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Dose Coefficients and Derived Air Concentrations for Accelerator-Produced Radioactive Material

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DOSE COEFFICIENTS AND DERIVED AIR CONCENTRATIONS FOR ACCELERATOR-PRODUCED RADIOACTIVE MATERIAL

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INTRODUCTION

Nitrogen-13 (^{13}N) and oxygen-15 (^{15}O) are produced in nuclear medicine departments by accelerators used in Positron Emission Tomography (PET) procedures. Both radionuclides decay by emission of positrons which, after losing their kinetic energy, annihilate with electrons of the absorbing media. The annihilation of the positron results in two 0.511 MeV photons emitted at 180°, which serves as the basis for imaging.

Radiations emitted by ^{13}N and ^{15}O are summarized in Table 1. The positrons are emitted with an energy ranging from zero to a maximum value of 1.19 MeV and 1.73 MeV for ^{13}N and ^{15}O, respectively. The positron spectra for the two nuclides are shown in Figure 1.

Table 1. Radiations emitted by ^{13}N and ^{15}O[a]

			Emitted Energy (MeV)	
Nuclide	$T_{1/2}$	Decay Mode	Positron	Gamma
N-13	9.96 m	β+	0.490	1.02
O-15	2.033 m	β+	0.735	1.02

[a]From Publication 38 of the International Commission on Radiological Protection (ICRP, 1983)

The Nuclear Regulatory Commission (NRC) recently was given jurisdiction over certain accelerator-produced radioactive material including products of PET procedures and requires radiation dose estimators, including dose coefficients, Annual Limits on Intake (ALIs), and Derived Air Concentrations (DACs), to evaluate occupational and public exposures to this material. The primary modes of exposure to these radionuclides are expected to be external dose from submersion in contaminated air and dose from internally deposited activity due to inhalation of the contaminated air.

The ICRP's tabulations of dose coefficients for intake of radionuclides by workers or members of the public are limited to radionuclides with half-lives of 10 min or greater and thus exclude ^{13}N or ^{15}O. Tabulations of ALIs and DACs in Federal Guidance Report No. 11 (EPA, 1987) and 10 CFR Part 20, Appendix B, are derived from ICRP dose coefficients for workers (ICRP Publication 30, 1979, 1980, 1981, 1988) and hence also exclude ^{13}N and ^{15}O.

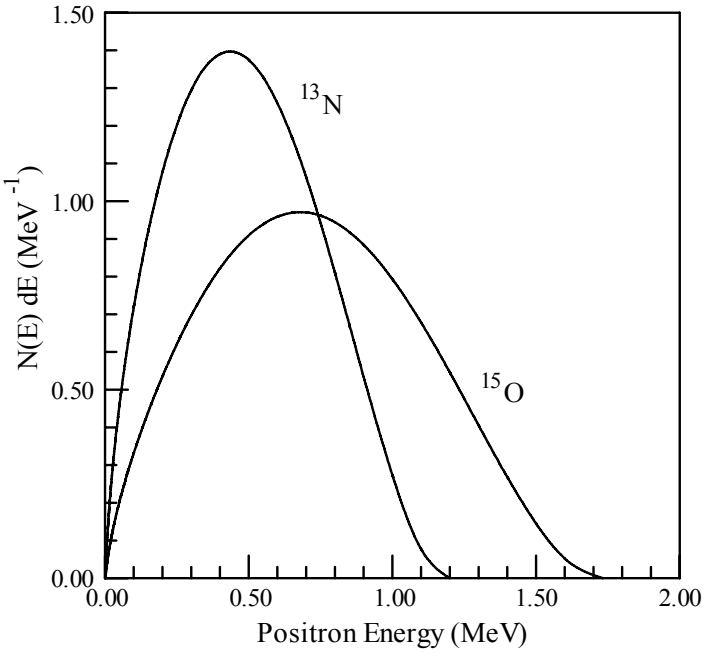

Figure 1. Positron differential energy spectrum for ^{13}N and ^{15}O.

10 CFR Part 20 provides default ALIs for radionuclides not listed explicitly in the Regulations. For radionuclides with decay mode other than alpha emission or spontaneous fission and with radiological half-life less than 2 hours, the default inhalation ALI is 200 μCi. This default value is of questionable applicability to radionuclides with half-lives of a few minutes.

External dose coefficients for exposure to ^{13}N and ^{15}O in air, water, and soil are provided in Federal Guidance Report No. 12 (EPA, 1993) for the effective dose equivalent as defined in ICRP Publication 26 (1977) and for several individual tissues. These coefficients can be used to derive ALIs and DACs for submersion in air contaminated with ^{13}N or ^{15}O.

Independently derived "effective dose factors" for air submersion are given for ^{13}N or ^{15}O in NCRP Report No. 123 (NCRP, 1996). These dose factors are from a compilation (Kocher, 1983) that pre-dates Federal Guidance Report No. 12 and are about 10% lower than the corresponding effective dose equivalent values given in Federal Guidance Report No. 12.

Biokinetic models and dose coefficients for selected chemical and physical forms and modes of administration of ^{13}N and ^{15}O are summarized in an ICRP document on doses to patients from radiopharmaceuticals (ICRP Publication 53, 1987). The biokinetic models in that document are specialized to diagnostic or therapeutic applications in

nuclear medicine but provide a starting place for modeling the biokinetics of some forms of inhaled ^{13}N and ^{15}O by workers or members of the public.

The purposes of this project are to develop inhalation dose coefficients for occupational or public exposure to prevalent forms of accelerator-produced ^{13}N and ^{15}O, determine inhalation ALIs and DACs implied by these dose coefficients, and compare the inhalation DACs with DACs based on submersion in contaminated air. Inhalation dose coefficients, ALIs, and DACs are provided for the following cases: (1) inhalation of ^{13}N as nitrogen gas, (2) inhalation of ^{13}N as ammonia, (3) inhalation of ^{15}O as water vapor, and (4) inhalation of ^{15}O gas (molecular oxygen). For consistency with the dosimetric quantities given in 10 CFR 20, the inhalation dose coefficients, ALIs, and DACs tabulated in this report are based on tissue weighting factors given in ICRP Publication 26 (1977). For completeness, comparison is made with a second set of values based on tissue weighting factors recommended more recently in ICRP Publication 60 (1991). The weighting factors given in Publication 26 and Publication 60 are listed in Table 2.

A key task in this project is the development of biokinetic models describing deposition and retention of prevalent forms of ^{13}N and ^{15}O in the respiratory tract, the level and time course of absorption to blood, and the systemic biokinetics of absorbed activity. The biokinetic models developed for inhaled ^{13}N gas, ^{13}N ammonia, ^{15}O as water vapor, and ^{15}O gas are described in Appendices A, B, C, and D, respectively.

