ANL-4661

May '51

Argonne National Laboratory

ON THE DETERMINATION OF RETENTION BEHAVIOR AND EXPECTED TOTAL METABOLIC EXCRETION OF RADIOISOTOPES FROM DAILY EXCRETION DATA

by

Sylvanus A. Tyler and Joan Gurian

DATE
INITIALS
Records Administrator, SGO

18-22 July 1994
Washington Federal Record Center
RG 112, Office of the Surgeon General
Department of the Army
Accession #
Box #:
File:

ARM1 940805 031

ANL-4661
Health and Biology

ARGONNE NATIONAL LABORATORY
P. O. Box 5207
Chicago 80, Illinois

ON THE DETERMINATION OF RETENTION BEHAVIOR AND EXPECTED TOTAL METABOLIC EXCRETION OF RADIO-ISOTOPES FROM DAILY EXCRETION DATA

Sylvanus A. Tyler and Joan Gurian

Biological and Medical Research Division

May 1951

Operated by The University of Chicago
under
Contract W-31-109-eng-38

18-22 July 1994
Washington Federal Record Center
RG 112, Office of the Surgeon General
Department of the Army
Accession #: 56A0198
Box #: 20
File: 700.2

Distribution	No. of Copies
Argonne National Laboratory	77
Armed Forces Special Weapons Project	1
Atomic Energy Commission, Washington	3
Battelle Memorial Institute	1
Brush Beryllium Company	1
Brookhaven National Laboratory	4
Bureau of Medicine and Surgery	1
Carbide and Carbon Chemicals Division (K-25 Plant)	4
Carbide and Carbon Chemicals Division (Y-12 Area)	4
Cleveland Area Office	1
Columbia University (J. R. Dunning)	1
Columbia University (G. Failla)	1
E. I. du Pont de Nemours and Company	5
General Electric, Richland	6
Idaho Operations Office	6
Iowa State College	2
Kellex Corporation	1
Kirtland Air Force Base	1
Knolls Atomic Power Laboratory	2
Los Alamos Scientific Laboratory	3
Mallinckrodt Chemical Works	1
Massachusetts Institute of Technology (A. R. Kaufmann)	1
Mound Laboratory	3
National Advisory Committee for Aeronautics	1
National Bureau of Standards (R. D. Huntoon)	1
Naval Medical Research Institute	1
Naval Radiological Defense Laboratory	2
New Brunswick Laboratory	1
New York Operations Office	3
North American Aviation, Inc.	1
Oak Ridge National Laboratory (X-10 Site)	10
Patent Branch, Washington	1
RAND Corporation	1
Sandia Corporation	1
Santa Fe Operations Office	1
Savannah River Operations Office	1
Sylvania Electric Products, Inc.	1
Technical Information Service, Oak Ridge	75
U. S. Geological Survey (T. B. Nolan)	1
U. S. Public Health Service	2

18-22 July 1994
Washington Federal Record Center
RG 112, Office of the Surgeon General
Department of the Army
Accession #: 56A0198
Box #: 20
File: 700.2

Distribution Continued	No. of Copies
University of California at Los Angeles	1
University of California Radiation Laboratory	6
University of Rochester	2
University of Washington	1
Western Reserve University	4
Westinghouse Electric Corporation	2

Supplementary Distribution

Dr. R. Antonelli	1
Armed Forces Institute of Pathology	1
Army Medical Library, Director	1
Atomic Energy Project, Chalk River	4
Chief of Naval Research	1
Dr. B. Harris	1
Harshaw Chemical Corporation	1
Isotopes Division (Mr. McCormick)	1
Library of Congress, Acquisition Department (J. W. Cormn)	2
Medical Research and Development Board	1
National Bureau of Standards (Library)	1
National Institute of Health	1
National Research Council, Ottawa	1
Naval Research Laboratory	1
Nevis Cyclotron Laboratories	1
Nucleonics	1
Oak Ridge Institute of Nuclear Studies	1
United Kingdom Scientific Mission (M. Greenhill)	10
USAF, Air Surgeon (Col. A. P. Gagge)	1
USAF, Director of Research and Development (Major Fred W. Bruner)	1
USAF, Wright-Patterson Air Force Base (CADO)	5
U. S. Army, Army Medical Service Graduate School (Col. W. S. Stone)	1
U. S. Army, Atomic Energy Branch (Lt. Col. A. W. Betts)	1
U. S. Army, Director of Operations Research (Dr. Ellis Johnson)	1
U. S. Army, Office of the Chief Signal Officer (Curtis T. Clayton thru Major George C. Hunt)	2
U. S. Army, Technical Command (Col. J. H. Rothschild, Attn: Technical Library)	3
University of Chicago Toxicity Laboratory	1
UT-AEC Agricultural Research Program (Charles S. Hobbs)	1
Total	298

