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● *Dosimetric Models: ICRP and NCRP Approaches*

AEROSOL DEPOSITION IN THE NOSE AS A FUNCTION OF BODY SIZE

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Abstract—The effect of body size on nasal doses from inhaled aerosols has not been measured directly in people. Two basic types of computational models are used to calculate inhaled particle deposition in adults. One type uses an impaction parameter that incorporates particle aerodynamic diameter and the average airflow rate. The second type uses the nasal pressure drop and particle aerodynamic diameter. Although both types of models have been adjusted to give reasonably accurate deposition efficiencies for adults, they predict very different deposition efficiencies when they are applied to young children. This is not surprising because the airflow-type model has no body-size-dependent parameters, unlike the pressure-drop-type model. The objective of our studies was to test these two types of computational models using idealized hollow nasal models of two sizes, representing the adult and young child. The results indicate that a pressure-drop relationship fits the aerosol deposition data very well. When the properly scaled physiological air flows and minute ventilations are used in a nasal dose calculation, the young child is seen to have potentially larger nasal doses than those of an adult.

INTRODUCTION

Particle deposition models

ACCURATE, validated models for predicting the regional deposition of inhaled particles are needed for several reasons. Risk estimates for inhaled air contaminants require knowledge of doses delivered to various regions of the respiratory tract. In comparative toxicology, it is clearly important to understand species differences in regional deposition of inhaled particles. Also, in the field of respiratory therapy, aerosol medications can be efficiently designed for people, livestock, companion and other animals only if good regional deposition models exist. The fact that no universally applicable model for the regional deposition of inhaled aerosols exists is a consequence of the enormous difficulty of the modeling problem. Such a universal model would have to handle the full range of mammalian lung structures, the full range of ventilation states both within and across species, and the large variety of aerosol particle shapes, sizes, and characteristics such as hygroscopicity and electrical charge. During the past 50 y of deposition modeling, progress has been made only in a few aspects of the overall problem.

A requirement for predictive models, both mechanistic and empirical, is that they have input information of three types: anatomical, airflow, and aerosol characteristics (Findeisen 1935; Yeh et al. 1976). Furthermore, the predictive models should be validated eventually by comparison of predictions and measurements of deposition in living subjects.

A review of each of the deposition models that have been proposed in the last half-century and their success in describing actual deposition data would be unwieldy. However, several publications, including those of Morrow et al. (1966), Mercer (1975), Lippmann (1977), Hounam and Morgan (1977), Ferron et al. (1985), Chan and Lippmann (1980), and Agnew et al. (1984), cover the subject relatively well. In brief, despite differences in the deposition equations used, in the way of describing respiratory tract anatomy, and in other features, essentially all of the diverse models satisfactorily fit the clinical deposition data for normal adults inhaling spherical particles at states of ventilation characteristic of those near rest.

Consideration of children

When children are considered, it is useful to establish the terminology and to consider growth as a function of age. Neonate, or newborn, refers to the period just after birth to about 4 wk. Infant (Latin for "not speaking") generally refers to the first 2 y of life, but sometimes the term is used for the first year or so (prior to achieving the ability to walk). Child refers to the ages between infancy and the onset of puberty—roughly from 2 y to about 10 or 12 y of age. The beginning of the adolescent period is marked by the appearance of secondary sex characteristics and ends with the cessation of growth, i.e., about 11 y to about 19. However, the term "child" can also be used broadly for the entire period of growth. In adequately nourished children there are two periods of relatively rapid

growth in height: from birth to an age of about 2 y, and from the onset of adolescence to about 16 y.

Increases in body height and mass vary considerably among individuals, cultures, races, generations, and even between the sexes, after about age 10 y. An important implication is that age *per se* is not a good primary parameter for correlation with ventilation or airway dimensions. It is better to initially relate deposition calculations to body dimensions and body mass and later use specific growth curves to relate the results to age.

