PROPOSED RETENTION MODEL FOR HUMAN INHALATION EXPOSURE TO $^{241}AmO_2$

James A. Mewhinney, William C. Griffith and Bruce A. Muggenburg

Lovelace Inhalation Toxicology Research Institute, P.O. Box 5890, Albuquerque, NM 87115, U.S.A.

Human exposures to ^{241}Am have been reported for four cases with measurements of lung retention near the exposure time (1-3), and five cases with long-term measurements of skeleton retention (4-6). These data were used to evaluate a model of ^{241}Am dissolution and retention developed using data from inhalation exposures of dogs to $^{241}AmO_2$. In several of the reports on human inhalation exposure, discrepancies have been shown with predictions of the Task Group Lung Model (1,3,4). The dissolution and retention model used in this paper takes into account the effects of particle size, distribution of particle sizes, and density of particles on lung retention. It is shown that the proposed dissolution and retention model is consistent with human inhalation exposures to ^{241}Am.

MATERIALS AND METHODS

The dissolution and retention model was developed using data from inhalation studies in Beagle dogs exposed to one of three sizes of monodisperse aerosols (0.75, 1.5, and 3.0 μm aerodynamic diameter) or a polydisperse aerosol (1.8 μm activity median aerodynamic diameter) of $^{241}AmO_2$ (7). Animals were sacrificed in pairs from 8 to 730 days after inhalation exposure to determine the organ retention and distribution patterns. Metabolic data from the studies using monodisperse aerosols were used to evaluate the effect of particle size on retention. Model parameters derived from the studies using monodisperse aerosols were used for modeling the study using polydisperse aerosols with adjustments only being made for the rate of mechanical clearance from lung to gastrointestinal tract. Model parameters from the study using polydisperse aerosols in Beagle dogs were compared with the human exposures in this paper.

The dissolution and retention model in Figure 1 described the lung as consisting of three regions — the nasopharynx, tracheobronchial and pulmonary — each cleared by competing pathways of mechanical clearance of particles to the gastrointestinal tract or dissolution and absorption into the general circulation. Dissolution and absorption was modeled as occurring through a dissolution pool and a compartment for the fraction of dissolved ^{241}Am bound locally to lung constituents. The locally bound ^{241}Am represents ^{241}Am seen as a diffuse distribution of single alpha tracts on autoradiographs of lung from the Beagle dog studies (7). Dissolution of the particles was described by equations developed by Mercer (8) who assumed the

This research was performed under U.S. Department of Energy Contract No. EY-76-C-04-1013 in facilities fully accredited by the American Association for the Accreditation of Laboratory Animals.

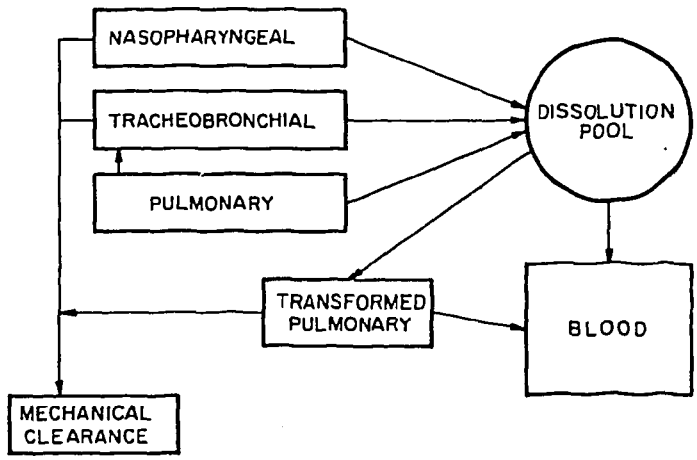

Figure 1. Dissolution and retention model for lung showing mechanical clearance pathways on the left to the gastrointestinal tract and dissolution pathways (described by equations of Mercer (8)) on the right from the 3 regions of lung to the dissolution pool. Other pathways for skeleton, liver, kidney, and soft tissue were modeled as exchanging with the blood compartment.

rate of dissolution is proportional to surface area of deposited particles. These equations take into account the distribution of particle sizes, density of particles, and shape of particles. The dissolution and retention model forced a total materials balance and used first order rate constants to describe transport, uptake and retention. In contrast, the Task Group Lung Model used by ICRP 30 (9) describes the clearance of lung as single exponential rates from subpools of the 3 regions of the lung. Also in contrast to ICRP 30, the model of retention in organs took into account redistribution of the absorbed ^{241}Am by representing the skeleton, liver, kidney, and soft tissue as two compartments in series exchanging ^{241}Am with the general circulation.