The structure and dosimetric features of the ICRP's current Human Respiratory Tract Model (HRTM) (ICRP, 1994) are applied, insofar as a respiratory model is required. (For example, no respiratory model is needed for ^{15}O as water vapor because instantaneous absorption of inhaled ^{15}O to blood is assumed.) The HRTM is better suited to the analysis than the Task Group Lung Model (TGLM) (ICRP, 1979) used in ICRP Publication 30 (and hence underlying the exposure limits in 10 CFR 20) because the forms of ^{13}N and ^{15}O addressed here are all gases or vapors. The HRTM was designed in part to address gases and vapors while the TGLM was designed specifically to address inhaled particles.

Systemic biokinetic models for specific forms of ^{13}N and ^{15}O given in the ICRP document on radiopharmaceuticals (ICRP, 1987) were used as starting places for modeling the inhalation exposures addressed here. Because activity in blood is estimated to represent a large portion of the cumulative activity of these two short-lived radionuclides after their absorption from the respiratory tract, a detailed blood distribution model (ICRP, 2002) is applied in the dosimetric calculations. This approach differs from the ICRP's standard dosimetric assumption for workers or members of the public that activity in blood is distributed among tissues in proportion to tissue mass. For example, the lungs, heart, and liver contain much larger portions of the total blood volume than their masses as percentages of total-body mass would indicate.

Table 2. Tissue weighting factors given in ICRP Publication 26 (1977) and ICRP Publication 60 (1991)[a]

	Tissue weighting factor (w_T)	
Organ or tissue	**ICRP Pub. 26**	**ICRP Pub. 60**
Gonads	**0.25**	**0.20**
Bone marrow (red)	**0.12**	**0.12**
Colon	**--**	**0.12**
Lung	**0.12**	**0.12**
Stomach	**--**	**0.12**
Bladder	**--**	**0.05**
Breast	**0.15**	**0.05**
Liver	**--**	**0.05**
Esophagus	**--**	**0.05**
Thyroid	**0.03**	**0.05**
Skin	**--**	**0.01**
Bone surface	**0.03**	**0.01**
Remainder	**0.30[a]**	**0.05[b,c]**

[a]The value 0.30 is applied to the average dose to the five remaining tissues receiving the highest dose, excluding the skin, lens of the eye, and the extremities.

[b]Remainder is composed of the following tissues: adrenals, brain, extrathoracic airways, small intestine, kidneys, muscle, pancreas, spleen, thymus, and uterus.

[c]The value 0.05 is applied to the mass-weighted average dose to the Remainder tissue group, except when the following "splitting rule" applies: If a tissue of Remainder receives a dose in excess of that received by any of the 12 tissues for which weighting factors are specified, a weighting factor of 0.025 (half of Remainder) is applied to that tissue and 0.025 to the mass-averaged committed equivalent dose in the rest of the Remainder tissues.

DERIVED DOSE COEFFICIENTS, ALIs, AND DACs

Inhalation

Derived dose coefficients for inhalation of ^{13}N as nitrogen gas or ammonia and inhalation of ^{15}O as water vapor or molecular oxygen are given in Table 3. The dose calculations were performed using the software package DCAL (Eckerman et al., 2006). They are for a reference adult and are based on the biokinetic models described in Appendices A-D. The last two lines of Table 3 list the effective dose equivalent H_E based on tissue weighting factors given in ICRP Publication 26 (1977) and, for comparison, the effective dose E based on tissue weighting factors recommended in ICRP Publication 60 (1991).

Table 3. Dose coefficients (Sv Bq^{-1}) for inhalation of important forms of ^{13}N or ^{15}O

Tissue	^{13}N Nitrogen gas	^{13}N Ammonia	^{15}O Water vapor	^{15}O Oxygen gas
Adrenals	6.53E-14	3.21E-13	1.50E-12	5.70E-13
Urinary Bladder	1.07E-15	1.83E-12	3.33E-13	4.12E-14
Bone Surfaces	2.60E-14	4.02E-13	7.16E-13	1.05E-13
Brain	3.80E-15	8.98E-13	1.11E-12	2.25E-13
Breast	6.79E-14	2.70E-13	3.08E-13	6.69E-14
St Wall	3.19E-14	2.82E-13	1.67E-12	2.78E-13
SI Wall	5.45E-15	2.95E-13	1.88E-12	4.35E-13
ULI Wall	6.56E-15	2.88E-13	1.80E-12	3.51E-13
LLI Wall	1.92E-15	2.95E-13	1.78E-12	3.35E-13
Kidneys	2.00E-14	6.53E-13	2.24E-12	1.45E-12
Liver	5.35E-14	6.83E-13	1.78E-12	3.48E-13
ET Region	2.59E-14	3.45E-10	3.21E-13	4.91E-14
Lung	3.29E-12	3.00E-13	1.73E-12	1.86E-12
Muscle	2.67E-14	3.92E-13	3.31E-13	5.41E-14
Ovaries	2.95E-15	3.04E-13	7.53E-13	9.94E-14
Pancreas	4.79E-14	3.23E-13	1.98E-12	3.66E-13
Red Marrow	3.47E-14	3.70E-13	8.12E-13	1.31E-13
Skin	1.35E-14	2.80E-13	2.79E-13	3.98E-14
Spleen	4.47E-14	2.93E-13	2.04E-12	5.33E-13
Testes	3.99E-16	2.64E-13	5.08E-13	5.69E-14
Thymus	7.96E-14	4.28E-13	3.47E-13	7.75E-14
Thyroid	2.59E-14	4.38E-13	1.56E-12	1.59E-12
Gall Bladder	2.17E-14	3.31E-13	4.95E-13	8.80E-14
Heart	1.17E-13	3.23E-13	1.38E-12	3.76E-13
Uterus	2.30E-15	3.27E-13	3.93E-13	5.45E-14
Remainder (Pub 26)	7.27E-14	6.98E-11	1.99E-12	6.73E-13
Remainder (Pub 60)	2.53E-14	1.73E-10	1.33E-12	8.79E-14
H_E (Pub 26)	**4.33E-13**	**2.12E-11**	**1.20E-12**	**5.26E-13**
E (Pub 60)	4.17E-13	9.04E-12	1.16E-12	4.45E-13

Table 4 lists radionuclide- and form-specific ALIs and DACs for workers implied by the tissue dose equivalents and effective dose equivalents H_E given in Table 3 and primary guidance given in ICRP Publication 26. Corresponding ALIs and DACs for members of the public are given in Table 5.

