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COMPARTMENT MODELS OF RADIOIODINE IN MAN

by

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Modèles de compartiments de radio-iode chez l'homme

par

J.R. Johnson

Résumé

Les équations différentielles qui régissent l'écoulement de l'iode au travers d'un modèle à trois compartiments du métabolisme de l'iode chez l'homme ont été résolues et les solutions comparées à celles obtenues au moyen de modèles à deux compartiments. Les conditions limites utilisées ont été celles appropriées pour une seule exposition très forte au radio-iode. L'équation d'excrétion urinaire établie à partir des solutions obtenues pour le modèle à trois compartiments comporte un minimum, quatre jours après le temps d'exposition. Ce minimum peut servir à calculer une valeur maximale pour la charge de la thyroïde en ayant recours à une seule mesure de débit d'excrétion urinaire et en conjonction avec cette valeur il est possible de calculer une fréquence d'échantillonnage urinaire optimale pour les différentes espèces de radio-iode.

L'Energie Atomique du Canada, Limitée
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<u>ABSTRACT</u>

The differential equations governing the flow of iodine through a three-compartment model of iodine metabolism in man have been solved and the solutions compared to those obtained from two-compartment models. The boundary conditions used were those appropriate for a single acute exposure to radioiodine. The urinary excretion equation derived from the solutions to the three-compartment model exhibits a minimum at four days after the exposure time. This minimum can be used to calculate a maximum value for thyroid burden using a single urinary excretion rate measurement, and in conjunction with this value, an optimum urinary sampling frequency for the different radioiodines can be calculated.

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AECL-5244

TABLE OF CONTENTS

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1. INTRODUCTION

Compartmental analysis[1], as applied to biological systems, is a method of analysing the flow of a particular material through a complex system by dividing it into a group of N interconnected subsystems, or compartments. Each of these compartments has, at most, 2(N-1) routes by which the material can be transferred between compartments, and a small number (usually 0 or 1) of routes by which the material can enter or leave the system. This method has mathematical simplicity if the assumptions are made that material flow in each route is proportional to the amount of material in the compartment the material is leaving, and that material can only flow one way in any given route.

The flow of material through the system can then be described by a set of ordinary differential equations

$$\frac{dy_i(t)}{dt} = \sum_{j=1}^{N} a_{ji} y_j(t) + x_i(t) \qquad (1)$$

where $y_i(t)$ is the amount of the material in compartment i at time t, $x_i(t)$ is the rate of input into compartment i from outside the system, a_{ji} is the rate constant (λ_{ji}) for material flow from j to i, and a_{ii} is defined as the negative sum of all rate constants for material leaving compartment i, that is

$$a_{ii} = -\sum_{j=1}^{N} \lambda_{ij}$$

The set of equations (1) has general solutions given by

$$y_i(t) = \sum_{j=1}^{N} b_{ij} e^{C_j t} \quad (2)$$

where b_{ij} and C_j are functions of the λ_{ij} and the $x_j(t)$.

The total rate of material entering the system is

$$X(t) = \sum_{i=1}^{N} x_i(t) \quad (3)$$

and that leaving the system

$$E(t) = X(t) - \sum_{i=1}^{N} \frac{dy_i(t)}{dt} \quad (4)$$

It follows from the form of equation (2) that for any system that can be described in this manner, solutions can be found to any degree of accuracy required, simply by increasing the number of compartments used to describe the system. In practice however, the usefulness of this methodology is limited to systems that can be described adequately by a small number of compartments for which the rate constants can be determined, either directly or indirectly.

The metabolism of iodine in man has been described by a three-compartment model [2]. These compartments are

1) Inorganic compartment, consisting of all extra-thyroidal iodine that is not bound to thyroid-produced organic molecules and which may be excreted or taken up by the thyroid for conversion into organic iodine.
2) Thyroid compartment, consisting of all iodine in the thyroid.
3) Organic compartment, consisting of all extra-thyroidal iodine bound to thyroid-produced organic molecules and capable of being excreted or being converted back to inorganic iodine.

This three compartment model is described in more detail below, and the solutions of the differential equations (solved using boundary conditions appropriate to a single instantaneous input of radioactive iodine into the inorganic compartment) are compared to two simplified models, each consisting of two compartments. The equations derived from one of these simplified models are similar to the retention and excretion equations recommended by the International Commission on Radiological Protection [3] (ICRP), which are also compared to the solutions of the three-compartment model.

The decay of radioiodine has not been included in the following equations. It can be included simply by multiplying all solutions by $\exp(-\lambda_r t)$, where λ_r is the appropriate decay constant for the radioactive iodine being considered.

2. SOLUTIONS TO THE MODELS' DIFFERENTIAL EQUATIONS

A. The Three Compartment Model

The three-compartment model used is shown in Figure 1. Excretion by exhalation and perspiration, and in faeces have been ignored in this model as these routes represent at most a few percent of the total excretion[2] and their inclusion would not change the solutions appreciably. The values of the rate constants given in Table 1 were calculated from the values from Table 3 of reference 2. They are "illustrative values for normal persons"; that is, they are mid-range values for persons having a normal thyroid function found by measuring the steady-state values for stable iodine in persons whose iodine intake was maintained at a constant value.

