IMAGE EVALUATION TEST TARGET (MT-3)

150mm

6"

FINAL REPORT

on the project

Aerosol Deposition in the Human Respiratroy System

(Grant No. 5 R01 00923)

submitted to

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I. Summary of Work Accomplished

The objective of this research was to develop mathematical models for aerosol deposition in the human respiratory system. The emphasis was placed upon intersubject variability. During the grant period December 1, 1979 to August 31, 1982, the following studies were completed:

1. Empirical modeling of head deposition
2. Development of lung deposition models
   a. derivation of deposition formulas
   b. study of particle charge effect
   c. deposition of ultrafine particles
   d. extensive comparison with experimental data
3. Development of probabilistic deposition models
   a. deposition of polydisperse aerosols
   b. lung deposition with different airway structures
   c. statistical deposition model with random airway structures
4. Modeling of bronchial particle clearance

II. Detailed Report

1. Empirical Modeling of Head Deposition

Inhaled particles deposit along the air passages in the head before entering the lung. The dynamics of particle motion in this region is very comple, due to the complexity of the passage geometry. The residence time of the particles in this passage, however, is relatively short (~ 0.2 sec). Thus, for micron-sized particles, sedimentation is insignificant and the major mechanism of deposition is impaction.

There were two previous theoretical studies on nasal deposition at inspiration. These studies had not provided a useful formula for predicting deposition. At the present time, useful deposition formulas can only be derived empirically. Based upon a comprehansive analysis of all existing experimental data, we have obtained expressions for mean deposition efficiency $\bar{\eta}$ for nasal inspiration, nasal expiration and mouth inspiration. The mouth expiration efficiency was assumed to be zero from experimental data. In addition, statistical properties associated with each deposition efficiency due to inter- and intrasubject variabilities were determined. It was found that all variabilities follow a normal distribution. The standard deviation for each case was determined. Expressions for head deposition with combined nose and mouth breathing were also derived. The head deposition results were published in the American Industrial Hygiene Association Journal (see No. 1 on the publication list given below).

2. Development of Lung Deposition Models

a. Derivation of deposition formulas

It is well known that for compact particles in charge equilibrium, deposition in the lung airways is due principally to the mechanisms of impaction, sedimentation and diffusion. Among all of these mechanisms, impaction is most difficult to deal with and no adequate deposition formula is available at this time. Using a bend model and neglecting the secondary flow in the bend, we obtained a simple expression for impaction deposition in the form

$$\eta = 0.768\,(St)(\theta) \qquad \text{for } (St)(\theta) \ll 1 \tag{1}$$

where $St = \rho d_p^2 u/(9\mu d)$ is the Stokes number, $\theta = \ell/(4d)$ is the bend angle, ρ and d_p are respectively the density and diameter of the particle, u is the mean flow velocity, μ is the air viscosity, and ℓ and d are the length and diameter of the airway. Calculated efficiency from this equation agrees fairly well with the impaction deposition measurements by Schlesinger et al. in a lung cast which consists of five generations of bifurcating airways.

For freshly generated aerosols, particle charge effect on deposition can also be important. It has been previously shown by us that in most cases, electrostatic image force on the particle will contribute to deposition. A deposition formula to account for this contribution was derived to give

$$\eta = 2.88\,E^{1/3} \tag{2}$$

where $E = \theta n^2 e^2/(6\pi^2 \varepsilon_o \mu d_p u)$ in which n is the charge number, e is the electronic charge, and ε_o is the permittivity.

Several deposition formulae for sedimentation have been derived in the literature. Those which proved to be most useful were by Pich, and by Yu and Thiagarajan. Pich's formula was derived for a horizontal tube. For application to a system of randomly oriented airways, an average angle of inclination with vertical ϕ was chosen so that $\sin \phi = \pi/4$. The use of measured values of ϕ from a lung cast in the deposition model gives only small effect. The formulae derived by Yu and Thiagarajan are more general and they include the effect of uphill-downhill flow as well as that of particle concentration profile at the airway entrance. We have used both pich's and Yu's formulae in the calculation. Yu's formulae give better deposition results when compared with the experimental data, but the difference is not large.

