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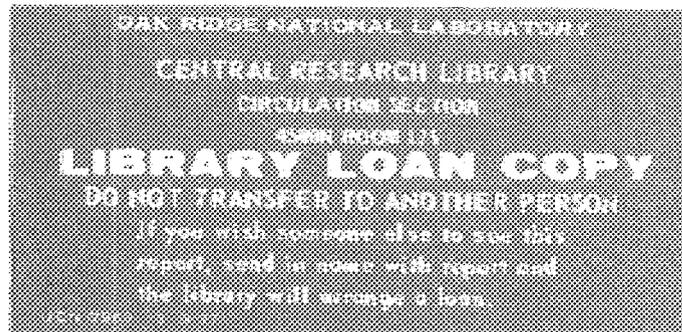
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NATIONAL
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MARTIN MARIETTA

Age- and Sex-Specific Estimation of Dose to a Normal Thyroid from Clinical Administration of Iodine-131

George G. Killough
Keith F. Eckerman



Prepared for the
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TO A NORMAL THYROID FROM CLINICAL
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NOTICE This document contains information of a preliminary nature.
It is subject to revision or correction and therefore does not represent
a final report.

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ABSTRACT

This report describes the derivation of an age- and sex-dependent model of radioiodine dosimetry in the thyroid and the application of the model to estimating the thyroid dose for each of 4,215 patients who were exposed to ^{131}I in diagnostic and therapeutic procedures. In most cases, the data available consisted of the patient's age at the time of administration, the patient's sex, the quantity of activity administered, the clinically determined uptake of radioiodine by the thyroid, and the time after administration at which the uptake was determined. The model was made to conform to these data requirements by the use of age-specific estimates of the biological half-time of iodine in the thyroid and an age- and sex-dependent representation of the mass of the thyroid. Also, it was assumed that the thyroid burden was maximum at 24 hours after administration (the ^{131}I dose is not critically sensitive to this assumption). The metabolic model is of the form

$$A(t) = K \cdot (\exp(-\mu_1 t) - \exp(-\mu_2 t)) \quad \mu\text{Ci}$$

where $\mu_i = \lambda_r + \lambda_i^b$ ($i = 1, 2$), λ_r is the radiological decay-rate coefficient, and the λ_i^b are biological removal-rate coefficients. The values of λ_i^b are determined by solving a nonlinear equation that depends on assumptions about the time of maximum uptake and the eventual biological loss rate (through which age dependence enters). The value of K may then be calculated from knowledge of the uptake at a particular time. The dosimetric S-factor (rad/ μCi -day) is based on specific absorbed fractions for photons of energy ranging from 0.01 to 4.0 MeV for thyroid masses from 1.29 to 19.6 g; the functional form of the S-factor also involves the thyroid mass explicitly, through which the dependence on age and sex enters. An analysis of sensitivity of the model to uncertainties in the thyroid mass and the biological removal rate for several age groups is reported. This model could prove useful in the dosimetry of very short-lived radionuclides. Tables of age- and sex-dependent coefficients are provided to enable readers to make their own calculations. An addendum (Appendix C) extends the method to other radioiodines and gives age- and sex-dependent dose conversion factors for most isotopes.

INTRODUCTION

This report describes work performed at Oak Ridge National Laboratory (ORNL) for the National Center for Devices and Radiological Health (DRH) of the Food and Drug Administration (FDA) in support of the Diagnostic ^{131}I Study conducted by DRH and funded by the U.S. Nuclear Regulatory Commission.* The task of ORNL was to examine a computer file consisting of records of administration of ^{131}I to 4,216 patients for completeness of data needed to estimate the radiation dose to the thyroid gland, and to compute the thyroid dose for each administration for which the data were sufficient.

The file to which ORNL was given access contained 5,382 records, with most records corresponding to single administrations of ^{131}I . A few records, however, represented follow-up observations for previously-recorded administrations. And some records were duplicates. Many records were incomplete in the data needed to estimate the thyroid dose. In some cases, these records could reasonably be completed by using information from other records on the same patient; in other cases they could not, and no dose estimate was possible.

The data file was revised and supplemented at ORNL in the following respects:

- Duplicate records were deleted.
- Incomplete records were supplemented from other records for the same patient when such supplementation appeared reasonable.
- Dose to the thyroid was computed for each administration for which the record was complete or could be supplemented as indicated above. The computed dose was added to the record.

The dosimetric model was constructed specifically for the information contained in this file. The model requires the patient's age and sex, the quantity of radioactivity administered, the fractional uptake of ^{131}I by the thyroid, and the time interval from the administration to the determination of fractional uptake.

This report discusses the revised data file and details of the dosimetric model for ^{131}I . It is intended as a reference for the use of DRH in carrying out the Diagnostic ^{131}I Study, as well as documentation of the model for possible use in other applications. The contents of the data file are not listed in this report.

THE PATIENT DATA FILE

The data file furnished to ORNL by DRH (which we shall call "the original file") consisted of 5,382 records of 50 characters each and represented a population of 4,216 patients. Each record corresponded to a particular administration of ^{131}I to a patient and determination of the fractional uptake of the radioiodine by the patient's thyroid. In some cases, multiple records existed for a single administration. In some of these instances, fractional uptake of the ^{131}I had been measured at two or more times after administration, but in others the multiplicity appeared redundant. Each record consisted of 16 fields, with definitions and formats as shown in Table 1.

Some of the records were incomplete in one or more fields. Approximately 11 percent of the records lacked data in one or more of the fields giving the exposure, the fractional uptake, and the time at which the uptake was determined. At the time the file was received

* Office of Nuclear Regulatory Research, Division of Radiation Programs and Earth Sciences, FIN B5771.

Table 1. Organization of Records in the Patient Data File

Characters	Format	Definition
1-6	xxxxxx	Patient identification. The first two digits are the code for the institution where the isotope was administered.
7-13	xxx.xxx	Age of patient (months) at the time of the administration.
14	x	Sex of patient (1 = male, 2 = female, 3 = unstated)
15-16	xx	Birth month
17-18	xx	Birth day
19-20	xx	Birth year
21-22	xx	Month of administration
23-24	xx	Day of administration
25-26	xx	Year of administration
27-31	xxx.x	Amount of ^{131}I administered (μCi)
32-35	xx.x	Fractional uptake of radioiodine by the patient's thyroid (%)
36-37	xx	Time interval (hours) after administration when fractional uptake was determined
38	x	Region of country in which the institution is located: 1 - Northeast: New York, Massachusetts 2 - North Central: Ohio, Iowa, Illinois 3 - South Central: Kansas, Missouri 4 - Western: California, Colorado
39-43	xxx.x	First diagnosis at the time of the procedure (ICDA8 code)
44-48	xxx.x	Second diagnosis at the time of the procedure (ICDA8 code)
49-50	xx	Institution code: 04 - University of Kansas Medical Center 05 - University of Iowa Hospital 06 - Dr. John Sinkey, Toledo, Ohio 10 - Stanford University Hospital 11 - University of Cincinnati Hospital 19 - Cleveland Clinic 24 - St. Louis University 25 - Washington University Hospital 27 - University of Illinois Hospital 28 - Sutter General Hospital, Sacramento, California 39 - Columbus Childrens Hospital, Columbus, Ohio 54 - Miami Valley Hospital, Dayton, Ohio 56 - Alta Bates Hospital, Dayton, Ohio 62 - Silver Cross Hospital, Joliet, Illinois 64 - University of California Hospital, San Francisco, California 71 - Columbia Presbyterian Hospital, New York, New York 73 - Strong Medical Center, Rochester, New York 74 - Shelton Clinic, Los Angeles, California 77 - University of Colorado Medical Center, Denver, Colorado 81 - Menorah Medical Center, Kansas City, Missouri 92 - Childrens Hospital, Boston, Massachusetts
51-59	xxxxx.xx[*]	Model-calculated dose to the thyroid (rad). The asterisk, when it is present, indicates that measured uptake is incompatible with model assumptions. In such cases, the dose corresponds to the assumption that removal of iodine from the thyroid prior to the time of maximum burden occurs only by radioactive decay (refer to the discussion of the retention function $A^*(t)$).

by ORNL, a similar number of records had missing or erroneous birth dates, or in some cases, an age field that was inconsistent with other records for the same patient. The latter inconsistencies were attributed by DRH to an incorrect computer algorithm, and corrections were furnished by DRH staff. At the same time, the DRH staff provided missing sex data and a number of miscellaneous corrections to records in the file.

In dose computations performed at ORNL, the corrected age field was used rather than the computed interval between the date of birth and the date of administration.

In some cases, missing uptake data could reasonably be estimated from another record for the same patient. A recurring pattern in the file consisted of a pair of records for a patient, indicating two administrations of ^{131}I . The first record would be complete with respect to uptake data. The second record would portray a somewhat larger administration 1 to 5 days later, for a diagnostic scan, and would lack uptake data. At the request of DRH, such cases were identified, and the uptake data from the earlier record were copied to the later record for dose computation. Approximately 90 patients had records that fell into this pattern.

We have alluded to multiple records corresponding to the same administration. For example, the last three records for patient #190370 corresponded to a single administration of $7\ \mu\text{Ci}$ on January 7, 1958; uptakes of 21%, 24%, and 25% were measured 5, 6, and 7 hours after administration, respectively. In situations of this kind, only the last record has been used to estimate the dose to the thyroid.

Other multiple records were apparently the result of redundant replication, and each was restored to a single record.

The file resulting from the corrections and revisions described above includes a 17th field, which gives the computed dose to the thyroid (rad) in each record for which the computation of dose is possible. We shall call this file "the revised file."

While ORNL will have no role in the epidemiological study that will be supported by the data in the revised file, we wish to make two observations about these data that we believe may bear upon the work.

First, the variability of the fractional uptake suggests the presence of subjects with abnormal thyroid conditions. The model that was derived for estimating the dose is based on euthyroid patients and may give biased estimates when it is applied to an abnormal population. The revised file presents dose numbers for all patients whose records contain sufficient data, whether the model may have been appropriately applied or not.

Second, we assume that a patient's total thyroid dose will be computed by adding the dose from each record for that patient. There are some examples in the file, however, for which this procedure seems likely to overestimate the total dose. These examples involve the administration of similar amounts of ^{131}I at short intervals, such as one day. For example, two of the records for patient #190295 include the information in the following table:

Date of admin.	Exposure (μCi)	Uptake (%)	Time (hr)	Dose (rad)
9/25/56	17.2	25	6	120.87
9/26/56	26.7	40	6	300.12

The second dose is not independent of the first, because the second measured uptake includes iodine from the first administration that has not yet been removed from the body by biological processes and radioactive decay. Although it seems reasonable in this case to assume that the second fractional uptake value could be taken to be the same as the first (25%), there are other cases in the file for which the second (or a later) recorded uptake is

less than the earlier one (e.g., the first two records for patient #40267). Thus a consistent policy for adjusting the uptake values does not immediately suggest itself. The investigators in the Diagnostic ^{131}I Study need to be aware of the existence of such effects and take them into account in using this data base.