The differential equations for this model are

Inorganic compartment

$$\frac{dI(t)}{dt} = -(\lambda_1+\lambda_2)\ I(t) + \lambda_4 O(t) + X(t) \qquad (5)$$

Thyroidal compartment

$$\frac{dT(t)}{dt} = \lambda_1 I(t) - \lambda_3 T(t) \tag{6}$$

Organic compartment

$$\frac{dO(t)}{dt} = \lambda_3 T(t) - (\lambda_5 + \lambda_4) O(t) \tag{7}$$

Urinary Excretion Rate

$$E_u(t) = X(t) - \frac{dI}{dt} - \frac{dT}{dt} - \frac{dO}{dt}$$

$$= \lambda_2 I(t) + \lambda_5 O(t) \tag{8}$$

The analytical solutions (see Appendix) to these equations, using the constants from Table 1 and the boundary conditions

$$\begin{aligned} X(t) &= 0 \\ I(0) &= I_o \\ T(0) &= O(0) = 0 \end{aligned} \tag{9}$$

are

$$I(t) = I_o \left[1.000\ e^{-2.85t} - 9.86 \times 10^{-4}\ e^{-0.0609t} + 9.45 \times 10^{-4}\ e^{-0.00586t} \right] \tag{10}$$

$$T(t) = I_o \left[-0.327\ e^{-2.85t} + 0.0175\ e^{-0.0609t} + 0.310\ e^{-0.00586t} \right] \tag{11}$$

$$O(t) = I_o \left[0.0010\ e^{-2.85t} - 0.0517\ e^{-0.0609t} + 0.0507\ e^{-0.00586t} \right] \tag{12}$$

$$E_u(t) = I_o \left[1.92\ e^{-2.85t} - 2.15 \times 10^{-3}\ e^{-0.0609t} + 2.07 \times 10^{-3}\ e^{-0.00586t} \right] \tag{13}$$

B. Two-Compartment Models

Two possible two-compartment models that can be used to approximate the three-compartment model are shown in figures 2 and 3.

1. Short-Term Model

This model is constructed by ignoring the organic compartment. Its differential equations are

$$\frac{dI(t)}{dt} = -(\lambda_1+\lambda_2)I(t) + \lambda_3(1-p)T(t) + X(t) \qquad (14)$$

$$\frac{dT(t)}{dt} = -\lambda_3 T(t) + \lambda_1 I(t) \qquad (15)$$

$$E_u(t) = \lambda_2 I(t) + p\lambda_3 T(t) \qquad (16)$$

where $p = \lambda_5/(\lambda_4+\lambda_5)$

The analytical solutions to these equations, using the boundary conditions (9) and the constants from Table 1 are

$$I(t) = I_o \left[0.999e^{-2.85} + 9.14x10^{-4}e^{-0.00609t}\right] \qquad (17)$$

$$T(t) = 0.326I_o \left[e^{-0.00609t} - e^{-2.85t}\right] \qquad (18)$$

$$E_u(t) = I_o \left[1.92e^{-2.85t} + 2.0x10^{-3}e^{-0.00609t}\right] \qquad (19)$$

2. Long-Term Model

This model is constructed by ignoring the inorganic compartment. Its differential equations are

$$\frac{dT(t)}{dt} = (1-q)\ \lambda_4 O(t) - \lambda_3 T(t) + X(t) \qquad (20)$$

$$\frac{dO(t)}{dt} = -(\lambda_4+\lambda_5)O(t) + \lambda_3 T(t) \qquad (21)$$

$$E_u(t) = (q\lambda_4+\lambda_5)O(t) \quad (22)$$

where $q = \lambda_2/(\lambda_1+\lambda_2)$

The solutions to these equations, using the boundary conditions

$$T(0) = (1-q)I_o = \frac{\lambda_1}{\lambda_1+\lambda_2} I_o \quad (23)$$

$$O(0) = 0$$

and the constants of Table 1, are

$$T(t) = I_o \left[0.017e^{-0.0609t} + 0.309e^{-0.00582t}\right] \quad (24)$$

$$O(t) = 0.0515\ I_o \left[e^{-0.00582t} - e^{-0.0609t}\right] \quad (25)$$

$$E_u(t) = 0.0407\ O(t) \quad (26)$$

3. ICRP-10 Equations

The equations recommended by the ICRP for use in cases of acute ("instantaneous") occupational exposure to radioiodine are for retention

$$R(t) = I_o \left[0.7e^{-1.98t} + 0.3\ e^{-0.00693t}\right] \quad (27)$$

and for urinary excretion

$$Y(t) = I_o \left[1.4\ e^{-1.98t} + 2\text{x}10^{-3} e^{-0.00693t}\right] \quad (28)$$

The constants in these equations are those which best approximated the available data using two-exponential functions to describe retention following acute occupational exposures. As such they are not expected to give the same results as the three-compartment model or even the short-term model, as acute occupational exposures will seldom result in a significant instantaneous input of the radioiodine into the inorganic compartment. However, for times greater than a few days post exposure, the shapes of the total retention and excretion functions should be similar to the three-compartment model solutions, assuming that the three compartment model adequately describes the metabolism of iodine in man.

It should be noted that equations 27 and 28 could also be derived using a two-compartment model consisting of inorganic and thyroidal compartments without an interconnecting route, and with 70% of I_o going instantaneously to the inorganic compartment and 30% to the thyroidal compartment*. The solutions to this model are

$$I(t) = 0.7\ I_o e^{-1.98t} \qquad (29)$$

$$T(t) = 0.3\ I_o e^{-0.00693t} \qquad (30)$$

and $E_u(t)$ is given by equation 28.

The solutions to the above models have been plotted in Figures 4, 5 and 6 to facilitate comparison between them.

* The ICRP did not intend that this interpretation should be attached to their equations (C.G. Stewart; private communication).

3. RELEVANCE OF THE MODELS TO RADIATION PROTECTION PROCEDURES

A. General Discussion

The ICRP considers the thyroid to be the critical organ for occupational exposure to soluble radioiodine [4]. If soluble radioiodine is inhaled or ingested the ability of the thyroid to concentrate and store iodine results in the dose to the thyroid being a larger fraction of the allowable dose than that to any other organ, or to the whole body. It is therefore the amount of radioiodine in the thyroid, and its retention, which is of primary interest to those concerned with radiation protection from radioiodine exposure.

