INTAKE RETENTION FUNCTIONS AND THEIR APPLICATIONS TO BIOASSAY AND THE ESTIMATION OF INTERNAL RADIATION DOSES

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INTRODUCTION

Intake retention functions that give the fraction of an intake expected to be present in a specified in vivo or in vitro bioassay compartment at any time after a single acute exposure or after the onset of a continuous exposure are needed for the proper design and conduct of bioassay programs. This paper summarizes the derivation of these functions from a multicompartmental model and a recursive catenary kinetics equation that completely describe the metabolism of radioelements from intake to excretion, accounting for the delay in uptake from compartments in the respiratory and gastrointestinal tracts and the recycling of radioelements between systemic compartments. Because the metabolic model of a worker will not in general be known and because bioassay data from an exposed worker generally is not sufficient to obtain the worker's model, we recommend that ICRP Publication 30 or any other appropriate metabolic models or excretion functions be used to obtain parameter values for our model. In a separate paper we show how to transform a known excretion function into a pseudo systemic uptake retention function and pseudo constant fraction of systemic excretion, which then can be incorporated into our model and algorithm directly[1]. The estimation of intakes and internal radiation doses and the use of intake retention functions in the design of bioassay programs are discussed along with several examples in the oral presentation of this paper at the 7th IRPA Congress.

MODEL DESCRIPTION

The multicompartmental model describing the metabolism is depicted in Figure 1 by various one-way catenary pathways from intake to excretion. Intake pathways can include, for example, inhalation, ingestion, and absorption from a wound. The word catenary refers to a chain of compartments, and a one-way catenary system means one in which the radioelement is modeled to move in only one direction. The last compartment of all catenary systems is designated in Figure 1 as the 'total excretion compartment', which may be thought of as a 'bucket' where all excretion is collected. Although only one-way transfers between compartments are depicted, the model does in fact account for the recycling of elements between systemic compartments by use of a systemic uptake retention function for the whole body whose parameter values incorporate this recycling. This function is shown at the bottom of Figure 1 as a sum of m exponential terms. The word compartment is used in its mathematical sense, and it may or may not represent a real structured physiological entity in the body.