Table 4. Occupational ALIs and DACs for inhalation of selected forms of ^{13}N and ^{15}O based on tissue weighting factors given in ICRP Publication 26 (1977)

		ALI		DAC	
Nuclide	Form	Bq	μCi	Bq m^{-3}	μCi ml^{-1}
^{13}N	Nitrogen gas	1.2×10^{11}	3.1×10^{6}	4.8×10^{7}	1.3×10^{-3}
	Ammonia	1.4×10^{9}	3.9×10^{4}	6.0×10^{5}	1.6×10^{-5}
^{15}O	Water vapor	4.2×10^{10}	1.1×10^{6}	1.7×10^{7}	4.7×10^{-4}
	Oxygen gas	9.5×10^{10}	2.6×10^{6}	4.0×10^{7}	1.1×10^{-3}

Table 5. ALIs and DACs for inhalation by members of the public of selected forms of ^{13}N and ^{15}O based on tissue weighting factors given in ICRP Publication 26 (1977)

		ALI		DAC	
Nuclide	Form	Bq	μCi	Bq m^{-3}	μCi ml^{-1}
^{13}N	Nitrogen gas	3.8×10^{8}	1.0×10^{4}	1.6×10^{5}	4.3×10^{-6}
	Ammonia	4.8×10^{6}	1.3×10^{2}	2.0×10^{3}	5.4×10^{-8}
^{15}O	Water vapor	1.4×10^{8}	3.8×10^{3}	5.8×10^{4}	1.6×10^{-6}
	Oxygen gas	3.2×10^{8}	8.6×10^{3}	1.3×10^{5}	3.6×10^{-6}

The ALIs for workers are based on an annual dose limit of 0.05 Sv (5 rem) for limitation of stochastic effects and 0.5 Sv (50 rem) for prevention of deterministic effects. The DACs for workers are based on these ALIs and an annual air intake of 2400 m^3. An ALI or DAC for members of the public is the corresponding value for occupational intake divided by 300. The reduction factor 300 includes a factor of 50 to relate the dose limit for workers to the lower limit for members of the public (e.g., for stochastic effects, 0.05 Sv or 5 rem for workers compared with 0.001 Sv or 100 mrem for the public), a factor of 3 to adjust for the difference in exposure time and inhalation rate for workers and members of the public, and a factor of 2 as an adjustment of occupational values so that they are applicable to other age groups (Eckerman, 1996).

The calculation of ALIs and DACs for workers is illustrated for the case of inhalation of ^{13}N as nitrogen gas. As specified in Publication 26, the ALI implied by inhalation dose coefficients for a radionuclide is the minimum of the annual intake A_1 that would result in an effective dose equivalent H_E of 0.05 Sv and the intake A_2 that would result in a dose equivalent of 0.5 Sv to the tissue receiving the highest dose. The value A_1 is calculated as follows:

$$A_1 = 0.05 \text{ Sv} / H_E = 0.05 \text{ Sv} / 4.33 \times 10^{-13} \text{ Sv Bq}^{-1} = 1.15 \times 10^{11} \text{ Bq}.$$

The value A_2 is determined in this case by the dose coefficient for the lungs because this is the highest coefficient for any tissue:

$$A_2 = 0.5 \text{ Sv} / \text{max tissue coefficient} = 0.5 \text{ Sv} / 3.29 \times 10^{-12} \text{ Sv Bq}^{-1} = 1.52 \times 10^{11} \text{ Bq}.$$

The smaller of A_1 and A_2 (1.15×10^{11} Bq) is the implied ALI. The implied DAC for workers is the ALI divided by the occupational intake of air during one year: 1.15×10^{11}

Bq / 2400 m^3 = 4.79 x 10^7 Bq m^{-3}. The implied ALI and DAC for members of the public (Table 5) are 1.15 x 10^{11} Bq / 300 = 3.83 x 10^8 Bq and 4.79 x 10^7 Bq m^{-3} / 300 = 1.60 x 10^5 Bq m^{-3}, respectively. Values in Tables 4 and 5 are rounded to two significant digits.

For comparison with values in Table 4 and 5, alternate ALIs and DACs for inhalation of ^{13}N or ^{15}O were derived on the basis of tissue weighting factors and primary guidance given in ICRP Publication 60 (1991). Publication 60 specifies that compliance with regulations should be based on the risk of stochastic effects as represented by the effective dose *E*. In this case the ALI for workers would be 0.05 Sv / *E* and the DAC for workers would be (0.05 Sv / *E*) / 2400 m^3. Calculations show that the inhalation ALIs and DACs based on guidance in ICRP Publication 60 are slightly (3-15%) higher than values in Tables 4 and 5 for each of three cases: inhalation of ^{13}N as gas, inhalation of ^{15}O as water vapor, and inhalation of ^{15}O as gas. For inhalation of ^{13}N ammonia, the ALI and DAC based on Publication 60 are roughly four times higher than corresponding values based on Publication 26. The reasons for this difference are discussed here at length because this illustrates a situation where application of Publication 60 can yield a much different ALI than Publication 26, namely, the situation in which one tissue receives a much higher dose than other tissues. In the case of inhaled ^{13}N ammonia the tissue is the extrathoracic (ET) region of the respiratory tract, the presumed site of deposition of 90% of inhaled ammonia (Appendix B). The estimated dose to ET largely determines both the effective dose equivalent H_E defined in Publication 26 and the effective dose *E* defined in Publication 60. In the calculation of the effective dose *E*, the dose to the ET region is given a weight of 0.025 based on the splitting rule for Remainder (see Table 2, footnote c). In the calculation of the effective dose equivalent H_E, the dose to ET is given a weight of 0.06 as one of the five tissues of Remainder (see Table 2, footnote a). This would result in a sizable difference in the two derived ALIs (roughly a factor of 2.4 = 0.06/0.025) if the ALI were determined solely by the effective dose coefficient and the stochastic limit of 0.05 Sv in each case. In the guidance of Publication 26, however, the deterministic limit of 0.5 Sv for any tissue must also be considered, and this determines the ALI if the dose equivalent to any tissue is more than 10 times the effective dose equivalent. This is the case for inhaled ^{13}N ammonia, for which the estimated dose equivalent to ET is about 16 times the effective dose equivalent. Thus, based on guidance in ICRP Publication 26, the ALI for inhaled ^{13}N ammonia is about 16/10 = 1.6 times more restrictive than the value implied by the stochastic limit alone. The net result is roughly a fourfold difference (in effect, 2.4 x 1.6) in the ALIs determined by the two difference sets of guidance, i.e., Publication 26 versus Publication 60. However this difference in ALIs is relative small compared to the much greater difference in DACs between inhalation and air submersion evaluated below.

Air Submersion

Dose rate coefficients for submersion in air contaminated with ^{13}N or ^{15}O are given in Table 6. These values are taken from the CD distributed with Federal Guidance Report No. 13 (except that the effective dose *E* was calculated separately) and are based on the methods of Federal Guidance Report No. 12 (1993). The effective dose coefficients for

air submersion are virtually the same for ^{13}N and ^{15}O due to similarities in their photon emissions. For either radionuclide H_E differs by only ~7% from the effective dose E based on tissue weighting factors of ICRP Publication 60. H_E and E are both reasonably consistent with the "effective dose factor" of 4.40 x 10^{-14} Sv-m^3 / Bq-s (after conversion of units) given for both ^{13}N and ^{15}O in NCRP Report No. 123 (1995). Nuclear decay data for both ^{13}N and ^{15}O appear to be well established, as are the models used to calculate external dose coefficients for relatively high-energy photon emitters. In short, the external dose rate coefficients for ^{13}N and ^{15}O for the case of air submersion appear to be established within fairly narrow bounds.

