CONF-8410171--1

METABOLISM OF ORGANICALLY BOUND TRITIUM

CONF-8410171--1
DE85 002576

C. C. TRAVIS

Health and Safety Research Division
Oak Ridge National Laboratory
P. O. Box X
Oak Ridge, Tennessee 37831

DISCLAIMER

Operated by Martin Marietta Energy Systems, Inc. with the U. S. Department of Energy under Contract DE-AC05-84OR21400

Validation of tritium model

C. C. Travis
Health and Safety Research Division
Oak Ridge National Laboratory
P. O. Box X
Oak Ridge, Tennessee 37831

C. C. Travis
Health and Safety Research Division
Oak Ridge National Laboratory
P. O. Box X
Oak Ridge, Tennessee 37831

Metabolism of Organically Bound Tritium

Abstract

The classic methodology for estimating dose to man from environmental tritium ignores the fact that organically bound tritium in foodstuffs may be directly assimilated in the bound compartment of tissues without previous oxidation. We propose a four-compartment model consisting of a free body water compartment, two organic compartments, and a small, rapidly metabolizing compartment. The utility of this model lies in the ability to input organically bound tritium in foodstuffs directly into the organic compartments of the model. We found that organically bound tritium in foodstuffs can increase cumulative total body dose by a factor of 1.7-4.5 times the free body water dose alone, depending on the bound-to-loose ratio of tritium in the diet. Model predictions are compared with empirical measurements of tritium in human urine and tissue samples, and appear to be in close agreement.

KEYWORDS: TRITIUM, ORGANIC UPTAKE, METABOLIC MODEL, DOSE, MODEL VALIDATION

INTRODUCTION

Tritium, the heaviest and only radioactive isotope of hydrogen, is produced naturally as a result of cosmic ray interactions in the stratosphere. Significant quantities of tritium are also released to the environment through nuclear weapons testings, nuclear power reactors, fuel reprocessing plants, and consumer products. Once released to the atmosphere, tritium is oxidized to tritiated water (^3HOH), enters the global hydrological cycle, and is widely dispersed throughout the environment. Transfer to man is by inhalation, skin absorption, or ingestion of food or drinking water. Once in the human body, tritium mixes rapidly with extracellular and intracellular tissue water, with a fraction replacing hydrogen bound in organic molecules of tissue. Loose tritium is defined as that which can be removed from plant or animal tissue by mild distillation techniques or lyophilization. Bound tritium is that which remains after this process and which may be removed by combustion. Bound tritium is composed of both stable tritium (that which is primarily attached to carbon and is usually only released during enzyme-mediated reactions) and labile tritium (that which is attached to oxygen, sulfur, nitrogen or phosphorus and will readily exchange with tritium in tissue water).

Various models have been proposed to describe the kinetics of tritium in the human body. The most widely accepted of these is Bennett's three-compartment model (1) which has been adapted by the National Council on Radiation Protection (NCRP) (2). The NCRP model is presented in Figure 1. This model assumes that all ingested tritium, whether organically bound or free, enters directly into the free body water compartment. On the basis of predictions made by this model, the NCRP (2) indicates that organically bound tritium in the body may be adequately accounted for by multiplying the free body water dose by a factor of 1.2.

All tritium models currently in use ignore the fact that organically bound tritium in foodstuffs may be directly assimilated in the bound compartments of body tissue without previous oxidation. We have developed a fourcompartment model of hydrogen metabolism in the body (see Figure 2) which allows for input of organically bound tritium directly into organic compartments representing tissue solids (3). Predictions made with this model indicate that properly accounting for metabolism of organically bound tritium in foodstuffs can increase cumulative dose estimates by as much as a factor of four to five over doses estimated for free body water alone.

While our model structure is similar to previous models (we have four compartments compared to two or three), the primary difference lies in the ability to input organically bound tritium directly into the compartments representing tissue solids, rather than into the free body water compartment. Model parameters (transfer rates and compartment masses) were selected so that the response to a pulse of tritiated water input directly into the water compartment (compartment A) would duplicate the tritium retention data reported by Snyder et al. (4) and Sanders and Reinig (5) (see Figure 3). The purpose of this paper is to discuss the dosimetric implications of our four-compartment model and to present a preliminary validation using measurements of background levels of loose and bound tritium in Italian subjects and their diets.

