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TRACHEOBRONCHIAL DEPOSITION PREDICTIONS FOR INFANTS, CHILDREN AND ADOLESCENTS

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Abstract—It is believed that the regional deposition patterns for inhaled particles can be mathematically predicted for simple cases considering three mechanisms (impaction, sedimentation, and diffusion) along with anatomical and air flow information. We have performed calculations of tracheobronchial (TB) particle deposition for a human body mass range of 3.3 Kg to 70 Kg (birth to adulthood) over a range of ventilations. These calculations predict for most particle diameters between 0.01 and 10.0 μm and most states of physical activity, that smaller individuals will exhibit greater TB deposition efficiencies than larger individuals. When one considers the greater ventilation per Kg body mass for smaller people, it appears that the initial deposited TB dose for young children may often be well above that for the adult.

INTRODUCTION

ALTHOUGH SEVERAL investigators have provided quantitative descriptions of the dimensions of adult human airways few have described their growth. Morphometric models for the adult tracheobronchial airways have been published by WEIBEL (1963), HORSFIELD *et al.*, (1971) and by YEH and SCHUM (1980). Limited information on bronchial dimensions in children has been published, but it is not complete enough to establish growth patterns for the TB tree (ENGEL, 1913; SCAMMON 1923).

The full number of bronchial airways is usually assumed to be present at birth and alveolarization of bronchioles continues postnatally in a proximal direction. Bronchial airway growth generally parallels changes in stature, but there is confusion regarding details (THURLBECK, 1977). The reasons for the lack of agreement on airway growth patterns include differences in techniques used by various investigators, significant variability among subjects, airway sampling problems and the lack of normal tissue. Despite the lack of quantitative information, the need to estimate environmental risks led to the use of theoretically based tracheobronchial growth curves by HOFMANN (1982). Because HOFMANN's dose calculations for particles inhaled by children did vary significantly as a function of age, the importance of accurately defining tracheobronchial growth is underscored.

YEH *et al.* (1976) described the factors influencing inhaled particle deposition and the anatomical input needed for modelling. The phenomena of diffusion, inertial impaction and gravitational sedimentation were assumed to be adequate for describing the relevant particle behaviour. YEH's calculations are in good agreement with particle deposition data for healthy humans. The anatomical information required includes airway tube lengths, diameters, branching angles, and inclinations to gravity. The

techniques for obtaining this information from replica casts of airways involve establishing an idealized model of an airway branch, defining the appropriate dimensions on this branch, and performing measurements on the casts.

METHODS

Twenty tracheobronchial airway casts made by J. MORTENSEN were used for morphometric measurements. The subjects, aged 11 days to 21 years, had no recognizable chronic lung disease, and died of causes not believed to alter the tracheobronchial dimensions. Data taken at the time of casting included body mass and length, and chest circumference. Dow Corning RTV 310 Silastic was placed into an injector which displaced saline as it slowly filled the lung *in situ* until the material would not flow (about 1 hour of filling). The silicone rubber was cured *in situ*, the lungs were removed and the tissue digested. A trimmed cast ready for measurement is shown in Fig. 1. Measurements were made by the authors.

Each airway measured was identified by a unique binary number (PHALEN, *et al.*, 1978). Over 90% of the measurements on the casts were independently measured by two morphometrists, a parity test performed, and any tubes for which there were major disagreements were measured again. For each of the lung casts, every airway down to the 3rd generation was measured (trachea = generation 0). In addition, a terminal bronchiole in the right upper lobe of each cast was marked with a thread tie and the pathway to the bronchiole measured. The pathway was typically 11 divisions. For each measured airway, length, diameter, and branching angle were recorded. Measurements were also made on several terminal bronchioles and the two divisions just proximal to them. In total, about 25 individual airways were measured in each cast.

Airway lengths and diameters were found to be linearly correlated with body length. Linear regression equations for each generation were used as multipliers for YEH and SCHUM's (1980) adult tracheobronchial dimensions in order to obtain age-specific airway dimensions as a function of body length (assumed equal to height). Although our measurements could be used to define adult dimensions, our data were focused on an upper lobe while YEH and SCHUM's data were on the whole lung. Thus our growth equations were scaled to yield YEH and SCHUM's adult tracheobronchial model when a body height of 175 cm is used.

