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PRESENT STATUS OF POLONIUM TOLERANCE ESTIMATIONS

by:

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Internal Distribution (Rochester)	
Library	98-99
Dr. A. H. Dowdy	100
Dr. Blair	101
Dr. Bale	102
Dr. Hursh	103
Dr. Stannard	104-107
Dr. Noonan	108
Mr. Casarett	109
Dr. Hodge	110
Dr. Howland	111

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TABLE OF CONTENTS

PRESENT STATUS OF POLONIUM TOLERANCE ESTIMATIONS

ABSTRACT

This report contains a summary of biological information on distribution, excretion, and toxicity of polonium; a comparison of results obtained when maximum permissible exposure rates for man are calculated from available data by different methods; and a critical evaluation of the present status of Po tolerance estimates. A maximum permissible body content of the order of 0.2 μc/70 Kg man is obtained by two methods. Applying an urinary excretion rate of 0.1% of body content/day, effective half-life of 34 days, and certain corrections for the non-exponential nature of Po excretion, maximum permissible air and water concentrations and urinary excretion rates have been computed.

Extrapolation from present data to calculations of tolerance levels in man is still difficult, and there appears to be no substitute for actual long term experiments. On the other hand, permissible exposure levels quoted herein appear to be, to a large extent, consistent with conservative practice.

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PRESENT STATUS OF POLONIUM TOLERANCE ESTIMATIONS

Maximum permissible levels for exposure to polonium were estimated in several classified letters during the period 1944-45[1-4], particular emphasis being placed upon the urinary excretion rate to be expected when the tolerance body content had been reached. In 1947, Morgan included tolerance concentrations for polonium in air and water among his calculated limits for a series of radioactive substances[5]. The methods of calculation used for these estimates are diverse and the "tolerance" values are divergent by a factor of ten or more in many instances. This spread is due in part to differences in basic assumptions, in part to the choice of biological constants. The present report will summarize the scattered material on this subject, attempt to evaluate the present tolerance levels in terms of the biological information available, and point out areas where more data should be obtained to place tolerance estimates for this substance on a firmer basis.

I. Determination of Maximum Permissible Body Content

A. Methods of Computation. Three main methods have been utilized for estimation of maximum permissible body contents of polonium. These are:

(1) Assumption of a most sensitive organ and computation of the critical concentration of radioactive material present in this organ under conditions such that the organ receives an assumed maximum permissible exposure over an indefinitely long period of time (Method 1).

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(2) Comparison of x-ray and polonium toxicity, and application of an acceptable x-ray tolerance figure (Method 2).

(3) Comparison of radium and polonium toxicity with application of an accepted maximal body content of radium (Method 3).

Each method contains elements of uncertainty as well as certain advantages, and all depend upon the validity of current tolerance levels for x-ray or radium exposure. These methods and the attendant biological information are discussed individually below.

B. Method 1 - "Most Vulnerable Organ".

(1) Description of method. Assumptions:

(a) That 0.1 r/day of x-ray or γ-radiation can be tolerated indefinitely.

(b) That, due to the greater specific ionization or α particles, an equivalent biological effect is obtained at one tenth the above level or 0.01 rep/day[7].

A convenient form for the calculation of the critical content in the most sensitive organ may be written as follows:

Let

X = Organ content in μc.

W_o = Organ weight in grams.

E = Average energy of the particle in MeV.

1 rep = 5.18×10^7 MeV/gr. tissue*.

*The roentgen equivalent physical (abbrev., rep.) is usually defined as 83 ergs per gram tissue. If this definition is employed, as done for the above calculation, it seems likely that a β-rep differs somewhat from an α-rep when compared on an ion-pair per gram tissue basis. This assumption is based upon the finding that it takes in air about 32.5 ev/(ion pair) for beta radiation as compared with 36 ev/(ion pair) for alpha and neutron radiation. If a comparable energy relation holds

Then

$$\text{Reps/day} = \frac{X \times \text{dis./}\mu\text{c/min} \times \text{min/day} \times E}{W_o \times \text{MeV/rep}},$$

or in the case of polonium for the maximum permissible content of organ

$$0.1 = \frac{X \times 2.22 \times 10^6 \times 1440 \times 5.3.}{W_o \quad 5.18 \times 10^7}$$

$$X = 3.06 \times 10^{-5} W_o.$$

To find body content corresponding to critical organ content,

$$X_B = \frac{3.27 \times 10^{-5} W_o}{\text{fraction in organ}}.$$

The above method represents in principle that employed by Morgan[2,5] for estimation of body content and limiting air and water values for polonium[2,3] as well as a number of other radioactive materials[5] and that used by Rose[4]. Body contents of the order of 0.25 μc/70 Kg man were estimated by these workers as equivalent to 0.01 rep/day to the most sensitive organ (kidney).

(2) Discussion of Method 1. It is clear that this method requires adequate biological information regarding the most vulnerable body organ and the per cent of body content contained therein. Studies on the distribution and metabolism of polonium have been reported from this laboratory[6,8-10] and pathological findings associated with these studies have been summarized[11]. Some of the distribution data on rats are reproduced in Figure 1. Of the vital body organs, kidney and lymph nodes acquire the highest con-

*cont.
for tissue, the assumption noted above would apply. However, the uncertainty involved is small (order of 10%) compared with, for instance, the uncertainty in choice of a factor of ten to allow for ion density of alpha as compared with beta radiation. For this reason and also in the interests of using the rep as a fixed dose unit, the present calculations have not attempted to apply a correction to put the dose on an ion pair/gram basis equivalent to beta doses.

