method it can be shown that γ is most readily evaluated from the relationship $A = 1/\gamma^b$, where A is the 1-day intercept of the power function line. When a suitable portion of the t values are not large enough to define suitably the power function asymptote, estimates of the constants may sometimes be determined by using Eq. 16 directly and employing the general method for fitting nonlinear 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—for example, by intravenous injection. When such is not the case, it is necessary to introduce appropriate correction factors, such as, for example, intestinal absorption which, as a rule, is not quantitative. Marinelli *et al.* (*26*) have demonstrated that radium sulfate that is inhaled into the human lung does not go readily into solution. This situation was analyzed, by 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 that is 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, Eq. 9 can be used to determine the amount of isotope which, if absorbed daily, can be expected 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 from Eqs. 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 strontium and calcium 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 Norris *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 life span 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 1, which include the period of childhood, were calculated on the basis of adult values and are incorrect to this extent.

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 with those discussed with reference to retention. Since radiation dosage accumulates as the product of concentration of the radioelement and time, the integrated dosage over t days, D_t, is

$$D_t = kf(R) \qquad (17)$$

where k is the radiation dosage rate per day per microcurie in the skeleton (*33*). The quantity $f(R)$ is in every case 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 Eq. 16 or, alternatively, integrate from 1 to t and add the best graphically determined estimate for the contribution from 0 to 1 day. From Eqs. 5 and 10 the appropriate values for $f(R)$ are, for single administration ($\lambda > 0$):

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

for a single administration ($\lambda = 0$):

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

for continuous administration ($\lambda \doteq 0$):

$$f(R) = \int_0^t \frac{A}{b+1}\,t^{b+1}dt = \frac{A}{(b+1)(b+2)}\,t^{b+2} \qquad (20)$$

The $f(R)$ for continuous administration with $\lambda > 0$, Eq. 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 C^{45} accumulated by continuous exposure have been calculated and included in Table 1.

In such calculations there is the major complication that bone-seeking elements, when administered over short periods of time relative to the life span, 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 to be expected that the skeleton will be uniformly radioactive (*34*), 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 of time, t, there may exist considerable differences, depending upon the mode of accumulation. This is best illustrated by comparing the two extreme cases: (i) a single administration of the bone-seeking element in such quantity that the tolerable body burden will obtain at time t, and (ii) 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, Eqs. 4 and 10 with $\lambda \doteq 0$ provide the following relationship:

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

$$q/C = t/(b+1) \qquad (21)$$

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 ($\lambda \doteq 0$) becomes:

$$\frac{D_t}{\bar{D}_t} = \frac{\frac{Aq}{b+1}\,t^{b+1}}{\frac{AC}{(b+1)(b+2)}\,t^{b+2}} = q(b+2)/Ct \qquad (22)$$

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

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

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 achieved by daily increments. This is a minimum figure since this manner of exposure necessarily results in a more uniform concentration (that is, 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 radioelements.

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.

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.

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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 percent retention of radon and its daughters in the skeleton, the total energy dissipated is 10.8×10^6 ev/disintegration. Thus assuming uniform distribution, the dose to the human skeleton (mass of 7000 g) from 1 microcurie of radium becomes:
$$k = \frac{3.7 \times 10^4 \times 8.64 \times 10^4 \times 10.8 \times 10^6}{7 \times 10^3 \times 6.24 \times 10^{11} \times 10^2} = 0.079 \text{ rad}/\mu\text{c day}.$$
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News of Science

Awards and Prizes at AAAS Meetings

To meet requests for information, an outline of the essential facts of the seven awards administered by the AAAS, and announced or presented at the annual meetings of the Association, is given here.

The Newcomb Cleveland Prize. This oldest award of the Association, originally known as the "AAAS Thousand Dollar Prize," has been administered since 1923. The donor, the late Newcomb Cleveland of New York, a life member of the Association, preferred to remain anonymous until his death in 1951. His bequest ensures the continuation of the prize, now given his name by the AAAS Board of Directors.

The Newcomb Cleveland Prize is unique in that it is given to the author(s) of a noteworthy paper, representing an outstanding contribution to science, presented in a regular session, sectional or societal, during the AAAS annual meeting. The Prize Committee, necessarily rather large, is composed of board members and others appointed by the president; their decision is reached at the end of the last day. It was always Cleveland's wish that this prize should be awarded each year to one of the younger scientists. Among the winners to date, each has received additional recognition and three have become Nobel Prize winners, in the later years indicated: Hermann J. Muller (1927) 1946; Wendell M. Stanley (1936) 1946; and I. I. Rabi (1939) 1944. The Newcomb Cleveland Prize will be awarded for the thirty-first time at this year's Washington meeting.

It is not necessary that the prize winner be a member of the Association. To be eligible a paper should consist primarily of the presentation for the first time of the results of the author's own research. Presidential and vice-presidential addresses, review papers, and comparable material that deals with either the research of others or with a review of the author's own previously published research accomplishments are not eligible. The prize committee will be listed in the 1958 General Program-Directory, available in early December.

Theobald Smith Award in Medical Sciences. The Theobald Smith Award in Medical Sciences of the AAAS was established in 1936 by Eli Lilly and Company, and will be given for the fourteenth time at this year's meeting. Again, without exception, the previous winners have received additional recognition subsequently.

The award, which consists of $1000 and a bronze medal, is given for "demonstrated research in the field of the medical sciences, taking into consideration independence of thought and originality." Travel expenses incurred in attending the AAAS meeting and receiving the medal are paid in addition. The recipient must be less than 35 years of age on 1 January of the year in which the award is to be made, and a citizen of the United States. Candidates do *not* apply for consideration but are nominated by AAAS fellows. The award is announced at the Association's annual