RESULTS

Predictions of lung clearance by the dissolution and retention model are shown for two particle sizes in Figure 2. Also shown are four cases of human inhalation exposures with early lung retention data (1-3) and the lung clearance of ^{241}Am as a Class W compound predicted by ICRP 30. Figure 3 shows predicted uptake by skeleton for three different particle sizes using the dissolution and retention model and for ^{241}Am as a Class W compound predicted by ICRP 30 (9). In applying the ICRP 30 lung model, it was assumed there was no absorption from the nasophyaryngeal and tracheobronchial regions since absorption from these regions appears to be low.

DISCUSSION

As can be seen from Figure 2, the dissolution and retention model can account for differences in early lung clearance observed in

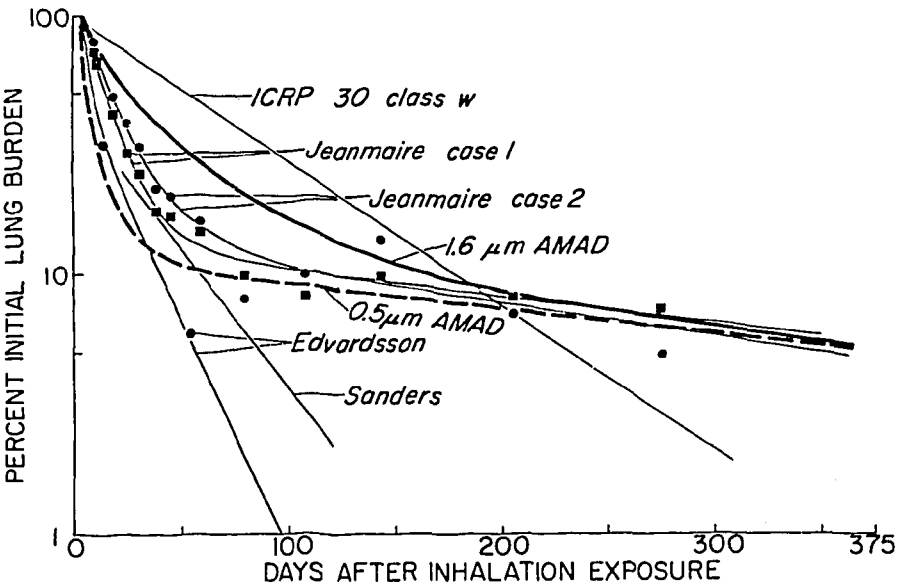

Figure 2. Comparison of early clearance from the lung for four human exposure cases (1-3), predictions of the dissolution and retention model, and predictions of ICRP 30 for ^{241}Am as a Class W compound (9). Lung retention is expressed as percent of the 4-day lung burden. Predictions of the dissolution and retention model are for a 0.5 μm activity median aerodynamic diameter (AMAD) aerosol (dashed line) and a 1.6 μm AMAD aerosol (heavy solid line) with a geometric standard deviation of 2 and density of 8 g/cm^3.