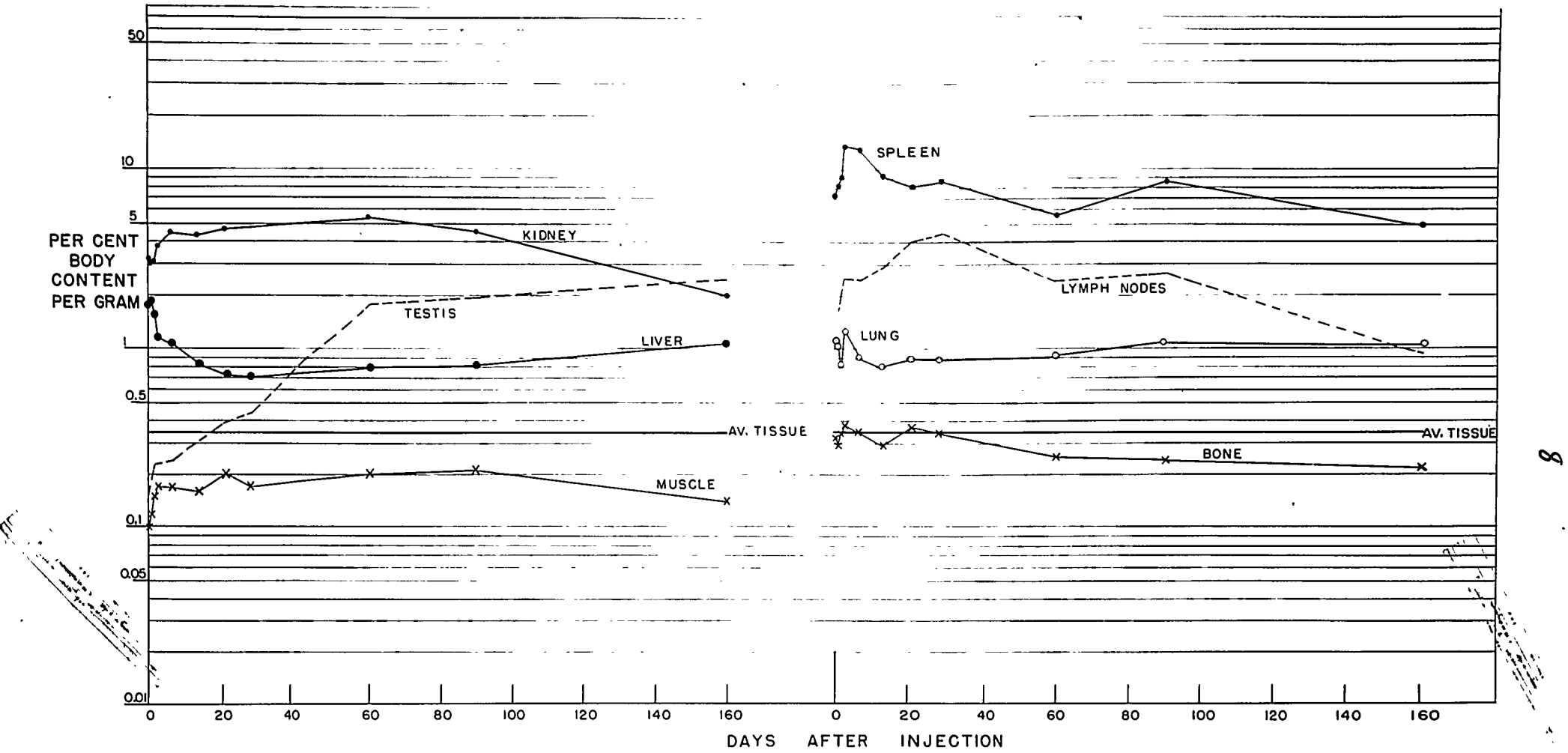

Fig. 1. Distribution of Polonium, as Per Cent of Body Content per Gram (Wet Weight), in Tissues of Rats Sacrificed Serially following Intravenous Administration of 10 to 20 Microcuries of Polonium Chloride per Kilogram

centrations of polonium.

Designation of a most vulnerable organ on the basis of its acquiring the highest concentration of radioactive material raises the question as to whether or not biological effect parallels the concentration of polonium in an organ. The following facts indicate that this may not be a simple problem:

(a) Early pathological reports indicated no significant renal damage at dosage levels which cause marked shortening of life, serious damage to hemopoietic organs and marked depression in numbers of circulating erythrocytes and leucocytes[11].

(b) More recent experiments on rats at lower dosage levels (10 and 20 μc/Kg) indicate the presence of a progressive renal lesion (apparently ischemic in type) which is more marked and more progressive at the lower dosage level. At 10 μc/Kg dose hemopoietic damage, while present, is not marked and is subject to considerable repair.

(c) The life span of rats appears to be significantly decreased at dosage levels of the order of 5 μc/Kg[10]. Complete data on pathology and blood changes are not available as yet for assay of the organ or system most affected at this level, but it appears that hemopoietic damage is negligible at this level[21].

(d) Rat testes showed marked atrophy at 10μc/Kg. Changes at 5 μc/Kg and below appear slight according to present knowledge.

The renal lesion, described in (b) above, involves a reaction whereby arteriolar walls are thickened as a result of proliferation

and swelling of endothelial cells, arteriolar lumens are narrowed, and the blood supply to the renal parenchyma probably reduced gradually. A change of this type may be inhibited at higher dosage levels or lack sufficient time to develop before death of the animal. The relation of this lesion to longevity is now under investigation. The critical lower dosage levels [cf. item (c)] must be assayed carefully because the kidney lesion might fail to appear at levels which still cause appreciable shortening of life. Thus there might result a critical dosage range above or below which the kidney may not be justifiably considered the most vulnerable organ. The lower limit, if any, of this range is the one of importance as well as variation of the kidney response with species**.

The presence of a progressive renal lesion at a dosage level (10 μc/Kg) associated with only mild or moderate changes in blood and blood-forming organs lends support to the choice of kidney as the most vulnerable organ until proven otherwise. It is clear, however, that a direct relation between organ content of polonium and biological effect cannot be assumed. There may exist critical concentration ranges for several functions, including spermatogenesis; and the relation of these ranges to the tolerance body content calculated on assumption of maximal exposures equivalent to 0.01 rep/day requires determination. Add to this the knowledge that polonium may not be distributed uniformly in many organs as revealed by auto-

---

**Preliminary pathology studies on two dogs[13] receiving 15 μc/Kg revealed marked renal damage, greater than expected from the available data on rats.

radiograph studies[10] and it is obvious that there can be no substitute for chronic exposure experiments on a variety of species.