DESCRIPTION OF THE MODEL

The model that we have applied to the age, sex, and uptake data in the revised file estimates absorbed dose (rad) to the thyroid resulting from a known fractional uptake by the thyroid at a specified time after a clinical administration of ^{131}I . To an extent that we believe is consistent with observations, the model distinguishes age differences and to a lesser degree, those related to sex. We emphasize that *the model is based on data from euthyroid subjects; its elaboration to abnormal thyroid conditions has not been undertaken.*

The model consists of two components, corresponding to the two factors in the right-hand side of the dose equation

$$\dot{D}(t) = S(\text{thyroid} \leftarrow \text{thyroid}) \cdot A(t) \quad (1)$$

where $\dot{D}(t)$ = absorbed dose rate (rad day^{-1}) to the thyroid at time t , $S(\text{thyroid} \leftarrow \text{thyroid})$ = dosimetric "S-factor" ($\text{rad } (\mu\text{Ci-day})^{-1}$) for ^{131}I in the thyroid, and $A(t)$ = activity burden (μCi) of ^{131}I in the thyroid at time t . In our model, S depends on age and sex, and $A(t)$ depends on age at the time of administration of the ^{131}I .

The ^{131}I activity in the thyroid, $A(t)$, is based on a metabolic model of iodine in the body. Several levels of detail have been incorporated into existing models. Multicompartment models aim at providing mechanistic representations of iodine kinetics (e.g., Berman, 1972), but the numerous parameters of such models are not readily expressed as functions of age. The International Commission on Radiological Protection (ICRP, 1979) has adapted a model of Riggs (1952) for its purposes of radiation protection for occupationally exposed adults. The Riggs/ICRP model (Fig. 1a) consists of three compartments. The first is a "transfer compartment," into which the radioiodine is originally introduced and from which the iodine is removed with biological half-time 0.25 days; 70% is excreted through the urine, and the remaining 30% is available for uptake by the thyroid. Iodine is cleared from the thyroid compartment with a half-time of 80 days into an organic iodine pool, which loses iodine through excretion and feedback to the transfer compartment of iodine from dehalogenation of thyroxine and triiodothyronine.

The transfer compartment has proved useful in avoiding overestimation of dose to the thyroid by short-lived radioiodines, which decay significantly before reaching the thyroid, and we wished to retain this feature in the model implicitly. The feedback pathway, on the other hand, makes little contribution to the time integral of activity in the thyroid for ^{131}I . To support this assertion, we have performed calculations with the three-box model of Fig. 1a and a two-box counterpart that lacks the organic-iodine compartment (Fig. 1b). When $1 \mu\text{Ci}$ of ^{131}I is introduced into the transfer compartment at time $t = 0$, the two models agree in the following respects:

- Both model thyroids have their maximum activity between 1.2 and 1.3 days after administration.
- Both maximum uptakes by the thyroid are 26% of the administered activity.
- For both models, the time integral of activity in the thyroid is $3.1 \mu\text{Ci-days}$ per μCi taken into the body.

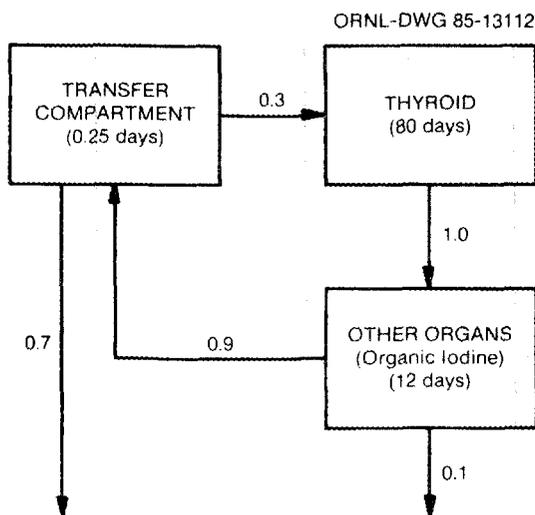


Figure 1a. The Riggs/ICRP metabolic model for iodine. Times in the boxes are biological removal half-times. The connecting arrows are labeled with the corresponding pathway fractions.

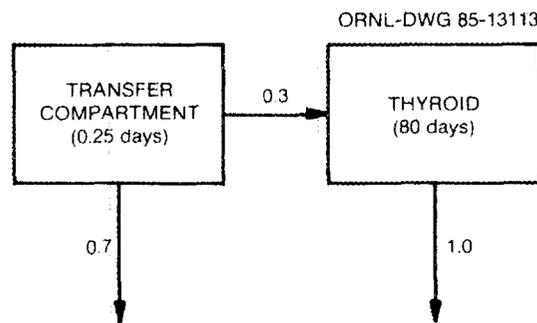


Figure 1b. Two-box metabolic model for iodine, which predicts, for ^{131}I , the same time-integrated radioactivity in the thyroid as the three-box model of Fig. 1a.

For our purposes, the model of Fig. 1b is essentially the functional equivalent of that of Fig. 1a and offers the advantage of fewer parameters.

But the formulation of the two-box model represented by Fig. 1b was not yet ideal for application to the FDA DRH computer file. We needed to be able to specify directly the fractional uptake of the administered isotope by the thyroid. The coefficient 0.3 (in the presence of the other parametric values) gives a maximum uptake of 26% and thus corresponds roughly to the maximum fractional uptake. But some patients' records contained measured uptakes only at times that were unlikely to correspond to the maximum. A model that would accommodate such a pattern of data was needed. To construct one, we proceeded along the following lines of reasoning.

The retention function

When the differential equations that describe the two-box model of Fig. 1b are solved explicitly, the representation of the thyroid compartment has the form

$$A(t) = K \cdot (\exp(-\mu_1 t) - \exp(-\mu_2 t)), \quad (2)$$

where $\mu_i = \lambda_i^b + \lambda_r$ ($i = 1, 2$) are effective decay-rate coefficients, $\lambda_i^b = (\ln 2)/T_i^b$ are biological decay-rate coefficients (the T_i^b are biological removal half-times), and λ_r is the radiological decay-rate coefficient for the radioiodine of interest.

Please note: Throughout this discussion, we assume that $A(t)$ is normalized to the intake of $1 \mu\text{Ci}$ of radioactive iodine into the body. Consequently, in applications, $A(t)$ must be multiplied by the actual number of μCi administered. Note also that $A(0) = 0$, because the initial intake is in the transfer compartment.

We take K , λ_1 , and λ_2 as unknown parameters and impose three constraints to determine their values:

1. $A(t)$ is required to have its maximum at a specified time, $t = t_{\max}$. Normally we will take $t_{\max} = 1$ day, corresponding to the clinical assumption that maximum uptake occurs in approximately 24 hours. For ^{131}I we tested the sensitivity of the time integral of $A(t)$ to the choice of t_{\max} by varying this parameter over a range from 0.5 to 2 days. The maximum deviation of the time integral of $A(t)$ from its reference value was 11%.
2. The function $y^b(t) = \exp(-\lambda_1 t) - \exp(-\lambda_2 t)$ is required to have a specified "apparent" biological half-time, T^* , with respect to a given interval, $t_1 \leq t \leq t_2$ ($t_1 \geq t_{\max}$). We normally set $t_1 = t_{\max}$ and $t_2 = 15$ days, in accordance with the common experimental practice of reporting a single clearance-rate parameter based on the first 15 days' observations. We express this requirement by the equation

$$\frac{y^b(t_2)}{y^b(t_1)} = \exp\left(-\frac{\ln 2}{T^*}(t_2 - t_1)\right). \quad (3)$$

3. Finally, we require that at a specified time, T , the fractional uptake, u , of iodine to the thyroid can be assigned: $A(T) = u$. The time T at which the fractional uptake is actually determined often does not coincide with t_{\max} ; for example, the file contains a number of observations at $T = 6$ hours.

Within the parameter range of interest in this work, the requirements 1-3 given above determine the parameters K , λ_1 , and λ_2 as functions of t_{\max} , t_1 , t_2 , T^* , T , and u . The numerical calculation of K , λ_1 , and λ_2 in a given case involves solving a nonlinear equation. We give the details of the procedure in Appendix A, and Appendix B lists a FORTRAN77 subroutine for carrying out the calculation.

Table 2. Age-Dependent Retention Parameters for ^{131}I in the Thyroid

Age (years)	Rate coefficients (day ⁻¹)		Age (years)	Rate coefficients (day ⁻¹)	
	μ_1	μ_2		μ_1	μ_2
0	0.1324	3.3691	10	0.1032	3.6759
1	0.1403	3.2977	11	0.1020	3.6900
2	0.1328	3.3654	12	0.1010	3.7021
3	0.1241	3.4491	13	0.0997	3.7187
4	0.1182	3.5089	14	0.0988	3.7301
5	0.1140	3.5540	15	0.0980	3.7398
6	0.1108	3.5891	16	0.0973	3.7484
7	0.1083	3.6172	17	0.0967	3.7559
8	0.1062	3.6403	≥18	0.0962	3.7626
9	0.1046	3.6596			

Table 2 displays the rate coefficients μ_1 and μ_2 of Eq. 2 vs. age. The tabulation is based on the parameter values $t_1 = t_{\max} = 1$ day and $t_2 = 15$ days. The following example illustrates how the retention function corresponding to a particular uptake observation is determined. Suppose that $25 \mu\text{Ci}$ of ^{131}I is administered to a ten-year-old male, and after 6 hours it is determined that the thyroid has taken up 9%. Let us calculate the fractional retention function. From Table 2 we have the effective rate coefficients $\mu_1 = 0.1032$, $\mu_2 = 3.6759 \text{ day}^{-1}$, and we are given that for $t = 6 \text{ hours} = 0.25 \text{ day}$,

$$K \cdot (\exp(-0.1032 \times 0.25) - \exp(-3.6759 \times 0.25)) = 0.09$$

so that $K = 0.09/0.5756 = 0.1564$. Since the maximum value occurs at $t_{\max} = 1$ day, we may compute it as follows:

$$u_{\max} = 0.1564 \times (\exp(-0.1032 \times 1) - \exp(-3.6759 \times 1)) = 0.1371$$

or 13.7% (3.4 μCi).

For some combinations of input parameters, however, the formulation just described and illustrated gives misleading results. Such an occurrence results from an estimate of the fractional uptake u at time T that predicts a maximum uptake $u_{\max} = A(t_{\max})$ that exceeds any amount that the thyroid could possibly take up by time t_{\max} , given the structural assumptions of the model and the values of the remaining input parameters. A necessary constraint may be expressed by the inequality

$$A(t_{\max}) < \exp(-\lambda_r t_{\max}), \quad (4)$$

because the value $\exp(\lambda_r t_{\max})$ is an upper bound for the fraction of the administered radioactivity that survives radioactive decay and is available for uptake by the thyroid at time t_{\max} . This upper bound is conservative, because some of the radioiodine would also be removed from the body by biological processes during the interval $[0, t_{\max}]$. But the constraint of Eq. 4 is not built into the model as we have formulated it so far. Our remedy for physically impossible cases is to replace the retention function $A(t)$ by $A^*(t)$, which is computed in the same way, but with $T = t_{\max}$ and $u = u_{\max} = \exp(-\lambda_r t_{\max})$. This use of the conservative upper bound for u_{\max} insures that A^* will not underestimate the uptake, given the model's structure and the other parameter values. But the use of A^* also has the advantage of avoiding dose estimates that are grossly in excess of what is physically possible. The choice, of course, is not consistent with the original input value of u .