18-22 July 1994
Washington Federal Record Center
RG 112, Office of the Surgeon General
Department of the Army
Accession #: 56A0198
Box #: 20
File: 700.2

ON THE DETERMINATION OF RETENTION BEHAVIOR AND EXPECTED TOTAL METABOLIC EXCRETION OF RADIOISOTOPES FROM DAILY EXCRETION DATA

by

Sylvanus A. Tyler and Joan Gurian

INTRODUCTION

In most research designed to investigate the excretion and retention behavior of radioisotopes injected into laboratory subjects, excretion data can be obtained with greater ease and accuracy than retention data. For this reason, it has long been the practice among investigators to derive the retention function from excretion information and to estimate the total excretion by summing excretion values over a finite set of discrete collection times. The expression,

$$E(t) = \overline{E}_1 t^b \qquad b < 0, \qquad (1)$$

where E (t) is the excretion per 24 hours via urine and/or feces after correction for decay, t is time in days from injection, and $\overline{E}_1$ and b are arbitrary constants determined from the linear, log-log regression line, is accepted by many investigators as representative of the metabolic* excretion-time behavior of injected tracer materials.[1-4] Another way by which the time-course of excretion via urine and feces can be described is by sums of exponential terms:

$$E(t) = \sum_{i=1}^{k} A_i e^{\alpha_i t} \qquad k \leq n - 1,\ \alpha_i < 0 \qquad (2)$$

where n is the total number of daily collections, and A_i and α_i are constants determined empirically. This description of excretion data more nearly coincides with the generally accepted postulates concerning the phenomenon of metabolic exchange and permits a more exact determination of the expected total excreted material from the excretion components that can be measured over the time interval investigated. The cumulative excretion and retention functions are immediately obtained.

THE PROBLEM

From daily-measured activity of the excreta, corrected for radioactive decay since administration,

1. determine on the basis of the empirical excretion trend

*Excretion corrected for decay.

18-22 July 1994
Washington Federal Record Center
RG 112, Office of the Surgeon General
Department of the Army
Accession #: 56A0198
Box #: 20
File: 700.2

established by the excretion values at n daily collection times, the expected amount of injected material that will be excreted; and

2. construct the corresponding cumulative excretion and retention functions.

For convenience, let the excretion data E_i ($i = 1, 2, \cdots n$) for the n consecutive daily collections be given in per cent of total injected material. Then describe the excretion-time trend as accurately as possible by a graphic method of fitting exponentials.*(5) Usually, the sum of two or three exponential terms is sufficient for a good fit. If expression (2) is the general excretion function, the total expected excretion (T) in per cent of the injected dose is given by the infinite sum **

$$T = \sum_{t=1}^{\infty} \left[\sum_{i=1}^{k} A_i e^{\alpha_i t} \right] = \sum_{i=1}^{k} \left[A_i e^{\alpha_i} \Big/ 1 - e^{\alpha_i} \right] \qquad (3)$$

$$k < n - 1 \,,\ \alpha_i < 0$$

and the cumulative excretion (C.E.) and retention (R(t)) functions can immediately be written.

$$\text{C.E.} = \sum_{i=1}^{k} \frac{A_1 e^{\alpha_i}}{1 - e^{\alpha_i}} \left(1 - e^{\alpha_i t}\right) \qquad (4)$$

$$R(t) = 100 - \text{C.E.} = 100 - \sum_{i=1}^{k} \frac{A_i e^{\alpha_i}}{1 - e^{\alpha_i}} \left(1 - e^{\alpha_i t}\right) \qquad (5)$$

For k = 2, expressions (2), (3), (4), and (5) become

$$E(t) = A_1 e^{\alpha_1 t} + A_2 e^{\alpha_2 t} \qquad \alpha_1, \alpha_2 < 0 \qquad (6)$$

$$T = \frac{A_1 e^{\alpha_1}}{1 - e^{\alpha_1}} + \frac{A_2 e^{\alpha_2}}{1 - e^{\alpha_2}} \qquad (7)$$

---

*The excretion values should be taken as corresponding to the day of collection since the time-points are considered as discrete.