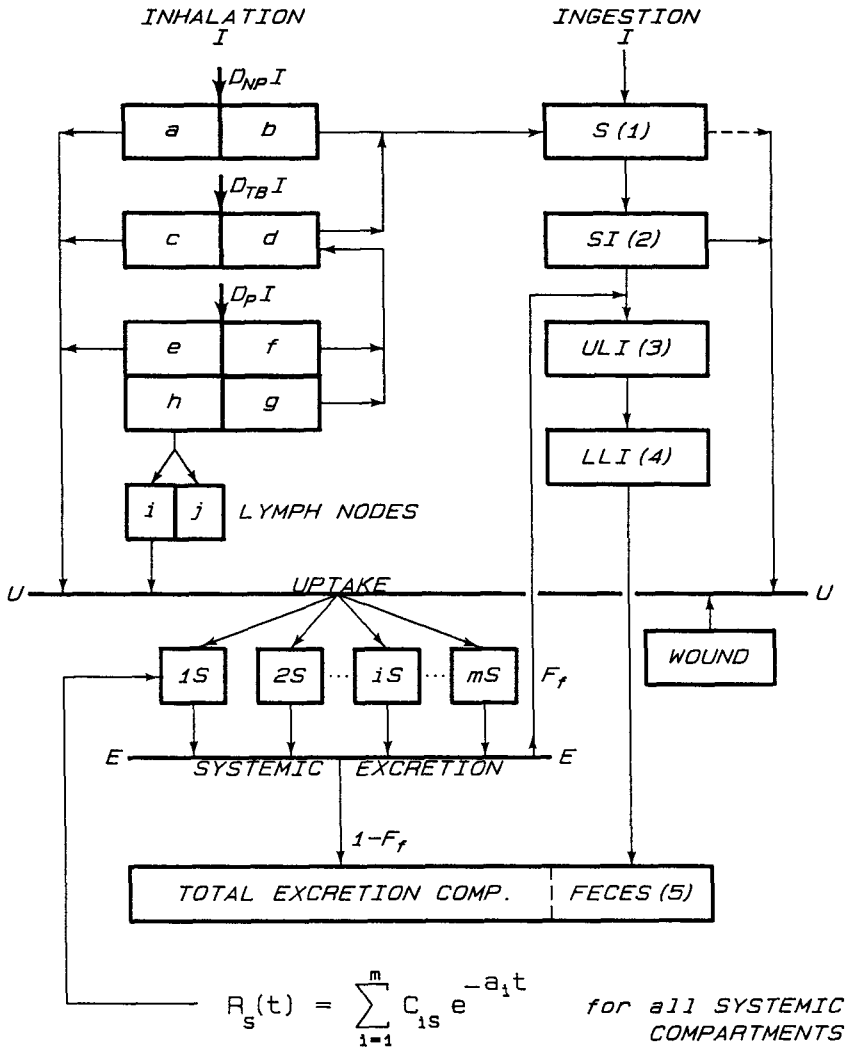

Figure 1. Catenary pathways from intake to excretion. Respiratory tract compartments are 'a' to 'j' inclusive. Gastrointestinal tract compartments are 1 to 4. The stable element uptake retention function $R_S(t)$ for the whole body is given by a sum (i=1 to m) of exponential terms with constant coefficients C_{iS}, which give the effective fractions of an uptake U that deposit in each ith systemic compartment. Each ith exponential $\exp(-a_i t)$ of $R_S(t)$ is treated as a deposition retention function of a systemic catenary compartment, which is cleared directly to systemic excretion E at an instantaneous fractional rate given by the eigenvalue or effective rate constant a_i of the exponential term. The fractions F_f and $(1-F_f)$ are the effective fractions of systemic excretion by the fecal and all other excretion pathways respectively.

Arrows in Figure 1 shown leaving a compartment indicate the specific compartmental biological removal pathways, each of which is characterized by a specific biological translocation rate constant. In addition, radioactive elements are removed from each compartment by radioactive decay, which is implicit and characterized by the decay constant λ of the particular radioelement. Because the metabolism can be described in terms of simple one-way transfers between compartments composing various catenary systems, the recursive catenary kinetics expression shown below by Equation 1 can be used to obtain explicit equations for the fraction of an intake expected to be present in all in vivo and in vitro bioassay compartments of interest. Although this description of the metabolism may seem oversimplified, it is mathematically consistent with more sophisticated models that rely on the use of convolution integrals for predicting the contents of systemic and excretion compartments following intakes.

CATENARY KINETICS EQUATION

By application of the following catenary kinetics equation to the model depicted in Figure 1, the fraction of an intake I expected to be present in an in vivo or an in vitro (i.e., accumulated excretion) compartment of interest is obtained:

$$i_n(t) = \sum_C F_C \prod_{p=1}^{n-1} k_{p,p+1} \sum_{j=1}^{n} \frac{\exp(-k_j t)}{\prod_{\substack{p=1 \\ p \neq j}}^{n} (k_p - k_j)} \qquad (1)$$

where:

$i_n(t) = \langle q_n(t) \rangle / I$ = fraction of acute intake I of radioelement expected to be present at time t in nth compartment as a result of contributions from all chains C,

$\langle q_n(t) \rangle$ = expected content of radioelement in nth compartment,

F_C = fraction of intake deposited in first compartment of chain C,

$k_{p,p+1}$ = rate constant giving the instantaneous fraction of the content of compartment p translocated per unit time to the (p+1)th compartment,

k_j = rate constant describing total removal of radioelement from jth compartment and given by $K_j + \lambda$, where K_j is the total of all biological translocation rate constants and λ is the decay constant, and

n = numerical index for that catenary compartment in chain C whose intake retention function is being obtained.

After values are substituted for the deposition fractions

F_C and rate constants in Equation 1, factors are multiplied, and the resulting coefficients of common exponential terms are added, then the intake retention function is expressed by a simple sum of exponential terms with constant coefficients. The coefficients are independent of the decay constant or half-life of the radioelement; so, they also apply to the intake retention function for the stable element, which can be obtained from Equation 1 by replacing each total removal rate constant k_j in each exponential by the total biological removal rate constant K_j.

OTHER INTAKE RETENTION FUNCTIONS

By applying the general catenary kinetics equation to the appropriate chains in Figure 1, single acute inhalation intake retention functions can be obtained for specific organs, organ systems, and excretion by summing the functions for the appropriate compartments. This includes: (1) the nasal passage (compartments a and b), (2) the lungs (compartments c-j), (3) the GI tract (compartments 1-4), (4) the systemic whole body (compartments 1S-mS), (5) a specific systemic organ x, e.g., the thyroid, by replacing $R_S(t)$ in Figure 1 by the organ's stable element uptake retention function $R_x(t)$ expressed by a sum of m exponential terms with constant coefficients (compartments 1x-mx), (6) accumulated total systemic excretion (compartment E), (7) accumulated total fecal excretion (compartment 5), (8) accumulated urinary excretion (F_u times the intake retention function for compartment E if F_u is constant or if a pseudo function $R_S(t)$ and pseudo constant F_u value are used), and (9) the total body (the sum of (1) - (4) above).

Once the single acute intake retention functions have been determined for the radioelement, other functions such as continuous intake functions, incremental excretion intake functions for single or continuous intakes, excretion rate intake functions for single or continuous intakes, and functions that yield the number of disintegrations in any *in vivo* compartment can be obtained by simply replacing the exponentials in the terms for the single intake functions by another time function. We have summarized these replacement functions and have discussed their applications in a more detailed manuscript of the subject of this paper, which we will provide upon request.

REFERENCES

1. K.W. Skrable, L.C. Sun, G.E. Chabot, C.S. French, and T.R. LaBone, "Pseudo Uptake Retention Functions for the Whole Body for Estimating Intakes from Excretion Bioassay Data", Radiation Protection Dosimetry 18(3), 133-139 (1987).