Hofmann et al. (1979) were apparently among the first to perform detailed calculations of doses to the tracheobronchial and pulmonary regions from inhaled aerosols as a function of age. They considered the impaction, sedimentation, and diffusion mechanisms of deposition and computed anatomical airway sizes and airflow rates on the basis of curve-fitting to existing data and scaling assumptions (Hofmann et al. 1979; Hofmann 1982). Hofmann concluded that for Rn daughters, ". . . the α dose rate in the respiratory tract is strongly age-dependent . . .," reaching a maximum at about 6 y. Age-dependent risk-modifying factors were recommended for dose calculations. This modeling work is significant because it pointed out a potentially important problem. The main limitations of the work were that only small particles (less than $0.3 \mu\text{m}$ in diameter) were considered, the nose was not included, and the anatomical data were, of necessity, derived rather than measured.

Thomas and Healy, of the Los Alamos National Laboratory, developed a more comprehensive age-related particle deposition model (Thomas and Healy 1985) that included nasal, tracheobronchial, and pulmonary regions. The model used as anatomical input a greatly simplified 11-generation structure (after Landahl 1950), which was theoretically scaled for humans aged 1 mo and older. Again, the model generally predicts greater tracheobronchial deposition efficiencies as age decreases. Predictions for nasal and pulmonary regions were very dependent on particle size (the range examined was 0.001 to $9.9 \mu\text{m}$), and large age-related differences were predicted. For nasal deposition, Pattle's impaction equation (1961) was used.

Phalen et al. (1985) performed anatomical measurements on 20 replica tracheobronchial casts from infants, children, adolescents, and young adults and used the information to compute particle deposition in the tracheobronchial region. The results were qualitatively in agreement with those of Hofmann and of Thomas and Healy, but showed a generally stronger age-related dependence for particle capture efficiencies. For example, there was a 10-fold difference in dose between an adult and a newborn, at rest, for inhalation of a $1\text{-}\mu\text{m}$ aerodynamic diameter aerosol. This arose from two factors, the higher tracheobronchial collection efficiency and the greater minute ventilation per unit body mass of the newborn.

Xu and Yu (1986) published a relatively complete theoretical model for particle deposition in the ". . . human from birth to adulthood." Airway dimensions were scaled theoretically as functions of age, taking into account

published data for several anatomical and physiological quantities. Impaction was considered to be the mechanism for deposition of particles in the airways of the head, and by scaling upper airway dimensions to existing measurements of tracheal diameter they predicted that deposition in the head (for mouth breathing) would increase with decreasing age for particle diameters between 2 and $10 \mu\text{m}$. For deposition in the tracheobronchial and alveolar regions, significant age dependencies (both more and less than for adults) were predicted. However, the total deposition probabilities for mouth-breathing increased as age decreased down to an age of about 2 y, then decreased, for younger children, for particle diameters between 0.01 and $10 \mu\text{m}$.

Nasal growth and aerosol deposition

The nasal region is of particular interest because little is known about its growth and the effect of growth on particle deposition. Dimensions of the nasal cavity are known for adult humans and other mammals (Swift and Proctor 1977; Schreider and Raabe 1981; Patra 1986). The nasal cavity undergoes considerable growth postnatally, as can be seen from sectional anatomical studies (e.g., Ritter 1978), but this growth has not been measured quantitatively. On the other hand, the pressure drop across the nose in infants has been directly measured (Stocks and Godfrey 1978).

Direct measurements of nasal collection efficiency as a function of breathing parameters and particle aerodynamic size have been published for adults but not for children (Hounam et al. 1971; Lippmann 1977; Heyder and Rudolf 1977; Yu et al. 1981). The aerodynamic diameter (the diameter of a 1-g cm^{-3} density sphere with the same terminal settling velocity as the particle in question) has been shown to be an appropriate particle size parameter for expressing such deposition for sizes above the free-molecule regime. These studies have shown that when particle size and either airflow rate or nasal pressure drop are increased, they are associated with an increase in the particle deposition efficiency in the nose.