DOSIMETRY

Our primary purpose in developing a compartmental model of hydrogen metabolism was to obtain better indications of the dosimetric consequences of human exposure to organically bound tritium. To answer this question, we input a single tritium pulse of 1 uCi/kg into both Bennett's model and our four-compartment model. In Bennett's model, the entire intake was input into the body water compartment, whereas in the four-compartment model, the intake was

divided proportionately into compartments A, B, and C, based on the fraction of daily hydrogen intake values (A=0.908; B=0.014; and C=0.078). Using Bennett's model, cumulative total body dose in uCi days/kg after 2000 days is 20.33. As should be the case, this dose is approximately 1.2 times the dose from the free body water compartment alone (16.49 uCi days/kg). Our four-compartment model, which allows for input of organically bound tritium directly into the compartments representing tissue solids, yields a cumulative dose after 2000 days of 29.5 uCi days/kg, a factor of 1.7 times the dose contributed by the free body water compartment.

In estimating body burdens, the ratio (R) of total bound to total loose tritium (including drinking water) ingested daily by an individual is an important quantity. Under conditions where tritium is uniformly dispersed in the environment (equilibrium conditions), tritium has the same specific activity in both the bound and loose compartments (i.e., the bound to loose ratio which is defined as the ratio of the specific activity in the bound compartment to that in the loose compartment, is 1). However, under equilibrium conditions the R value for total ingested tritium is low (R=0.15) since the average human diet is composed of much more loose than bound hydrogen (and consequently tritium). In order to determine the effect of the parameter R on dose estimations, we repeated our dose calculation again using a single pulse input of 1 uCi/kg and varying the bound-to-loose ratio in foodstuffs. Figure 4 shows the ratio of cumulative total body dose to free body water dose after 2000 days (as predicted by the four-compartment model) as a function of the ratio R. Bennett's model estimates are included for comparison. The figure shows that for a hypothetical diet in which the total intake of bound tritium is ten times larger than the total intake of loose tritium (R=10), cumulative total body dose after 2000 days would be a factor of 4.5 times higher than the dose contributed by the free body water along.

In summary, under conditions of a unit bound-to-loose tritium ratio in individual foods items, Bennett's model predicts a cumulative dose to the body after 2000 days that is 1.2 times the free body water dose, whereas our model predicts a cumulative dose 1.7 times the body water dose. Under the dietary conditions described by Bogen (6), the four-compartment model predicts a cumulative dose two times that predicted for the free body water compartment. For higher bound-to-loose ratios in the diet (up to R=10), the cumulative dose could be up to 4.5 times that of the free body water compartment, while Bennett's model still predicts a ratio of 1.2. The difference here lies in the capability to input organically bound tritium directly into the organic compartments of the four-compartment model.

VALIDATION OF FREE BODY WATER COMPARTMENT

Belloni et al.[1] summarized the findings of a study on background tritium content in the Italian diet and its transfer to man. Daily dietary intake and excretion of tritium were measured for seven healthy subjects. Bound and loose concentrations were reported for foodstuffs and blood, and loose concentrations were reported for urine for each subject. Bound to loose tritium ratios measured in individual food items of the Italian diet ranged from 2.3 for flour to 48.1 for meat.[2] These measurements are contrary to the commonly held assumption that bound-to-loose ratios in food items under background conditions should be one (2,7). Bogen et al.(8) have also measured bound to loose ratios in food items in a New York diet and found them to range from 1.2 - 5.6.

The ratio (R) of dietary tritium in the seven Italian diets was found to range from 0.5 - 8.9. Tritium concentrations in urine were found to average 3.6 times tritium concentrations in the loose fraction of the diet (with a range of 0.7 - 9.0). Again, these measurements are contrary to the commonly held belief that urine concentrations will be similar to the tritium concentration

in the loose fraction of the diet. These higher concentrations of tritium in urine result from long-term retention of bound tritium in the body and its subsequent release into the body water compartment. Using data on the dietary intake of tritium for the seven subjects, we will first validate the free body water compartment of our model by comparing model predictions with reported concentration of tritium in the urine of each subject.