**See appendix for derivation.

18-22 July 1994
Washington Federal Record Center
RG 112, Office of the Surgeon General
Department of the Army
Accession #: 56A0198
Box #: 20
File: 700.2

$$C.E. = \frac{A_1 e^{\alpha_1}}{1-e^{\alpha_1}}(1-e^{\alpha_1 t}) + \frac{A_2 e^{\alpha_2}}{1-e^{\alpha_2}}(1-e^{\alpha_2 t}) \tag{8}$$

$$R(t) = 100 - C.E.$$

It often happens that the first day excretion value (E_1) is considerably lower or higher than the value expected, based on the general trend of the remaining values.

$$\begin{cases} E(1) - E_1 \\ E(t) = \sum_{i=1}^{k} A_i e^{\alpha_i t}, \quad k \leq n-2, \alpha_i < 0, t = 2,3,4 \cdots \end{cases} \tag{9}$$

In this case, ignore the value of E_1 in fitting and obtain the total excretion by adding to the sum from day two on, the excretion for day one.

$$T = E_1 + \sum_{t=2}^{\infty}\left[\sum_{i=1}^{k} A_i e^{\alpha_i t}\right] = E_1 + \sum_{i=1}^{k}\left[A_i e^{2\alpha_i}/1-e^{\alpha_i}\right] \quad k \leq n-2 \quad \alpha_i < 0 \tag{10}$$

The corresponding cumulative excretion and retention functions are:

$$C.E. = E_1 + \sum_{i=1}^{k}\left[\frac{A_i e^{2\alpha_i}}{1-e^{\alpha_i}}\right]\left[1-e^{(t-1)\alpha_i}\right] \quad t = 1,2,3 \cdots \tag{11}$$

$$R(t) = 100 - E_1 - \sum_{i=1}^{k}\left[\frac{A_i e^{2\alpha_i}}{1-e^{\alpha_i}}\right]\left[1-e^{(t-1)\alpha_i}\right] \quad t = 1,2,3 \cdots \tag{12}$$

Similarly, if for s consecutive collection times beginning with the first time point, the corresponding excretion values depart markedly from the

18-22 July 1994
Washington Federal Record Center
RG 112, Office of the Surgeon General
Department of the Army
Accession #: 56A0198
Box #: 20
File: 700.2

time trend characterizing the remaining excretion values,* the total excretion is found by use of the following expression

$$T = \sum_{j=1}^{s} E_j + \sum_{i=1}^{k} \left[A_i e^{(s+1)\alpha_i} \Big/ 1 - e^{\alpha_i} \right] \quad k \leq n - s - 1 \qquad (13)$$

$$\alpha_i < 0$$

and the C.E. and R(t) functions are adjusted accordingly.

COMMENTS

The time interval over which daily excretions are usually measured is too short and the methods used for tracer detection are far from sensitive enough to reveal, quantitatively, many components that contribute to the total excreted material. Thus, the calculated T underestimates the true excretion total. Elimination of this error can only be achieved by completely analyzing the processes taking place and getting error-free data. Since satisfying these conditions is usually impossible, approximating methods, the goodness of which depends on their adherence to the known kinetics of the system investigated, must be used.

ACKNOWLEDGMENT

The writers gratefully acknowledge (1) the technical assistance rendered by Mr. W. Feurzeig and (2) the advice and criticism given by Drs. A. M. Brues, D. L. Buchanan, E. L. Powers, A. J. Finkel, and Mr. G. Sacher.

