ESTIMATES OF DOSE FROM XENON-133 TO INFANTS AND CHILDREN FOR IMMERSION IN AN INFINITE CLOUD AND FOR MEDICAL USES*

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Within the next 50 years, with the increase in nuclear power production, there is the possibility of population exposure to noble gases which are released to the atmosphere. However, apart from the future industrial exposure, some of the noble gases are being used extensively in nuclear medicine for persons of all ages. Among the principal uses of the radioactive noble gases in nuclear medicine are the assessment of regions of decreased ventilation and perfusion in the lungs and regional blood flow in other areas of the body. The radiopharmaceuticals are either prepared as a labeled gas which the patient inhales or injected as a solution containing the dissolved gas.

Committee 2 of the International Commission on Radiological Protection (ICRP, 1960) has based its recommendations for $(MPC)_a$ on the basis of the adult individual being submersed in a large cloud of radioactive gas. This concept of an adult submersed in a cloud is not applicable for medical applications which will primarily be internal exposures. Nevertheless, there is a relationship of the two types of exposure as we shall see.

When an individual is immersed in an atmosphere of ^{133}Xe , his tissues absorb or take up a certain portion of xenon until the body fluids are in equilibrium with the

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atmosphere. The temperature at which the experiment is carried out influences the solubility--the higher the temperature, the lower the solubility (Yeh and Peterson, 1964 and 1965). Although a few in vivo studies have been done with ^{133}Xe using rats, rabbits and dogs (Andersen and Ladefoged, 1967; Clifton, 1968; Conn, 1961), most biological experiments have been done in vitro using substances such as olive oil, paraffin oil, distilled water, plasma and red blood cells. The solubility of ^{133}Xe in various fluids or tissues has been expressed by Ostwald's solubility coefficient or, alternatively, by the tissue-blood partition coefficient and other ratios. For our study we chose the data taken at 37°C and expressed as Ostwald's solubility coefficient at equilibrium which for radioactive ^{133}Xe equals $(\mu\text{Ci } ^{133}\text{Xe}/\text{ml fluid})/(\mu\text{Ci } ^{133}\text{Xe}/\text{ml air})$.

From Kitani's (1972) review of much of the published literature, it appears that Ostwald's solubility coefficient for both in vivo and in vitro studies is 10 to 20 times higher for substances with a high fat content than for those with a low fat content. He also references Ostwald's solubility coefficients for ^{133}Xe at 37°C in olive oil as ranging from 1.79 to 1.883 with a mean of about 1.84, and in paraffin oil, from 1.96 to 2.079 with a mean of about 2.03. Because we have not found data on the solubility of ^{133}Xe in vivo in human adipose tissue, we based our solubility coefficients on olive oil and paraffin. We selected 1.9 as the solubility coefficient for ^{133}Xe in human fat. Ostwald's solubility coefficients in vitro for nonfatty substances such as distilled water, saline, red blood cells, plasma, human blood, rabbit muscle homogenate and beef brain homogenate ranged from 0.074 to 0.186 (Kitani, 1972; Ladefoged and Andersen, 1967; Muehlbaeche et al., 1966; Veall and Mallett, 1965; Yeh and Peterson, 1965)

with a mean of 0.11. Based upon the solubility coefficient for these substances, a value of 0.1 was chosen as being representative for these nonfatty tissues.

Three tissues are considered for deposition of ^{133}Xe --adipose tissue; the skeleton, because it contains considerable fat in the marrow; and the remaining tissues of the body. Reference man weighs 70 kg, and of this, 15 kg are adipose tissue. Of this 15 kg, 12.5 kg are considered to be separable adipose tissue, that is, rather large deposits of adipose tissue which are anatomically easily separable from surrounding tissues. Because adipose tissue consists of 80% fat, there are about 10 kg of fat in these tissues. Using our estimated Ostwald solubility coefficient, C , for the separable adipose tissue of the body,

$$C_{\text{adipose tissue}} = \frac{(10,000)(1.9) + (2500)(0.1)}{12,500} = 1.54 \text{ pCi/ml } (\sim \text{pCi/g}).$$