We illustrate the handling of such exceptions with the case of a six-year-old who was given 20 μCi of ^{131}I and was reported to have taken up 41.4% after 2 hours = 0.083 day. For age six years, $\mu_1 = 0.1108$ and $\mu_2 = 3.5891 \text{ day}^{-1}$ (Table 2), and we are given

$$K \cdot (\exp(-0.1108 \times 0.083) - \exp(-3.5891 \times 0.083)) = 0.414$$

so that $K = 0.414/0.2485 = 1.666$. This retention function predicts a maximum fractional uptake, at $t_{\max} = 1$ day, of

$$u_{\max} = 1.666 \times (\exp(-0.1108 \times 1) - \exp(-3.5891 \times 1)) = 1.45$$

or 145%, which is impossible. We must conclude that the observation was taken, recorded, or transcribed incorrectly, or that the patient's uptake of the radioiodine was approaching its maximum somewhat earlier than the assumed 24 hours. Having no further information about the patient or the procedure, we discard the observation of 41.4% after 2 hours and instead assume that $u = u_{\max} = \exp(-\lambda_r t)$ at $t = t_{\max} = 1$ day. With $\lambda_r = (\ln 2)/(8.04 \text{ days}) = 0.0862 \text{ day}^{-1}$, this gives $u_{\max} = 0.917$ and

$$K \cdot (\exp(-0.1108 \times 1) - \exp(-3.5891 \times 1)) = 0.917$$

so that $K = 0.917/0.8675 = 1.057$. As we noted earlier, the recomputed retention function $A^*(t)$ cannot be consistent with the reported 41.4% at 2 hours; instead, the value after 2 hours is

$$\begin{aligned} u &= A^*(0.084) = 1.057 \times (\exp(-0.1108 \times 0.083) - \exp(-3.5891 \times 0.083)) \\ &= 0.263 \end{aligned}$$

or 26.3%. The interpretation of this default retention function is that during the first 24 hours, radioiodine is lost from the body only by radioactive decay, whereas after 24 hours it is removed by a combination of radioactive decay and biological processes. Thus, the default represents an upper bound for retention curves having their maximum values at $t = 1$ day and having the same values of the parameters t_1 , t_2 , and T^* .

Whenever the procedure that we have just illustrated had to be applied to a case, the resulting dose estimate was marked with an asterisk as it was written into the revised data file (Table 1). The incidence of such occurrences was confined to a small fraction of the records.

The biological half-time, T^* , of iodine in the thyroid has been estimated in numerous studies with different age groups and is one of the parameters considered by Dunning and Schwarz (1981) in a review of literature for euthyroid patients. Dunning and Schwarz estimated distributions of T^* for each of several age groups ranging from newborn to adult. Their mean value of 85 days for the adult is similar to the 80-day value used by the ICRP (1979). We will use a function that interpolates the mean values given by Dunning and Schwarz (1981) as an age-dependent representation of T^* (Fig. 2).

Thus, Eq. 2, together with constraints 1-3 described previously, defines an age-specific metabolic model of iodine retention in the thyroid. The model can be tied directly to population data through its biological half-time parameter T^* and to specific individual clinical data through the uptake parameters T and u , and it depends only marginally on a parameter (t_{\max}) to which we have less direct access.

The dosimetric S-factor

The remaining factor in the dose-rate equation (Eq. 1) is the S-factor, which depends on the mass of the thyroid, which in turn depends strongly on age and to a much lesser extent on sex. We outline the considerations used in obtaining the S-factors for the model.

We express the S-factor, which represents absorbed dose rate to (target) organ Y per unit radioactivity of the radionuclide of interest in (source) organ X , in the form

$$S(Y \leftarrow X) = k \sum_i n_i E_i \Phi_i(Y \leftarrow X) \quad (5)$$

where

$$\begin{aligned} n_i &= \text{mean number of radiations of type } i \text{ per nuclear transformation} \\ E_i &= \text{mean energy per radiation of type } i \text{ (MeV)} \\ \Phi_i(Y \leftarrow X) &= \text{specific absorbed fraction for radiation type } i \text{ (g}^{-1}\text{)} \\ k &= 2.13 \text{ (rad-g)/}(\mu\text{Ci-hr-MeV)}. \end{aligned}$$

In the present context, $X = Y = \text{thyroid}$. The absorbed dose rate from non-penetrating radiation as a function of thyroid mass M_{th} is

$$S_{\text{np}}(\text{thyroid} \leftarrow \text{thyroid}) = \frac{2.13 \sum_i n_i E_i}{M_{\text{th}}},$$

because $\Phi = 1/M_{\text{th}}$ for such radiations. For ^{131}I , 0.191 MeV of non-penetrating radiation is emitted per nuclear transformation (ICRP, 1983). Thus,

$$S_{\text{np}}(\text{thyroid} \leftarrow \text{thyroid}) = \frac{2.13 \times 0.191}{M_{\text{th}}} = \frac{0.406}{M_{\text{th}}} \text{ rad}/\mu\text{Ci-hr}.$$

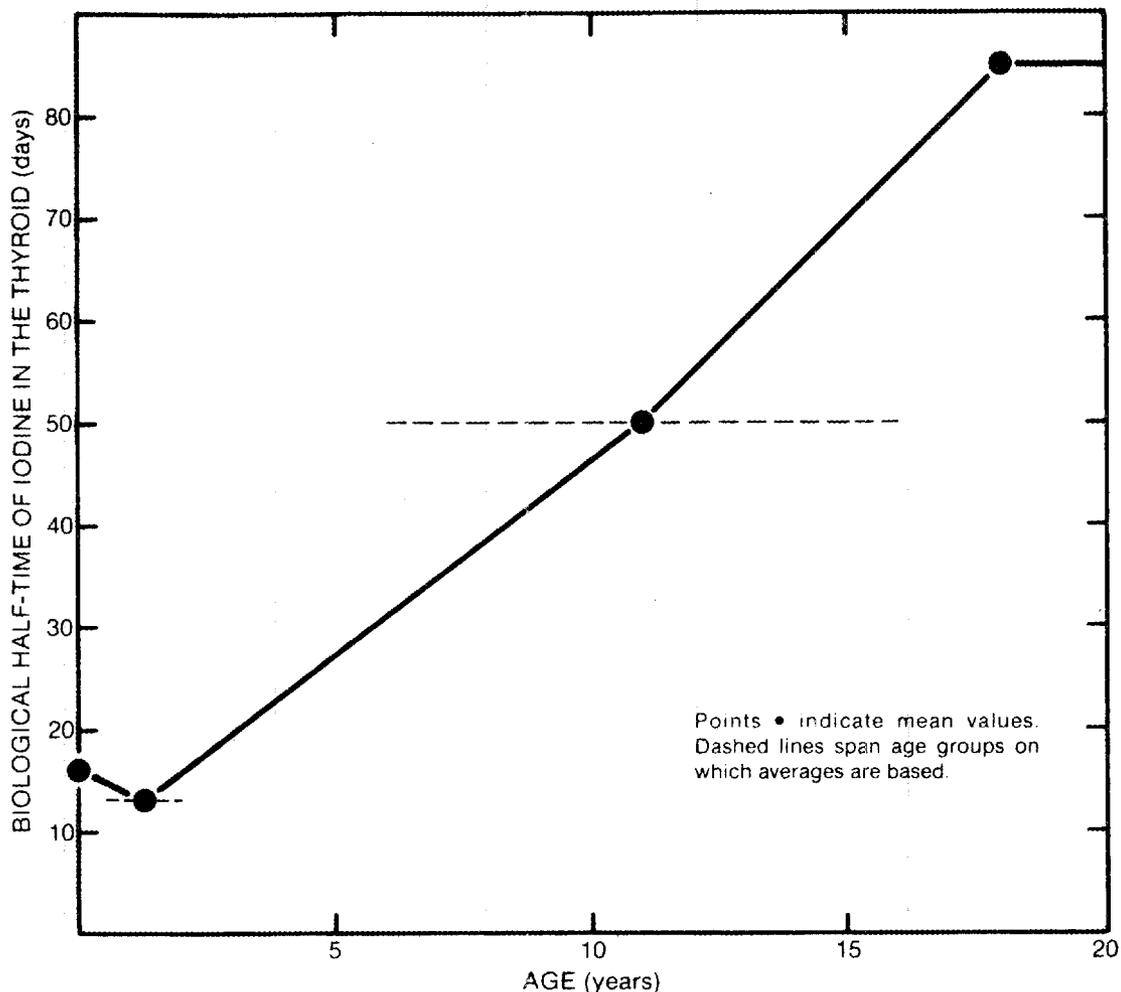


Figure 2. Biological half-time of iodine in the thyroid as a function of age, based on estimates of Dunning and Schwarz (1981).

Monte Carlo calculations of the specific absorbed fraction for photons of energy ranging from 0.01 to 4.0 MeV have been performed for thyroid mass values from 1.29 to 19.6 g (Table 3). An S-factor for the penetrating radiations of ^{131}I was calculated for each specific thyroid mass (Table 4) and fitted to a power function of thyroid mass. The resulting expression is

$$S_p(\text{thyroid} \leftarrow \text{thyroid}) = 1.014 \times 10^{-2} M_{\text{th}}^{-0.666}.$$

This function fits the data with reasonable accuracy. The total S-factor is the sum of the components for non-penetrating and penetrating radiations:

$$S(\text{thyroid} \leftarrow \text{thyroid}) = \frac{0.406}{M_{\text{th}}} + 1.014 \times 10^{-2} M_{\text{th}}^{-0.666}. \quad (6)$$

It remains for us to express the thyroid mass, M_{th} , as a function of age and sex. Kay et al. (1966) analyzed the masses at autopsy of thyroids of 537 subjects of both sexes and of ages ranging from pre-natal to 19 years (all but eight were under 15 years of age). Kay

**Table 3. Photon Specific Absorbed Fraction for the Thyroid
As a Function of Thyroid Mass**

Photon energy (keV)	$\Phi(\text{thyroid} \leftarrow \text{thyroid}) \text{ kg}^{-1}$					
	1.29 g	1.78	3.45	7.93	12.4	19.6
10	533.	390.	215.	100.	66.4	42.9
15	280.	209.	123.	62.7	43.5	29.3
20	145.	110.	67.6	36.4	26.0	18.1
30	49.0	37.0	23.9	13.7	10.2	7.41
50	15.4	11.7	7.68	4.45	3.43	2.42
100	8.73	6.90	4.58	2.62	2.03	1.44
200	9.42	7.72	5.09	2.88	2.20	1.55
500	10.2	8.70	5.71	3.22	2.43	1.66
1,000	9.89	8.18	5.45	3.02	2.29	1.54
2,000	8.26	6.86	4.57	2.56	1.90	1.31
4,000	6.83	5.46	3.38	2.04	1.49	1.05

Table 4. Iodine-131 S-Factor as a Function of Thyroid Mass

Thyroid mass (g)	$S \text{ (rad}/\mu\text{Ci-hr)}$		
	Non-penetrating	Penetrating	Total
1.29	0.314	8.32×10^{-3}	0.323
1.78	0.228	6.95×10^{-3}	0.235
3.45	0.118	4.56×10^{-3}	0.123
7.93	0.0512	2.57×10^{-3}	0.0538
12.4	0.0327	1.95×10^{-3}	0.0347
19.6	0.0207	1.35×10^{-3}	0.0221

et al. fitted the data with the regression line

$$M_{\text{th}} = 1.48 + 0.648a \pm 1.94 \text{ g}, \quad (7)$$

where a = age in years and 1.94 g is the residual standard error. Over the range of ages considered, the difference in thyroid mass between sexes was not found to be significant. To construct our function, we have used the regression line of Eq. (7) for both sexes and ages ranging from newborn to 15 years. For adults, we have adopted the average values 17.5 ± 6.8 g (male) and 14.9 ± 6.7 g (female) from a study of New York City cases (Mochizuki et al., 1963; ICRP, 1975). The articulation of the two data sets was accomplished by interpolating linearly, for each sex, between the value of M_{th} given by Eq. 7 for $a = 15$ years and the appropriate adult value at $a = 25$ years. After 25 years, the functions are considered to be constant (Fig. 3). This scheme furnishes, for each age and sex, a value of M_{th} , which is substituted into Eq. 6 to obtain the S-factor.