The body-size scaled tracheobronchial data were used as input into the particle deposition equations of YEH and SCHUM (1980). Values for airflow rates for humans of various ages, both at rest and during maximal exercise, were taken from a compilation of published values (ALTMAN and DITTMER, 1971). The particle deposition calculations were performed using 3 ventilation states corresponding to low activity (10 litres/min for the adult), light exertion (20 litres/min for the adult), and heavy exertion (60 litres/min for the adult). Ventilation was scaled downward as linear functions of body mass. The air flow rates for selected ages, along with body height and mass are given in Table 1.

The particle diameters used for deposition calculations ranged from 0.01 to 10.0 micrometers; unit density and spherical shape were assumed.

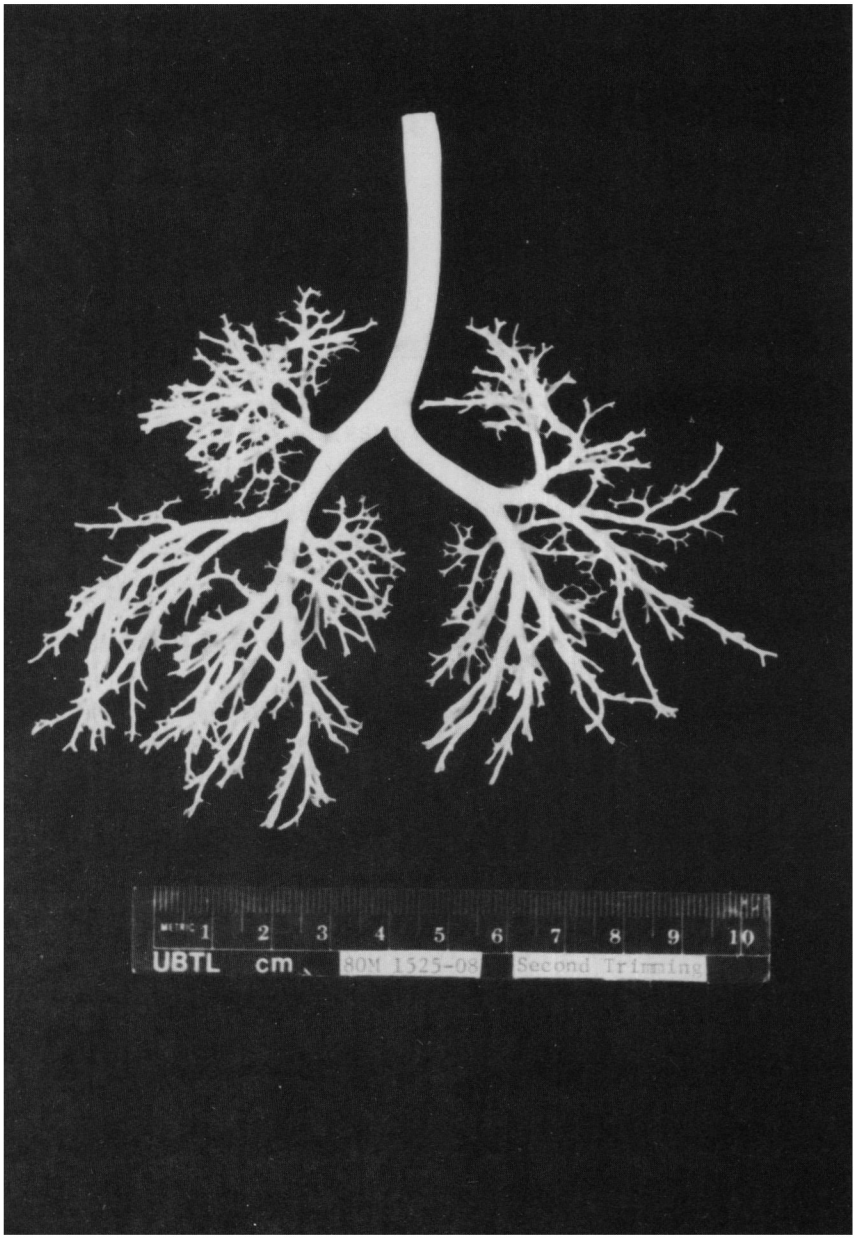


FIG. 1. Trimmed airway cast made in situ in a 4-month-old male. The cast was made by Dr. Mortensen, UBTL, Salt Lake City, UT, U.S.A.