Deposition formulae for diffusion was adopted from earlier studies of Landahl for turbulent flow and Ingham for laminar flow. These formulae appear to be sufficiently accurate for deposition calculation.

b. Study of particle charge effect

Equations (1) and (2) were used in a theoretical study of particle deposition in the human tracheobronchial tree considering the simultaneous action of the inertial and electrostatic forces on the particle. Calculated deposition in the trachea agrees well with the data by Chan et al. It was also shown that particle charge can produce a significant enhancement in deposition in the tracheobronchial region. For example, inhaled particles having mass median aerodynamic diameter of 2 μm and carrying 200 electronic charges per particle resulted in tracheobronchial deposition of 39% as compared to 3% for unchaged particles of the same size during inhalation. This may have important implications in health hazard assessment.

The effect of particle charge on total lung deposition was also studied using a lung deposition model that we developed and compared with the data by Tarroni et al. The agreement between our model and data is favorable. However, the data appear to show the existence of a threshold charge number per particle and below this number particle charge has no effect on deposition. This is not found from our model, and we are making further studies on this point in an attempt to explain the discrepancy.

The deviation of impaction deposition formulae and the study of charge effect on lung deposition were reported in several papers and at meeting presentations (see No. 2 to 5 on the publication list).

c. Deposition of ultrafine particles

For particle size below 0.1 μm, diffusion is the major mechanism of deposition. Deposition calculations were made for these ultrafine particles with the use of our lung model. The results showed that deposition varies with a parameter $D\tau$ regardless of the particle size, where D is the diffusion coefficient and τ is the period of a respiratory cycle. The effect of flowrate was found to be small. It was also shown that ultrafine particles are better tools than large particles for measuring airway dimensions. Publication No. 6 reports these results.

Deposition data for ultrafine particles are very scarce because of experimental difficulties. Some data of Heyder et al. for 0.2 μm particles were used to compare with our calculated results and agreement is good for this particle size. Recently, we have been approached by Dr. K. Tu of the Environmental Measurements Laboratory, DOE, who has just completed some deposition measurements for particle sizes smaller than 0.1 μm. Extensive comparisons of our results with Dr. Tu's data are underway.

d. Extensive comparison with deposition data of large particles

Dr. Heyder and his colleagues at Frankfurt, Germany, have collected total deposition data at mouth breathing of spherical, uncharged di-2-ethylhexyl sebacate and iron-oxide particles with diameters ranging from 0.2 μm to 8 μm under a variety of well controlled breathing conditions. They established that the physical factors responsible for deposition under this condition are particle diameter, particle density, mean flowrate and mean residence time, and made measurements by systematically varying these parameters. To validate our deposition models, we have calculated total deposition for all their experimental conditions. Good agreement was found for all cases. Although regional deposition was not measured in this experiment, it can be readily determined from our model study. It has been demonstrated how regional deposition varies with each physical factor and how this variation contributes to the observed change in total deposition.

There are not enough data on regional deposition for a well controlled experiment under various conditions of particle mass density, mean flowrate and mean residence time. Recent measurements by Stahlhofen et al. using iron-oxide particles tagged with ^{198}Au covered a wide range of particle sizes. Their data were used for comparison with our calculated deposition. The data of Stahlhofen et al. show that at mouth breathing, both the head (H) and tracheobronchial (TB) depositions are insignificant if the aerodynamic particle diameter is below 2 µm. However, this was not exactly found in calculation. The calculation shows a small amount of tracheobronchial deposition for particle aerodynamic diameters below 2 µm. A manuscript reporting various comparisons between calculated depositions and experimental data will be published in the Journal of Aerosol Science (No. 7 in the publication list).

3. Development of Probabilistic Deposition Models

Uncertainties in aerosol deposition arise from several origins. These are particle source, airway morphology and respiratory conditions. We have studied each of these factors separately in order to understand their effects on deposition.

a. Deposition of polydisperse aerosols

Since airborne particles in the environment are normally composed of particles of different sizes, a study was conducted to study deposition of a polydisperse aerosol of uniform composition using our deposition models. We assumed that the aerosol had a lognormal distribution. For this aerosol, it was shown by the Task Group that mass deposition fraction depends upon two aerosol factors. These are mass medium aerodynamic diameter $\bar{D}_m$ and geometrical standard deviation σ_g.