Table 5 shows S-factors for males and females and for ages newborn to 25 years. We illustrate the dose computation procedure by referring to an earlier example of a ten-year-old male who was given 25 μCi of ^{131}I and found to have taken up 9% to the thyroid after 6 hours. The fractional retention function was found to be

$$A(t) = 0.1564 \times (\exp(-0.1032t) - \exp(-3.6759t)).$$

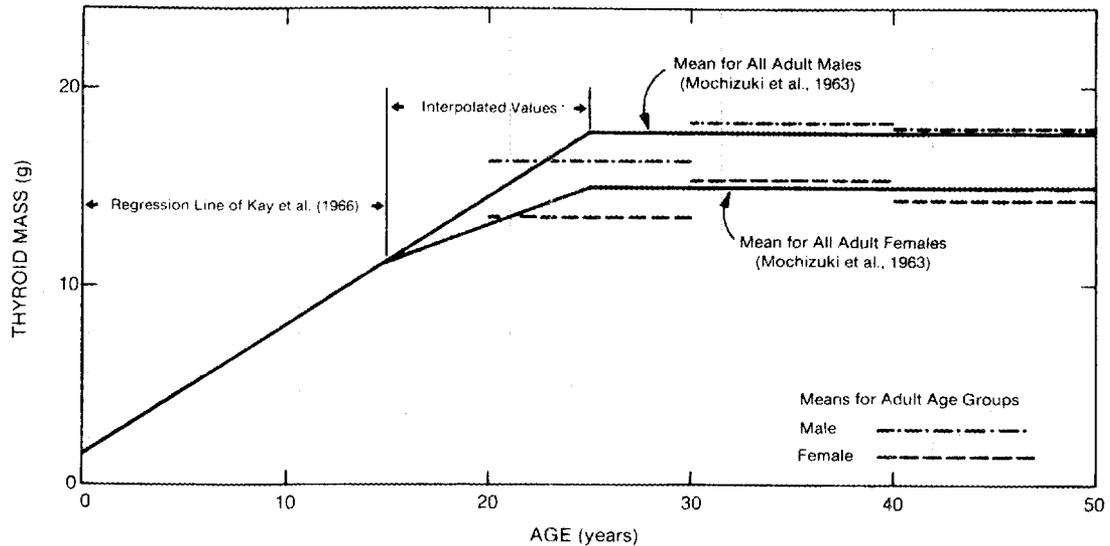


Figure 3. Mass of the thyroid as a function of age.

Table 5. Sex- and Age-Dependent S-Factors for ^{131}I in the Thyroid

Age (years)	S-factors (rad/ μCi -day)		Age (years)	S-factors (rad/ μCi -day)	
	Male	Female		Male	Female
0	6.7709	6.7709	13	1.0367	1.0366
1	4.7259	4.7259	14	0.9740	0.9740
2	3.6332	3.6332	15	0.9187	0.9187
3	2.9529	2.9529	16	0.8706	0.8898
4	2.4883	2.4883	17	0.8273	0.8627
5	2.1509	2.1509	18	0.7882	0.8372
6	1.8946	1.8946	19	0.7527	0.8132
7	1.6933	1.6933	20	0.7203	0.7906
8	1.5309	1.5309	21	0.6906	0.7692
9	1.3972	1.3972	22	0.6632	0.7490
10	1.2852	1.2852	23	0.6380	0.7298
11	1.1899	1.1899	24	0.6146	0.7115
12	1.1080	1.1080	≥ 25	0.5929	0.6942

Integration gives

$$\bar{A} = \int_0^{+\infty} A(t) dt = \frac{0.1564}{0.1032} - \frac{0.1564}{3.6759} = 1.473 \mu\text{Ci-days per } \mu\text{Ci intake.}$$

(The infinite limit of integration, in the case of ^{131}I , gives the same result as an integration time of 50, 70, or 100 years.) The S-factors in Table 5 are in units of rad/ μCi -day. Hence the dose to this patient's thyroid is estimated to be

$$\begin{aligned} D &= 25 \mu\text{Ci} \times 1.285 \text{ rad}/\mu\text{Ci-day} \times 1.473 \mu\text{Ci-day}/\mu\text{Ci} \\ &= 47.3 \text{ rad to the thyroid.} \end{aligned}$$

Calculation with the model

Table 6 gives the results of a calculation performed with this composite dosimetric model. Dose to the thyroid (rad/ μCi) is tabulated by age and sex. For this tabulation, the fractional maximum uptake was based on the age-specific mean values from the review of Dunning and Schwarz (1981). For comparison, corresponding estimates of ^{131}I dose to the thyroid by Dunning and Schwarz (1981), Johnson (1981), ICRP (Eckerman et al., 1981), Medical Internal Radiation Dosimetry (MIRD) Committee (1975), and the U.K. National Radiological Protection Board (NRPB, 1983) are shown alongside.

Table 6. Iodine-131 Dose to the Thyroid by Age and Sex (rad μCi^{-1})

Age	Present model		Johnson, 1981		Dunning and Schwarz, 1981 (Both sexes)	ICRP methodology ^a (Both sexes)	MIRD, 1975 (Both sexes)	NRPB, 1983 ^b (Both sexes)
	Male	Female	Male	Female				
0	25.1	25.1	15.1	15.1	25.3			
1	14.4	14.4	10.8	10.8				13.7
2	11.4	11.4	7.95	7.95	14.2 ^c			
3	10.0	10.0						
4	9.0	9.0						
5	8.2	8.2	5.34	5.34				
6	7.5	7.5						
7	7.0	7.0						
8	6.5	6.5						
9	6.1	6.1						
10	5.9	5.9	3.35	3.35				4.4
11	5.6	5.6			8.5			
12	4.8	4.8						
13	4.1	4.1						
14	3.5	3.5						
15	2.9	2.9	2.29	2.29				
16	2.5	2.5						
17	2.0	2.1						
18	1.6	1.7	1.38	1.66	1.4	1.8	1.3 ^d	1.6
19	1.5	1.7						
20	1.5	1.6						
21	1.4	1.6						
22	1.3	1.5						
23	1.3	1.5						
24	1.2	1.4						
25	1.2	1.4						

^aEckerman et al. (1981).

^bStather et al. (1983).

^c0.5-2 years.

^dBased on maximum uptake to the thyroid of 25% and thyroid mass 20 g.

In general, the agreement among these estimates of dose per unit intake is good, but the comparison with the factors of Johnson (1981), which for the younger age groups are systematically less than our factors, deserves further comment. In the case of our model, the fractional uptake and the biological half-time for iodine in the thyroid are considered

to be observables and are furnished from clinical or experimental data. In the model of Johnson, however, these quantities are not specified directly but are defined implicitly by the model's kinetics. We have estimated their values by solving the differential equations of the model after following the calibration procedure set forth by Johnson (1981). The following table compares the values of the fractional uptake and the biological half-time with the corresponding parameters from Dunning and Schwarz (1981) for newborn infants and adults:

		Present model	Johnson (1981)
Maximum level of iodine in the thyroid (%)	Newborn	46	25
	Adult	19	25
Effective biological half-time of iodine in the thyroid (days)	Newborn	16	72
	Adult	85	142

For newborns, the Johnson model simulates a much lower fractional uptake than the Dunning and Schwarz value that was used in our model. This disparity in uptake fractions explains most of the difference in the dose conversion factors; because of the 8-day half-life of ^{131}I , the much slower removal simulated by the Johnson model's kinetics cannot offset the gap in uptakes. In the case of adults, however, the fractional uptakes are reversed, but the difference between them is less. For longer-lived radioiodines (^{125}I and ^{129}I), the contrast in the apparent biological half-times between the two models becomes significant, and the dose conversion factors calculated with the Johnson model for the youngest age groups are marginally larger than the corresponding factors calculated with our model.

The discrepancies in the two models' predictions lie almost entirely in their metabolic representations; their S-factors for corresponding age groups differ by at most a few percent.

SENSITIVITY OF THE DOSE MODEL TO UNCERTAINTIES IN ITS PARAMETERS

We have tested the sensitivity of the dose estimate to uncertainties in two of the model parameters by replacing those parameters with probability distributions and estimating the corresponding distribution of the dose. The parameters are the biological half-time of iodine in the thyroid (T^*) and the mass of the thyroid (M_{th}). The calculations, which were performed by pseudorandom sampling from the input probability distributions, were carried out for each of the four age groups considered by Dunning and Schwarz (1981):

- newborn
- children 0.5–2 years
- adolescents 6–16 years
- adults ≥ 18 years.

For each age group, the corresponding estimate by Dunning and Schwarz of the mean value of fractional uptake by the thyroid was used. Substitution of different values of fractional uptake—such as clinically determined uptakes—would, of course, lead to different distributions of dose, but the distributions we have computed should give a reasonable impression of variability in the dose estimates for fixed fractional uptake.

Other fixed parameters and their values that were used in the simulations were t_{max} (1 day), t_1 (1 day), t_2 (15 days), and T (1 day).

The biological half-time of iodine in the thyroid, T^* , and the mass of the thyroid, M_{th} , were treated, for each age group, as independent random variables on the assumption that independence would represent an extreme case. The distribution of T^* was assumed to be lognormal with values of the logarithmic mean and standard deviation, μ and σ , taken from Dunning and Schwarz (1981). For each nonadult group, M_{th} was assumed lognormally distributed with logarithmic parameters μ and σ computed from the mean and standard deviation (α and β) given by Kay et al. (1966). Sexes were consolidated in accordance with the conclusion of Kay et al. that in the nonadult groups the difference in thyroid mass between males and females is not statistically significant. The equations are

$$\mu = \ln \frac{\alpha}{\sqrt{1 + \beta^2/\alpha^2}} \quad \sigma^2 = \ln(1 + \beta^2/\alpha^2).$$

These equations were obtained by solving the inverse equations given by Aitchison and Brown (1969; Sect. 2.3). For adults, we followed a similar procedure, but with differentiation by sex, using lognormal distributions with parameters based on autopsies performed in New York City for individuals aged 20 to 30 years. These autopsy data were originally reported by Mochizuki et al. (1963) and were reprinted in the Reference Man Report (ICRP, 1975).

Figure 4 gives an indication of the distribution of dose for each of the age groups. In absolute terms, the variability shown in Fig. 4 is large for the newborn and children's groups (99th percentile = 75 and 41 rad, respectively) and progressively smaller with increasing age. But in relative terms, the variability changes little with age: the coefficients of variation (standard deviation divided by the mean) for all of these groups cluster closely about the value 0.5.

Note: The uncertainty analysis described in this section represents a departure from the procedure reported by Killough and Eckerman (1985). The present analysis is based on variances β^2 in thyroid mass that are specific to age, whereas for the previous work it was assumed that all sub-adult groups had a common variance. We are indebted to F.O. Hoffman, ORNL Environmental Sciences Division, for suggesting that we perform the analysis with thyroid mass variance specific to each age group.

DISTRIBUTION OF DOSE AMONG PATIENTS IN THE FDA DRH DATA FILE

A detailed accounting of the information in the FDA DRH file is beyond the scope of this report. For the general reader, however, it may be of interest to see how dose as estimated by the model is distributed within the population of patients represented by the file. Table 7 shows the frequency (i.e., number of patients) within each of seven age groups and 10 levels of radiation dose to the thyroid from administered ^{131}I . For inclusion in Table 7, each patient's total dose was computed by adding the result of each administration. Patients for whom no dose could be computed were represented by zero and were tallied in the column for < 1 rad.