Thus, if reference man is immersed in an atmosphere containing $1 \mu\text{Ci/m}^3 (= 1 \text{ pCi/ml})$, the separable adipose tissue would contain $1.54 \times 12,500 = 1.9 \times 10^4 \text{ pCi}$ of ^{133}Xe at equilibrium according to this calculation which assumes a specific gravity of 1 for adipose tissue. We only consider the separable adipose tissue in this calculation, because most of the remaining adipose tissue is widely scattered throughout the body in small deposits of diameter less than the range of many of the beta particles. On the other hand, the separable adipose tissue exists in rather large masses of tissue where beta-like energy can be assumed to be completely absorbed without undue loss of accuracy.

The skeleton of reference man weighs 10 kg, and of this, 1900 g are fat and 8100 g are considered to be nonfatty tissue. Therefore,

$$C_{\text{skeleton}} = \frac{(1900)(1.9) + (8100)(0.1)}{10,000} = 0.442 \text{ pCi/ml.}$$

In this case we considered the specific gravity of the skeleton as 1.5, and on a mass basis

$$\frac{0.442}{1.5} = 0.295 \text{ or } 0.3 \text{ pCi/g.}$$

Thus, with reference man in equilibrium with an atmosphere containing $1 \mu\text{Ci/m}^3$ as before, his skeleton would be expected to contain $0.3 \times 10,000 = 3 \times 10^3$ pCi of ^{133}Xe in tissue. Actually most of this ^{133}Xe is in the yellow marrow, and a separate dose calculation for the beta-like energy will be made for this tissue. However, the distribution of the marrow is rather general throughout the skeleton, and for the photons we will use the specific absorbed fraction (SAF) or absorbed fraction of energy per gram of tissue for the skeleton in estimating dose. Fat has now been accounted for in the separable adipose tissue (12,500 g) and skeleton (10,000 g). In the remaining 47,500 g of soft tissue of the total body, there are 1500 g of so-called essential fat. Therefore, the Ostwald solubility coefficient for the remaining soft tissue is

$$C_{\text{soft tissue}} = \frac{(1500)(1.9) + (46,000)(0.1)}{47,500} = 0.157 \text{ pCi/ml } (\sim \text{pCi/g}).$$

Our reference man at equilibrium with the atmospheric level of $1 \mu\text{Ci/m}^3$ in air thus will have $0.16 \times 47,500 = 7.6 \times 10^3$ pCi of ^{133}Xe in the soft tissues other than separable adipose tissue and skeleton. To summarize, at equilibrium we would expect to find 1.9×10^4 pCi of activity in the separable adipose tissue; 3×10^3 pCi of activity in the skeleton, much of it being in the yellow marrow; and 7.6×10^3 pCi of activity in the remaining tissues of the body.

An average dose rate from beta-like energy released in the body tissues due to the ^{133}Xe absorbed in those tissues can be estimated by assuming complete absorption of beta-like energy in these tissues which does not seem unreasonable. Using the decay-scheme data of Dillman (see Fig. 1), we obtain in rads/day:

$$D_{\beta} \text{ (separable adipose tissue)} = 1.08 \times 10^{-5}$$

$$D_{\beta} \text{ (skeleton average)} = 2.14 \times 10^{-6}$$

$$D_{\beta} \text{ (remainder of body)} = 1.14 \times 10^{-6}$$

The beta dose to the yellow marrow would be the same as the estimate of dose to the separable adipose tissue.

It is not entirely easy to represent the distribution of activity given above in terms of the Monte Carlo calculations of the absorbed fractions of photon energies that have been carried out, the reason being that the phantom as used in MIRD Pamphlet 5 (Snyder et al., 1969) has no region as representative of the separable adipose tissue. This tissue consists of the subcutaneous fat as well as other large deposits of fat around the kidneys, intestines, omentum, etc., and all of this is contained in a compartment labeled "other tissues" in the phantom as used in the calculations. This "other tissue" compartment simply consists of the remaining tissues of the body after 22 organs, which are identified separately as regions, are removed. It has a mass of 48,210 g. The separable adipose tissue is distributed rather generally throughout this region since the subcutaneous fat extends from head to foot and the adipose tissue about the kidneys occupies a rather central region. Values of SAF are available, although not published, for this region as a target tissue. By use of the reciprocity

theorem or by subtraction from values obtained with the total body as source, the SAF may be obtained for this region as a source (Snyder et al., 1972).