Since there is room for doubt regarding choice of the most vulnerable organ, pending completion of adequate physiological tests, the values for tolerance body contents in man (assuming 0.01 rep/day exposure) computed on the basis of different organs being the most sensitive are gathered in Table 1. The spread in values due to differences in distribution is considerable and presents a clear indication of the need for more precise determination of the sensitivity factor. It may be useful to note, however, that, pending further investigation of organ sensitivities, use of kidney as a basis results in the lowest (and more conservative) tolerance figures, excepting use of spleen.

C. Method 2. Comparison of X-ray and Polonium Toxicity.

(1) Description of method. This method was ultilized by Bale[1] and the form of the calculation may be represented as follows:

$$\frac{\text{Daily X-ray dose lethal to 50\% animals in 20 days}}{\text{Single Polonium dose lethal to 50\% animals in 20 days}} = \frac{\text{X-ray tolerance dose (man)}}{\text{Polonium tolerance dose (man)}},$$

and the polonium tolerance dose is calculated.

Assumptions:

(a) That 0.1 r/day is a permissible exposure level for x-radiation.

(b) That the $\frac{\text{X-ray}}{\text{Polonium}}$ lethality ratio as established in animals*** is valid for man.

***Specifically rats in the data we shall consider.

Table 1

TOLERANCE TO POLONIUM BASED ON TISSUE CONTENT

Tissue	Days after Dose	Average Po Content*	Concn. Factor	Tolerance	
				Body Content**	Urinary Excretion
	Days	% Body Content/Gram		μc	d/min/24 hr sample
Spleen	10	12.2	30.5	0.083	183
	300	3.8	9.5	0.265	583
Kidney	10	5.5	13.7	0.184	405
	300	1.5	3.8	0.664	1460
Liver	10	1.8	4.5	0.560	1232
	300	0.8	2.0	1.26	2770
Bone Marrow	10	3.0	7.5	0.336	739
	300	0.5	1.3	1.94	4270
Testis	10	0.2	0.5	5.04	11090
	300	1.7	4.2	0.601	1321

*Rat data: average weight 250 grams
**70 Kg man, calculated on basis 0.01 rep/day, is equivalent to 0.036 μc/Kg if distribution were uniform.

(c) That the biological half-life of polonium is sufficiently long with respect to 20 days that the daily dose received from the injected polonium is not markedly reduced over the period of the experiment.

(d) That the relative effectiveness of x-ray radiation and the alpha radiation of polonium as signified by lethal actions remains unchanged for long time chronic exposure.

Utilizing this method and available 20-day lethality data on rats Bale[1] arrived at a tolerance body content of 2.7 μc/70 Kg man.

(2) Discussion of Method 2. The assumptions on which this method is based may be examined. Assumption (a) is common to the first two methods of calculation and is a generally accepted value. Assumption (b), i.e., that the x-ray/polonium lethality ratio as determined on rats applies to man, cannot, of course, be directly substantiated by experiment. Excretion and tissue distribution studies with polonium as carried out on man[10] show no major discrepancy when compared to similar data on rats. Such evidence may be regarded as supporting this approach. Assumption (c) is, of course, not strictly true since the biological half-life of 34 days (see page 26) for polonium is not long with respect to the 20-day span used in the calculation. This, however, is not a very serious error since the average polonium activity, taking into account excretion and decay for the 20-day period, turns out to be 71% of the amount fed as a single dose.

Assumption (d) involves the essential principle of the method and is the most difficult to assess. In an effort to test the validity

of this assumption we have compared the x-ray and polonium doses for a series of average survival times from 20 days to 300**** days. The x-ray data is taken from experiments on rats performed by Hagen and Simmons[18] and the comparable polonium data from reports of Boyd, et al[11,17].

It is clear that when such long survival times are concerned, the single initial polonium dose is not a valid measure of the day by day radiation from polonium. Accordingly, the polonium dose has been recalculated for each survival time as an equivalent average dose making allowance for excretion and radioactive decay (Table 2)†. This procedure is certainly open to the criticism that the lethal effect of a constantly diminishing dose is not necessarily equivalent to "an equivalent average dose" supplied at a lower constant level for the term of survival. However, some support for this manipulation of the data can be argued from a consideration of the degree of constancy of the equivalent total lethal dose for different survival times arrived at by multiplying the number of days average survival by the equivalent average dose as given in Table 2. It is found that the μc-days so calculated varies about twelve per cent for survival times from 20 to 200 days. This permits the cautious generalization that approximately the same amount of μc-days is required to kill a rat by polonium regardless of the rate at which the dose is administered. At least, the rate of application of the dose appears to be

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****(The polonium lethality at 300 days is subject to considerable error.)

†The procedure used was to plot the per cent activity remaining as a function of time after a single dose of polonium. Twenty day segments were cut out and weighed accurately and 0-20, 0-40, etc. segment weights were compared with the weight of a rectangular segment representing 100 % of the dose for a comparable time.

Table 2

COMPARISON OF X-RAY AND POLONIUM TOXICITY IN RATS, PLUS CALCULATED* TOLERANCE BODY CONTENT OF POLONIUM IN MAN

Average Survival Time	Dose			Dose Ratio X-Ray/Po	Tolerance Body Content
	X-Ray**	Polonium (Single Dose)	Polonium/ (Effective Av.)		
Days	r/day	μc/Kg	μc/Kg		μc/70 Kg man
20	80	45.0	31.9	2.5	2.80
40	55	27.5	16.1	3.4	2.03
60	42	22.2	11.2	3.7	1.89
80	39	20.0	8.9	4.4	1.61
100	35	18.3	7.2	4.9	1.47
200	22	13.5	3.2	6.9	1.05
300	12	9.5	1.5	8.0	.91

*$\frac{\text{X-ray lethal}}{\text{X-ray tolerance}} = \frac{\text{Polonium lethal}}{x}$; x = polonium tolerance.

**Reference 18.

/Calculated from references 11 and 17. The polonium values given are average activities calculated from single dose, rat experiments corrected for elimination and decay (see text).

less important than it is with x-radiation.

Tentatively accepting the validity of the equivalent average polonium dose, ratios of the lethal effectiveness of x-ray vs. polonium for different average survival times have been calculated and are presented in the fourth column of Table 3. It is hard to escape the conclusion that if assumption (d) is valid, the ratio of lethal effectiveness should show no change. Yet this ratio does change by a factor slightly less than 3 over the interval for which data is presented. "Maximum permissible body content" figures for polonium are presented in the fifth column of the table and show a steady decrease as calculated for increasing survival times.