Our deposition results show that total and regional depositions of a polydisperse aerosol may deviate considerably from that of a monodisperse counterpart. These deviations can be explained in terms of the average mobility effect and deposition limitation effect of the polydisperse aerosol as well as the sequential filtering effect of the various compartments in the respiratory system. A manuscript (No. 8 on the publication list) reporting our results will be published in the American Industrial Hygiene Association Journal.

b. Lung deposition models with different airway structures

The deposition model that we previously developed was based upon Weibel's dichotomous, symmetric lung model A. In a real lung, the airways are believed to be asymmetric and Weibel's model thus does not give the correct number of airway structures. Pioneering models of asymmetric airways were proposed by Horsefield and Cumming for the tracheobronchial tree and by Parker et al. for distal airways. A combination of these models for the entire lung was suggested by Olson et al. Hansen and Ampaya also proposed an asymmetric lung model beyond the first 10 generations of Weibel's model. Recently, Yeh and Schum presented an airway model for each lobe of the lung. Their data include the branching angle and the angle of inclination with the vertial. The number of airways at each generation, however, follows the dichotomous model of Weibel.

To examine the effect of the airway geometry on particle deposition in the lung, a comparative study was made using the four lung models described above (publication No. 9). It was found that at the same lung volume, deposition varied with the lung model and the differences were small in total deposition, and became more profound in regional depositions. At the airway generation level, deposition distributions were found to be markedly different for large particales. It should be pointed out that various lung models developed from different lung casts and measurement schemes. Deposition differences obtained various lung models reflect, therefore, a certain extent of the intersubject deposition variability observed in the experiment.

c. Statistical deposition models

We have devoted considerable effort to develop lung deposition models from a probabilistic approach. Dr. Heyder has provided us with detailed total and regional deposition data for 20 subjects obtained under various controlled breathing conditions. Thus, intersubject variability in this set of data is due only to anatomical differences in the subjects. We considered the probabilistic modeling of this problem using two approaches. One was to consider each airway generation as a compartment with a probabilistic description of its airway size (assumed fixed airway length to diameter ratio). Under certain assumptions, we obtained close-form expressions for the mean and variance of deposition at each airway generation. However, the expression for the variance is very complex and its evaluation was abandoned due to difficulty in implementing the algorithm. The advantage of this approach is that it permits geometrical variability in each airway generation.

The second approach was based upon a regional consideration since only regional deposition could be measured at this time. In this approach, we used two independent probabilistic scaling factors α and β for airway volume, α for the tracheobronchial region and β for the alveolar region, and σ_α and σ_β are their corresponding coefficients of variation. These two factors represent anatomical differences between individuals. From the data of Heyder for the 20 subjects, it was shown that the total lung volume (FRC) follows a lognormal distribution. The coefficient of variation was found to be 0.249. We assumed the same value for σ_α and σ_β and considered the head as a random filter with characteristics that we obtained before, total and regional mean depositions and their standard deviations σ were calculated for a controlled mouth breathing condition. Remarkable agreement is found between theory and experiment for deposition variability. Except for the alveolar deposition, the results also show that the amount of variability depends upon particle size, increasing as particle size increases. The detailed result of the probabilistic deposition model described above has been presented in a paper to be published in Aerosol Science and Technology (No. 10 in the publication list).

4. Modeling of Particle Clearance in the Tracheobronchial Tree

Inhaled particles deposited in the tracheobronchial tree are cleared by mucociliary transport. The rate of this clearance depends upon the mucociliary transport velocity and particle deposition pattern along the airways. Experimentally, the clearance can be measured by tracking the activity of radio-labelled aerosols retained in the thorax with time. Thus, the experimental retention curves so obtained contain valuable information on particle deposition.

A collaborative research with Dr. M. Lippmann at the New York University Medical Center was initiated last summer to study this problem. A monodisperse ferric oxide aerosol tagged with radioactive technitium was used in the inhalation experiment. The subsequent retention of particles in the lung was measured by sodium iodide scintillators for the next 8 hours.