Figure 5 compares the amount of radioiodine in the thyroid (the thyroid "burden") as a function of time after an acute exposure for the four models discussed above. It can be seen that for times longer than two days post exposure, there is little to choose between the models. The difference in the retentions given by the models is less than that expected from the difference in the rate constants between individuals.

It is possible to directly measure the thyroid burden using a standard NaI(Tl) crystal and multichannel analyser system. The limit of detection with such a system will depend on the iodine isotope and the characteristics of the measuring system but values less than one one-thousandth of the maximum permissible thyroid burden [4] for the iodine radionuclides of practical interest should be readily measurable. It is not usually convenient to measure a worker's thyroid burden as a function of time every time he is suspected of being exposed to radioiodine. What is usually done is to set a secondary standard for the maximum daily urinary excretion of radioiodine and require that workers submit urine samples for analysis when exposures are suspected. This secondary standard is set by using some derived or measured relationship between thyroid burden and urinary excretion rate, with a suitable safety factor, to insure that the thyroid burden is less than an agreed upon maximum for any conditions of exposure. This secondary standard is usually called an action level or investigation level and if it is exceeded, follow-up urine analysis, or direct iodine in thyroid measurements, and often both, are performed to evaluate the worker's thyroid burden.

It is clear from examining the shape of the solution to the three-compartment model for urinary excretion rate (Figure 6) that a two-compartment model, or a two-exponential phenomenological equation (ICRP-10), cannot describe urinary excretion of radioiodine for all times after an exposure. A minimum of two two-compartment models is required, each suitable for a different time region.

If the thyroid burden were to be estimated from urinary excretion data obtained on, say, the sixth day after the exposure occurred using either the short-term model or the ICRP equations, the thyroid burden could easily be underestimated by a factor of four, whereas the long-term model would give a very good e-timate of the thyroid burden (assuming of course that the rate constants used adequately describe the individual's iodine metabolism).

The most conservative action level that can be derived for a single urine sample would be to use the urinary excretion rate at four days post exposure to calculate the initial uptake I_o. This uptake will be a maximum provided the urinary excretion rate is corrected for radioactive decay and that the sample is collected soon enough after the exposure that the excretion rate has not decreased, due to radioactive decay of the radioiodine and/or due to the third term in equation 13, below the minimum at the fourth day after exposure. This maximum initial uptake can be used to calculate a maximum thyroid dose, as demonstrated below.

B. Examples Using ^{131}I

1. Time of Exposure and Initial Body Burden from Two Urine Samples

Suppose a urine sample was analysed that contained an amount A of ^{131}I which was in excess of the action level. A second sample was asked for but due to circumstances beyond the control of the analyst it was not obtained until three days after the first. It was found to contain an amount B of ^{131}I, and the decay corrected ratio of A to B is 10; i.e.

$$\frac{A}{B} \exp\left[\frac{-3\ell n2}{t_{1/2}}\right] = 10$$

$t_{1/2}$ = 8.05 days for ^{131}I

From examination of Figure 6, the ICRP equations would give an exposure time of approximately 2 days before sample A was collected and an initial estimate of the ^{131}I total burden of $I_o \simeq A \exp\left[\frac{2\ell n2}{8.05}\right] / 0.03$. The three-compartment model would give approximately the same time for the exposure but would estimate I_o as $I_o \simeq A \exp\left[\frac{2\ln 2}{8.05}\right]/0.006$, or a factor of five greater than the ICRP estimate.

While it would be unusual indeed to base the calculations of dose to the thyroid on only two urine samples where more urinary excretion data and/or direct thyroid burden measurements may be easily acquired, it is a common practice to evaluate the seriousness of an exposure case for possible future action by using the ICRP equations. Use of these equations, within a particular time interval, can easily underestimate the thyroid burden by a factor of five. Unless the size of a safety factor in the secondary standard over and above that required to account for the variability of an individual's rate constant is large enough to include this factor, or unless the three compartment model is used to derive the secondary standard, some exposures that should have been evaluated by direct thyroid measurements could have been ignored because they have been assumed to be below a significant level.

2. <u>Maximum Initial Body Burden from a Single Urine Sample</u>

The maximum initial body burden can be calculated using a single urine sample under certain conditions. The urinary excretion rate on day four post exposure is a minimum; if I_o', the initial body burden, is calculated assuming the sample was collected on day four, I_o' will be the maximum value I_o^{max}, provided that

$$\frac{E_u(t)}{E_u(4)} \times \frac{\exp(-\lambda_r t)}{\exp(-\lambda_r 4)} \geq 1 \qquad (31)$$

where λ_r is the radioactive decay constant.

That is, if the increase in the urinary excretion rate for times greater than t=4 days is greater than the decrease in the amount of material excreted due to radioactive decay, then up to a time t_{max} during which this is true, I'_o will be a maximum.

Equation 31 can be rewritten as

$$t \leq 4 + \frac{1}{\lambda_r} \ln \left[\frac{E_u(t)}{E_u(4)} \right] = t_{max} \qquad (32)$$

The values of $E_u(t)$ are obtained from the solutions to the three-compartment model and can be calculated from equation 13.