It is believed that, in view of the trend of the variation of the lethal effectiveness ratio, no sound tolerance value for polonium can be arrived at by application of this method of calculation, and that values arrived at on the basis of short survival times are very likely to be high.

D. Method 3. Comparison of Radium and Polonium Toxicity.

(1) Description of method. Method 3 is in principle very similar to method 2. The form of the calculations may be represented:

$$\frac{LD_{50} \text{ for radium in 20 days}}{LD_{50} \text{ for polonium in 20 days}} = \frac{0.1\ \mu c \text{ radium}}{\text{Max. permissible body content of Po.}}$$

Assumptions:

(a) That 0.1 μc of radium in the body is the maximum permissible amount.

(b) That radium and polonium experimental lethality data as collected on rats are applicable to man.

Table 3

CALCULATION OF POLONIUM TOLERANCE ON BASIS OF TOXICITY VERSUS RADIUM*

Ratio $\frac{\text{Toxicity Po}}{\text{Toxicity Ra}}$	Tolerance Amount in Body	Tolerance Urinary Excretion Rate per Day
	μc	d/min
0.5	0.2	440
1.0	0.1	220
17	0.0059	13
28	0.0036	8
90	0.0011	2

*Assuming tolerance concentration for Ra in body = 0.1 μg.

(c) That the ratio of the effectiveness of polonium and radium as established by lethality experiments applies equally well to the production of minimal injury of the low dose chronic type.

The relative toxicities of polonium, plutonium, and radium are illustrated in Fig. 2, reproduced from data gathered in this laboratory[17]. The upper radium line represents radium of higher purity (containing less polonium) than the lower radium line. This point is discussed in detail in the original report[17], but it is clear that pure radium[//] is very much less toxic than polonium if comparison is made on the basis of lethality in less than 100 days. On the other hand, for chronic exposure, they are more nearly equal in toxicity as evidenced by the trend toward confluence (or crossing) of the radium and polonium lines in Fig. 2. If the trend illustrated should continue, radium might be actually more toxic than polonium on a long term basis.

(2) Discussion of method 3. Assumption (a) is a generally accepted figure which has been justified elsewhere[19] at some length.

Assumption (b) is not likely to be in very great error in view of the similarity of tissue distribution and excretion data for polonium in rats and man. Similar data exists for radium. It turns out that the lethal effectiveness of polonium vs. radium is, like the case

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[//] Even though commercial radium may contain appreciable amounts of polonium, it is anticipated that much the same relationships would hold except that its short term toxicity might be somewhat greater.

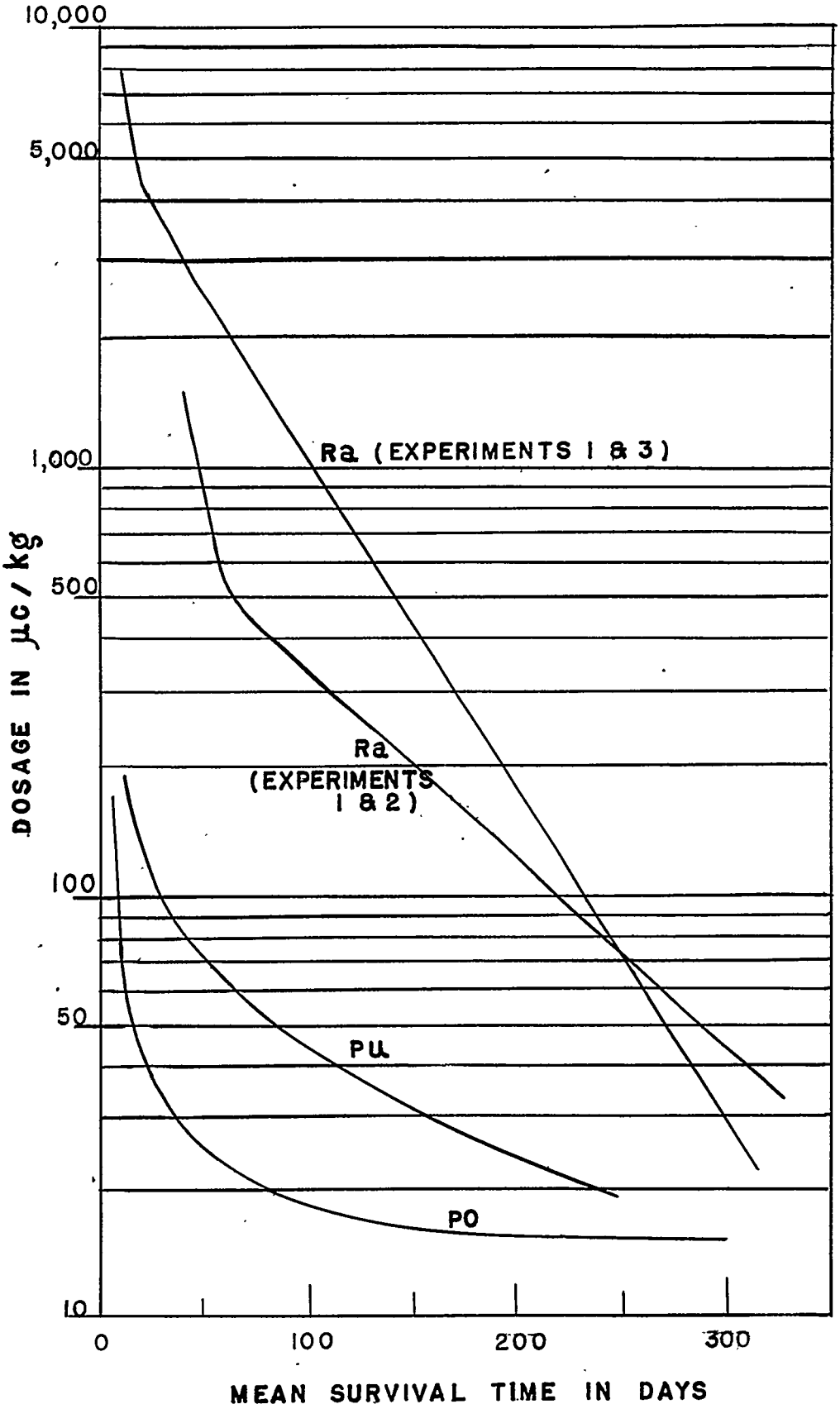


Fig. 2 Survival Time of Rats vs. Microcuries of Polonium, Plutonium, and Radium Injected per Kilogram of Body Weight

of polonium vs. x-ray, a function of the dosage level. This is true even when differences in specific activity, alpha particle range, radioactive decay, retention, and daughter products are considered[11,17], as illustrated in Fig. 3. Thus assumption (c) may not be valid, and the objections raised in regard to Method 2 may apply equally well to this method. However, an important practical difference arises from the fact that the polonium-radium lethal dose ratio is increasing with lower doses and longer survival times, thus placing tolerance calculations based on shorter times on the conservative side.