In a few cases, considerable intervals of time elapsed between administrations to a given patient, and there may be a few individuals whose experience spanned more than one age group. In all cases, the age corresponding to the most recent administration was arbitrarily assigned to the individual for the purposes of the table. Such situations are too rare to have an important effect on the tabulated frequencies.

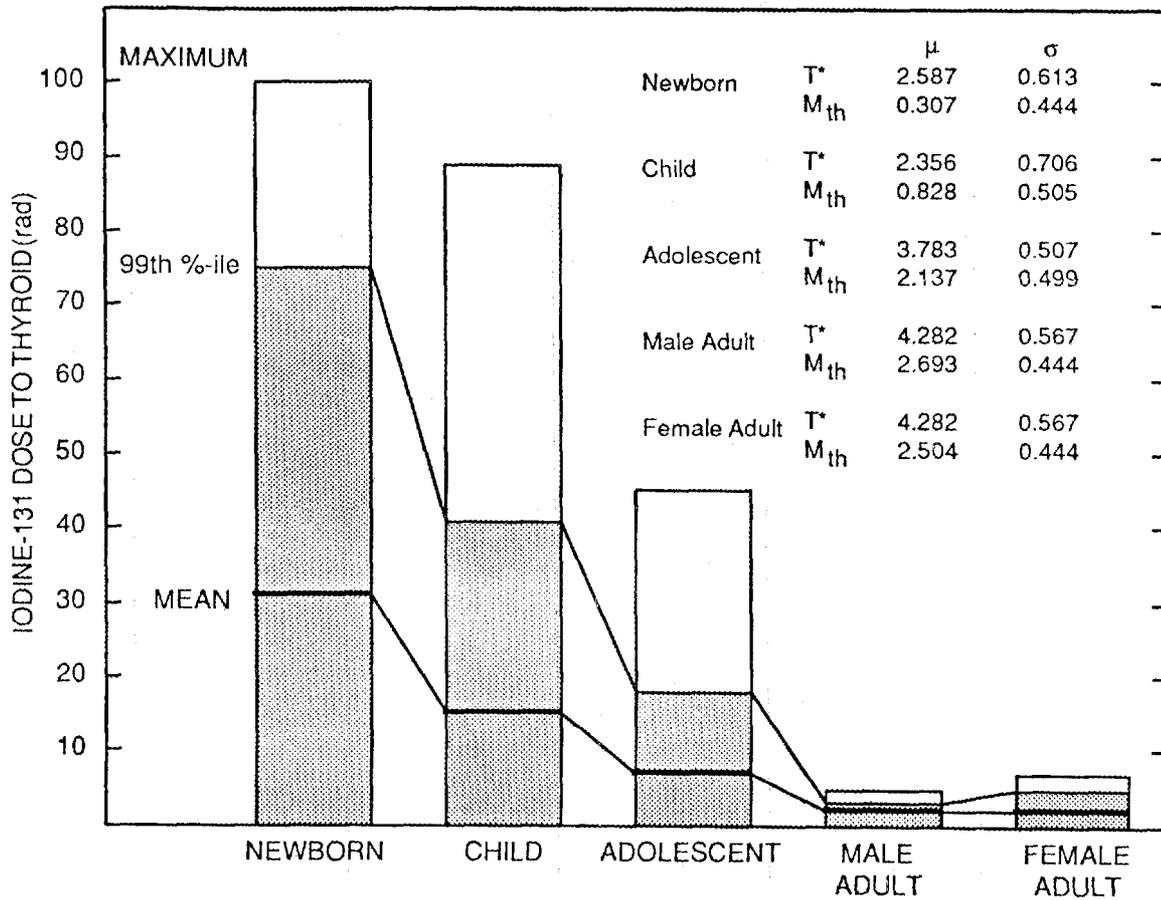


Figure 4. Distributions of thyroid dose corresponding to uncertainties in biological half-time T^* and mass M_{th} .

Table 7. Joint Frequency of Thyroid Dose and Age for Subjects In the FDA DRH Data File

	Dose (rad)										Total
	< 1	1-5	5-10	10-50	50-100	100-500	500-1000	1000-2000	2000-3000	> 3000	
Newborn	0	0	0	1	0	0	2	0	0	0	3
0-6 mo.	31	23	14	32	10	27	7	2	0	0	146
6 mo.-1 yr.	15	8	9	18	5	22	5	1	0	0	83
1-6 yr.	39	42	43	184	112	179	15	6	3	3	626
6-12	38	49	63	372	279	274	19	8	1	1	1104
12-18	77	56	82	664	432	357	16	7	0	2	1693
> 18	35	24	31	198	124	130	14	5	0	0	561
Total	235	202	242	1469	962	989	78	29	4	6	4216

Readers are reminded once again that the doses were estimated in a way appropriate for subjects with normal thyroid function, and the incidence of abnormal thyroid function in the population under study could bias the frequencies presented in Table 7.

SUMMARY AND CONCLUSIONS

We have described the derivation and application of an age- and sex-specific model of ^{131}I dosimetry for the thyroid. The model was specially formulated for the data base that will support the Diagnostic ^{131}I Study conducted by DRH; in particular, the model accommodates values of fractional uptake to the thyroid that were determined at various times after administration, including but not restricted to the time of maximum thyroid burden. The model has been applied to all records of the data file for which the uptake and retention data are complete or can be estimated from other records for the same patient, and each computed thyroid dose has been incorporated into the appropriate record.

Tests of sensitivity of the model's predictions to uncertainties in the biological half-time of iodine in the thyroid and the mass of the organ were performed. These tests showed large absolute variability in the dose for newborns and children, but relative measures of dispersion, such as the coefficient of variation, differ little among age groups. Inasmuch as there was no clinical determination of thyroid mass nor of biological half-time of iodine in the thyroid for the patients in this study, our estimates of variability in dose due to uncertainty about these variables could be of interest to the investigators in the Diagnostic ^{131}I Study and also to those who make generic applications of the model.

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REFERENCES

- Aitchison, J., and J.A.C. Brown. 1969. *The Lognormal Distribution*, Cambridge University Press.
- Berman, M. 1972. "Iodine Kinetics," Chapter 11 in: *The Thyroid and Biogenic Amines* (J.E. Rall and I.J. Kopin, editors), Vol. I of *Methods in Investigative Endocrinology* (S.A. Berson, series editor). North-Holland Publishing Company.
- Cristy, M., and K.F. Eckerman. *Specific Absorbed Fractions of Energy at Various Ages from Internal Photon Sources*. ORNL/TM-8381 Vol. 1 - Vol. 6 (in preparation).
- Dunning, D.E., Jr., and G. Schwarz. 1981. "Variability of Human Thyroid Characteristics and Estimates of Dose from Ingested ^{131}I ." *Health Phys.* 40(5): 661-675.
- Eckerman, K.F., M.R. Ford, and S.B. Watson. 1981. *Internal Dosimetry Data and Methods of ICRP—Part 2, Vol. 1: Committed Dose Equivalent and Secondary Limits*, NUREG/CR-1962 Volume 1, ORNL/NUREG/TM-433/VI.

- Forsythe, G.E., M.A. Malcolm, and C.B. Moler. 1977. *Computer Methods for Mathematical Computations*. Englewood Cliffs, New Jersey: Prentice-Hall.
- International Commission on Radiological Protection. 1983. *Radionuclide Transformations—Energy and Intensity of Emissions*, ICRP Publication 38. Oxford: Pergamon Press.
- International Commission on Radiological Protection. 1979. *Limits for Intakes of Radionuclides by Workers*, ICRP Publication 30 Part 1, *Ann. ICRP* 2(3/4): 88–93.
- International Commission on Radiological Protection. 1975. *Report of the Task Group on Reference Man*, ICRP Publication 23. Oxford: Pergamon Press.
- Johnson, J.R. 1981. "Radioiodine Dosimetry." *J. Radioanal. Chem.* 65(1–2): 223–238.
- Kay, C., S. Abrahams, and P. McClain. 1966. "The Weight of Normal Thyroid Glands in Children," *Arch. Path.* 82: 349–352.
- Killough, G.G., and K.F. Eckerman. 1986. "An Age- and Sex-Dependent Model for Estimating Dose to a Normal Thyroid." *Proc. Fourth International Radiopharmaceutical Dosimetry Symposium*, Oak Ridge, Tennessee, November 5–8, 1985 (in press).
- Medical Internal Radiation Dosimetry (MIRD) Committee. 1975. "Summary of Current Radiation Dose Estimates to Humans from ^{123}I , ^{124}I , ^{126}I , ^{130}I , ^{131}I , and ^{132}I as Sodium Iodide," Dose Estimate Report No. 5, *J. Nucl. Med.* 16(9): 857–860.
- Mochizuki, Y., R. Mowafy, and B. Pasternack. 1963. "Weights of Human Thyroids in New York City," *Health Phys.* 9: 1299–1301. Data reproduced in ICRP Publication 23 (1975), p. 198.
- Riggs, D.S. 1952. "Quantitative Aspects of Iodine Metabolism in Man," *Pharmacol. Rev.* 4: 284–370.
- Stather, J.W., J.R. Greenhalgh, and N. Adams. 1983. "The Metabolism of Iodine in Children and Adults," *NRPB Radiol. Prot. Bull.* No. 54 (ISSN 0308-4272).

Appendix A

COMPUTATIONAL PROCEDURE FOR THE THYROID UPTAKE AND RETENTION FUNCTION

This appendix gives details of the determination of the fractional uptake and retention function for ^{131}I in the thyroid given by Eq. 2. The basis for the determination of the parameters μ_1 , μ_2 , and K is three constraints, which we recapitulate:

First constraint

The fraction $A(t)$ defined in Eq. 2 must take its maximum value at a specified time, $t = t_{\max}$.

This constraint requires that the derivative of $A(t)$ vanish at $t = t_{\max}$:

$$\frac{dA}{dt} = -K(\mu_1 e^{-\mu_1 t_{\max}} - \mu_2 e^{-\mu_2 t_{\max}}) = 0,$$

from which we obtain

$$\frac{\mu_1}{\mu_2} = e^{(\mu_1 - \mu_2)t_{\max}}. \quad (\text{A1})$$

We introduce the following transformation of $(\mu_1, \mu_2) \mapsto (r, s)$:

$$\begin{aligned} r &= \mu_1 / \mu_2 \\ s &= \mu_2 - \mu_1 \quad (0 \leq \mu_1 < \mu_2) \end{aligned} \quad (\text{A2})$$

with inverse

$$\begin{aligned} \mu_1 &= rs / (1 - r) \\ \mu_2 &= s / (1 - r) \quad (0 \leq r < 1, s > 0). \end{aligned} \quad (\text{A3})$$

Using Eq. A1, we may express s explicitly in terms of r :

$$s = -t_{\max}^{-1} \ln r. \quad (\text{A4})$$

This relationship will enable us to eliminate s and obtain a single equation in r .

Second constraint

The biological retention function

$$q^b(t) = e^{\lambda_r t} A(t) = K(e^{-\lambda_1 t} - e^{-\lambda_2 t}) \quad (\text{A5})$$

is to have a specified biological half-time, T^* , with respect to a given interval $t_1 \leq t \leq t_2$, where $t_1 \geq t_{\max}$, in the sense that the equation

$$\frac{q^b(t_2)}{q^b(t_1)} = \exp\left(-\frac{\ln 2}{T^*}(t_2 - t_1)\right) \quad (\text{A6})$$

must be satisfied.