For ^{131}I equation 32 becomes

$$t_{max} = 4 + 11.6 \ln \left[\frac{E_u(t)}{E_u(4)} \right]$$

$$= 17 \text{ days}$$

$$\left[\begin{array}{l} \text{For } ^{125}\text{I } (t_{1/2} = 60 \text{ days}) \; t_{max} = 120 \text{ days} \\ \text{For } ^{133}\text{I } (t_{1/2} = 0.87 \text{ days}) \; t_{max} = 4 \text{ days} \end{array} \right]$$

Therefore for ^{131}I, a sampling frequency of one urine sample every 17 days is sufficient to insure that, if the urinary excretion rate is below some value, say U_{max}, then its initial uptake I_o, must be below I_{max},

where

$$I_{max} = \frac{U_{max} e^{\lambda_r 4}}{E_u(4)/I_o} \qquad (33)$$

and $E_u(4)/I_o$ can be obtained from equation 13 or figure 6.

The dose to the thyroid from an initial uptake of I_{max} of radioiodine is

$$Q_{max} = \int_0^{\infty} e^{-\lambda_r t} T_{max}(t)\, dt \ (\mu Ci\text{-days})$$

where $T_{max}(t)$ is obtained from equation 11 with I_{max} replacing I_o. Then

$$Q_{max} = \frac{U_{max} e^{\lambda_r 4}}{E_u(4)/I_o} \left[\frac{-0.327}{\lambda_r+2.85} + \frac{0.0175}{\lambda_r+0.0609} + \frac{0.310}{\lambda_r+0.00586} \right]$$

For ^{131}I ($\lambda_r = 0.0861$ day^{-1})

$$Q_{max} = \frac{U_{max} x1.41}{3.58x10^{-4}} \quad 3.38$$

$$= 1.33x10^4\ U_{max} (\mu Ci\text{-days})$$

for U_{max} in µCi/day.

The maximum dose in rem is

$$D_{max} = 51.2\ Q_{max} E/m$$

where 51.2 is the factor for converting from µCi-days to rem if E, the effective energy, is in MeV and m, the mass of the organ, is in grams. Using values for ^{131}I in the thyroid from reference 4, D_{max} becomes

$$D_{max} = 51.2 \times 1.33x10^4\ U_{max} \times \frac{0.23}{20}\ (\text{rem})$$

$$= 7.84x10^3\ U_{max} (\text{rem})$$

for U_{max} in µCi/day

The quarterly limit on dose to the thyroid is one-half the yearly limit of 30 rem, and the ICRP recommends an investigation level[3] of one-tenth the quarterly limit, or 1.5 rem potential dose. That is to say, if an exposure to radioiodine could deliver, in 50 years, 1.5 rem to the thyroid, it should be investigated.

If,

$$U_{max} = 1.5/7.84x10^3 \ \mu Ci/day = 425 \ dpm/(days \ urine) \quad (34)$$

is not exceeded, this recommended investigation level for ^{131}I will not be exceeded provided that the urine sample was obtained within 17 days of the acute uptake.

4. CONCLUSION

The solutions to a three-compartment model of radioiodine in man have shown that in a particular interval of time after uptake the two-compartment model normally used can lead to significant errors in the prediction of the thyroid burden using urinary excretion data. Urinary excretion data is invaluable in assessing exposure to radioiodine in two respects. Firstly it allows one to estimate the seriousness of the exposure without bringing an employee "in" for direct thyroid measurements. Secondly it is often useful in estimating the time at which the exposure occurred. That is, if two urine samples a few days apart are obtained, and the first contains much more radioiodine than the second, one knows immediately that the exposure occurred at most a few days before the first sample was obtained: whereas if one were to rely on direct thyroid measurements to estimate the time that the exposure occurred, the first thyroid measurement would have to be made within 24 hours of the exposure, as can be seen by examining Figure 5.

Urinary excretion data should only be used to estimate the maximum thyroid burden as large errors are possible in the estimation of the actual burden, and direct thyroid burden measurements are a simple procedure. Urinary excretion data can be used, however, to isolate incidences where direct thyroid measurements are warranted.

TABLE 1

RATE CONSTANTS CALCULATED FROM TABLE 3 OF REFERENCE 2

Route	Rate Constant λ_i in $(\text{Days})^{-1}$	Half-Life Days
1	0.93	0.74
2	1.92	0.36
3	0.0087	79
4	0.053	13
5	0.0050	139