Table 3 gives tolerance body contents and urinary excretion rates (assuming 0.1 % of body content excreted/day) as a function of toxicity ratios at various times selected from Fig. 2. In view of the trend in Figures 3 and 4, a toxicity ratio of 1.0 or less is considered the most likely figure for chronic exposure and tolerance body contents of 0.1 to 0.2 μc more reasonable than the very low figures obtained at higher toxicity ratios.

E. Tolerance Body Content. The inadequacies of present data have been stressed in the sections above. On the other hand, some sort of working figure is desirable even though subject to revision. It is obvious that insufficient data are available for use of Method 2. If the most reasonable figures are selected on the basis of present information, Methods 1 and 3 yield comparable figures.

Thus, utilizing Method 1, assuming maximum exposure of 0.01 rep/day to the most sensitive organ, that kidney is the most sensitive, that normal kidneys average 300 grams per pair, and that kidney contains on the average 5% of the body content of polonium:

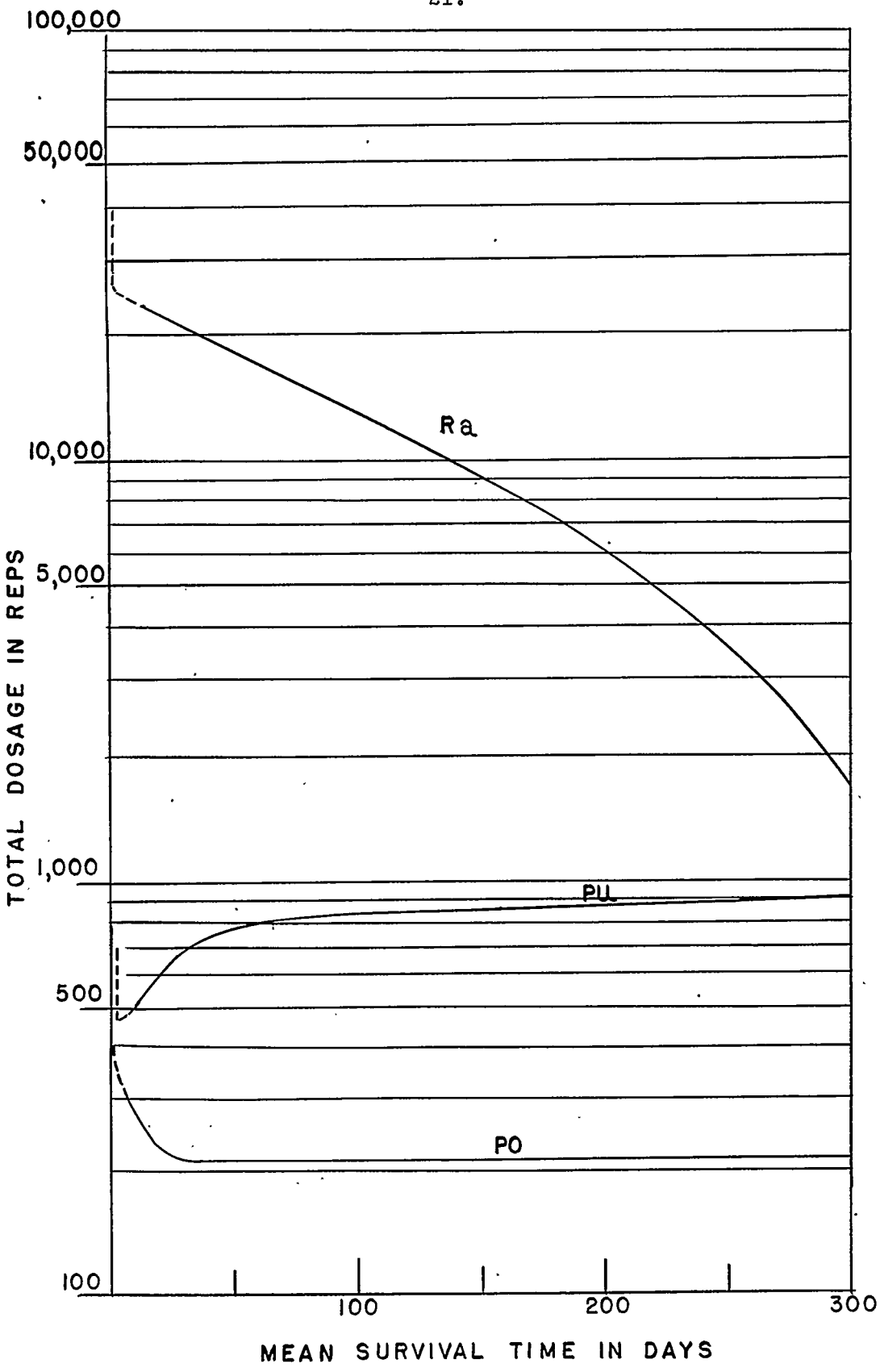
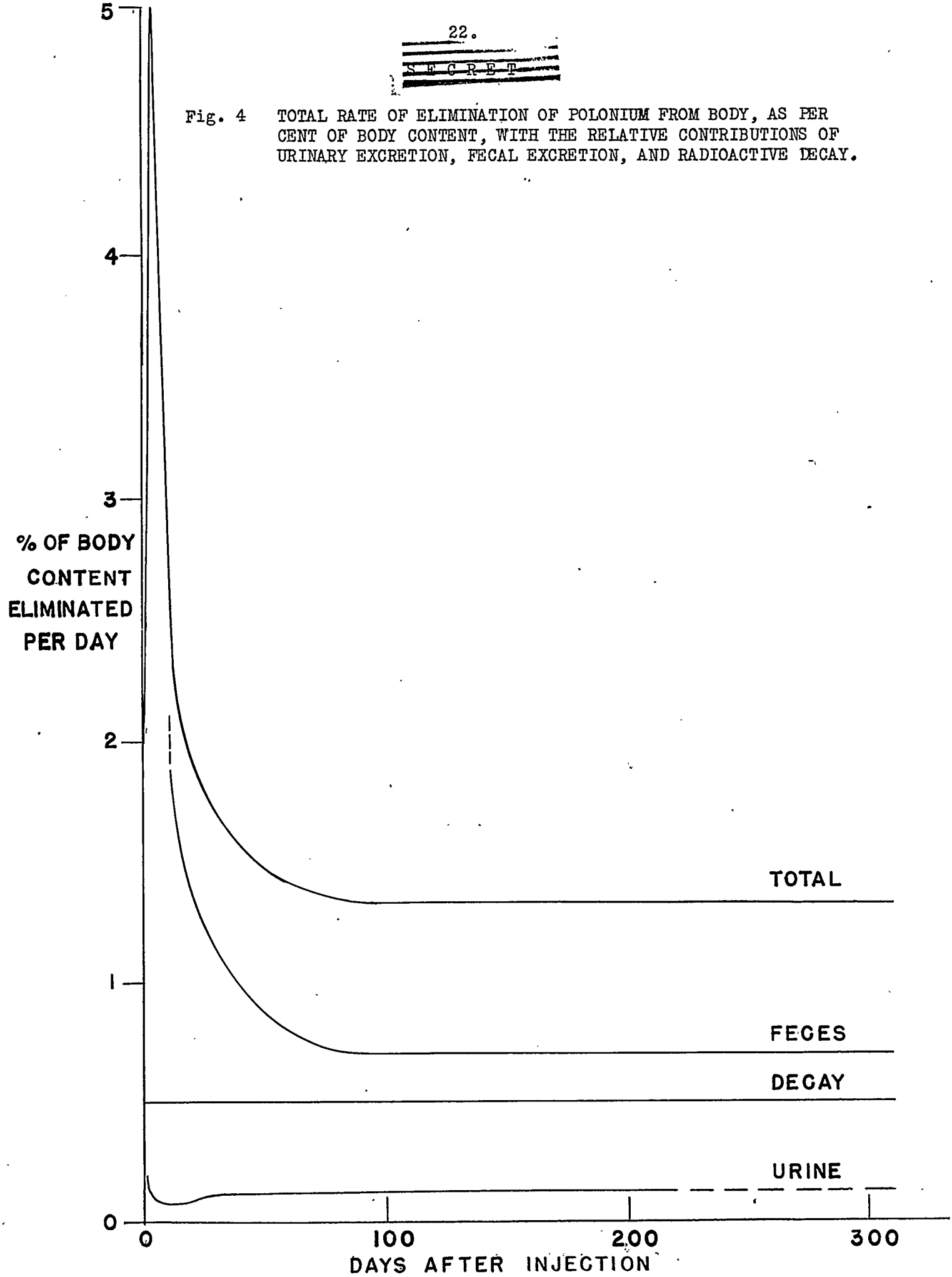