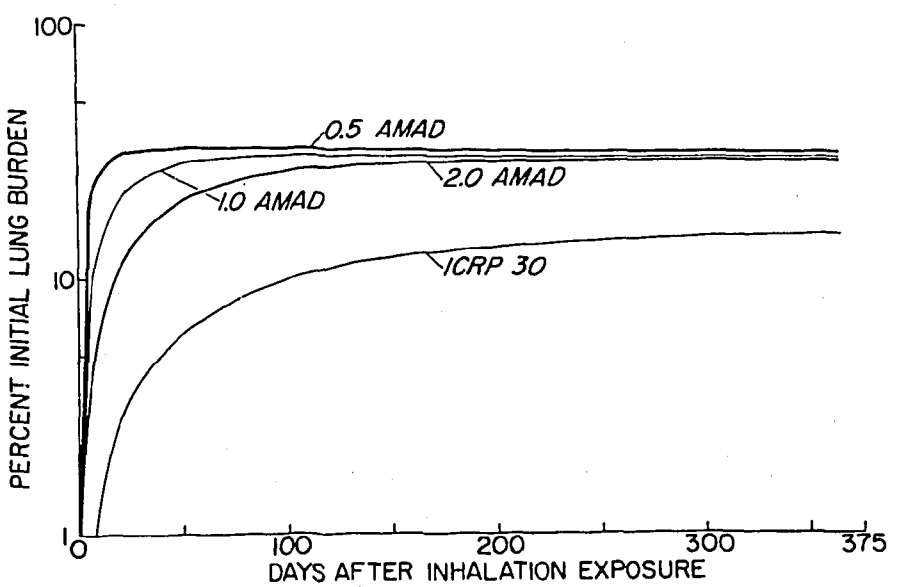

Figure 3. Predictions of skeletal uptake and retention from the dissolution and retention model for three particle sizes (geometric standard deviation of 2 and density of 8 g/cm^3) compared with the predictions of the ICRP 30 model of ^{241}Am as a Class W compound.

the human exposure cases by considering a range of activity median aerodynamic diameters from 0.5 μm to 1.6 μm. The surface area solubility rate constant was the same as that observed in dog studies (1.5×10^{-6} g/cm^2/day) and in *in vitro* solubility studies of AmO_2 (7). The particles were assumed to be spherical; however, this is not an essential assumption since changing the shape factor for irregular particles will have the same effect as changing the median particle size (8). Although characteristics of the aerosols were not reported for the human exposures, the parameters used to describe the aerosols in the calculations are typical of aerosols characterized in industrial facilities (10).

Comparison of the dissolution and retention model predictions with human inhalation exposure cases in which only long-term retention data were available for skeleton show reasonable agreement. Some discrepancies exist between the calculated half times of skeleton retention in humans of 17 years (5), 28 years (5), and 100 years (4,6), and the dissolution and retention model prediction of 10 years. These discrepancies probably occur because of a wide age range in human exposure cases (6 years to adults) and because the data used in developing the dissolution and retention model extends to only 2 years after inhalation exposure, making prediction of the long-term half-life in skeleton uncertain.

As shown in Figure 2, clearance of ^{241}Am from lung for the human exposure cases was more rapid than predicted in the ICRP 30 model with ^{241}Am as a Class W compound (9). The ICRP 30 model also fails to predict the presence of a long-term retained fraction as observed in several of the human exposures (1,4,5,6). Figure 3 shows the ICRP 30 model underpredicts the long term skeletal burden by a factor of 2 because the fraction of ^{241}Am absorbed from lung is underpredicted (4,7). Also the rate at which ^{241}Am accumulates in skeleton is underpredicted because ICRP 30 predicts a slower rate of absorption of ^{241}Am from the lung than was observed in the human exposures.

REFERENCES

1. Jeanmaire, L. and Ballada, J. (1971): In: Proceedings, Radiation Protection Problems Relating to Transuranium Elements, UR-4612, p 531.
2. Sanders, Jr. S. M. (1974): Health Phys., 27, 359.
3. Edvardsson, K. A. and Lindgren, L. (1976): In: Proceedings, Diagnosis and Treatment of Incorporated Radionuclides, IAEA, Vienna, p 497.
4. Fry, F. A. (1976): Health Phys., 31, 13.
5. Cohen, N., LoSasso, T. and Wrenn, M. E. (1978): In: New York University Institute of Environmental Medicine Radioactivity Studies Progress Report, COO-3382-17, p III-1.
6. Toohey, R. E. and Essling, M. A. (1980): Health Phys. (in press).
7. Mewhinney, J. A. and Griffith, W. C. (1978): In: Inhalation Toxicology Research Institute Annual Report, LF-60, p 43.
8. Mercer, T. T. (1967): Health Phys., 13, 1211.
9. ICRP Publication 30 (1979): Limits for Intakes of Radionuclides by Workers: Permagon Press: Oxford.
10. Raabe, O. G., Newton, G. J., Wilkinson, C. J., Teague, S. V. and Smith, R. C. (1978): Health Phys., 35, 649.