Because of the complexity of nasal airflow patterns and nasal anatomy, rigorous mechanistic theoretical models for predicting aerosol deposition in the nose are difficult to formulate (Scott et al. 1978). Therefore, various semi-empirical relationships between deposition efficiency and particle size have been proposed (Pattle 1961; Hounam et al. 1971; Heyder and Rudolf 1977; and Yu et al. 1981). The proposed models are said to be semi-empirical because aerosol deposition efficiency is quantitatively related to a function of particle size and airflow rate by means of a regression fit to empirical data, rather than by theoretical mechanistic considerations. These types of models have been developed for and successfully applied to adults.

To date, these semi-empirical relationships have been of two major types, which are typified by eqn (1) and (2):

$$E_N = -0.62 + 0.475 \log(D_a^2 F) \quad (1)$$

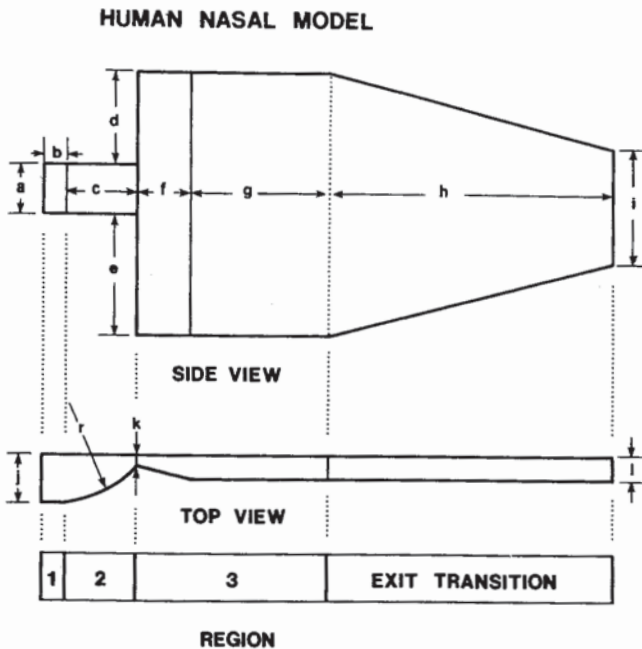


Fig. 1. Internal shape of the human nasal cavity hollow models used in the aerosol deposition studies.

$$E_N = -0.975 + 0.66 \log(D_a^2 P), \quad (2)$$

where E_N is the fraction of inhaled particles of a given aerodynamic diameter D_a (in μm) that deposit in the nose, F is the average airflow rate in liters per minute, and P is the average pressure drop across the nose (in $\text{mm H}_2\text{O}$).

Equation (1) (after Pattle 1961), which incorporates the average airflow rate, was used by the Task Group on Lung Dynamics of the International Commission on Radiological Protection for calculating adult nasal doses (Morrow et al. 1966). One notes that eqn (1) has no parameter that takes into account the size or shape of the nasal cavity. This is probably the major reason that *in vivo* human nasal deposition efficiency data show an unusually large degree of scatter when plotted vs. $\log(D_a^2 F)$ (Mercer 1975; Yu et al. 1981).

Equation (2) (after Hounam et al. 1971), on the other hand, does account for nasal size and shape through the use of the parameter P , the nasal pressure drop. Equation (2) represents the human data with less scatter than does eqn (1) (Mercer 1975). The possibility arises that if P is known for an individual, including a small child, eqn (2) might provide better predictions of the nasal deposition efficiencies of inhaled aerosols than would eqn (1).

It is noteworthy that, for an individual, the flow and

pressure drop across the nose are related to one another through the resistance parameter, R (in $\text{mm H}_2\text{O}$ per liter per min), by the following approximate relationship:

$$P = RF^x, \quad (3)$$

where x has been measured to be approximately $\frac{3}{2}$ by Hounam et al. (1971). Studies by Heyder and Rudolf (1977), involving four adult human subjects, demonstrated that a relationship of the following type [which is a modification of eqn (2)] provided the best description for their own deposition data:

$$E_N = A + B \log(D_a^2 P^{2/3}). \quad (4)$$

(Note that $\frac{2}{3}$ is the reciprocal of $\frac{3}{2}$, the exponent that relates P and F .)

None of the investigators previously mentioned directly addressed how their semi-empirical relationships would apply to growing individuals, i.e., newborns, infants, children, and adolescents. It is therefore logical to test the proposed relationships to see whether they could also be used to describe nasal deposition in smaller individuals.