Fig. 3 Survival Time of Rats as a Function of the Total Alpha Particle Energy Dissipated in Body (Expressed as Roentgen Equivalents Physical)

Fig. 4 TOTAL RATE OF ELIMINATION OF POLONIUM FROM BODY, AS PER CENT OF BODY CONTENT, WITH THE RELATIVE CONTRIBUTIONS OF URINARY EXCRETION, FECAL EXCRETION, AND RADIOACTIVE DECAY.



$$X_B = \frac{3.27 \times 10^{-5} W_o}{\text{fraction in organ}} = \frac{3.27 \times 10^{-5} \times 300}{.05} = 0.196 \mu c.$$

Utilizing Method 3, assuming polonium and radium are equally toxic for chronic exposure, and that 0.1 μc Ra = maximumpermissible body content:

$$X_B = 0.1 \mu c \text{ Ra} = 0.1 \mu c \text{ Po}.$$

Since the toxicity of radium might actually be greater than that of polonium over long periods, a ratio of 0.5 might be chosen in which case Methods 1 and 3 would both indicate approximately 0.2 μc as the tolerance body content. This is the value chosen here for further calculations.

II. Rate of Elimination of Polonium

A. Elimination in Urine and Feces. Fig. 4 presents a composite picture of elimination rates from the metabolism experiments on rats in which the polonium was administered intravenously. In terms of per cent of body content excreted per day (in contrast to the per cent of dose commonly reported) a reasonably constant urinary excretion rate of about 0.1% per day can be estimated. Data on four human subjects[10,15,16] and three dogs[14] indicate no marked deviation in excretion rates on the average, from the rat data, but tests on one rabbit[10] indicate more rapid initial urinary excretion of polonium in this species. The cumulative effect of radiation damage on the kidney may complicate determinations of urinary excretion rates at the high dosage levels used in the animal experiments, and the human tests should perhaps be more extensive; but, as a first approximation, a urinary excretion rate value of 0.1% of the body content per day has been chosen for future computations.

The rate of elimination in the feces (and therefore the total elimination) is relatively more rapid during the first 30 days after a given dose and is, therefore, not constant with time when expressed in terms of per cent of body content. For this reason elimination of polonium from the body cannot be considered exponential.

Figure 5 indicates the total polonium excretion as a function of time along with the relative contributions of excretion and decay. This graph was calculated from material available in our files[10].

B. Effective Half-life. This parameter can be determined empirically from Fig. 5. Rats eliminate half of a single dose in about 45 days. The radioactive decay reduces this figure to 25 days.

These values differ appreciably from the 200-day elimination half-life and 82-day effective half-life quoted by Morgan[2,5]. The exact origin of these latter values is not clear to us. Tests on dogs[14] and humans[10,15,16] do not indicate wide variations in elimination rate among species.