To use the values of SAF, we assume the 1.9×10^4 pCi of activity assigned to separable adipose tissue will have the same SAF's as does the "other tissues" compartment. This assumption is probably least accurate in estimating dose to the adipose tissue itself but would not be expected to be a major error in calculating dose to other tissues than separable adipose tissue. To represent the distribution of sources in the phantom, we need to have 1.9×10^4 pCi of activity in the "other tissues" compartment representing only the contribution of separable adipose tissue, 3×10^3 pCi of activity in the skeleton, and 7.6×10^3 pCi of activity in the remaining tissue. This is best done by putting $7.6 \times 10^3 \times 70,000/47,500$ pCi = 11.2×10^3 pCi distributed uniformly in the total body and noting that this already accounts for 1.6×10^3 pCi of activity in the skeleton and thus leaves only 1.4×10^3 pCi additional required there and also noting that this accounts for $11.2 \times 10^3/70,000 \times 12,500 = 2 \times 10^3$ pCi of activity in the adipose tissues. Thus only $19 \times 10^3 - 2 \times 10^3 = 17 \times 10^3$ pCi of activity need be put in the "other tissues" compartment. Recapitulating, we require 11.2×10^3 pCi distributed uniformly in the total body, 1.4×10^3 pCi distributed uniformly in the skeleton, and 17×10^3 pCi distributed uniformly in the "other tissues" compartment which represents adipose tissue. The resulting dose rates to various organs and tissues of the body are shown in Table 1. In general, the dose from photons emitted within the body is less for organs near the surface than for those near the central axis; of course, this does not apply for the beta component of dose.

The dose rates given in Table 1 result from the ^{133}Xe present in the body tissues of a man immersed in a semi-infinite cloud of ^{133}Xe at 1 pCi/ml. The dose from the

^{133}Xe present in the external cloud is given in the last column of the table. It appears that the individual's internal organs get much more dose from the photons emitted from the external cloud than from ^{133}Xe absorbed in the tissues. The beta rays emitted from the cloud would effectively penetrate only to a depth of about 0.05 cm and fall off from a level of 8×10^{-4} rad/day at a depth of 0.007 cm. The average over this distance is about 1.8×10^{-4} rad/day. However, dose to the lung from ^{133}Xe in the air space of the lung does not appear to vary markedly with age. For example, data on reference man (ICRP, to be published) and from the Report of the Task Group on Lung Dynamics (ICRP, 1966) indicate that the adult, the ten-year-old and the newborn would have average values for air space in the lung of about 4 l, 1.6 l and 0.24 l, respectively, and lung masses of 1000 g, 425 g and 51 g, respectively. Thus the dose from beta rays would be proportional to

$$\frac{4}{1000}, \frac{1.6}{425}, \frac{0.24}{51} \approx 0.004, 0.0038, 0.0047.$$

Dose from photons would be even less important for the younger ages than is indicated in Table 1 for the adult due to the greater escape of photons from the smaller organs. All of these calculations assume the air in the lung airways is in equilibrium with the outside air, that is, at a level of $1 \mu\text{Ci}/\text{m}^3$.

Because fatty tissue concentrates ^{133}Xe more than other tissues in the body, it is necessary to determine the amount of fat in the body as a function of age. This is presented in Fig. 2. In the newborn, fat comprises about 12% of the total body weight, while in the adult, about 14 or 15% of the total body weight is fat. The amount of fat as a percentage of the total body weight at each specified age may be estimated

from this figure. For the ten-year-old, about 17% of the total body weight is fat. This would indicate that the ten-year-old individual might receive a slightly higher dose than any other age less than 20 years. Also, the data as plotted in this figure indicate that after age ten, there may be a sex difference--the female receiving the higher dose due to the larger amount of fat. It may be that the elderly will be the critical individual, but in all cases the percentage of fat seems to vary by a factor of about two from that of the adult male. Moreover, as remarked previously, the beta dose will not be greatly different, since there are no large differences in fat composition of tissues and, hence, in uptake of ^{133}Xe . Thus, dose from beta rays should be largely independent of age. The dose from photons would appear to be less on the average for children and infants due to the fact that there is a greater escape of photon energy from their bodies due to their smaller size. Also, it will be noted that beta rays are the major contributor to dose, and this dose would not be expected to change much with age. These conclusions are based on various individuals being exposed to and in equilibrium with the infinite cloud of ^{133}Xe .