TABLE 1. BODY MASS, HEIGHT, AND CALCULATED MINUTE VENTILATION AT 3 LEVELS OF ACTIVITY FOR SELECTED AGES. VALUES FOR MASS AND HEIGHT ARE FROM GRAPHICAL FITS OF PUBLISHED DATA (ALTMAN AND DITTMER, 1971; 1972)

Age (years)	Mass (kg)	Height (cm)	Calculated Minute Ventilation (l/m) Low Activity	Light Exertion	Heavy Exertion
0	3.3	50	1.52	3.00	8.92
2	13.0	88	2.75	5.48	16.4
4	16.4	104	3.18	6.34	19.0
6	22.0	115	3.89	7.77	23.2
8	27.0	127	4.53	9.05	27.1
10	34.0	138	5.42	10.8	32.4
12	43.0	150	6.56	13.1	39.3
14	54.0	162	7.96	15.9	47.8
16	63.0	170	9.10	18.2	54.6
18	70.0	175	10.0	20.0	60.0

RESULTS

A. *Tracheobronchial Morphology*

Tracheal dimensions vs. body height were fitted by linear regression (corr = 0.97). The derived regression equations can be used to compute tracheal length L_0, or diameter D_0 for any body height H. Adult values are computed using 175 cm for H.

$$L_0(\text{mm}) = 0.51\ H(\text{cm}) + 10.8 \qquad D_0(\text{mm}) = 0.10\ H(\text{cm}) + 2.06$$

Although bronchi are distinguished by cartilage in their walls, airways in generations 1 to 8 were called bronchi as a working definition. When bronchial dimensions for each generation were plotted vs. body height, they demonstrated linear relationships with that parameter. Least squares fits yielded the following growth equations:

	SE;r (mm)		SE;r (mm)
$L_1 = 0.18\ H + 12.1$	3.0; .95	$D_1 = .069\ H + 3.53$	.84; .97
$L_2 = 0.07\ H + 5.55$	1.7; .88	$D_2 = .046\ H + 3.25$	.92; .92
$L_3 = 0.053\ H + 0.38$	1.0; .93	$D_3 = .033\ H + 2.50$	.37; .98
$L_4 = 0.035\ H + 3.83$	1.6; .75	$D_4 = .017\ H + 3.54$	.57; .83
$L_5 = 0.033\ H + 4.33$	.91; .88	$D_5 = .014\ H + 3.29$	.43; .85
$L_6 = 0.022\ H + 5.05$	1.1; .71	$D_6 = .012\ H + 2.25$	.51; .78
$L_7 = 0.013\ H + 7.35$	.74; .66	$D_7 = .007\ H + 2.51$	.30; .78
$L_8 = 0.008\ H + 7.27$	.86; .42	$D_8 = .004\ H + 2.52$	.17; .78

The standard error (SE) is the mean standard error around the best-fit line; r is the correlation coefficient.

Growth equation constants for bronchioles (generation 9 to 15) were interpolated using a straight line (on a semi-log plot) connecting the measured generations. The resulting equations for L and D (mm) vs H (cm) are shown below.

$$L_9 = .009\,H + 5.10, \qquad D_9 = .003\ \ H + 2.05$$
$$L_{10} = .007\,H + 4.34, \qquad D_{10} = .002\ \ H + 1.63$$
$$L_{11} = .006\,H + 3.41, \qquad D_{11} = .001\ \ H + 1.39$$
$$L_{12} = .005\,H + 2.72, \qquad D_{12} = .0009\,H + 1.02$$
$$L_{13} = .004\,H + 2.05, \qquad D_{13} = .0006\,H + 0.815$$
$$L_{14} = .003\,H + 1.60, \qquad D_{14} = .0004\,H + 0.660$$
$$L_{15} = .002\,H + 1.33 \qquad D_{15} = .0002\,H + 0.565$$

Although YEH and SCHUM (1980) have used 60° for gravity angles of distal airways (on the assumption of random orientation in 3 dimensions), measured angles often approach 45°. Thus 45° was assumed as the gravity angle of airways beyond generation 13.

B. *Computed Particle Deposition*

Particle deposition efficiencies, expressed as a fraction of those entering the trachea, were calculated as functions of age, particle diameter, and ventilatory state. Fig. 2 shows the computed deposition efficiencies for particle diameters from 0.01 to 10.0 micrometers for 3 representative ages and 3 states of ventilation. The minimum at about 0.5 micrometers is due to the fact that for such size particles, sedimentation, impaction, and diffusion are all inefficient deposition mechanisms. In general, increasing age is associated with decreasing particle deposition efficiency. This is not necessarily the case at high flow rates and large particle diameters as seen in Fig. 2c. All calculations were for inhalation only.