The ideal way to test the applicability to children of eqn (1) and (2) would be to perform a series of aerosol deposition studies in children while simultaneously measuring E_N , F , and P . Unfortunately, such direct studies would be costly and technically difficult and, because there would be little or no direct benefit to the subjects, might be unconscionable for ethical reasons.

Another method for estimating the nasal deposition efficiency of children and also testing the semi-empirical relationships is to build large and small nose-like hollow models representing various body sizes, and then perform aerosol deposition studies in the models. We used the latter approach, and the remainder of this paper will describe aerosol deposition studies in two sizes of simplified hollow models and some of the implications of the results.

METHODS

Study design

Four hollow silicone-rubber models were constructed, two representing the anterior regions of one side of an adult nose and two representing the anterior regions of one side of the nose of a young child. Each hollow model was mounted, in turn, on a test stand so that air could be drawn through in a controlled fashion while the pressure drop across the model was being measured. Monodisperse aerosol particles of two sizes were generated into the air stream, and an optical particle counter was

Table 1. Dimensions (cm) of hollow nasal casts used in aerosol deposition studies. In Fig. 1, dimensions a through l are thicknesses and lengths, and r is radius of curvature. Note that infant model is half the size of adult model.

	a	b	c	d	e	f	g	h	i	j	k	l	r
Adult	1	0.5	1.5	2.0	2.5	1.0	3.0	6.0	2.5	1.0	0.32	0.5	2.0
Infant	0.5	0.25	0.75	1.0	1.25	0.5	1.5	3.0	1.25	0.5	0.16	0.25	1.0

used to measure particle counts. The deposition efficiency in the cast was determined by alternating particle counts with the cast in and out of the system. Each deposition measurement was performed at least twice for each combination of flow, pressure drop, and particle diameter. The mean values of each set of deposition data were calculated, the data were pooled and then fitted to linear-log equations of the types shown in eqn (1), (2), or (4), and the mean standard errors around the best-fitted lines and the correlation coefficients were determined.

Design and construction of hollow models

According to several investigators, the majority of the nasal deposition of inhaled particles occurs just beyond the region of minimal cross section, i.e., the slit-like nasal valve (Itoh et al. 1985; Scott et al. 1978; Fry and Black 1973). This "hot spot" of deposition is caused by the significant air turbulence that is generated by an abrupt increase in airway cross-sectional area. Knowledge of this fact permits simplification of the hollow models by omitting the very complex nasal turbinate region, presumably producing only minor underestimation of the total aerosol deposition efficiency. For example, Scott et al. (1978) predicted that over 90% of the deposition for 2- μm -aerodynamic-diameter particles would be in the preturbinate region at a ventilation rate of 10 L min⁻¹.

Each nasal cavity can be thought of as having five regions: the entrance or naris; a region of decreasing cross section leading to the nasal valve; the anterior nasal chamber; the main chamber with the turbinates; and the nasopharynx, a "bend" where the two nasal cavities join. Dimensions of these regions for the adult have been published by Scott et al. (1978), who used them to calculate the particle deposition efficiency and pressure drop in the nose. Because these calculations were in good agreement with the clinical data on pressure drop and aerosol deposition for human subjects, we constructed hollow models that were patterned after the first three regions described by Scott et al. (1978) with one exception: our region 3 (anterior nasal chamber) was enlarged to give a cross-sectional area consistent with that for the adult, as published by Swift and Proctor (1977). The shape of the interior cavity of models is shown in Fig. 1. Our young-child models were geometrically similar to the adult models, but each dimension was reduced by 50% (Table 1). The assumption of geometrical similarity of the nasal cavity for young children and adults is an approximation made necessary by a lack of accurate growth-related data. This approximation appears to be reasonable from in-

Table 2. Physiologic variables for adults and infants used in calculating inhalation doses. Note that ratio of minute ventilation to body mass is much larger for infant than for adult.