The function $q^b(t)$, through λ_1 and λ_2 and the transformation of Eq. A2, depends on the parameters r and s ; the latter parameter can be eliminated by Eq. A4, leaving q as a function of t with parameter r . The explicit dependence can be shown to be

$$q^b(t; r) = K r^{[r/(1-r)](t/t_{\max})} e^{\lambda_r t} (1 - r^{t/t_{\max}}). \quad (\text{A7})$$

When Eq. A7 is substituted into Eq. A6, the result is a nonlinear equation in the variable r , which can be solved numerically to obtain the solution $r = r^*$. Then from Eqs. A3 and A4, we may compute

$$\begin{aligned} s^* &= -t_{\max}^{-1} \ln r^* \\ \lambda_1 &= \mu_1 - \lambda_r = r^* s^* / (1 - r^*) - \lambda_r \\ \lambda_2 &= \mu_2 - \lambda_r = s^* / (1 - r^*) - \lambda_r \end{aligned} \quad (\text{A8})$$

and thus the ratio $q^b(t)/K$ (Eq. A5) is determined.

Third constraint

For a specified time T and fractional uptake u by the thyroid, we must have

$$A(T) = u \quad \text{if} \quad A(t_{\max}) \leq \exp(-\lambda_r t_{\max}). \quad (\text{A9})$$

In the event that $A(t_{\max}) > \exp(-\lambda_r t_{\max})$, we substitute the function $A^*(t)$, which is computed by the requirement

$$A^*(t_{\max}) = \exp(-\lambda_r t_{\max}). \quad (\text{A10})$$

In case the condition of Eq. A9 holds, the determination of the constant K is as follows:

$$K = \frac{u}{e^{-\mu_1 T} - e^{-\mu_2 T}}. \quad (\text{A11})$$

Otherwise

$$K = \frac{1}{e^{-\lambda_1 t_{\max}} - e^{-\lambda_2 t_{\max}}}. \quad (\text{A12})$$

Summary of the computational procedure

Substitute Eq. A7 into Eq. A6 and solve for $r = r^*$. Then use Eq. A8 to calculate μ_1 and μ_2 . Finally, obtain K from Eq. A11 or Eq. A12, according to whether or not the inequality

$$u \cdot \frac{e^{-\lambda_1 t_{\max}} - e^{-\lambda_2 t_{\max}}}{e^{-\lambda_1 T} - e^{-\lambda_2 T}} \leq e^{-\lambda_r T}$$

is satisfied.

Appendix B

COMPUTER IMPLEMENTATION OF THE DOSE MODEL

The FORTRAN77 subroutine IRET (Iodine RETention) goes a bit beyond its name and computes integrated activity and dose, as well as returning the rate constants λ_1 and λ_2 and the coefficient K . It is provided to assist the reader who needs to examine the details of the calculation and should be studied primarily in connection with Appendix A. Subroutine IRET invokes the nonlinear equation solver ZEROIN (or more precisely, a double-precision version of it), which was taken from Forsythe et al. (1977; p. 164ff). Other equation solvers might be substituted, but those requiring the evaluation of one or more derivatives will demand additional effort on the part of the user, because no code for calculating derivatives is included in the listings that follow.

```

SUBROUTINE IRET(LMR,TMAX,TCAP,U,T1,T2,AGE,SEX,
$             AWIGL,DOSE,K,LM1,LM2)
C
C ESTIMATES PARAMETERS OF A THYROID-IODINE RETENTION FUNCTION OF THE FORM
C
C   FCN(T) = K*(EXP(-(LMR+LM1)*T) - EXP(-(LMR+LM2)*T)),
C
C WHERE LMR = RADIOLOGICAL DECAY CONSTANT (1/DAY) FOR THE PARTICULAR ISOTOPE
C OF IODINE, AND K, LM1, AND LM2 ARE THE UNKNOWN PARAMETERS. THE CRITERIA FOR
C THEIR DETERMINATION ARE:
C
C   (1) THE MAXIMUM VALUE OCCURS AT A SPECIFIED TIME, TMAX > 0.
C   (2) THE VALUE AT A SPECIFIED TIME, TCAP, IS A GIVEN NUMBER, U.
C   (3) THE APPARENT BIOLOGICAL HALF-TIME IN THE RANGE (T1,T2),
C       WHERE TMAX <= T1 < T2, IS A GIVEN VALUE TSTAR.
C
C INPUT PARAMETERS:  LMR (1/DAY),
C                   TMAX, TCAP (DAYS),
C                   U (FRACTION),
C                   T1, T2 (DAYS),
C                   AGE (YEARS),
C                   SEX (1=M, 2=F)
C RETURNED VALUES: AWIGL (MICROCURIE-DAYS PER MICROCURIE INTAKE),
C                   DOSE (RAD),
C                   K (MICROCURIE-DAYS),
C                   LM1, LM2 (1/DAY)
C
C   IMPLICIT REAL*8 (A-H,O-Z), INTEGER (I-N)
C   REAL*8 K,LMR,LM1,LM2,MTH
C   INTEGER SEX
C   EXTERNAL FCN
C   DIMENSION X(2),F(2),WA(13)
C   COMMON CVAR(5)
C   QBYA(T,X1,X2)=DEXP(-(X1+LMR)*T)-DEXP(-(X2+LMR)*T)
C
C COMPUTE APPARENT BIOLOGICAL HALF TIME OF IODINE IN THE THYROID AS A
C FUNCTION OF THE AGE VALUE THAT WAS JUST READ IN. THE PIECEWISE LINEAR

```

```

C FUNCTION EVALUATED BELOW IS BASED ON THE REVIEW OF DUNNING & SCHWARZ.
  IF (AGE .GE. 0DO .AND. AGE .LT. 1.25DO) THEN
    TSTAR=16DO-2.4DO*AGE
  ELSEIF (AGE .GE. 1.25DO .AND. AGE .LT. 13DO) THEN
    TSTAR=8.26DO+3.80DO*AGE
  ELSEIF (AGE .GE. 13DO .AND. AGE .LT. 18DO) THEN
    TSTAR=-5DO+5DO*AGE
  ELSE
    TSTAR=85DO
  ENDIF
C SOLVE THE EQUATIONS FOR LM1, LM2, AND A FOR THE METABOLIC MODEL
C
C MOVE VALUES OF DUMMY PARAMETERS TO COMMON AREA TO MAKE THEM AVAILABLE
C TO FCN
  CVAR(1)=LMR
  CVAR(2)=TMAX
  CVAR(3)=T1
  CVAR(4)=T2
  CVAR(5)=TSTAR
  AR=.001DO
  BR=.99DO
  TOL=1D-6
C INVOKE DOUBLE-PRECISION VERSION OF ZEROIN (FORSYTHE, MALCOLM, AND MOLER,
C 1977) TO SOLVE EQ. A6 FOR R, WHERE THE DEPENDENCE OF QB(T) ON R IS GIVEN
C BY EQ. A5.
  R=ZEROIN(AR,BR,FCN,TOL)
  S=-DLOG(R)/TMAX
  LM1=R*S/(1DO-R)-LMR
  LM2=S/(1DO-R)-LMR
  K=U/QBYA(TCAP,LM1,LM2)
C EVALUATE THE INTEGRAL OF THE THYROID BURDEN (Q) FROM 0 TO 50 YEARS
  AWIGL=K*((1DO-DEXP(-(LM1+LMR)*18250.DO))/(LM1+LMR)
  $ -(1DO-DEXP(-(LM2+LMR)*18250.DO))/(LM2+LMR))
C COMPUTE THE S-FACTOR (REM/MICROCURIE-DAY) FOR THE GIVEN AGE AND SEX
  IF (AGE .GE. 0DO .AND. AGE .LE. 15DO) THEN
    MTH=1.48DO+0.648DO*AGE
  ELSEIF (AGE .GT. 15DO .AND. AGE .LE. 25DO) THEN
    IF (SEX .EQ. 1) THEN
      MTH=1.75DO+0.63DO*AGE
    ELSE
      MTH=5.65DO+0.37DO*AGE
    ENDIF
  ELSE
    IF (SEX .EQ. 1) THEN
      MTH=17.5DO
    ELSE
      MTH=14.9DO
    ENDIF
  ENDIF
C MTH = AGE- AND SEX-DEPENDENT MASS OF THE THYROID IN GRAMS
C THIS APPROACH USES THE REGRESSION CURVE MTH=1.48+.648*AGE FROM
C KAY ET AL. (1966) FOR BOTH SEXES, AND FROM 15 TO 25 YEARS EXTRAPOLATES

```

C LINEARLY TO OBTAIN THE VALUES 17.5 (MALE) AND 14.9 G FROM NEW YORK CITY DATA
C PRESENTED IN REFERENCE MAN (ORIGINALLY FROM MOCHIZUKI ET AL., 1963).

SFACT=(4.0598D-1/MTH+1.014D-2*MTH**(-0.666DO))*24.DO

C THIS S-FACTOR IS SPECIFIC TO IODINE-131

DOSE=SFACT*AWIGL

RETURN

END

FUNCTION FCN(R)

IMPLICIT REAL*8 (A-H,O-Z), INTEGER (I-N)

REAL*8 LMR, LB1, LB2

LOGICAL FIRST

COMMON LMR, TMAX, T1, T2, TSTAR

DATA FIRST/.TRUE./

QB(T)=DEXP(R/(1DO-R)*T/TMAX*DLR)*DEXP(LMR*T)

\$ *(1DO-DEXP(T/TMAX*DLR))

C

IF (.NOT. FIRST) GOTO 10

FIRST=.FALSE.

DL2=DLOG(2.DO)

10 CONTINUE

DLR=DLOG(R)

FCN=QB(T2)-QB(T1)*DEXP(-DL2/TSTAR*(T2-T1))

RETURN

END

Appendix C

ADDENDUM: DOSE CONVERSION FACTORS FOR OTHER RADIOIODINES

The foregoing portions of this report describe the development of dosimetric information for the Diagnostic ^{131}I study conducted by the National Center for Devices and Radiological Health (DRH) and represents a final report for that work. This appendix discusses work that we have performed recently to extend the method to radioactive isotopes of iodine other than mass number 131. This recent work incorporates certain departures from the method employed for the DRH study, but the resulting doses to the thyroid from ^{131}I are for all practical purposes the same; hence there is no reason to revise any of the dose estimates that were written into the DRH data file. The following subsections explain the adjustments that were made in order to calculate age- and sex-dependent dose conversion factors ($\text{rad } \mu\text{Ci}^{-1}$) for other radioiodines. Dose conversion factors for most radioactive isotopes of iodine are tabulated (Table C1) as well as the coefficients and parameters of the model (Tables C2 and C3).

The Retention Function

The principal change of approach in deriving the retention function is that we now postulate the time, t_{max} , at which the *biological* retention function

$$q^b(t) = K(e^{-\lambda_1 t} - e^{-\lambda_2 t}) \quad (\text{C1})$$

takes its maximum value (the earlier method considered the maximum of the function $A(t) = e^{-\lambda_r t} q^b(t)$). And we have adopted $t_{\text{max}} = 2$ days as being typical of the normal thyroid (Bell, Davidson, and Scarborough, 1968). One may obtain the revised calculation from Appendix A by putting $\lambda_r = 0$ and making the replacements $\mu_i \leftarrow \lambda_i$, $i = 1, 2$, and $A(\) \leftarrow q^b(\)$ in Eqs. A1 through A12.