LITERATURE CITED

1. Anthony, D. K. Lathrop, and R. Finkle. 1946. Radiotoxicity of injected Sr^{89} for rats, mice and rabbits. Part II. Metabolism and organ distribution. CH-3846 (declassified).
2. Sacher, G. 1946. The excretion, retention, distribution and clinical effects of Sr^{89} in the dog. Part II. Statistical analysis of excretion and retention of Sr^{89} for individual dogs. CH-3866 (declassified).
3. Painter, E. et al. 1946. Clinical physiology of dogs injected with plutonium. CH-3858 (declassified).
4. Norris, W. P. and H. B. Evans. 1946. Studies of the metabolism and toxic action of injected radium. CH-3852 (declassified).
5. Feurzeig, W. and S. A. Tyler. 1950. A note on exponential fitting of empirical curves. Quarterly Report, Biological and Medical Divisions, Argonne National Laboratory, November, December, January, 1949-50, ed., A. M. Brues. ANL-4401 (unclassified), Pp. 14-29

*The number s << n.

18-22 July 1994
Washington Federal Record Center
RG 112, Office of the Surgeon General
Department of the Army
Accession #: 56A0198
Box #: 20
File: 700.2

APPENDIX

Given the exponential function

$$E'(t) = A' e^{\alpha' t} \qquad \alpha' < 0,\ A' \text{ a constant},\ t = \text{a positive integer} \tag{14}$$

To compute the nth partial sum

$$S_n = \sum_{t=1}^{n} E'(t) = \sum_{t=1}^{n} A' e^{\alpha' t}, \tag{15}$$

let $k = e^{\alpha'}$ and rewrite (15) in the form

$$S_n = A'k\,(1 + k + k^2 + \cdots\cdots + k^{n-1}) = \frac{A'\,k}{1-k}\,(1-k^n) \tag{16}$$

But S_n is equal to the cumulative excretion at $t = n$, thus

$$\text{C.E.} = \frac{A'\,e^{\alpha'}}{1-e^{\alpha'}}\,(1-e^{\alpha' t}) \tag{17}$$

The expected total excretion T is then

$$T = \lim_{n \to \infty} S_n = \frac{A' e^{\alpha'}}{1-e^{\alpha'}} \qquad \alpha < 0 \tag{18}$$

Similarly, for a function

$$\begin{cases} E''(1) = E''_1 \\ E''(t) = A'' e^{\alpha'' t} \end{cases} \qquad t = 2,3,4 \cdots, \tag{19}$$

the cumulative excretion function is

$$\text{C.E.} = E''_1 + \frac{A''\,e^{2\alpha''}}{1-e^{\alpha''}}\,(1-e^{(t-1)\alpha''}) \qquad t = 1,2,3,4 \cdots \tag{20}$$

18-22 July 1994
Washington Federal Record Center
RG 112, Office of the Surgeon General
Department of the Army
Accession #: 56A0198
Box #: 20
File: 700.2

and the expected total excretion (T) becomes

$$T = E_1'' + \frac{A'' e^{2\alpha''}}{1-e^{\alpha''}} \tag{21}$$

By applying these results and recalling the algebra of convergent series, the expressions for C.E. and T, associated with excretion functions expressed as sums of exponential terms, are easily obtained.

a. For $E(t) = \sum_{j=1}^{v} A_j e^{\alpha_j t}$ $\quad$ t = a positive integer, $\alpha_j < 0$, (22)

$$C.E. = \sum_{j=1}^{v} \frac{A_j e^{\alpha_j}}{1-e^{\alpha_j}} (1-e^{\alpha_j t}) \tag{23}$$

$$T = \sum_{j=1}^{v} \frac{A_j e^{\alpha_j}}{1-e^{\alpha_j}} \tag{24}$$

b. For
$$\begin{cases} E(1) = E_1 \\ E(t) = \sum_{i=1}^{m} A_i e^{\alpha_i t} \quad t = \text{a positive integer} > 1, \\ \qquad \alpha_i < 0 , \end{cases} \tag{25}$$

$$C.E. = E_1 + \sum_{i=1}^{m} \frac{A_i e^{2\alpha_i}}{1-e^{\alpha_i}} (1-e^{(t-1)\alpha_i}) \tag{26}$$

$$T = E_1 + \sum_{i=1}^{m} \frac{A_i e^{2\alpha_i}}{1-e^{\alpha_i}} \tag{27}$$

18-22 July 1994
Washington Federal Record Center
RG 112, Office of the Surgeon General
Department of the Army
Accession #: 56A0198
Box #: 20
File: 700.2