	Age (y)	Body Mass (kg)	Height (cm)	Minute Ventilation (L min ⁻¹)	
				Near Resting	Exertion
Adult	18	70	175	10	30
Infant	1/12	4	52	1.6	4.75

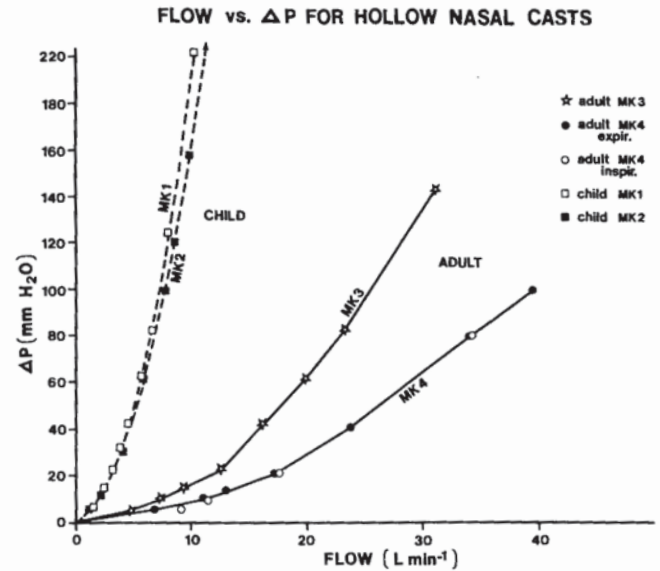


Fig. 2. Pressure-flow relationship for the four hollow nasal models used in the study. Although the two adult-sized casts were intended to be identical, differences in surface roughness at the narrowest region apparently led to the reproducibly distinct curves.

spection of the cross sections of the nasal cavities of children and an adult, published by Ritter (1978).

Assigning an appropriate age to the hollow half-size cast was not a trivial matter. At age 2 y, body height is about 50% of the adult value. However, the actual pressure-flow curves for the casts indicated that the small casts were more representative of the young infant, corresponding to an approximate age of about 1 mo. Because pressure drop, a key factor in aerosol deposition and nasal growth, is not quantitatively documented, an age of 1 mo was adopted. Using published body growth and ventilation data (Altman and Dittmer 1971, 1972; Phalen et al. 1985), we assigned a body mass of 4 kg and a body height of 52 cm to this age, as given in Table 2. The corresponding values for the adult are also shown in this table. In order to prevent turbulence at the exit from the model, the distal end had a gently tapered (15° taper) exit region that doubled the total length of the hollow model.

The hollow models were made by constructing solid plastic models of regions 1, 2, and 3, potting the models in RTV 700 silicone rubber molding compound,* removing the solid original models, filling the molds with a melted carnauba/paraffin mixture (about one-third carnauba wax) to make wax replicas, potting these wax replicas in silicone rubber, and melting and pouring out the wax. The four hollow models were sealed inside plastic cylinders, and connectors were added to allow for entry and exit of the aerosol-containing air. It was assumed that some variation in dimensions of the paired casts might occur, especially at the narrowest region, the nasal valve.

* General Electric Co., Waterford, NY.