Table 6. Dose coefficients for external exposure to ^{13}N or ^{15}O due to air submersion (Sv-m^3 / Bq-s)

Nuclide	^{13}N	^{15}O
Adrenals	3.98E-14	3.98E-14
Bladder Wall	3.96E-14	3.97E-14
Bone Surface	8.44E-14	8.46E-14
Brain	5.06E-14	5.07E-14
Breast	5.47E-14	5.48E-14
Esophagus	3.90E-14	3.91E-14
St Wall	4.23E-14	4.23E-14
SI Wall	3.75E-14	3.76E-14
ULI Wall	3.92E-14	3.93E-14
LLI Wall	3.82E-14	3.83E-14
Kidneys	4.25E-14	4.25E-14
Liver	4.27E-14	4.28E-14
Lungs	4.75E-14	4.76E-14
Muscle	4.64E-14	4.65E-14
Ovaries	3.55E-14	3.56E-14
Pancreas	3.73E-14	3.73E-14
Red Marrow	4.58E-14	4.59E-14
Skin	8.68E-14	1.04E-13
Spleen	4.30E-14	4.31E-14
Testes	4.78E-14	4.79E-14
Thymus	4.40E-14	4.41E-14
Thyroid	4.87E-14	4.88E-14
Uterus	3.66E-14	3.66E-14
H_E (ICRP Pub. 26)	**4.90E-14**	**4.91E-14**
E (ICRP Pub. 60)	4.57E-14	4.59E-14

For both ^{13}N and ^{15}O the occupational DAC implied by the effective dose coefficient H_E is 0.05 Sv / (4.9 x 10^{-14} Sv-m^3 / Bq-s x 2000 h x 3600 s/h) = 1.4 x 10^5 Bq m^{-3} (3.8 x 10^{-6} μCi/ml). The comparative value based on the 10-fold higher non-stochastic limit 0.5 Sv is considerably higher for each radionuclide because the dose to the most highly irradiated tissue does not greatly exceed the effective dose coefficient in each case. The DAC of 1.4 x 10^5 Bq m^{-3} is about a factor of 4 lower than the most restrictive DAC based on inhalation of ^{13}N and two orders of magnitude lower than the most restrictive DAC based on inhalation of ^{15}O (Table 4). Therefore the lower DAC based on submersion and the stochastic limit of 0.05 Sv is applicable.

For calculation of the DAC for members of the public based on an external dose coefficient for air submersion, the assumption is made that exposure occurs for the entire year (8760 h). No adjustment is made in the dose coefficient for application to children because the external dose from air submersion is not strongly dependent on body size, particularly for relatively high-energy photons. The implied DAC for members of the public for submersion in air contaminated with either ^{13}N or ^{15}O is 0.001 Sv / (4.9×10^{-14} Sv-m^3 / Bq-s x 8760 h x 3600 s/h) = 6.5×10^{2} Bq m^{-3} (1.8×10^{-8} µCi/ml). The DACs for members of the public based on external dose coefficients for air submersion are about a factor of 3 lower than the most restrictive DAC based on inhalation of ^{13}N and two orders of magnitude lower than the most restrictive DAC based on inhalation of ^{15}O. Therefore the lower DAC based on air submersion is applicable.

Conclusion

In summary, exposures to airborne ^{13}N and ^{15}O are limited by their contribution to external dose from air submersion rather than from the inhalation intakes of these radionuclides. The limiting DACs are tabulated below.

Derived Air Concentration - DAC

	Workers		Members of Public	
Nuclide	Bq m^{-3}	µCi ml^{-1}	Bq m^{-3}	µCi ml^{-1}
^{13}N	1.4×10^{5}	3.8×10^{-6}	6.5×10^{2}	1.8×10^{-8}
^{15}O	1.4×10^{5}	3.8×10^{-6}	6.5×10^{2}	1.8×10^{-8}

APPENDIX A. BIOKINETIC MODEL FOR ^{13}N INHALED AS NITROGEN GAS

The case of inhalation of ^{13}N as nitrogen gas is addressed in ICRP Publication 53, Radiation Dose to Patients from Radiopharmaceuticals (ICRP, 1987). Because gaseous nitrogen has low solubility in blood and tissues, the assumption was made in that document that inhaled ^{13}N gas does not enter the pulmonary circulation but mixes with air in the lungs and is exhaled over a period of minutes. Mean biological elimination rates of 4.27 min^{-1} (representing 11% of the inhaled activity) and 1.48 min^{-1} (89%) were measured following equilibration in eight human subjects (Rosenzweig et al., 1969). The slower elimination rate (1.48 min^{-1}) was applied in Publication 53 to 100% of the inhaled activity.

Two exposure situations were addressed in Publication 53: a single inhalation of ^{13}N gas with 20-second breathhold, and continuous inhalation of ^{13}N gas for one hour. The derived cumulative activity in the lungs per unit activity intake was 34.5 Bq-s / Bq for a single inhalation and 38.7 Bq-s / Bq for continuous inhalation.

The model used in the present report for ^{13}N inhaled as nitrogen gas is based on the model of ICRP Publication 53. Inhaled ^{13}N is assumed to be uniformly distributed in the lung volume. There is assumed to be no absorption of ^{13}N to blood. The assumed rate of elimination of ^{13}N from the lungs in expired air is 2185 d^{-1} or about 1.52 min^{-1}. This value was set to yield the same cumulative activity in the lungs as calculated in ICRP Publication 53 for the case of continuous inhalation of ^{13}N gas, i.e., 38.7 Bq-s / Bq.

APPENDIX B. BIOKINETIC MODEL FOR ^{13}N INHALED AS AMMONIA

Respiratory model for inhaled ammonia

Factors controlling retention of inhaled gases or vapors in the respiratory tract include their solubility in body fluids and reactivity with tissues and fluid lining the respiratory tract (ICRP, 1994). Gases or vapors that are highly water soluble such as ammonia dissolve predominantly in the lining of the nose and trachea, while reactive gases or vapors with low water solubility may deposit largely in the lungs.