Daily intake of loose tritium for each of the seven subjects was based on estimated tritium concentrations in surface water (400 pCi/L), while daily intake of bound tritium was obtained by multiplying total intake of loose tritium by the measured value of R for each subject (Table 1). For example, to obtain the daily intake of loose tritium (I_L) for subject 1 (see Table 1), one multiplies the total daily intake of water (3.94 L/d) by surface water concentration (400 pCi/L). The daily intake of bound tritium (I_B) for subject 1 is obtained by multiplying I_L by R=3.4. Tritium inputs into compartments A, B, and C of the four-compartment model are $I_L + 0.3\ I_B$, and $0.11\ I_B$, and $0.59\ I_B$, respectively (3). Model predictions were used to estimate the concentration of tritium in the body water compartment of each of the seven subjects. The concentration of tritium in urine is assumed similar to that of the body water[3]. Table 2 lists the measured concentration in urine for each of the seven subjects, and the values predicted by our four-compartment model and the NCRP model (2). It can be seen that the predictions of both models are very close to the measured values for all subjects except 4 and 5.

VALIDATION OF ORGANIC COMPARTMENTS

Recently, Belloni et al.[4] have presented a summary of data on tritium content of the diet and human tissues from a sample of the Italian population (see Table 3). Using the daily intake of loose and bound tritium from Table 3 as input into our four-compartment model, we predict equilibrium loose and bound body burdens

for the average Italian subject as 56,500 pCi and 90,900 pCi, respectively. This compares with the Belloni et al. estimate of 62,100 pCi and 93,960 pCi, respectively (see Table 3). A comparison between predicted and reported fresh tissue concentrations is given in Table 4. The close agreement of our model predictions with reported values indicates that our four-compartment model accurately represents the metabolism of tritium in the organic compartments of the human body (10).

The NCRP Model (2) as it now stands (inputting both loose and bound tritium into the free body water compartment) will not reproduce the concentration of tritium in the bound compartments as reported in the Italian study (see Table 4). These data support our claim that by not properly accounting for organically bound tritium in food, the NCRP methodology can underestimate cumulative dose from tritium by as much as a factor of 4-5, depending on the bound-to-loose ratio of tritium in the diet (3).

CONCLUSION

Under conditions of exposure to tritiated water, organically bound tritium in the human body contributes little to cumulative dose. To account for this metabolic incorporation of loose tritium into human tissues, it is currently suggested that cumulative dose estimates be multiplied by a factor of 1.2. However, if exposure is through tritium bound in food, the cumulative dose from organically bound tritium in the body may be large, and must be considered separately. Application of the four-compartment model to tritium dosimetry predicts a cumulative dose varying from 1.7 - 4.5 times the dose predicted for the free body water compartment along (see Figure 4), depending on bound-to-loose ratios of tritium in the diet.

Given the potential importance of tritium in both fission and fusion nuclear field cycles, we stress the need for further research on uptake of organically

bound tritium. This research should emphasize both human metabolism and microdosimetry of organically bound tritium.

FIGURE CAPTIONS

Figure 1. National Council of Radiation Protection and Measurements Three-Compartment Model of Hydrogen in the Body.