The fact that polonium elimination is not exponential with relation to body content introduces certain complications if the empirical figure obtained from Fig. 5 is used in estimating maximum permissible concentrations in air and water. A more suitable figure for the biological half-life may be arrived at as follows. The chronic condition is considered in which the polonium content of the body remains unchanged. The polonium load carried by the individual may be regarded as made up of a number of equal single doses acquired at regular time intervals. To simplify the calculation the time interval is taken as 20 days and attention is directed to a specific 20-day

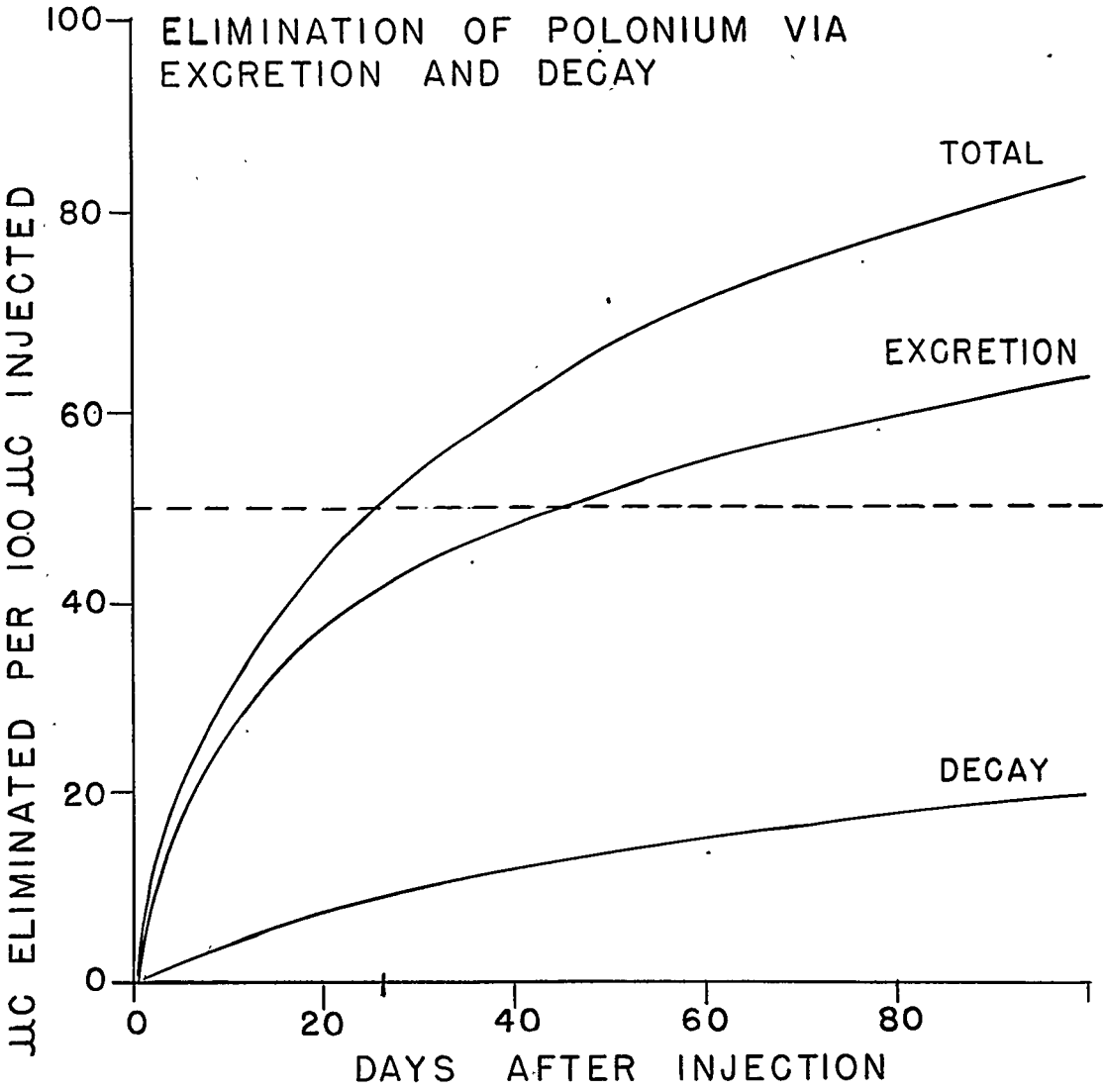


Fig. 5

interval in the course of the exposure. It is supposed that the equal doses were administered on the 1st day of this 20-day interval, on -20th day, -40 day, etc. until the -180th day. The amount of each dose that was excreted as well as the corresponding average amount of activity referred to each dose can be gotten for the specific 20-day interval. (This information can be derived from curves such as Fig. 5). With these figures an excretion rate in terms of per cent of body content per day can be arrived at for each of the doses considered. Each of the excretion figures so arrived at is weighed proportionally to the associated average body content and an effective average excretion rate determined.

When this calculation is carried out, the effective average excretion rate (i.e., expressed as if excretion were exponential) is found to be 1.52% of body content per day. If λ_B = biological "decay constant" and T_B = biological half life;

$$\lambda_B = .0152. \qquad T_B = \frac{.693}{.0152} = 45.5 \text{ days.}$$

Then effective half life (taking radioactive decay, T_R, into account as well as excretion) is:

$$\frac{T_B T_R}{T_B + T_R} = \frac{45.5 \times 140}{185.5} = 34 \text{ days.}$$

C. Tolerance Urinary Excretion Rate. If 0.2 μc is assumed as the maximum permissible body content in man and urinary excretion rate at 0.1% of body content per day, the activity in 24-hour urine samples should not exceed

$$\frac{0.2 \times 2.2 \times 10^6}{.001} = 440/\text{disintegrations/min/24 hour sample.}$$

This value is somewhat lower than some previous estimates. On the other hand, it approximates closely the value believed to be currently recommended for plant practice.