FIGURE 1

THREE-COMPARTMENT MODEL OF IODINE METABOLISM IN MAN

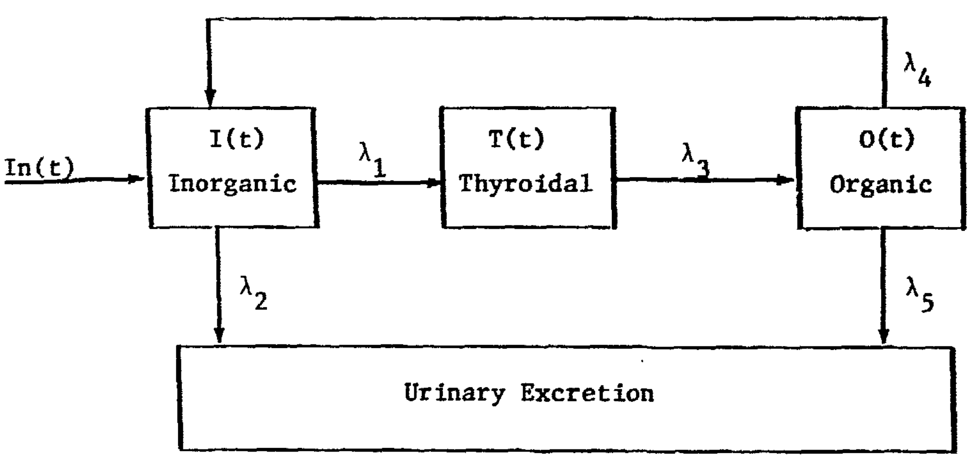


FIGURE 2

SHORT-TERM APPROXIMATION TO THE THREE-COMPARTMENT MODEL

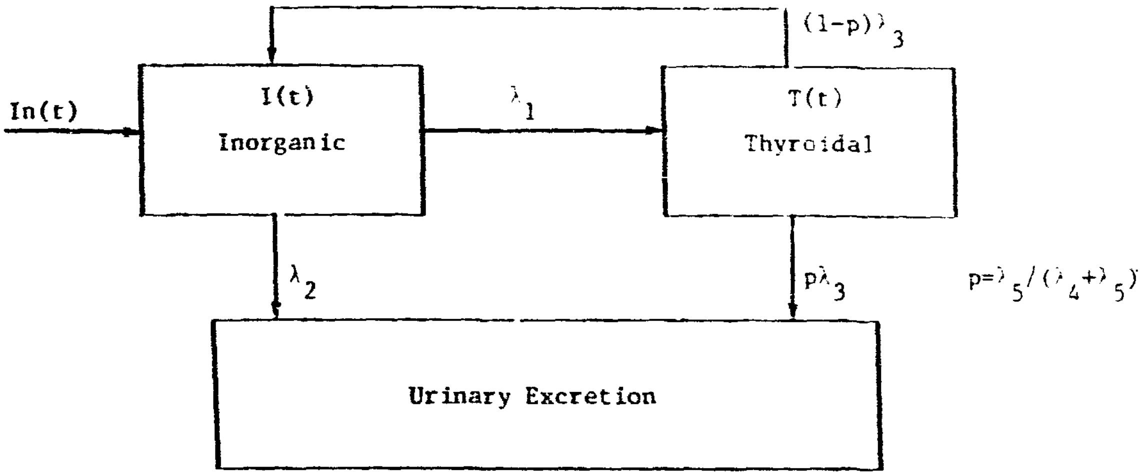


FIGURE 3

LONG-TERM APPROXIMATION TO THE THREE-COMPARTMENT MODEL

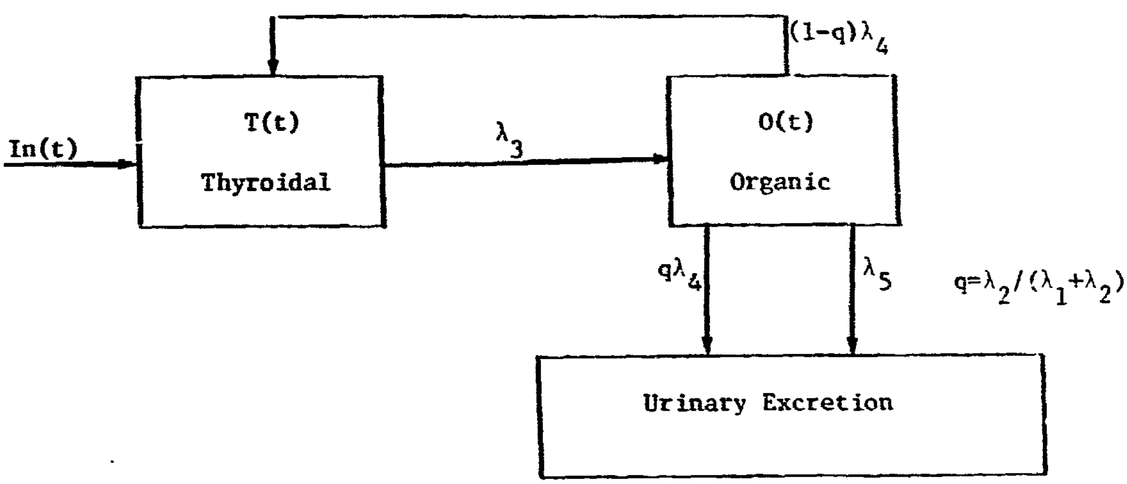


FIGURE 4
INORGANIC AND ORGANIC BURDENS

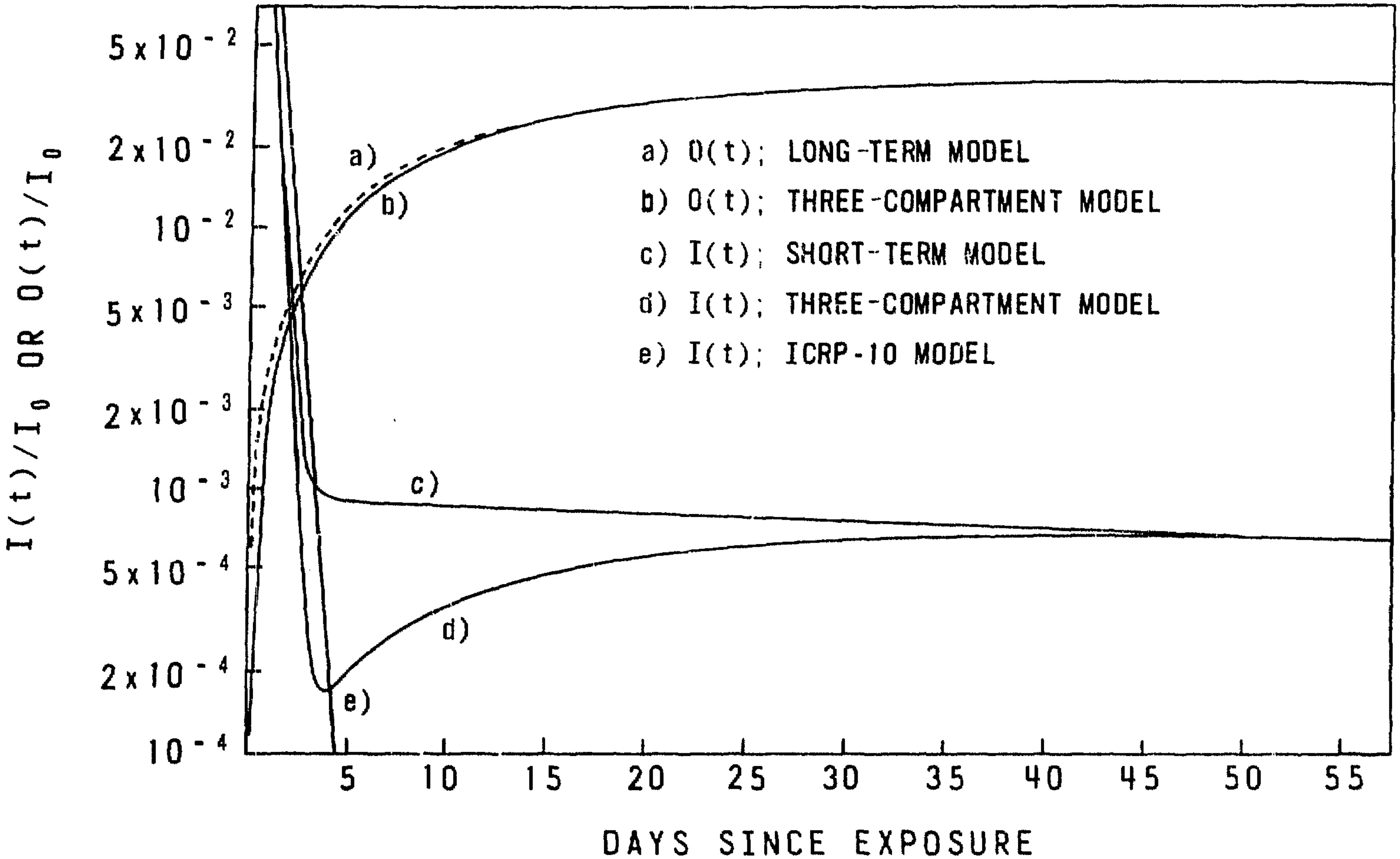


FIGURE 5

THYROID BURDEN

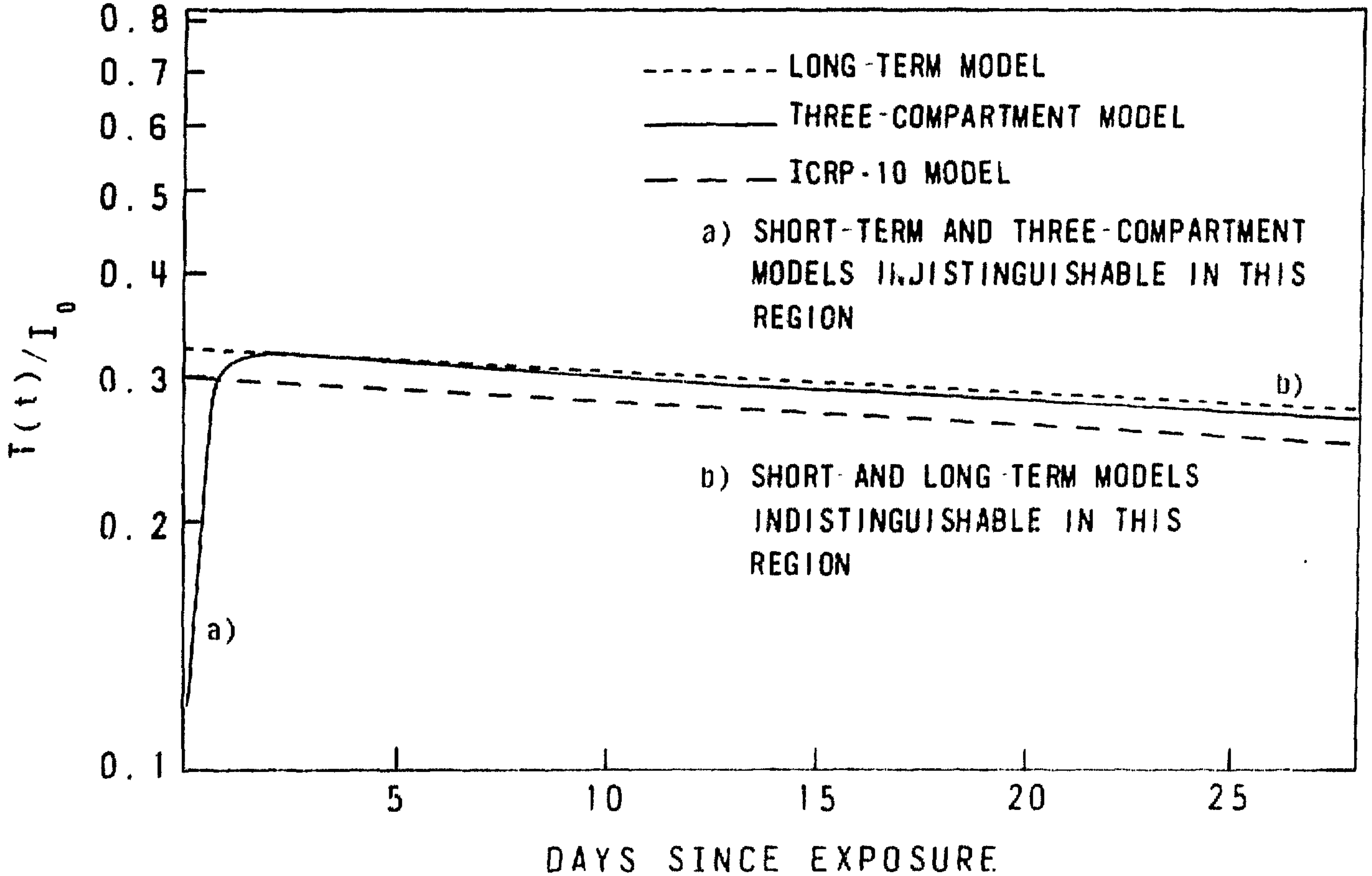
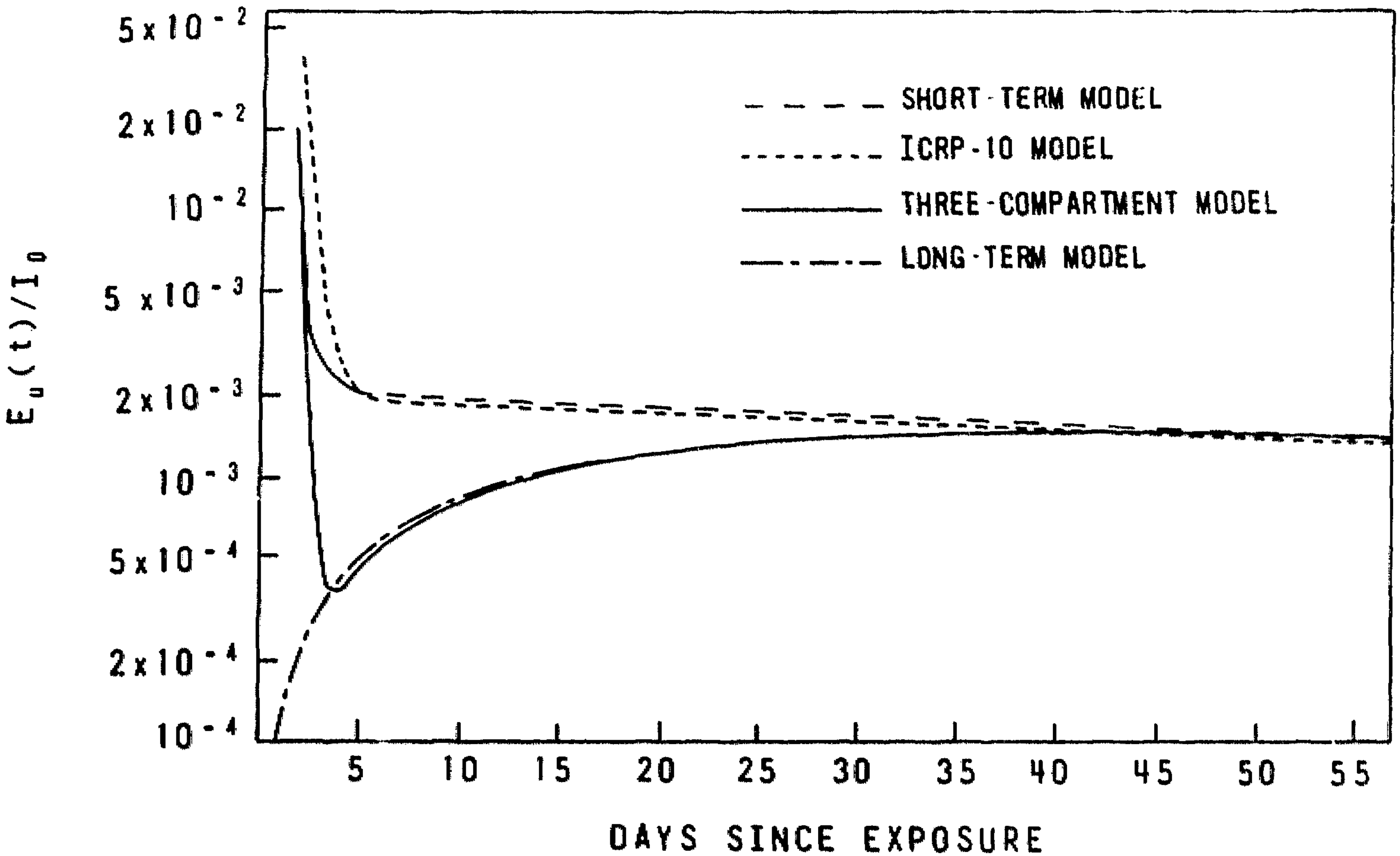


FIGURE 6

URINARY EXCRETION RATES