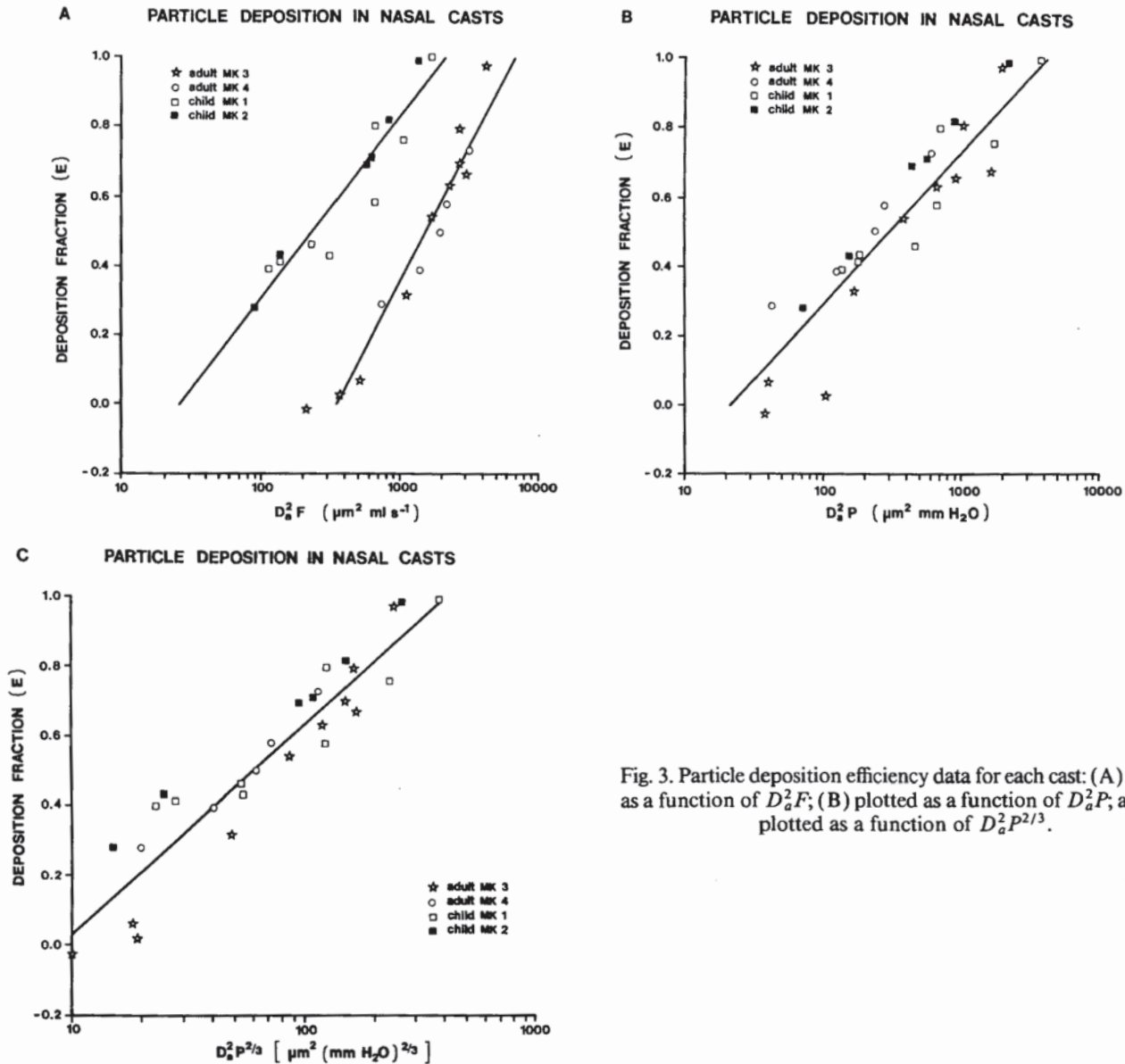


Fig. 3. Particle deposition efficiency data for each cast: (A) plotted as a function of $D_a^2 F$; (B) plotted as a function of $D_a^2 P$; and (C) plotted as a function of $D_a^2 P^{2/3}$.

Laboratory measurements

Pressure drop was measured to ± 2 mm with a water manometer, and the air flow for each data point was measured at least twice with a 7.5-L bell-type, water-seal spirometer. Pressure-volume curves were obtained before the aerosol deposition measurements were made. The aerosol deposition efficiency was determined by alternately taking particle counts with the cast in place, then bypassing it. Two or three such pairs of particle counts were used for each deposition determination.

Aerosol particles were counted with a Climet Model 208 optical particle counter† operated in a setting of either greater than 0.5 or greater than 1 μm . Before each laboratory study, we verified that no significant numbers of particles were generated that were outside the desired size range.

Aerosols were nebulized with a Lovelace-type nebulizer (Mercer et al. 1968) loaded with monodisperse polystyrene latex spheres‡ of either 0.8 or 2.02 μm nominal diameter (density = 1.05 g cm^{-3}). The particles were diluted in water 1:150 to limit agglomeration after drying the nebulizer droplets. Observation of a collected sample on a glass slide with an optical microscope indicated that 80% or more of the particles were singlets. Aerodynamic diameters were calculated by multiplying the particle diameter by the square root of the density.