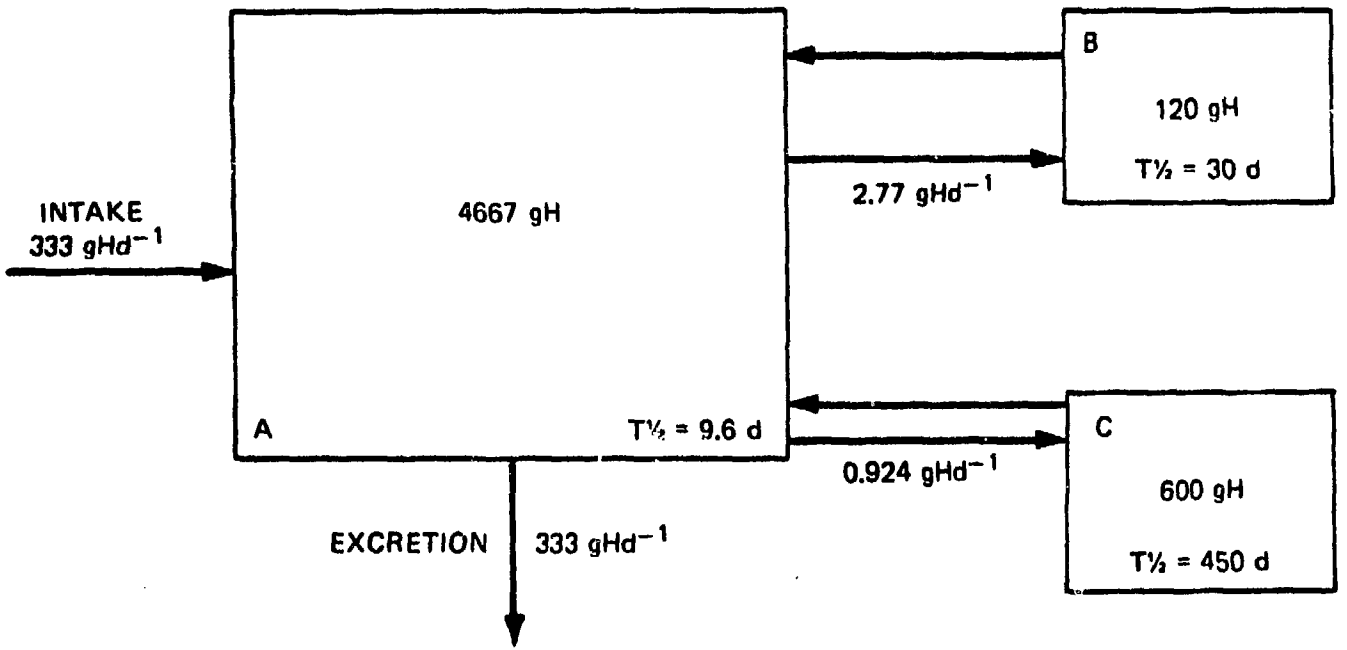
Figure 2. Four-Compartment Model of Hydrogen Metabolism.

Figure 3. Urinary excretion of Tritium in Man. The two Doted Lines are empirical tritium retention data and the solid line is the 4-compartment model retention curve.

Figure 4. Ratio of Cumulative Total Body Dose to Free Body Water Dose (after 2000 days) as a Function of the Ratio R of Total Bound to Loose Tritium Intake in the Diet.