In an early study of the retention of inhaled gases in the human nose and lung, an estimated 92% +/- 2% of inhaled ammonia was retained in the respiratory tract in two adult human subjects exposed for short durations (< 2 min) at a mean air flow (intake) rate of 6-7 liter/min (Landahl and Herrmann, 1950). In a separate experiment, about 83% was retained in the nasopharnyx at a flow rate of 18 liter/min, but only 63-71% was retained when the flow rate was tripled (Landahl and Herrmann, 1950). In another study of human subjects exposed to ammonia in air for 30 min, the percentage of inhaled ammonia retained in the nasal mucosa decreased progressively until equilibrium was reached at 23% (range: 4–30%) after 10–27 min of exposure (Silverman et al., 1949). The concentration of ammonia in exhaled air remained stable after this period and returned to pre-exposure levels within 3–8 min after the end of exposure. The subjects eliminated an estimated 70–80% of the deposited ammonia by exhalation (Silverman et al., 1949). In dogs exposed to ammonia in air, retention in the whole respiratory tract was in the range 73-83% and was not affected by concentration, respiratory rate, or tidal volume (Egle, 1973).

Silverman et al. (1949) could not detect significant changes in blood nitrogen concentrations in human subjects exposed for 30 min to air containing 500 ppm ammonia even though as much as 20-30% of inhaled ammonia was not accounted for by measurements of exhaled ammonia. By contrast, Kustov (1967) demonstrated a significant increase in blood urea nitrogen in human subjects exposed to a concentration of 20 ppm for 8 h. Continuous exposure of rats for 24 hours to ammonia concentrations up to 32 ppm resulted in significant increase in blood ammonia levels (Schaerdel et al. 1983). Exposures to 310–1,157 ppm led to significantly increased blood concentrations of ammonia within 8 hours of exposure initiation, but blood ammonia returned to pre-exposure values within 12 hours of continuous exposure and remained at that level from 12-24 hours (Schaerdel et al., 1983).

The respiratory model for inhaled ammonia used in this report is a variation of the ICRP's respiratory model (Figure B-1) as applied to highly soluble or reactive (Class SR-2) gases and vapors. According to the ICRP model, 100% of inhaled SR-2 material deposits in the ET_2 region, which consists of the posterior nasal and oral passages, the pharynx, the larynx, and associated lymphatic tissue. Subsequent retention in ET_2 and

absorption to body fluids may be estimated on the basis of substance-specific information. If no specific information is available, reference values for translocation of deposited Type F material (absorption rate 100 d^{-1} corresponding to a half-time of 10 min) or Type V material (instantaneous absorption) are usually applied.

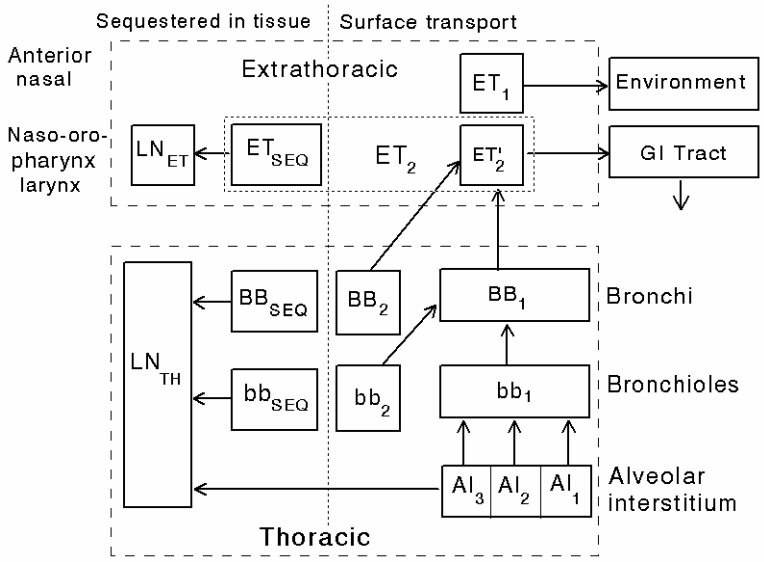

Figure B-1. Structure of the ICRP's respiratory tract model (ICRP, 1994). Arrows indicate directions of particle transfer. Gases and vapors are assigned material-specific directions of transfer.

In the present respiratory model for inhaled ammonia, it is assumed on the basis of data for human subjects that 90% of inhaled ammonia is deposited in ET_2. Transfer coefficients describing the behavior of deposited ammonia are given in Table B-1. In that table, ET_2-sur and ET_2-seq represent material subject to surface transport and material sequestered in tissues, respectively, and LN-ET represents the extrathoracic lymph nodes. Activity in ET_2-sur is assumed to be removed from the body in expired air with a half-time of 3 min, which is reasonably consistent with data of Silverman et al. (1949) for retention and exhalation of inhaled ammonia by human subjects. Other than for the assumption of removal in expired air, the parameter values in Table B-1 are consistent with the behavior of Type F material as defined by the ICRP.

Table B-1. Parameter values of the respiratory model for inhaled ammonia used in this report (compartments shown in Figure B-1; directions of movement specific to ^{13}N ammonia)

Origin[a]	Destination	Transfer coefficient (d^{-1})
ET_2-sur	Excreta	3.33E+02
ET_2-sur	Blood	1.00E+02
ET_2-seq	LN-ET	1.00E-03
ET_2-seq	Blood	1.00E+02
LN-ET	Blood	1.00E+02

[a]ET_2-sur is material in ET_2 subject to surface transport. ET_2-seq is material in ET_2 sequestered in tissues. LN-ET is extrathoracic lymph nodes.

Systemic model for ammonia absorbed from the respiratory tract

There is little direct information on the systemic biokinetics of ammonia after absorption from the respiratory tract. The systemic biokinetic model applied in this report to absorbed ammonia is a variation of the model applied to intravenously injected ^{13}N ammonia in ICRP Publication 53, Radiation Dose to Patients from Radiopharmaceuticals (ICRP, 1987). The ICRP model is based on measurements made on normal subjects and patients with liver disease following intravenous administration of ^{13}N ammonia (Lockwood et al., 1979; Lockwood, 1980). The injected material was rapidly removed from the circulation and metabolized in tissues, and some metabolic products were returned to the circulation. Body scans made up to 50 min post injection showed substantial amounts of ^{13}N in liver, brain, and urinary bladder with smaller amounts in the heart and kidneys. In normal subjects the mean transit time of ^{13}N ammonia in the circulation was 65 s, corresponding to a removal half-time of 45 s if first-order kinetics is assumed. About 7% of the injected activity was taken up by the liver in normal subjects (>10% in patients with severe liver disease), ~7% was taken up by the brain, and ~6% deposited in the urinary bladder contents. About 6% was returned to the circulation as ^{13}N metabolites with an estimated half-time of 2 min; a similar amount was measured in the urinary bladder and was estimated to enter the bladder with a half-time of 8 min.