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APPENDIX

The differential equations for the three compartment model of iodine metabolism are solved below. The method of obtaining the solutions is outlined in order that different rate constants may be substituted for those given in Table 1 and new solutions calculated.

The differential equation ((5), (6) and (7) with $X(t) = 0$) can be written as

$$\frac{dy_1}{dt} = -(\lambda_1+\lambda_2)y_1 + \lambda_4 y_3 \qquad \text{A-1}$$

$$\frac{dy_2}{dt} = -\lambda_3 y_2 + \lambda_1 y_1 \qquad \text{A-2}$$

$$\frac{dy_3}{dt} = -(\lambda_4+\lambda_5)y_3 + \lambda_3 y_2 \qquad \text{A-3}$$

and they have solutions

$$Y_i = \sum_{j=1}^{3} b_{ij} \exp(C_j t) \qquad \text{A-4}$$

By substituting A-4 into A-1, A-2 and A-3, and assuming that none of the C_j are equal, the following 9 equations are obtained (j=1, 2 and 3)

$$b_{1j}\, C_j = -(\lambda_1+\lambda_2)b_{1j} + \lambda_4 b_{3j} \qquad \text{A-5}$$

$$b_{2j}\, C_j = -\lambda_3 b_{2j} + \lambda_1 b_{1j} \qquad \text{A-6}$$

$$b_{3j}\, C_j = -(\lambda_4+\lambda_5)b_{3j} + \lambda_3 b_{2j} \qquad \text{A-7}$$

Appendix ..