Now consider an individual inhaling ^{133}Xe and who is not exposed to the infinite cloud. Specifically, we assume for definiteness that he inhales 1 μCi of ^{133}Xe . We note that the levels in the body tissues which produced the doses in the first three columns of Table 1 were maintained by inhaling 20 $\mu\text{Ci}/\text{day}$. This is a result of the assumption that the reference individual inhales about 20 m^3 of air and each cubic meter contains 1 μCi of ^{133}Xe . Since he breathes 20 μCi every day and receives the doses indicated in the first three columns of Table 1, conservation of energy requires that 20 μCi taken at one time produce total doses equal to the doses

per day given in the table. Dividing by 20, we obtain the total dose per μCi inhaled which is shown for the adult male in Table 2.

As noted earlier, there is little difference found in the dose rates received by the individuals of different ages when exposed to the infinite cloud; in fact, the differences are by about a factor of 2 either way from the dose rates for the adult male. Considering the breathing rates of the individuals of different ages, we have arrived at the rates shown at the heads of the columns of Table 2. This estimate is obtained by multiplying the frequency (breaths per minute) by the tidal volume (volume per breath). There is very little data available in the literature on the frequencies and tidal volumes at the specific ages in which we are interested. For both frequency and tidal volume we used the data of Altman and Dittmer (1964), Altman et al. (1958), ICRP Lung Report (1966), ICRP Reference Man Report (to be published), and Watson and Lowrey (1967). For frequency, we used the ages of 1 y, 2 y, 3 y, 5y, 10 y, 15 y and 20 y, and for tidal volume, we used data for ages newborn, 1, 2.5, 8.6, 10, 12, 14, 15, 16, 17.3 and 20 y. We plotted the available data for what ages we could find and estimated from the graph values for the specific ages in which we are interested. Although individual values are not firm, the trend of these data appears to be significant. Because the amount of air breathed per minute is dependent upon the activity of the individual, we likewise had to make estimates as to the number of hours for resting and light activity. As an example, for the newborn we estimated 16 hours of resting and 8 hours of light activity, while for the adult we estimated 8 hours for resting and 16 hours for light activity.

Now, considering the dose rates as relatively constant among individuals of different ages as maintained by breathing an atmosphere containing $1 \mu\text{Ci } ^{133}\text{Xe}$ per m^3 , we have only to repeat the procedure for the adult. Dividing the indicated dose per day by the μCi (equals m^3) of air breathed, we have the estimates of dose shown in Table 2. It will be noted that although there was not much difference in the daily doses due to immersion in the cloud, the dose per μCi inhaled increases regularly as age decreases. Thus the newborn receives a total dose per μCi inhaled that is approximately a factor of 10 higher than does the adult. This applies to all organs except the lung where the dose per μCi appears to be relatively constant. These estimates are being further explored and, although preliminary, may indicate a common region of interest for the health physicist and medical personnel.

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Table 1. Dose Rate (rad/day) to Various Organs and Tissues of Adult Man from Immersion in an Infinite Cloud of ^{133}Xe at a Concentration of 1 pCi/ml