The biokinetic model for ^{13}N ammonia used in ICRP Publication 53 is not described there in much detail, but the following model features can be inferred from the short description together with tabulated model predictions. Circulating ^{13}N is divided into two compartments, one representing ^{13}N ammonia (and referred to here as Blood) and one representing ^{13}N metabolites (Blood M). Activity in collective unspecified tissues (Other) is also divided into two compartments, one with no biological removal (Other 1), and one that returns ^{13}N to Blood M as ^{13}N metabolites (Other 2). Activity leaves Blood with a biological half-time of 45 s, with 7% depositing in Liver, 7% in Brain, 6% in Kidneys, 74% in Other 1, and 6% in Other 2. The half-time for biological removal from Other 2 to Blood M is 2 min. There is no biological removal from Blood M. Activity in Kidneys is transferred to Urinary Bladder Contents with a half-time of 3.47 min, corresponding to a mean transit time of 5 min (a generic value in ICRP Publication 53). There is no biological removal from Liver, Brain, Other 1, or Urinary Bladder Contents.

The systemic model for ammonia applied in this report is a modification of the ICRP's model described above, with the main difference being the treatment of ^{13}N metabolites. In the present model ^{13}N metabolites are assumed to originate in Liver, Brain, and Other, which requires that each of these tissues be divided into two compartments. For example, Liver is divided into Liver 1, which receives 94% of inflow from Blood, and Liver 2, which receives 6% of inflow from Blood, and outflow from Liver 2 is assigned to Blood M. Analogous assumptions are made for Brain 1 and Brain 2, and Other 1 and Other 2. Blood M is assumed to be the only source of ^{13}N entering Kidneys and subsequently Urinary Bladder Contents. Specifically, it is assumed that: ^{13}N ammonia leaves Blood with a half-time of 45 s, with 6.58% (0.94 x 7%) depositing in Liver 1, 0.42% (0.06 x 7%) in Liver 2, 6.58% in Brain 1, 0.42% in Brain 2, 80.84% (0.94 x 86%) in Other 1, and 5.16% (0.06 x 86%) in Other 2. The biological removal half-time from Other 2 to Blood M is 2 min. Activity transfers from Blood M to Kidneys with a biological half-time of 1 min. Activity in Kidneys is transferred to Urinary Bladder Contents with a half-time of 3.47 min, corresponding to a mean transit time of 5 min. There is no biological removal from Liver 1, Brain 1, Other 1, or Urinary Bladder Contents. Transfer coefficients derived from these assumptions are given in Table B-2.

Table B-2. Parameter values of the systemic model for ammonia injected into blood or absorbed from the respiratory tract

Origin	Destination	Transfer coefficient (d^{-1})
Blood	Liver 1	8.76E+01
Blood	Liver 2	5.59E+00
Blood	Brain 1	8.76E+01
Blood	Brain 2	5.59E+00
Blood	Other 1	1.08E+03
Blood	Other 2	6.87E+01
Liver 2	Blood M	4.99E+02
Brain 2	Blood M	4.99E+02
Other 2	Blood M	4.99E+02
Blood M	Kidneys	1.00E+03
Kidneys	Urinary Bladder Content	2.88E+02

APPENDIX C. BIOKINETIC MODEL FOR ^{15}O INHALED AS WATER VAPOR

Starting point: Model of ICRP Publication 80

The biokinetic model applied in this report to inhaled ^{15}O water is based on the same distribution and retention processes for O_2 water that were assumed in ICRP Publication 80 (1998). The present model is designed to approximate the distribution of cumulative activity of ^{15}O estimated in Publication 80, but the model formulation differs from that of Publication 80.

The model of ICRP Publication 80 is intended for application to patients intravenously injected with ^{15}O water for diagnostic purposes. Cumulative decays of ^{15}O ($T_{1/2}$ = 2.04 min) in an organ are based on the organ's blood perfusion rate and the consideration that a portion of accumulated ^{15}O water returns to blood at a rate depending on the water distribution space of the organ. The concentration of ^{15}O water in a given organ is derived by convolution of the arterial blood concentration (arterial input function) and the transit time function (impulse response) of the organ. The impulse response is $\exp[-(F/V_d) + \lambda)t]$ where F (ml min^{-1} g^{-1}) is the organ blood perfusion rate, V_d is the relative water distribution space for the organ (ml g^{-1}), and λ (min^{-1}) is the radioactive decay constant for ^{15}O. Following intravenous injection of ^{15}O water into a patient, the arterial blood concentration can be monitored and retention values for organs with known values of F and V_d can be calculated. Organ residence times for injected ^{15}O water and resulting dose estimates tabulated in ICRP Publication 80 are mean values derived from estimates determined by applying this model to patients at four different centers.

Description of the present model for inhaled ^{15}O water

The formulation of the present model for ^{15}O inhaled as water vapor is consistent with that of other first-order recycling models used by the ICRP in documents on occupational or environmental exposure to radionuclides. The model structure is shown in Figure C-1, and parameter values are given in Table C-1. Inhaled water vapor is assumed to pass instantaneously to blood. It is assumed that ^{15}O leaves blood at the rate 1000 d^{-1}, corresponding to a half-time of approximately 1 min. This is broadly consistent with the rate of decline of the activity concentration in arterial blood observed in patients injected with ^{15}O water (see Fig. 1 of Smith et al., 1994). With the exception of Liver and Other (remaining tissues), the rate of uptake of ^{15}O by individual tissues is assumed to be proportional to the percentages of cardiac output received (Table C-2). For example, the transfer coefficient (also called transfer rate) from Blood to Kidneys is 0.19 x 1000 d^{-1} = 190 d^{-1}, where 0.19 is the fraction of cardiac output received by the kidneys (Table C-2) and 1000 d^{-1} is the total outflow rate from blood. Liver is assumed to receive ^{15}O from portal as well as arterial blood, but availability of ^{15}O in portal blood is assumed to be reduced by 50% relative to arterial blood due to uptake and retention by tissues between the heart and portal vein. That is, the assigned percentage of outflow from blood received by Liver is the percentage of cardiac output received in arterial blood plus half the percentage received in portal blood: 6.5% + (0.5 x 19%) = 16%, corresponding to a

transfer coefficient from Blood to Liver of 160 d^{-1}. The transfer coefficient from Blood to Other is 1000 d^{-1} minus the sum of transfer coefficients to explicitly identified tissues.

The biological removal rate from a tissue to blood is F/V_d (min^{-1}), where F and V_d are as in the model of Publication 80. For example, the transfer coefficient from Adrenals to Blood is (0.003 x 6500 ml min^{-1} / 14 g) / 0.7 = 1.99 min^{-1} or 2900 d^{-1}, where 0.003 is the fraction of cardiac output received by the adrenal glands, 6500 ml min-1 is cardiac output, 14 g is the mass of the adrenal glands, and 0.7 is the relative water distribution space for the adrenal glands.