DISCUSSION

In general, at a given age our model airways are usually larger than those formerly reported. It is noted that our subjects tended to be larger in stature at a given age than children were in the past (ALTMAN and DITTMER, 1972). Thus, age is not as useful as height (or sitting height) for tracheobronchial growth curves.

For adults, the computed particle deposition efficiencies are comparable to laboratory measurements of tracheobronchial deposition in human subjects (summarized by LIPPMANN *et al.*, 1971). Our computations are also in basic agreement with other model calculations (TASK GROUP ON LUNG DYNAMICS, 1966; CHAN and LIPPMANN, 1980).

Comparable predictions for children for a wide range of particle sizes have not been published previously. HOFMANN (1982) published computed deposition probabilities (deposition per cm^2 of surface area) for submicron particles (0.08 μm) for tracheobronchial airways as a function of age. His computations generally predicted that deposition efficiency was highest in the newborn, decreased with increasing age to 21 years, and remained essentially constant for greater ages. Our calculations are in agreement with this prediction.

The model predictions indicate that smaller individuals will generally have greater particle deposition efficiencies within the tracheobronchial tree (as a fraction of particles entering the trachea) than larger individuals at a given activity state. The predictions apply most directly to mouth breathing individuals. Also, because minute ventilation at a given state of activity is approximately linearly related to body mass

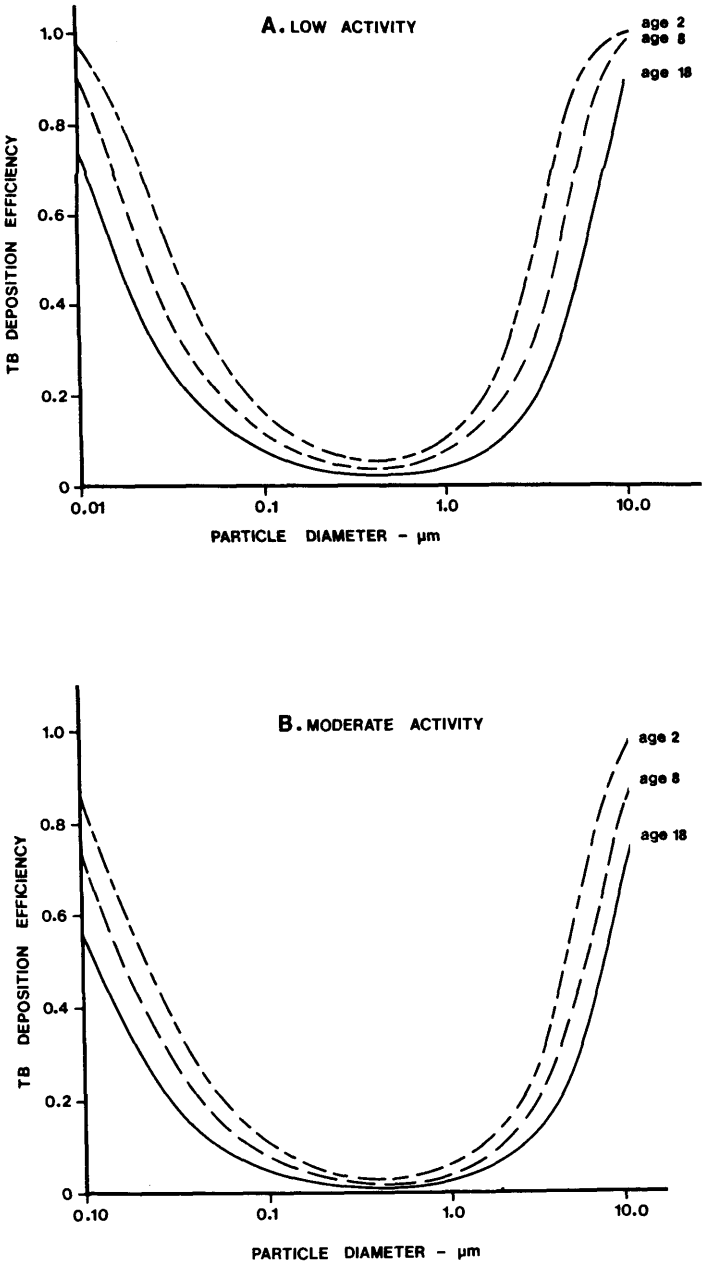
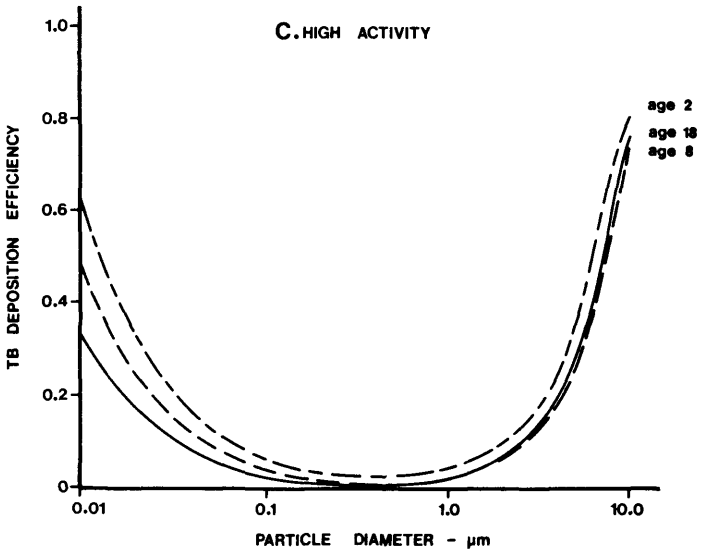