Target Organ	Source		Air
	Skeleton, Adipose Tissue and Total Body γ	β	
Adipose tissue	4.5×10^{-7}	1.1×10^{-5}	4.2×10^{-4}
Skeleton	5.3×10^{-7}	2.14×10^{-6}	8.4×10^{-4}
Red marrow	7.7×10^{-7}	4×10^{-6}	7.7×10^{-4}
Ovaries	5.5×10^{-7}	1.1×10^{-6}	2.1×10^{-4}
Testes	4.0×10^{-7}	1.1×10^{-6}	4.7×10^{-4}
Lungs	$4.5 \times 10^{-7*}$	$1.1 \times 10^{-6*}$	3.7×10^{-4}
	$8.6 \times 10^{-7**}$	$2.5 \times 10^{-5**}$	
Skin	2.1×10^{-7}	1.1×10^{-6}	$6.3 \times 10^{-4} \gamma$
			$1.8 \times 10^{-4} \text{ avg } \beta$
Other organs	$3.8 \times 10^{-7} \text{ to}$	1.1×10^{-6}	4.8×10^{-4}
	7.0×10^{-7}		

* Dose from ^{133}Xe absorbed in body tissues

** Dose from ^{133}Xe in air spaces of the lung

Table 2. Breathing Rate and Total Dose (μ rad) to Various Organs and Tissues of the Body
from Inhalation of 1 μ Ci ^{133}Xe

	Age					
	Newborn	1 y	5 y	10 y	15 y	20 y (adult)
Breathing rate (m^3/day)	1.8	3.4	12	18	20	20
Target organs						
Adipose tissue	6.67	3.53	1.0	0.67	0.60	0.60
Skeleton	1.50	0.79	0.23	0.15	0.14	0.14
Red marrow	2.67	1.41	0.40	0.27	0.24	0.24
Ovaries	0.94	0.50	0.14	0.094	0.085	0.085
Testes	0.83	0.44	0.13	0.083	0.075	0.075
Lungs*	1.3	1.3	1.3	1.3	1.3	1.3
Skin	0.72	0.38	0.11	0.072	0.065	0.065
Other organs (range)	0.83-1.0	0.44-0.53	0.13-0.15	0.083-0.10	0.075-0.090	0.075-0.090

* Dose from ^{133}Xe in air spaces of lung.

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XENON-133

BETA - MINUS DECAY

INPUT DATA			
Radiation	%/disintegration	Transition energy (MeV)	Other nuclear parameters
Beta-1	0.70	0.267 *	Allowed
Beta-2	99.3	0.346 *	Allowed
Other betas	<0.001		
Gamma-1	0.65	0.0796	M1 + E2, $\alpha_K = 1.0$, K/L = 1.5
Gamma-2	99.95	0.081	M1 + 2.6% E2, $\alpha_K = 1.35$, K/L = 6.0, K/(L + M) = 4.8
Gamma-3	0.05	0.161	M1 + E2, $\alpha_K = 0.205$ (T), $\alpha_L = 0.0274$ (T)

Ref: Lederer, C. M. et al, Table of Isotopes, 6th ed.
* Endpoint energy (MeV); (T) = Theoretical value.

OUTPUT DATA			
Radiation (I)	Mean number/disintegration (n)	Mean energy (MeV) (E)	Δ_i ($\frac{\text{g-rad}}{\mu\text{Ci-h}}$)
Beta-1	0.007	0.0753	0.0011
Beta-2	0.993	0.1006	0.2132
Gamma-1	0.0023	0.0796	0.0004
K int. con. electrons	0.0023	0.0436	0.0002
L int. con. electrons	0.0015	0.0742	0.0002
M int. con. electrons	0.0005	0.0786	0.0001
Gamma-2	0.3499	0.0810	0.0605
K int. con. electrons	0.4724	0.0450	0.0454
L int. con. electrons	0.0787	0.0757	0.0127
M int. con. electrons	0.0984	0.0800	0.0148
Gamma-3	0.0004	0.1605	0.0001
X-rays Ka-1	0.2297	0.0310	0.0152
Ka-2	0.1173	0.0306	0.0077
K β -1	0.0453	0.0350	0.0047
K β -2	0.0134	0.0360	0.0010
L	0.0737	0.0643	0.0007
Auger electrons: KLL	0.0358	0.0234	0.0019
KLX	0.0157	0.0297	0.0010
KXY	0.0026	0.0340	0.0002
LMM	0.438	0.0033	0.0031
MXY	1.13	0.0010	0.0024

DILLMAN, 1970

FIG. 1.

Fig. 2.
Body Fat as a Function of Postnatal Age in Males and Females. (ICRP
Reference Man Report to be Published)