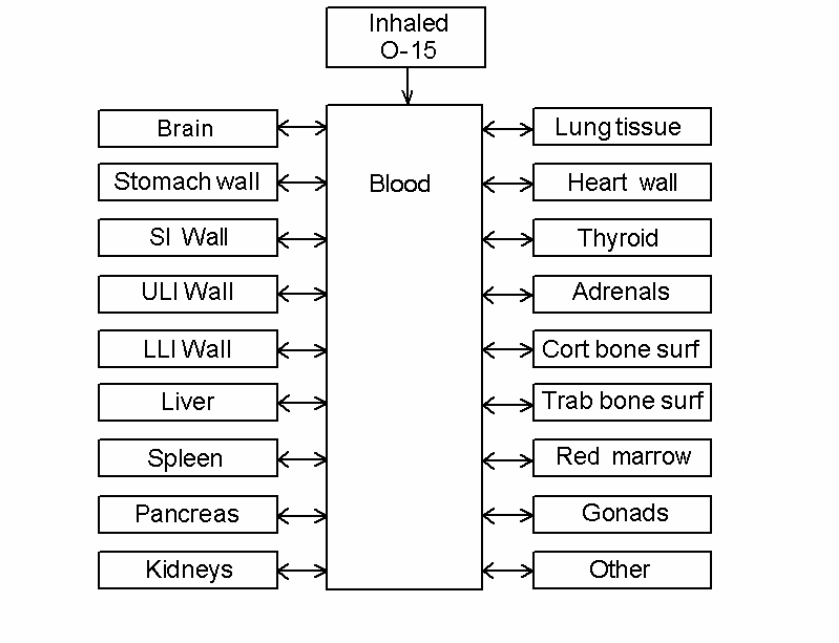

Figure C-1. Structure of the model applied in this report to inhaled ^{15}O water.

Table C-1. Parameter values of the systemic model for ^{15}O water		
Origin	Destination	Transfer coefficient (d^{-1})
Blood	Adrenals	3.00E+00
Blood	Brain	1.20E+02
Blood	Cortical bone surface	1.00E+01
Blood	Trabecular bone surface	1.00E+01
Blood	Stomach wall	1.00E+01
Blood	Small intestine wall	1.00E+02
Blood	Upper large intestine wall	2.28E+01
Blood	Lower large intestine wall	1.72E+01
Blood	Heart wall	4.00E+01
Blood	Kidneys	1.90E+02
Blood	Liver	1.60E+02
Blood	Lung tissue	2.50E+01
Blood	Ovaries	2.00E-01
Blood	Pancreas	1.00E+01
Blood	Red marrow	3.00E+01
Blood	Spleen	3.00E+01
Blood	Testes	5.00E-01
Blood	Thyroid	1.50E+01
Blood	Other	2.063E+02
Adrenals	Blood	2.90E+03
Brain	Blood	7.70E+02
Cortical bone surface	Blood	1.10E+02
Trabecular bone surface	Blood	2.80E+02
Stomach wall	Blood	6.90E+02
Small intestine wall	Blood	1.40E+03
Upper large intestine wall	Blood	1.00E+03
Lower large intestine wall	Blood	1.00E+03
Heart wall	Blood	1.30E+03
Kidneys	Blood	5.70E+03
Liver	Blood	9.20E+02
Lung tissue	Blood	4.70E+02
Ovaries	Blood	1.70E+02
Pancreas	Blood	7.40E+02
Red marrow	Blood	4.80E+02
Spleen	Blood	1.90E+03
Testes	Blood	1.30E+02
Thyroid	Blood	7.80E+03
Other	Blood	1.00E+02

Table C-2. Organ masses, blood flow rates, and relative water distribution used in the present model for ^{15}O water to estimate rates of uptake and removal of ^{15}O by tissues

Tissue	Mass (g)[a]	Blood flow rate (% cardiac output)[a]	V_d[b] (ml g^{-1})
Adrenals	14	0.3	0.7
Brain	1450	12	1
Bone			
Cortical	4400	1	0.2
Trabecular	1100	1	0.3
GI tract			
Stomach wall	150	1	0.9
SI wall	650	10	1
ULI wall	210	2.3	1
LLI wall	160	1.7	1
Heart wall	330	4	0.9
Kidneys	310	19	1
Liver	1800		0.9
Hepatic		6.5	
Portal		19	
Lung tissue	500	2.5	1
Ovaries	11	0.02	1
Pancreas	140	1	0.9
Red marrow	1170	3	0.5
Spleen	150	3	1
Testes	35	0.05	1
Thyroid	20	1.5	0.9
Other	53,900	30.13	0.5

[a]ICRP Publication 89 (2002).
[b]Rounded from values tabulated by Smith et al. (1994).

APPENDIX D: BIOKINETIC MODEL FOR ^{15}O INHALED AS MOLECULAR OXYGEN

Starting point: Model of ICRP Publication 53

The model for ^{15}O inhaled as molecular oxygen is patterned after the model of ICRP Publication 53 (1987) for continuous inhalation of ^{15}O-labeled O_2 by a resting adult male. The model of Publication 53 was changed to reflect 24-hour average breathing rates and updated reference characteristics of an adult male and to provide improved estimates of the distribution of absorbed ^{15}O.

The following reference values and assumptions were used in ICRP Publication 53: inhalation volume, 500 ml, distributed between alveolar space (350 ml) and dead space (150 ml); breathing rate, 12 per min; O_2 concentration in inhaled air, 21% by volume; functional residual volume of the lungs, 2400 ml; oxygen consumption, 240 ml/min; no absorption of O_2 to blood from the dead space; total blood volume, 5200 ml; concentration of O_2 in blood, 0.16 ml / ml blood; uniform distribution of absorbed O_2 in the total body; negligible elimination of absorbed ^{15}O from tissues; and the concentration of ^{15}O in the dead space is the average of that in the inhaled air and that of the alveolar air exhaled after 5 s. All parameter values of the ICRP model were derived from these assumptions. For example, the rate of loss of O_2 from the alveolar space in expired air was estimated as (350/2750) / (5 s) = 0.0255 s^{-1}; a transfer coefficient of ~0.009 s^{-1} from the alveolar space to blood was derived from the O_2 requirement for a resting adult of 240 ml / min; and it was estimated that O_2 transfers from blood to systemic tissues at the rate (240 ml O_2 / min) / (5200 ml blood x 0.16 ml O_2 / ml blood) = 0.2885 min^{-1} = 0.0048 s^{-1}.

Description of the present model for ^{15}O inhaled as molecular oxygen

The present model also is based on physiological features of an adult male but parameter values are derived from 24-h average (rather than resting) breathing patterns and O_2 consumption. The features of the adult male are taken primarily from ICRP Publication 89 (2002), the main exception being that the tidal volume is set for consistency with energy requirements as proposed by Layton (1994). The model structure is shown in Figure D-1 and parameter values are given in Table D-1.