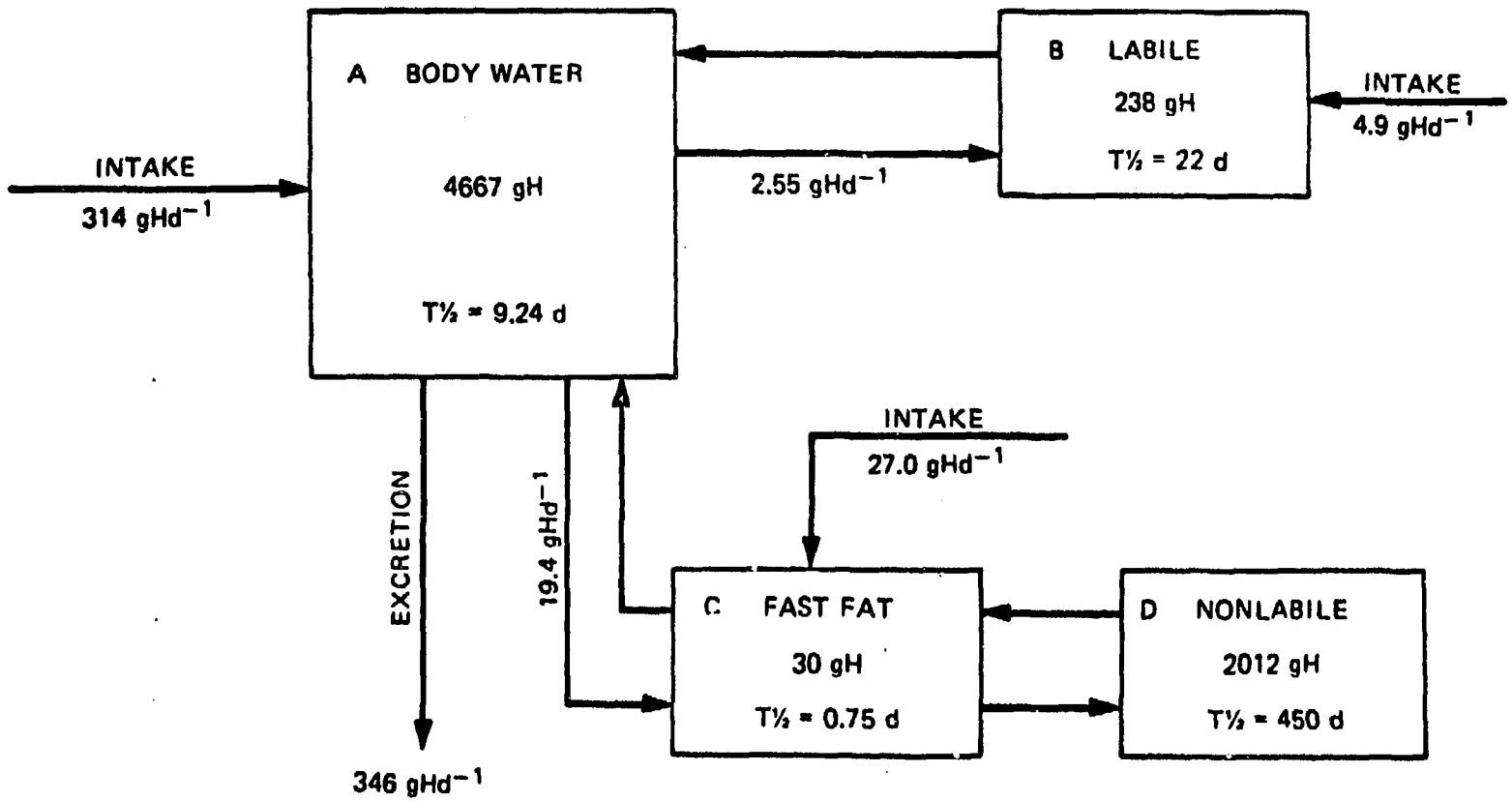
ORNL–DWG 82-18500

NATIONAL COUNCIL ON RADIATION PROTECTION AND MEASUREMENTS THREE-COMPARTMENT MODEL OF HYDROGEN IN THE BODY

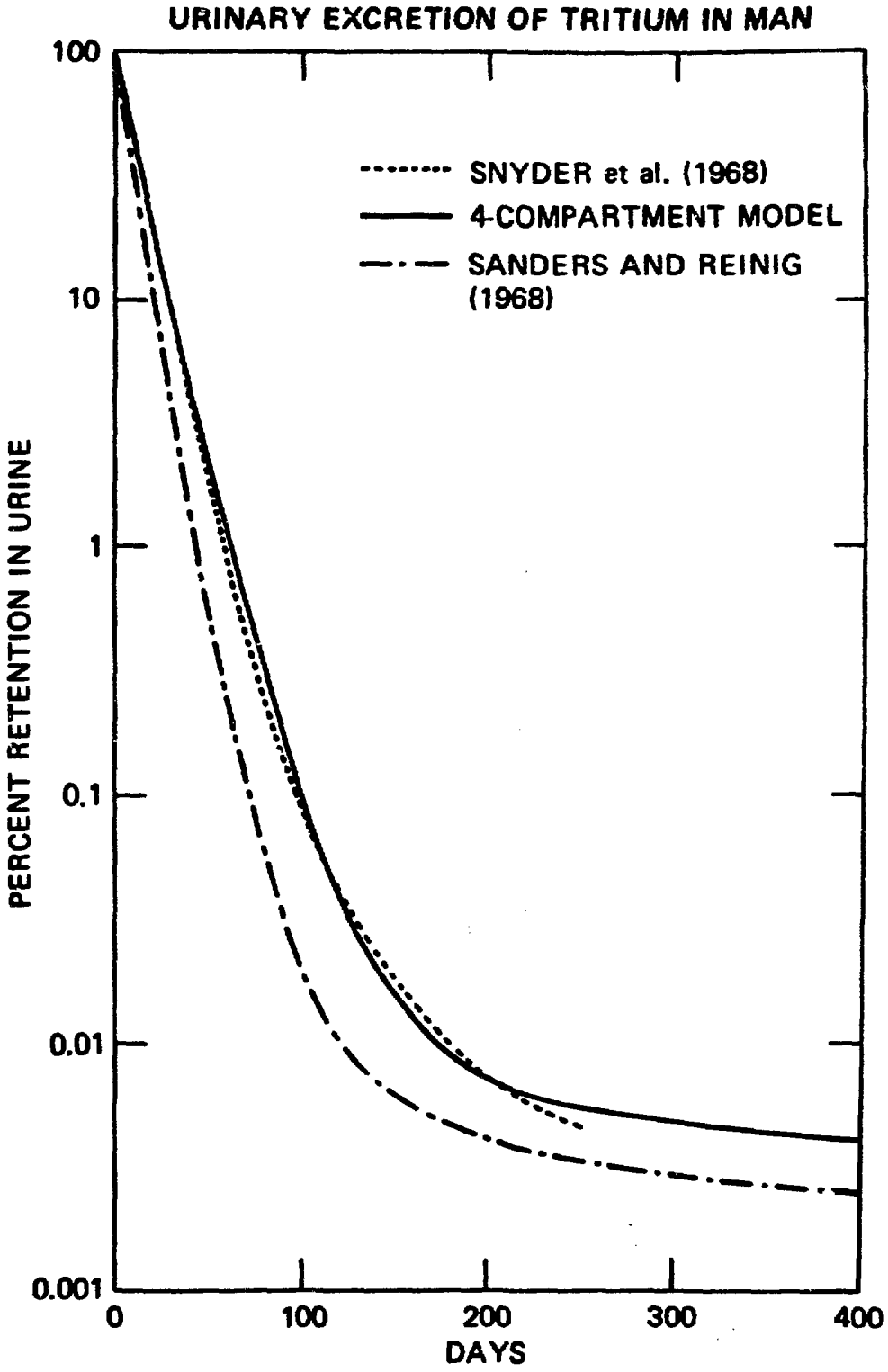


ORNL–DWG 82-18501

FOUR-COMPARTMENT MODEL OF HYDROGEN METABOLISM



ORNL–DWG 82-18502



ORNL–DWG 82-18506R

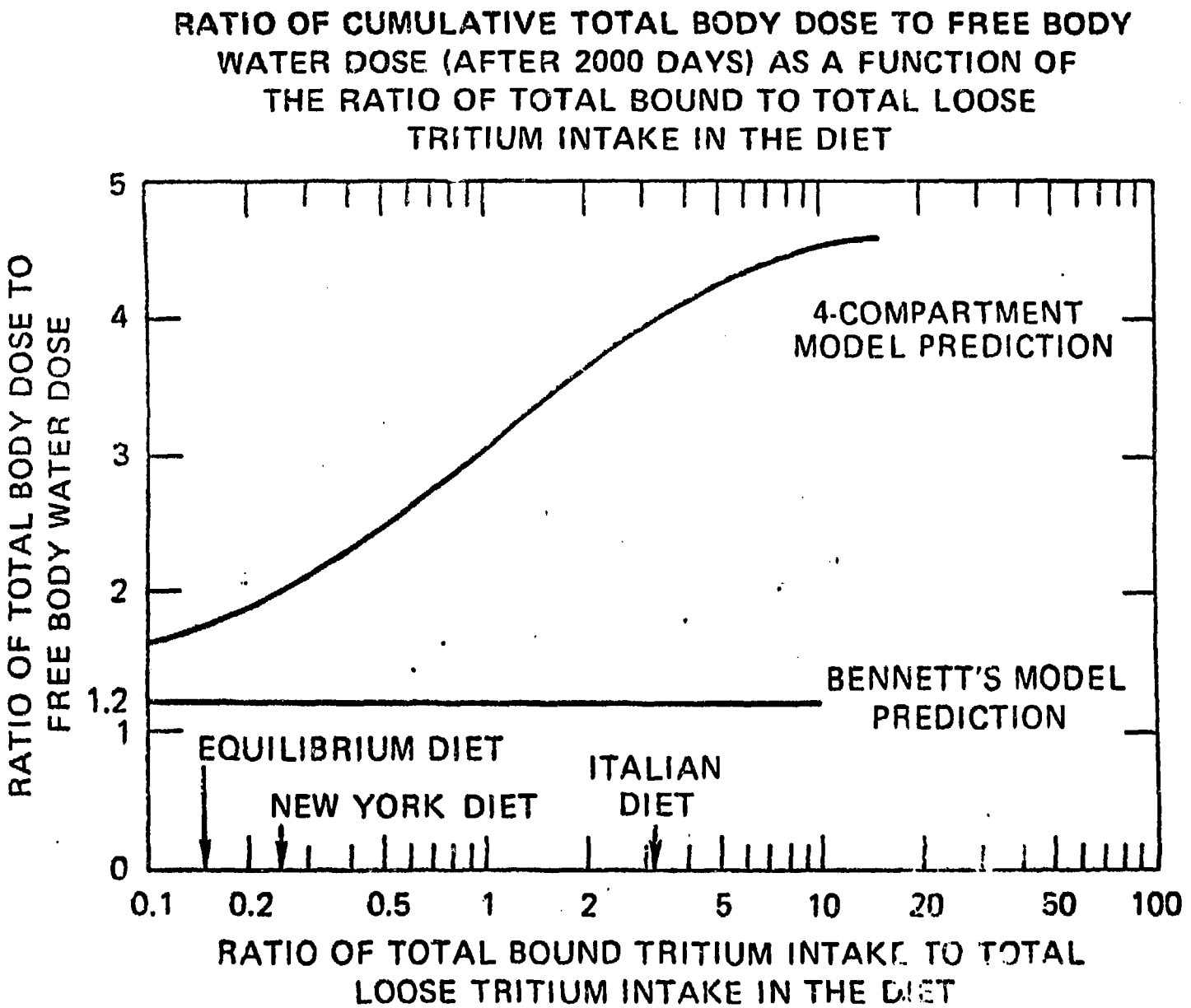


Table 1. Estimated parameters for Italian diet study

Subject	Weight[a] (kg)	Body water[a] compartment (L)	Urine[a] excreted (L/d)	Total water[b] intake (L/d)	R[a,c]
1	95	57	1.8	3.94	3.4
2	52	31	0.471	1.03	3.1
3	73	44	0.783	1.71	7.3