Table C2 lists the computed quantities K , λ_1 , and λ_2 for newborn and through age 18 years; the values for adults are the same as those for 18 years. The uptake fraction, u , and biological half-time, T^* , are taken from the review of Dunning and Schwarz (1981); T^* vs. age is plotted in Fig. 2, and uptake vs. age is shown in Fig. C1.

Table C2. Age-Dependent Retention Coefficients for Iodine in the Thyroid

Age	K	λ_1	λ_2	Age	K	λ_1	λ_2
0	5.268055(-1)	4.515202(-2)	1.920236	10	4.791605(-1)	1.544690(-2)	2.573194
1	4.652511(-1)	5.325276(-2)	1.818654	11	4.862500(-1)	1.426617(-2)	2.620971
2	4.445201(-1)	4.555638(-2)	1.914753	12	4.437564(-1)	1.325277(-2)	2.665159
3	4.430334(-1)	3.664530(-2)	2.048413	13	4.011307(-1)	1.188835(-2)	2.730168
4	4.449618(-1)	3.064626(-2)	2.157817	14	3.591805(-1)	1.096815(-2)	2.778261
5	4.487747(-1)	2.633288(-2)	2.250343	15	3.175215(-1)	1.018005(-2)	2.822688
6	4.537359(-1)	2.308210(-2)	2.330465	16	2.760936(-1)	9.498037(-3)	2.863931
7	4.594484(-1)	2.054477(-2)	2.401078	17	2.348510(-1)	8.900370(-3)	2.902521
8	4.656786(-1)	1.850898(-2)	2.464190	≥ 18	1.937611(-1)	8.374135(-3)	2.938654
9	4.722818(-1)	1.684042(-2)	2.521193				

Table C1. Dose to the Thyroid (rad μCi^{-1}) for Various Radioiodine Isotopes

Age	Male													
	^{121}I	^{122}I	^{123}I	^{124}I	^{125}I	^{126}I	^{128}I	^{129}I	^{130}I	^{131}I	^{132}I	^{133}I	^{134}I	^{135}I
0	4.9(-2)	4.7(-4)	2.7(-1)	1.6(+1)	7.7	2.9(+1)	1.5(-2)	2.5(+1)	2.4	2.5(+1)	2.7(-1)	6.2	5.6(-2)	1.2
1	2.9(-2)	2.7(-4)	1.6(-1)	9.6	4.3	1.6(+1)	8.8(-3)	1.4(+1)	1.5	1.5(+1)	1.6(-1)	3.7	3.3(-2)	6.8(-1)
2	2.3(-2)	2.1(-4)	1.3(-1)	7.4	3.7	1.3(+1)	6.8(-3)	1.2(+1)	1.1	1.1(+1)	1.2(-1)	2.8	2.6(-2)	5.2(-1)
3	2.0(-2)	1.9(-4)	1.1(-1)	6.4	3.6	1.2(+1)	5.9(-3)	1.2(+1)	9.5(-1)	1.0(+1)	1.0(-1)	2.3	2.2(-2)	4.5(-1)
4	1.8(-2)	1.7(-4)	9.4(-2)	5.6	3.6	1.1(+1)	5.3(-3)	1.2(+1)	8.3(-1)	9.0	9.3(-2)	2.0	2.0(-2)	3.9(-1)
5	1.6(-2)	1.5(-4)	8.4(-2)	5.1	3.5	9.9	4.8(-3)	1.2(+1)	7.4(-1)	8.2	8.4(-2)	1.8	1.8(-2)	3.5(-1)
6	1.5(-2)	1.4(-4)	7.7(-2)	4.6	3.4	9.2	4.4(-3)	1.3(+1)	6.8(-1)	7.5	7.7(-2)	1.6	1.7(-2)	3.2(-1)
7	1.4(-2)	1.3(-4)	7.1(-2)	4.3	3.4	8.6	4.1(-3)	1.3(+1)	6.2(-1)	7.0	7.2(-2)	1.5	1.6(-2)	2.9(-1)
8	1.3(-2)	1.2(-4)	6.6(-2)	4.0	3.3	8.2	3.9(-3)	1.3(+1)	5.8(-1)	6.5	6.7(-2)	1.4	1.5(-2)	2.7(-1)
9	1.3(-2)	1.2(-4)	6.2(-2)	3.7	3.3	7.8	3.6(-3)	1.3(+1)	5.4(-1)	6.2	6.3(-2)	1.3	1.4(-2)	2.6(-1)
10	1.2(-2)	1.1(-4)	5.8(-2)	3.5	3.2	7.4	3.5(-3)	1.4(+1)	5.1(-1)	5.8	6.0(-2)	1.2	1.3(-2)	2.4(-1)
11	1.1(-2)	1.1(-4)	5.6(-2)	3.3	3.2	7.1	3.3(-3)	1.4(+1)	4.9(-1)	5.6	5.7(-2)	1.1	1.3(-2)	2.3(-1)
12	9.9(-3)	9.1(-5)	4.8(-2)	2.9	2.9	6.1	2.9(-3)	1.3(+1)	4.2(-1)	4.8	5.0(-2)	9.8(-1)	1.1(-2)	2.0(-1)
13	8.6(-3)	7.9(-5)	4.1(-2)	2.5	2.6	5.3	2.5(-3)	1.2(+1)	3.6(-1)	4.1	4.3(-2)	8.4(-1)	9.4(-3)	1.7(-1)
14	7.4(-3)	6.7(-5)	3.5(-2)	2.1	2.3	4.5	2.1(-3)	1.1(+1)	3.0(-1)	3.5	3.6(-2)	7.1(-1)	8.0(-3)	1.4(-1)
15	6.2(-3)	5.7(-5)	2.9(-2)	1.7	2.0	3.8	1.8(-3)	9.9	2.6(-1)	2.9	3.1(-2)	5.9(-1)	6.8(-3)	1.2(-1)
16	5.2(-3)	4.8(-5)	2.4(-2)	1.4	1.7	3.2	1.5(-3)	8.7	2.1(-1)	2.4	2.6(-2)	4.9(-1)	5.7(-3)	1.0(-1)
17	4.3(-3)	3.9(-5)	2.0(-2)	1.2	1.4	2.6	1.2(-3)	7.5	1.7(-1)	2.0	2.1(-2)	4.0(-1)	4.7(-3)	8.2(-2)
18	3.4(-3)	3.1(-5)	1.6(-2)	9.3(-1)	1.1	2.1	9.7(-4)	6.2	1.4(-1)	1.6	1.7(-2)	3.1(-1)	3.7(-3)	6.5(-2)
19	3.3(-3)	3.0(-5)	1.5(-2)	8.9(-1)	1.1	2.0	9.3(-4)	5.9	1.3(-1)	1.5	1.6(-2)	3.0(-1)	3.5(-3)	6.2(-2)
20	3.1(-3)	2.8(-5)	1.4(-2)	8.5(-1)	1.0	1.9	8.8(-4)	5.7	1.3(-1)	1.4	1.5(-2)	2.9(-1)	3.4(-3)	6.0(-2)
21	3.0(-3)	2.7(-5)	1.4(-2)	8.2(-1)	1.0	1.8	8.5(-4)	5.4	1.2(-1)	1.4	1.5(-2)	2.7(-1)	3.3(-3)	5.7(-2)
22	2.9(-3)	2.6(-5)	1.3(-2)	7.9(-1)	9.6(-1)	1.7	8.1(-4)	5.2	1.2(-1)	1.3	1.4(-2)	2.6(-1)	3.1(-3)	5.5(-2)
23	2.8(-3)	2.5(-5)	1.3(-2)	7.6(-1)	9.3(-1)	1.7	7.8(-4)	5.0	1.1(-1)	1.3	1.4(-2)	2.5(-1)	3.0(-3)	5.3(-2)
24	2.7(-3)	2.4(-5)	1.2(-2)	7.3(-1)	9.0(-1)	1.6	7.5(-4)	4.8	1.1(-1)	1.2	1.3(-2)	2.4(-1)	2.9(-3)	5.1(-2)
25	2.6(-3)	2.3(-5)	1.2(-2)	7.1(-1)	8.7(-1)	1.6	7.3(-4)	4.7	1.0(-1)	1.2	1.3(-2)	2.4(-1)	2.8(-3)	4.9(-2)
	Female													
16	5.3(-3)	4.9(-5)	2.5(-2)	1.5	1.7	3.3	1.5(-3)	9.0	2.2(-1)	2.5	2.6(-2)	5.0(-1)	5.8(-3)	1.0(-1)
17	4.5(-3)	4.1(-5)	2.1(-2)	1.2	1.5	2.7	1.3(-3)	7.9	1.8(-1)	2.1	2.2(-2)	4.1(-1)	4.9(-3)	8.6(-2)
18	3.6(-3)	3.3(-5)	1.7(-2)	9.9(-1)	1.2	2.2	1.0(-3)	6.6	1.4(-1)	1.7	1.8(-2)	3.3(-1)	3.9(-3)	6.9(-2)
19	3.5(-3)	3.2(-5)	1.6(-2)	9.6(-1)	1.2	2.1	1.0(-3)	6.4	1.4(-1)	1.6	1.7(-2)	3.2(-1)	3.8(-3)	6.7(-2)
20	3.4(-3)	3.1(-5)	1.6(-2)	9.3(-1)	1.1	2.1	9.7(-4)	6.2	1.4(-1)	1.6	1.7(-2)	3.1(-1)	3.7(-3)	6.5(-2)
21	3.3(-3)	3.0(-5)	1.5(-2)	9.1(-1)	1.1	2.0	9.5(-4)	6.1	1.3(-1)	1.5	1.6(-2)	3.1(-1)	3.6(-3)	6.4(-2)
22	3.3(-3)	2.9(-5)	1.5(-2)	8.9(-1)	1.1	2.0	9.2(-4)	5.9	1.3(-1)	1.5	1.6(-2)	3.0(-1)	3.5(-3)	6.2(-2)
23	3.2(-3)	2.9(-5)	1.5(-2)	8.6(-1)	1.1	1.9	9.0(-4)	5.8	1.3(-1)	1.5	1.5(-2)	2.9(-1)	3.4(-3)	6.0(-2)
24	3.1(-3)	2.8(-5)	1.4(-2)	8.4(-1)	1.0	1.9	8.7(-4)	5.6	1.2(-1)	1.4	1.5(-2)	2.8(-1)	3.3(-3)	5.9(-2)
25	3.0(-3)	2.7(-5)	1.4(-2)	8.2(-1)	1.0	1.8	8.5(-4)	5.5	1.2(-1)	1.4	1.5(-2)	2.8(-1)	3.3(-3)	5.8(-2)