RESULTS AND CONCLUSIONS

The pressure-flow curves for the four single-channel hollow nasal models are shown in Fig. 2. Considering the substantial variability in the measurements on people, the

† Climet Instruments Co., Redlands, CA.

‡ Duke Standards, Palo Alto, CA.

Table 3. Regression fit parameters for hollow model deposition data where SE is standard error of y estimate.

Model Type (r^2 , SE)	Figure	Intercept	Slope
$\log D_a^2 F$ (0.34, 0.23)	4A	-0.016	0.34
$\log D_a^2 P$ (0.88, 0.097)	4B	-0.67	0.48
$\log D_a^2 P^{2/3}$ (0.89, 0.095)	4C	-0.57	0.60

casts appeared to be acceptable for subsequent deposition measurements.

Linear regressions of deposition efficiency vs. $\log(D_a^2 F)$, $\log(D_a^2 P)$ and $\log(D_a^2 P^{2/3})$ were performed. The curve-fitting data indicated that the independent variables $D_a^2 P$ and $D_a^2 P^{2/3}$, when log transformed gave good predictions of the observed deposition fraction E_N (Fig. 3 and Table 3). For the combined data from all casts, the correlation coefficients (r^2) for these fits were about 0.9, and the standard errors of the y (E_N) estimates were about 10%. This standard error is a measure of the average difference between the observations and the fitted line, and thus is an appropriate measure of goodness of fit of the equation under consideration. On the other hand, although the relationship based on $\log(D_a^2 F)$ fits individual cast data adequately, it does not provide a good fit to the combined data from all four casts.

From these experiments we concluded that the hollow models were reasonable surrogates for the nasal cavities of adults and infants and that the $\log(D_a^2 P)$ type relationships gave acceptable fits to the combined large- and small-cast data.

DISCUSSION

Because idealized nasal models were used, the results should be considered suggestive, rather than definitive, for predicting the nasal deposition efficiencies for the infant. As the turbinate and pharyngeal regions were not

included, the predicted E_N values may underestimate those of people. The curve in Fig. 2B does lie below the curve of Hounam et al. (1971). On the other hand, the models did appear to give reasonable pressure-flow and aerosol collection values for adults and therefore are likely to be applicable to the 1-mo-old infant as well.

It appears that, for the aerosol sizes and flow rates used, at an activity level near resting the infant and adult have similar nasal aerosol collection efficiencies. During mild exercise, however, our data suggest that the infant's nose may be more efficient in collecting particles than is the adult's nose. When deposition doses are calculated by multiplying collection efficiencies by minute ventilations and dividing by body masses, predicted infant doses will be significantly greater than those of the adult. It is interesting to note that, using a purely theoretical scaling approach, Xu and Yu (1986) also predicted, for the case of mouth-breathing, that young children would have higher deposition of particles in the head region than would adults for particle diameters between 2 and 10 μm .

We hope that the predictions will be verified eventually in studies with young human subjects. Until that time, the possible increase in nasal doses received by young children should be given consideration in estimating risks from inhaled aerosols. The relationship described by Hounam et al. (1971), shown in eqn (2), or the relationship described by Heyder and Rudolf (1977) could be used to estimate particle deposition in the nasal cavities of small individuals, provided that the pressure drop is known. Both very small, diffusion-dominated particles and very large particles ($>10 \mu\text{m}$ in aerodynamic diameter) may not be well described by a pressure-drop-type relationship, however.

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QUESTIONS AND COMMENTS

(Paper presented by R. F. Phalen, Community and Environmental Medicine, University of California, Irvine, CA.)

Q: F. J. Miller, U.S. EPA, Research Triangle Park, NC
Would you expect nasal pressure drop to still be an important parameter for nasal deposition at higher minute ventilations, especially when oronasal breathing occurs?

Phalen: Yes, but one would have to take into account the decreased airflow (and thus decreased pressure drop) through the nose during oronasal breathing.