III. Permissible Intake Rates

A. General Considerations. Since decisions regarding maximum permissible levels, in peace time at least, assume the possibility of years of exposure, the establishment of equilibrium between rates of intake and output from the body can be assumed. If elimination is assumed to be logarithmic with respect to time, rates of intake would be calculated as:

$$\text{Maximal Rate} = \frac{.693 \text{ maximum permissible body content.}}{\text{effective half-life}}$$

As outlined in section II, polonium elimination is not logarithmic but can be assumed to be so without large error by adjustment of the effective half-life value. This complicates the estimates, however, since the actual exposure may be neither continuous nor in single dose. If the half-life value (34 days) calculated in Section II is employed, the critical rate becomes:

$$\frac{.693 \times 0.2}{34} = 4.08 \times 10^{-3} \mu c/\text{day} = 2.83 \times 10^{-6} \mu c/\text{min.}$$

B. Absorption from the Gut. Only the order of magnitude can be set down for this datum. Two rats fed large quantities of polonium chloride in saline absorbed 2.4% and 4.8% of the dose[8,9]. The one human subject tested absorbed "less than 10% of the theoretical dose"[16]. A value of 4% has been arbitrarily chosen for use in calculating tolerance concentrations in water.

C. Absorption from the Lungs. While several experiments on rats have

been reported[10,20] using various techniques, experimental difficulties have been serious. The report of Kimball and Fink[20] was summarized as follows:

"The data outlined here indicate that: (1) A large proportion (probably over 30% and perhaps in some cases approaching 100%) of the vaporized polonium inhaled by the rat is retained in his lungs. (2) Most of the polonium captured by the lungs is absorbed into the blood stream giving essentially the effect of an intravenous injection, and (3) sufficient polonium may be retained in the lungs for a prolonged period to produce distinct effects in that organ."

Perusal of all available data points out the need for careful, long-term studies of the absorption, toxicity, and distribution in the body of inhaled polonium. For use in tolerance calculations it has been assumed that 65% of the inhaled dose is retained by the lungs, (a rough average of available data regardless of the theoretical merits or disadvantages of each figure) and that the body tissues will received about 80% as much polonium from that retained in the lungs as from a comparable intravenous injection. These figures are arbitrary, and justified only by the fact that the over-all tolerance picture is affected relatively less by the choice of these particular biological "constants" than by, for example, choice of the most vulnerable organ or of method of calculation.

D. Permissible Concentration in Air. It is commonly assumed in industrial hygiene practice that a man engaged in light factory work ventilates his lungs at the rate of 10 liters/min. This is

1.5 to 2 times the sitting-rest average, and represents a reasonable average for an 8-hour working day. This is equivalent to 4.8 cu. meters per 8-hr. day. For 24-hr. exposure the rate will be reduced and a total of about 10 cu. meters per 24-hour day is assumed.

Since only 65% of an inhaled dose is retained, the maximum rate of intake would be:

$$4.08 \times 10^{-3}\ \mu c/day \times \frac{1}{.65} = 6.28 \times 10^{-3}\ \mu c/day^{fff}$$

or:

$$\frac{6.28 \times 10^{-3}}{10} = 6.28 \times 10^{-4}\ \mu c/cu\ meter\ air\ for$$

continuous exposure or approximately 1380 disintegrations/min/cu meter of air.

If exposure occurs during an eight hour working day, maximum permissible air concentration becomes:

$$\frac{6.28 \times 10^{-3}}{4.8} = 1.31 \times 10^{-3}\ \mu c/cu\ meter\ air$$ or approximately 2900 d/min/cu meter.

It may be that this value does not take adequate account of the possibility of long term retention of Po in the lungs. It is thus possible that damage to the lungs would be sufficient to make them the "most vulnerable organ" in certain instances. On this account, the air value calculated above may be too high, but no concrete information is available regarding lung retentions during chronic exposure, and this factor cannot be evaluated quantitatively for the present.

E. Permissible Concentration in Water. Water intake levels vary tremendously with season and conditions of work. Only an approximate

fff The absorption from the lungs is not complete but possible damage from retained polonium may well compensate for incomplete absorption.

level can be chosen. For specific applications the tolerance values can be easily altered to accommodate variations in water intake. For general use it may be assumed that about two liters will be drunk per day.

It is assumed that 4% of the polonium entering the gut reaches the blood stream and is distributed to the tissues. Thus the maximum permissible rate of intake is

$$\frac{4.08 \times 10^{-3}}{.04} = 0.1\ \mu c/day = \frac{0.1}{2000} = 5 \times 10^{-5}\ \mu c/cc,$$

or 110 d/min/cc.

F. Safety Factors. No strictly engineering safety factors have been included in the above calculations since these may vary in relation to local conditions. Biological factors such as differences in individual sensitivity, intake and elimination rates, etc. are included to a certain extent in the toxicity determinations. Account of these may be considered inherent in the conservative choices made at various points. However, it is desirable to avoid unnecessary use of "biological safety factors" which are in turn multiplied several fold by the introduction of engineering safety factors in the local situation. Thus the tolerance levels outlined above might be treated as conservative biologically but not necessarily allowing for the human factors involved in plant operation.

IV. Summary

1. A maximum permissible body content of polonium of the order of 0.2 μc/70 Kg man is obtained by two methods. One method (comparison of x-ray and polonium toxicity) yields appreciably higher values. There are adequate reasons for discaring this latter method for the

present.

2. Previous reports have been summarized and applicable biological data reproduced herein. Urinary excretion rate is about 0.1% of body content per day. Fecal excretion is more rapid initially than after 80-100 days (in rats). Elimination from the body is, therefore, not exponential with respect to time. The effective half-life for a single dose in rats is about 25 days while after about 80 days elimination proceeds as if the effective half-life were 52 days. For continuous exposure situations and assuming logarithmic behavior, a calculated value of 34 days can be applied.

3. When the body contains 0.2 μc, the urine will contain 400-500 d/min in a 24 hour sample.

4. Maximum permissible air concentrations approximate 1380 d/min/cu meter for continuous exposure and 2900 d/min/cu meter for 8-hour daily exposure.

5. Maximum permissible water content is calculated on the basis of present data as of the order of 110 d/min/cc.

6. In spite of the amount of data on polonium toxicity already gathered, critical experiments for determination of toxicity under chronic exposure conditions apparently still need to be done. The present tolerance values are, therefore, subject to revision in the future; and there appears to be no substitute for actual performance of the long-term experiment. On the other hand, tolerance values calculated from the most acceptable data at hand do not vary widely from what is understood to be present plant practice.

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