4	50	30	0.800	1.75	8.9
5	82	49	0.805	1.76	0.5
6	68	41	0.920	2.01	1.2
7	60	36	0.444	0.972	7.2

[a]from footnote 1.

[b]estimated from Reference Man (9) water balance data.

[c]R = the ratio of total bound to total loose tritium (including drinking water) ingested daily.

Table 2. Comparison of measured to predicted urine concentration for seven Italian subjects

Subject	Urine concentration (pCi/mL)		
	Measured values[a]	Four-Compartment model prediction[b]	NCRP Model prediction[c]
1	1.4	1.4	1.4
2	0.7	0.6	0.6
3	1.8	1.5	1.5
4	0.7	2.7	2.7
5	1.9	0.3	0.3
6	0.5	0.5	0.5
7	0.9	1.0	1

[a]from footnote 1.

[b]Based on computer runs using model in Ref. 3.

[c]Based on computer runs using model in Ref. 2.

Table 3. Average tritium concentration in diet and tissue samples of Italian population[a]

Body soft tissue weight	59,000 g
^{3}H urinary concentration	1,500 pCi/L
Total loose tritium daily intake (I_L)	1 472 pCi/d
Total bound tritium daily intake (I_B)	2,714 pCi/d
Average tissue concentration of loose tritium[b]	1.053 pCi/g
Average tissue concentration of bound tritium[b]	1.593 pCi/g
Loose tritium body burden (X_L)	62,100 pCi
Bound tritium body burden (X_B)	93,960 pCi

[a]from footnote 4.