FIG. 2. Computed particle deposition efficiencies vs particle size for ages 2, 8 and 18 years at 3 ventilatory states; A) Low activity, B) Light exertion, and C) Heavy exertion.



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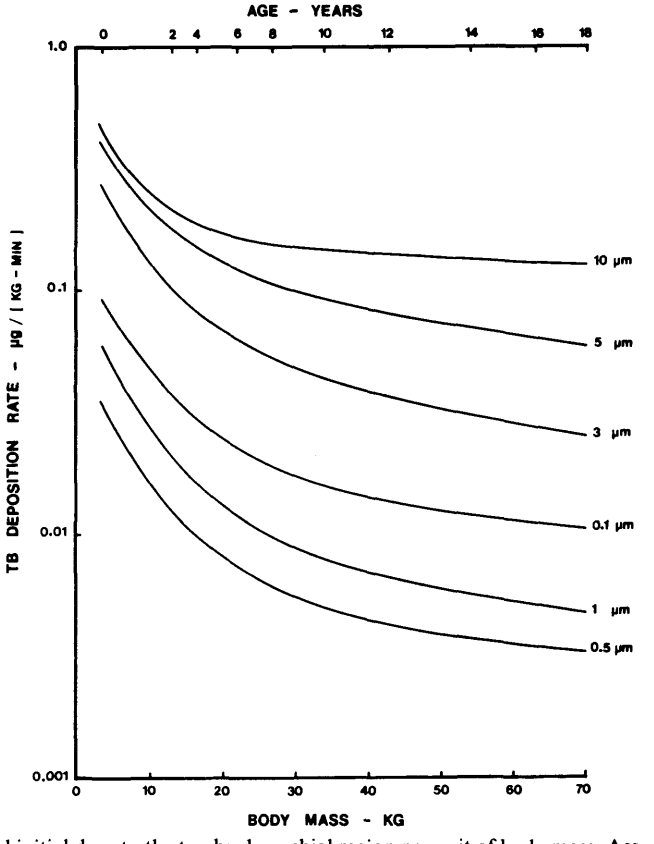

FIG. 3. Predicted initial dose to the tracheobronchial region per unit of body mass. Assumptions include equivalent upper airway deposition for all ages, inhalation of particles at 1 mg/m^3 concentration in air, and low activity ventilation ($\dot{V}_m$ 10 L/min for the adult, scaled downward for younger people).

plus an additional constant, under similar levels of activity the smaller person inhales more air per unit body mass. Therefore, higher initial tracheobronchial doses on a per unit body mass basis are predicted for smaller people. This conclusion was also arrived at qualitatively by HISLOP, *et al.* (1972). Figure 3 shows an example of this age-related dose effect for several particle sizes at low activity ventilation (10 L/min in the adult). If all other factors were identical between a young person and an adult, the young person might be at greater risk from many types of airborne particles. These other factors include deposition efficiency in the nasal, oral and pharyngeal airways and at the larynx; speed and efficiency of clearance of deposited material; efficiency of defences; and tissue sensitivity. Particle deposition efficiencies in the airways of the head as a function of body size are at present unknown. Because particle deposition in head airways can protect the remainder of the respiratory tract, research in this area deserves high priority. Although it is probable that children spend more time exercising than adults and thus may receive even greater doses than we have predicted, quantitative data are lacking so this factor was not included in the dose calculations.