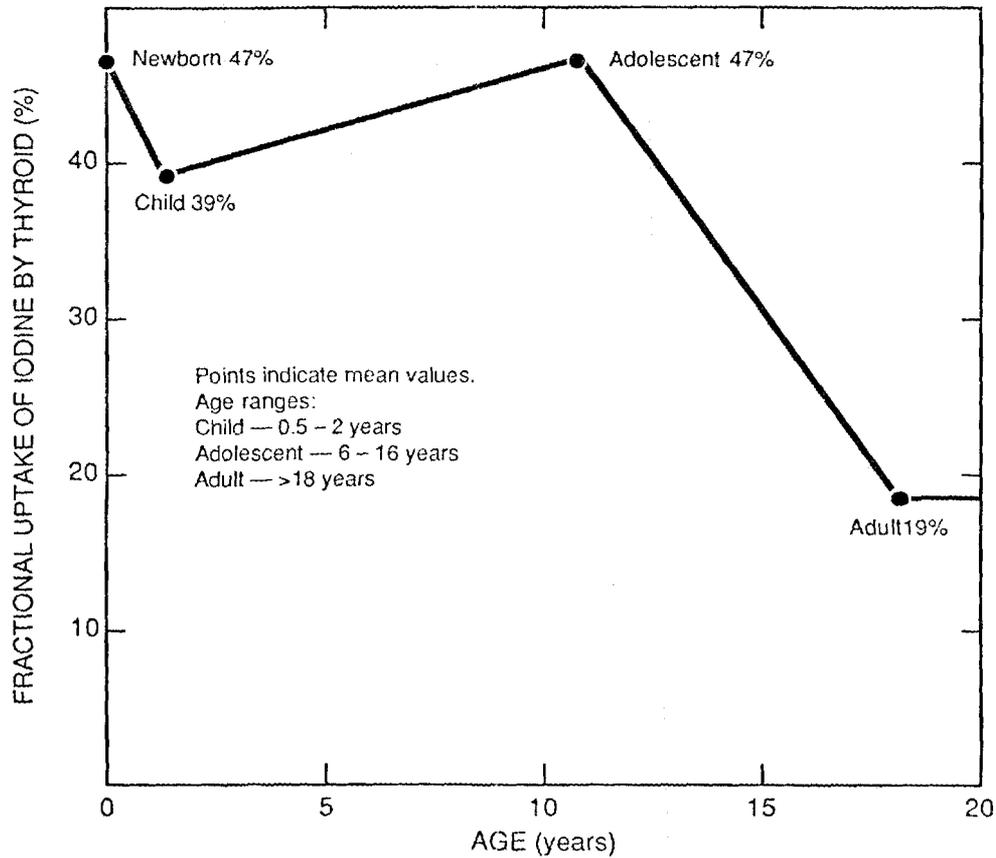


Figure C1. Fractional uptake of iodine to the thyroid as a function of age. The plotted points are mean values based on estimates reported by Dunning and Schwarz (1981).

For radioiodines with half-lives at most a few days, the dose is calculated by the formula

$$D = S(\text{thyroid} \leftarrow \text{thyroid}) \int_0^{50 \text{ years}} q^b(t) e^{-\lambda_r t} dt, \quad (\text{C2})$$

where $q^b(t)$ is given by Eq. C1 and the S-factor is calculated in a manner that is described in the next section. For the longer-lived isotopes, however (^{125}I and ^{129}I , with half-lives 60.14 days and 5.73×10^9 days, respectively), the dependence of the biological rate coefficients and the S-factor on age is a potentially significant effect in the integration, and Eq. C2 should be replaced by the more general formulation

$$D(a_0) = \int_0^{50 \text{ years}} s_\sigma(a_0 + t) A(t; a_0) dt, \quad (\text{C3})$$

where a_0 denotes the age at time $t = 0$, $s_\sigma(a_0 + t)$ is the age- and sex-dependent S-factor, and the age-dependent level of radioactivity in the thyroid, $A(t; a_0)$, is obtained by solving

Table C3. Iodine S-Factor Parameters by Isotope^a

Isotope	g	h	p
121 ^b	0.1747	1.557×10^{-2}	-0.6910
122	2.2365	2.612×10^{-2}	-0.6682
123	5.9640×10^{-2}	1.013×10^{-2}	-0.7147
124	0.4111	3.161×10^{-2}	-0.6770
125	0.0424	1.123×10^{-2}	-0.7458
126	0.3344	1.473×10^{-2}	-0.6805
128	1.5911	2.527×10^{-3}	-0.6740
129	0.1365	6.029×10^{-3}	-0.7416
130	0.6284	5.623×10^{-2}	-0.6654
131	0.4068	1.012×10^{-2}	-0.6658
132	1.0416	5.860×10^{-2}	-0.6663
133	0.8712	1.598×10^{-2}	-0.6651
134	1.3249	6.677×10^{-2}	-0.6671
135	0.7753	3.826×10^{-2}	-0.6696

^a The parameters g , h , and p , for which values are given in the table, correspond to the formula

$$S(\text{thyroid} \leftarrow \text{thyroid}) = \frac{g}{M_{\text{th}}} + hM_{\text{th}}^p \quad (\text{rad}/\mu\text{Ci}\cdot\text{h}).$$

^b The ¹²¹Te daughter of ¹²¹I is included by means of its own S-factor, given by

$$\begin{aligned} S_{\text{Te-121}}(\text{thyroid} \leftarrow \text{thyroid}) \\ = \frac{0.02128}{M_{\text{th}}} + 0.02128 M_{\text{th}}^{-0.6891} \quad (\text{rad}/\mu\text{Ci}\cdot\text{h}). \end{aligned}$$

The total S-factor is $S_{\text{total}} = S_{\text{I-121}} + S_{\text{Te-121}}$.

the differential equations

$$\begin{aligned} \frac{dY_1}{dt} &= -(\lambda_2(a_0 + t) + \lambda_r)Y_1 \\ \frac{dY_2}{dt} &= \rho\lambda_2(a_0 + t)Y_1 - (\lambda_1(a_0 + t) + \lambda_r)Y_2 \\ \frac{dY_3}{dt} &= s_\sigma(a_0 + t)Y_2, \end{aligned} \quad (\text{C4})$$

with initial conditions $Y_1(0) = 1 \mu\text{Ci}$ and $Y_2(0) = Y_3(0) = 0$. The state variable Y_3 equals $A(t; a_0)$. The symbol ρ is an abbreviation for $(1 - \lambda_1/\lambda_2)K$, where λ_1 , λ_2 , and K are evaluated for age $a_0 + t$. These three parameters were expressed as continuous functions of age by applying cubic spline interpolating functions to the previously calculated annual values in Table C2. A similar interpolation procedure was followed with values of the S-factor that were calculated for ages newborn through 25 years in increments of one year (cf. the following section) to produce the continuous function $s_\sigma(a_0 + t)$. The system C4 was solved with a discrete-variable integration routine. It is perhaps worth noting that this somewhat more elaborate calculation produced dose estimates that differed from those

obtained with the simpler procedure by at most about 4% for the newborns and only very trivially for other age groups.

Note: The indexing in the system of Eq. C4 may appear confusing at first sight. The state variable Y_1 is associated with the transfer compartment of the two-box model of Fig. 1b, and Y_2 represents the radioiodine in the thyroid. Rather than renumbering the state variables and writing the first two differential equations in the reverse order, we chose to adopt the more natural numbering of the state variables and allow the age-dependent coefficients λ_1 and λ_2 to retain their association with the previously defined notation.

The S-Factors

The computation of S-factors is identical to the procedure summarized by Eq. 6, except that the coefficients and exponent of the formula depend on the particular isotope of iodine. These parameters have been computed for the radioiodines from nuclear data given in ICRP Publication 38 (1983). We adopt the general notation

$$S(\text{thyroid} \leftarrow \text{thyroid}) = \frac{g}{M_{\text{th}}} + hM_{\text{th}}^p, \quad (\text{C5})$$

and the numbers g , h , and p are given in Table C3 for various radioactive isotopes of iodine.

Radioactive Progeny

Some of the radioiodines treated here produce one or more radioactive daughters (telluriums or xenons). The cases in point are

$^{121}\text{I}(2.12 \text{ h}) \rightarrow ^{121}\text{Te}(17 \text{ d})$ — The tellurium daughter was assumed to behave metabolically like the iodine. Its contribution to the dose was accounted for in the S-factor: $S_{\text{total}} = S_{\text{I-121}} + S_{\text{Te-121}}$.

$^{123}\text{I}(13.2 \text{ h}) \rightarrow ^{123}\text{Te}(10^{13} \text{ y})$ — Formation of this daughter is negligible.

$^{131}\text{I}(8.04 \text{ d}) \rightarrow ^{131\text{m}}\text{Xe}(11.9 \text{ d})$ — Yield of this xenon is about 1%. For this and other radioactive xenon daughters of iodine, ICRP practice is to assume that the noble gas escapes from the body before significant decay occurs, and we have adopted this assumption.

$^{133}\text{I}(20.8 \text{ h}) \rightarrow ^{133}\text{Xe}(5.245 \text{ d})$ with a 3% branch through $^{133\text{m}}\text{Xe}(2.188 \text{ d})$ — These xenons are neglected on the assumption that they escape from the thyroid before significant decay occurs.

$^{135}\text{I}(6.61 \text{ h}) \rightarrow ^{135}\text{Xe}(9.09 \text{ h})$ — This xenon is neglected on the assumption that it escapes from the thyroid before significant decay occurs.

Use of the Dose Conversion Factors

The dose conversion factors shown in Table C1 for most radioactive isotopes of iodine express absorbed dose to the thyroid due to nuclear transformations occurring within the gland. The dose in rad is based on the introduction of $1 \mu\text{Ci}$ into the blood. Thus, without modification, the factors can apply only to compounds of iodine that are highly soluble, that (in the case of inhalation) deposit almost totally in the respiratory airways, and that translocate rapidly from the respiratory passages or the GI tract into the blood. Elemental iodine vapor might be assumed to have these properties; but ICRP Publication 30 (1979) recommends that all compounds of iodine be treated with the ICRP lung model (inhalation class D), for which less than 100% of inspired material is deposited. Accordingly, for each isotope we

furnish an absorption fraction for inhalation that is based on the ICRP lung model, with particle diameter (AMAD) $1\ \mu\text{m}$ and solubility class D assumed. These absorption fractions are isotope-specific, because the fraction of the iodine that reaches the blood from the respiratory tract is dependent on the competition between radioactive decay and biological translocation processes. We remind the reader that neither age nor sex dependence is built into the ICRP lung model, and any application of the inhalation absorption fractions to the age- and sex-dependent dose conversion factors of Table C1 should be undertaken only with this deficiency in mind. The absorption fractions for inhalation are given in Table C4.

Table C4. Absorption Fractions (%) for Radioiodines Based on ICRP Models for the Lung^a and GI Tract^b

Isotope	121	122	123	124	125	126	128	129	130	131	132	133	134	135
Inhalation	34	5	48	60	63	62	19	63	48	61	34	52	26	43
Ingestion	75	8	95	99	100	100	38	100	95	100	77	97	56	90

^a Class D, AMAD = $1\ \mu\text{m}$ (ICRP, 1979).

^b Iodine is removed from the stomach directly to blood with biological mean-time 1 hour (ICRP, 1979).

For ingestion of radioiodines, ICRP practice is to assume complete absorption of the iodine from the small intestine (ICRP, 1979). We have computed absorption fractions for ingestion by assuming that the iodine being removed from the stomach to the small intestine goes instead directly into the blood (Table C4). These ingestion fractions are significant only for short-lived isotopes and therefore are of little use for environmental studies in which ephemeral isotopes will have decayed away during their transit to the target individual. But for certain other applications, it may be useful to take into account the decay of radioactive iodine in the stomach before it reaches the blood; hence for completeness, the absorption factors for ingestion are included in Table C4. Note also that these fractions are based on a model of the GI tract that is neither age- nor sex-dependent, and that the model involves time constants that vary greatly from one individual to another.

References

Note: All references, other than the following, are given in the main report.

Bell, G.H., J.N. Davidson, and H. Scarborough. 1968. *Textbook of Physiology and Biochemistry*. Edinburgh and London: E. & S. Livingstone Ltd.

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