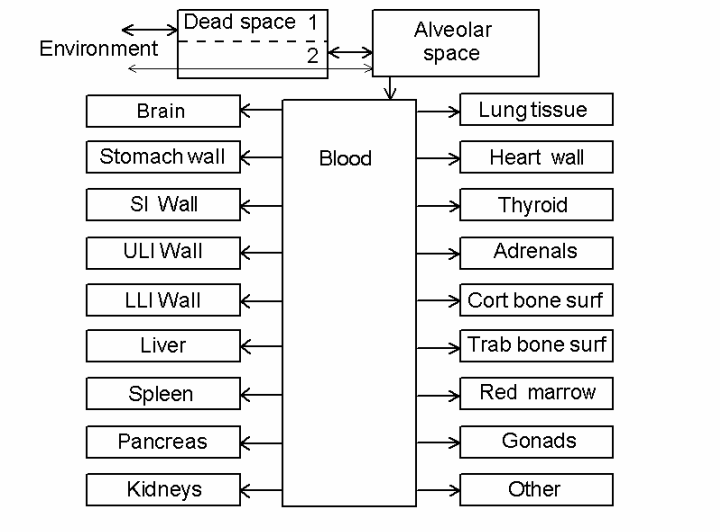

Figure D-1. Structure of the model applied in this report to ^{15}O inhaled as molecular oxygen.

Table D-1. Parameter values of the systemic model for ^{15}O inhaled as molecular oxygen

Origin	Destination	Transfer coefficient (d^{-1})
Blood	Adrenals	2.1228E+00
Blood	Brain	8.4912E+01
Blood	Cortical bone surface	7.0760E+00
Blood	Trabecular bone surface	7.0760E+00
Blood	Stomach wall	7.0760E+00
Blood	Small intestine wall	7.0760E+01
Blood	Upper large intestine wall	1.6133E+01
Blood	Lower large intestine wall	1.2171E+01
Blood	Heart wall	2.8304E+01
Blood	Kidneys	1.3444E+02
Blood	Liver	1.1322E+02
Blood	Lung tissue	1.7690E+01
Blood	Ovaries	1.4152E-01
Blood	Pancreas	7.0760E+00
Blood	Red marrow	2.1228E+01
Blood	Spleen	2.1228E+01
Blood	Testes	3.5380E-01
Blood	Thyroid	1.0614E+01
Blood	Other	1.4598E+02

The following characteristics of the adult male are taken from ICRP Publication 89: breathing rate averaged over 24 h, 15 breaths min^{-1} (after rounding); functional residual volume of the lungs, 3300 ml; volume of the dead space, 150 ml; total energy expenditure, 2800 kcal/d; and total blood volume, 5300 ml. As in ICRP Publication 53 it is assumed that the O_2 concentration in the inhaled air is 21% by volume, that O_2 is not absorbed to blood from the dead space; and that the concentration of O_2 in blood is 0.16 ml / ml blood.

The 24-h average ventilation rate and O_2 consumption rate were derived as follows. The quantity of energy liberated per liter of O_2 is 4.5-5.0 kcal, depending on the relative quantities of fat, carbohydrate, and protein in the diet (Guyton, 1982; Layton, 1994). Thus, O_2 consumption in a person with energy expenditure 2800 kcal/d is ~600 L O_2 d^{-1} (calculated range, 560-622 L O_2 d^{-1}). On the basis of reported measurements on human subjects, Layton (1994) concluded that the ventilation rate (L min^{-1} is approximately 27 (23-32) times the oxygen consumption rate regardless of activity level, age, or gender. Multipliers on the order of 36 were derived for pre-adult ages in a study not addressed by Layton (Zapletal et al., 1987), but the value 27 appears to be a reasonable central estimate, particularly for adults. Thus, total 24-h air intake is estimated as 600 L d^{-1} x 27 = 16,200 L d^{-1} or 11.25 L min^{-1}, which corresponds to 750 ml per breath based on 15 breaths min^{-1}.

The above reference values or derived values and assumptions were used to develop the following idealized representation of the respiratory behavior of ^{15}O-labeled molecular oxygen after inhalation in a single breath. Labeled O_2 enters the respiratory tract in 750 ml of inspired air that is distributed between the alveolar space (600 ml) and dead space (150 ml). Simultaneously, 150 ml of air remaining in the dead space at the end of the previous breath moves into the alveolar space, so that a total of 750 ml of air enters the alveolar space. Labeled O_2 is removed from the alveolar space through continuous uptake to blood plus exhalation of 750 ml of air every 4 s. Air removed from the alveolar space is distributed between the dead space (150 ml) and expired air (600 ml), forcing the previous deposit of air in the dead space to be expired. Thus, the initial deposition of labeled O_2 in the dead space is removed after 4 s. During the next inhalation of air the labeled O_2 that has moved from the alveolar space to the dead space returns to the alveolar space.

This idealized sequence of events is converted into a first-order model as follows. The respiratory tract is divided into three compartments: AR, representing labeled O_2 in the alveolar region, DS1 representing initial deposition of labeled O_2 in the dead space, and DS2 representing labeled O_2 that has moved into the dead space from AR. Fractional removal from AR per unit time is [750 / (750 + 3300)] / 4 s = 0.046296 s^{-1}, where 3300 ml is the functional residual volume. The transfer coefficient from AR to the environment (excreta) is (600 / 750) x 0.046296 s^{-1} = 0.03704 s^{-1} and from the alveolar space to DS2 is (150 / 750) x 0.046296 s^{-1} = 0.009259 s^{-1}. The transfer coefficient from DS1 to excreta is 0.25 s^{-1} based on a transit time of 4 s. The transfer coefficient from DS2 to AR is also 0.25 s^{-1}. If these parameter values for respiratory compartments are applied to continuous inhalation of O_2, the transfer coefficient from the alveolar space to blood required to

deliver 600 L O_2 d^{-1} is 0.01065 s^{-1}. After conversion to units of d^{-1}, transfer coefficients from respiratory compartments are as follows: AR to Blood, 920 d^{-1}; AR to Excreta, 3200 d^{-1}; AR to DS2, 800 d^{-1}; DS1 to Excreta, 21,600 d^{-1}; DS2 to AR, 21,600 d^{-1}.

Oxygen entering the blood from the alveolar region is estimated to leave blood at the rate (600 L O_2 / d^{-1}) / (5300 ml blood x 0.16 ml O_2 / ml blood) = 707.6 d^{-1}, where the numerator is the O_2 consumption rate by the body's tissues and the denominator is the O_2 content of blood. The distribution of O_2 that reaches blood is assumed to be determined by cardiac output, so that the portion of outflow from blood going to a tissue is the same as estimated earlier for O_2 water. The rate of transfer of oxygen from tissues back to blood is assumed to be negligible compared with the radiological decay rate of ^{15}O (0.34 min^{-1}).

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