To explain the experimental data, a compartmental model was proposed by us to describe mucociliary transport and particle clearance in the tracheobronchial tree (Publication Nos. 11-13). This model suggests a procedure by which mucociliary transport rate, airway dimensions and particle deposition at each airway generation are determined simultaneously from several retention curves. We represent each airway generation by an escalator. If there are 17 airway generations in the tracheobronchial tree such as in Weibel's model, then these are represented by 17 escalators with lengths $_0$ to $_{16}$ and moving with velocity v_0 to v_{16}. Let the mass of deposited particles in the ith generation be m_i and that in the nonciliated airways by M_P. Then the mass fraction of the deposited particles in the ith generation is

$$f_i = \frac{m_i}{M_{TV} + M_P} \tag{4}$$

where $M_{TB} = \sum_{i=0}^{16} m_i$ is the fraction deposition in the tracheobronchial region. From the mass balance, we obtain the following relationship between R(t) and f_i:

$$R(T_n) = 1 - \sum_{i=0}^{n} f_i \tag{5}$$

where $T_n = \sum_{i=0}^{n} t_i$ is the time required to clear particles completely from the first n generations.

For a given lung model, m_i or f_i can be calculated from our deposition models. Equation (5) then determines various values of t_i and $v_i = \ell_i/t_i$. To obtain some preliminary results, we used Weibel's lung model to determine f_i. Then from the retention curve we obtained the values of v_i. In the first two generations (trachea and main bronchi), the calculated v_i from this method agrees reasonably well with the experimental values. Mucociliary transport rates in fine airways have yet to be measured experimentally. Our results give estimates of these rates for the first time from the particle retention data.

III. Publications

1. C.P. Yu, C.K. Diu and T.T. Soong, "Statistical Analysis of Aerosol Deposition in Nose and Mouth", American Industrial Hygiene Association Journal, 42, 726 (1981).
2. C.K.Diu and C.P. Yu, "Deposition from Charged Aerosol Flows in a Two-Dimensional Bend", Journal of Aerosol Science, 11, 383 (1980).
3. C.K. Diu and C.P. Yu, "Deposition from Charged Aerosol Flows in a Pipe Bend", Journal of Aerosol Science, 11, 397 (1980).
4. T.L. Chan and C.P. Yu, "Charge Effects on Particle Deposition in the Human Tracheobronchial Tree", Fifth International Symposium on Inhaled Particles, Wales, England, September 8-12, 1980; full paper will be published in Annals of Occupational Hygiene.
5. C.P. Yu and C.K. Diu, "Deposition of Charged Polydisperse Aerosols in the Human Lung", 14th Aerosol Technology Meeting, Johns Hopkins University, Baltimore, Maryland, August 24-26, 1981, abstract published.
6. C.P. Yu and J.P. Hu, "Diffusional Deposition of Ultrafine Particles in the Human Lung", International Symposium on Aerosols in Mining and Industrial Work Environment, Minneapolis, Minn., November 1-6, 1981; extended abstract published: full paper will be published in the symposium proceedings.
7. C.P. Yu and C.K. Diu, "Total and Regional Deposition of Inhaled Aerosols in Humans", Journal of Aerosol Science, in press.
8. C.K. Diu and C.P. Yu, "Deposition of Polydisperse Aerosols in Humans", American Industrial Hygiene Association Journal, January 1983.
9. C.P. Yu and C.K. Diu, "A Comparative Study of Aerosol Deposition in Different Lung Models", American Industrial Hygiene Association Journal, 43, 54 (1982).

10. C.P. Yu and C.K. Diu, "A Probabilistic Model for Intersubject Deposition Variability of Inhaled Particles", Aerosol Science and Technology, December 1982.

11. C.P. Yu, "A Model of Particle Clearance in Human Tracheobronchial Tree", 34th Annual Conference on Engineering in Medicine and Biology, Houston, Texas, September 21-23, 1981, extended abstract published.

12. C.P. Yu, J.P. Hu, G. Leikauf, D. Spektor and M. Lippmann, "Mucociliary Transport and Particle Clearance in the Human Tracheobronchial Tree", International Symposium on Aerosols in the Mining and Industrial Environment, Minneapolis, Minn., November 1-6, 1981; extended abstract published: full paper will be published in the symposium proceedings.

13. C.P. Yu, "A Compartmental Model of Particle Clearance by Mucociliary Transport in the Human Tracheobronchial Tree", Proceedings of the Third International Conference on Mechanics in Medicine and Biology, Compiegne, France, July 1982.

IV. Staffing

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