[b]measured as fresh tissue.

Table 4. Comparison of measured to predicted tritium concentrations in tissue

	Measured Values[a]	Four-Compartment Model Prediction[b]	NCRP Model Prediction[c]
Bound tritium	1.59 pCi/g	1.54 pCi/g	0.15 pCi/g
Urine concentration	1.50 pCi/mL	1.60 pCi/mL	1.60 pCi/mL

[a]from footnote 4.

[b]Based on computer runs using model in Ref. 3.

[c]Based on computer runs using model in Ref. 2.

FOOTNOTES

1. Belloni, P., Clemente, G. F., Di Pietro, S., and Quaggin, S. (1979). Data Preliminari Sullo Studio del Trasferimento di Bassi Livelli di Tritio Dall' Ambiente All' Uomo, Comitato Nazional Energia Nucleare Technical Report, RT/PROT(79)5, Rome.

2. Belloni, P., Clemente, G. F., Di Pietro, S., Quaggia, S., and Santaroni, G. P. (1981). Livelli di Contaminazione da Tritio in Diete ed Alimente Italiani, Comitato Nazional Energia Nucleare Technical Report, RT/PROT(80)35, Rome.

3. Woodard, H. Q. (1970). The Biological Effects of Tritium, HASL-229, Health and Safety Laboratory, U.S. Atomic Energy Commission, New York, New York.

4. Belloni, P., Brener, F., Clemente, G. F., Di Pietro, S., and Ingrao, G. Tritium metabolism in the human body, Proceedings Seminar on the Environmental Transfer to Man of Radionuclides Released from Nuclear Installations, Brussels, Belgium, October 17-21, 1983 (in press).

REFERENCES

1. Bennett, B. G. Environmental tritium and the dose to man, pp. 1047-1053 in Proc. 3rd International Congress of the IRPA. Washington, D.C., U.S. Atomic Energy Commission, Technical Information Center, Oak Ridge, Tennessee. (1973).

2. National Council on Radiation Protection and Measurements (NCRP). Tritium in the Environment, NCRP Report No. 62, Washington, D.C. (1979).

3. Etnier, E. L., Travis, C. C., and Hetrick, D. M. Metabolism of organically bound tritium in man, Rad. Res. (in press).

4. Snyder, W. D., Fish, B. R., Bernard, S. R., and Ford, M. R. (1968). Urinary excretion of tritium following exposure of man to HTO -- a two exponential model, Phys. Med. Biol. 13: 547-559.

5. Sanders, S. M., Jr., and Reining, W. C. (1968). Assessment of tritium in man, in Proceedings of a Symposium for the Diagnosis and Treatment of Deposited Radionuclides (H. A. Kornberg and W. D. Norwood, eds.), Monographs on Nuclear Medicine and Biology, No. 2, pp. 534-542, Excerpta Medica, Amsterdam.

6. Bogan, D. C., Henkel, C. A., White, C. G., and Welford, G. A., (1973). Tritium intake in New York City, p. 639-646 in Tritium (A. A. Moghissi and M. W. Carter, Eds.), Messenger Graphics, Phoenix, Arizona.

7. International Atomic Energy Agency. (1979). Symposium on the Behavior of Tritium in the Environment, ed. S. Freeman, STI/PUB/498, IAEA, Vienna.

8. U.S. Nuclear Regulatory Commission, Regulatory Guide 1.109, Rev. 1. (1977). Calculation of Annual Doses to Man from Routine Releases of Reactor Effluents for the Purpose of Evaluating Compliance with 10 CFR Part50, Appendix I.

9. International Commission on Radiological Protection (ICRP) (1975). Report of the Task Group on Reference Man, Report No. 23, Pergamon Press, Oxford.

10. Travis, C. C., Etnier, E. L., and Hetrick, D. M., Validation of a Metabolic Model for Tritium, Rad. Res. (in press).