These nine equations, plus the boundary conditions given in equation 9 which can be re-written as

$$I(o) = \sum_{j=1}^{3} b_{1j} = I_o$$

$$T(o) = \sum_{j=1}^{3} b_{2j} = 0 \qquad \text{A-8}$$

$$O(o) = \sum_{j=1}^{3} b_{3j} = 0$$

give 12 equations in 12 unknowns (the b_{ij}'s and the C_j's), which for the above case, can be solved as follows:

Combining equations A-5 and A-7 gives

$$b_{1j}(C_j+\lambda_1+\lambda_2) = \frac{\lambda_4\lambda_3\, b_{2j}}{C_j+\lambda_4+\lambda_5}$$

which combined with A-6 gives

$$b_{1j}(C_j+\lambda_1+\lambda_2) = \frac{\lambda_4\lambda_3\lambda_1 b_{1j}}{(C_j+\lambda_4+\lambda_5)(C_j+\lambda_3)}$$

with the result that

$$(C_j+\lambda_1+\lambda_2)(C_j+\lambda_3)(C_j+\lambda_4+\lambda_5) = \lambda_1\lambda_3\lambda_4$$

That is, the C_j's are the solutions to the cubic equation.

$$C^3 + \alpha C^2 + \beta C + \delta = 0 \qquad \text{A-9}$$

with

$$\alpha = \lambda_1+\lambda_2+\lambda_3+\lambda_4+\lambda_5$$

$$\beta = \lambda_3(\lambda_1+\lambda_2+\lambda_4+\lambda_5) + (\lambda_1+\lambda_2)(\lambda_4+\lambda_5) \quad \text{A-10}$$

$$\delta = (\lambda_1+\lambda_2)\lambda_3(\lambda_4+\lambda_5) - \lambda_1\lambda_3\lambda_4$$

Substituting

$$C = x - \alpha/3 \quad \text{A-11}$$

into A-9 yields

$$x^3 - 3px - 2q = 0 \quad \text{A-12}$$

where

$$p = \frac{1}{3}\left(\frac{\alpha^2}{3} - \beta\right) \quad \text{A-13}$$

$$q = \frac{1}{2}\left(\frac{\alpha\beta}{3} - \frac{2}{27}\alpha^3 - \delta\right)$$

The form of the solutions to A-12 depends on the sign and relative magnitude[5] of p and q. All reasonable values for the rate constants of the model will result in values of α, β and δ such that $p > 0$ and $q^2 < p^3$, as can be shown by substituting numerical values into A-10 and A-13.

Therefore the solutions to A-12 are [5]

$$x_1 = 2(p)^{\frac{1}{2}} \cos\theta$$

$$x_2 = -\frac{x_1}{2} + (3p)^{\frac{1}{2}} \sin\theta \quad \text{A-14}$$

$$x_3 = -\frac{x_1}{2} - (3p)^{\frac{1}{2}} \sin\theta$$

Appendix ...

where

$$\theta = \frac{1}{3} \text{Cos}^{-1} (qp^{-3/2})$$

from which the C_j's can be calculated.

The b_{ij}'s can be expressed in terms of one another as

$$b_{1j} = \frac{b_{2j}}{\lambda_1} (C_j + \lambda_3) \qquad \text{A-15}$$

and, using A-5, A-6 and A-7

$$b_{3j} = \frac{b_{2j}}{\lambda_1 \lambda_4} (C_j + \lambda_3)(C_j + \lambda_1 + \lambda_4) \qquad \text{A-16}$$

The solutions of the differential equations will therefore be complete if solutions to the b_{2j}'s can be found. Three equations involving only the b_{2j}'s can be written using the boundary conditions given in A-8 and equations A-15 and A-16.

$$\sum_{j=1}^{3} b_{2j} = 0$$

$$\sum_{j=1}^{3} b_{2j} (C_j + \lambda_3) = \lambda_1 \sum_{j=1}^{3} b_{1j} = \lambda_1 I_o$$

$$\sum_{j=1}^{3} b_{2j}(C_j + \lambda_3)(C_j + \lambda_1 + \lambda_2) = \lambda_1 \lambda_4 \sum_{j=1}^{3} b_{3j} = 0$$

These three equations yield solutions for the b_{1j}'s of

Appendix ...

$$b_{21} = \frac{\lambda_1 I_o}{D} \quad (C_1+\lambda_4+\lambda_5)(C_2-C_3) \qquad \text{A-17}$$

$$b_{22} = \frac{\lambda_1 I_o}{D} \quad (C_2+\lambda_4+\lambda_5)(C_3-C_1) \qquad \text{A-18}$$

$$b_{23} = \frac{\lambda_1 I_o}{D} \quad (C_3+\lambda_4+\lambda_5)(C_1-C_2) \qquad \text{A-19}$$

where

$$D = C_1^{\,2} \; (C_2-C_3)+C_2^{\,2}(C_3-C_1)+C_3^{\,2}(C_1-C_2) \qquad \text{A-20}$$

The solutions represented by equation A-4 can now be calculated.

Putting the rate constants of Table 1 into equations A-10 yield

$\alpha = \; 2.9167$

$\beta = \; 0.1910$

$\delta = \; 0.00100$

which in turn yield, from A-13

$p = \; 0.88170$

$q = \; 0.82684$

The C_j's are therefore calculated to be, using A-11 and A-14

$C_1 = \; 2.8499$

Appendix ...

$$C_2 = -0.06089$$

$$C_3 = -0.005863$$

It is now a straight-forward procedure to calculate the b_{ij}'s using these values for the C 's and equations A-15 to A-19. The results are summarized in the following table.

j	C_j	b_{1j}	b_{2j}	b_{3j}
1	-2.85	1.000	-0.327	0.0010
2	-0.0609	-0.000983	0.0175	-0.0517
3	-0.00586	0.000945	0.310	0.0507

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