Our data can be used to shed new light on the ways in which human airways grow. All generations of airways appear to grow in length and in diameter in proportion to body height, but the slope is greater for larger airways so larger airways grow proportionately more rapidly than smaller ones.

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REFERENCES

ALTMAN, P.L. and DITTMER, D.S. (editors) (1971) *Respiration and Circulation*, Federation of American Societies for Experimental Biology. Bethesda, MD, pp. 40–41, and 78–84.

ALTMAN, P.L. and DITTMER, D.S. (editors) (1972) *Biology Data Book*, 2nd Edition, Volume 1. Federation of American Societies for Experimental Biology, Bethesda, MD, pp. 195–201.

CHAN, T.L. and LIPPMANN, M. (1980) Experimental measurements and empirical modelling of the regional deposition of inhaled particles in humans. *Am. Ind. Hyg. Assoc. J.* **41**, 399–409.

ENGEL, S. (1913) Form, Lage und Lageveranderungen des Bronchialbaumes im Kindesalter. *Arch. f. Kinderheilk* **60**, 267–288.

HISLOP, A., MUIR, D.C.F., JACOBSEN, M., SIMON, G. and REID, L. (1972) Postnatal growth and function of the pre-acinar airways. *Thorax* **27**, 265–274.

HOFMANN, W. (1982) Dose calculations for the respiratory tract from inhaled natural radioactive nuclides as a function of age. II. *Health Phys.* **43**, 31–44.

HORSFIELD, K., DART, G., OLSON, D.E., FILLEY, G.F. and CUMMING, G. (1971) Models of the human bronchial tree. *J. Appl. Physiol.* **31**, 207–217.

LIPPMANN, M., ALBERT, R.E. and PETERSON, H.T., Jr. (1971) The regional deposition of inhaled aerosols in man. *Inhaled Particles III.* W.H. Walton (editor), Unwin Brothers Limited, Old Working, Surrey, England, pp. 105–122.

PHALEN, R.F., YEH, H.C., SCHUM, G.M. and RAABE, O.G. (1978) Application of an idealized model to morphometry of the mammalian tracheobronchial tree. *Anat. Rec.* **190**, 167–176.

SCAMMON, R.E. (1923) The Trachea. In *Pediatrics*, L.A. Abt. (editor), W.B. Saunders, Philadelphia, pp. 344–348.

TASK GROUP ON LUNG DYNAMICS. (1966) Deposition and retention models for internal dosimetry of the human respiratory tract. *Health Physics* **12**, 173–207.

THURLBECK, W.M. (1977) Structure of the lungs, Chapter 1 in *Respiratory Physiology II*, Vol. 14. Edited by J.G. Widdicombe, University Park Press, Baltimore, MD, pp. 1–34.

WEIBEL, E.R. (1963) *Morphometry of the Human Lung*. Springer-Verlag, Berlin.

YEH, H.C., PHALEN, R.F. and RAABE, O.G. (1976) Factors in influencing the deposition of inhaled particles. *Environ. Health Perspect.* **15**, 147–156.

YEH, H.G. and SCHUM, G.M. (1980) Models of human lung airways and their application to inhaled particle deposition. *Bull. Math. Biol.* **42**, 461–480.

DISCUSSION

J. HEYDER: It is not considered that particle deposition takes place for those particles which are not deposited in the lung periphery and return to the tracheo-bronchial.

R. F. PHALEN: That is correct. Our model is relatively simple in that it is an inspiratory one only.

J. D. BRAIN: Your predictions are very interesting, and potentially important in estimating risk in children. My major concern with your estimates is that they begin with the trachea; the upper airways are ignored. We are faced with the frightening spectre of headless infants and children.

What is known about the geometry and collection efficiency of the nose, mouth and larynx as a function of age and body size?

What is known about transitions between mouth and nose breathing in children?

Finally, are there any experimental data on collection efficiency and particle distribution in children, which can be used to test your predictions?

R. F. PHALEN: We began with the tracheobronchial model because we had good anatomical information on the growth of that region. Ignoring the upper airways means that the predictions are probably most applicable to oral breathing. The nose which has unknown dimensions during growth could change the tracheobronchial doses considerably. Our early efforts on modelling nasal deposition indicate that the results will be very sensitive to the precise anatomy. Using a simple scaled pipe model for the nose we predict that children's noses have greater collection efficiencies than adults' noses. On the other hand, using published nasal pressure drop data for children and putting them into Houman's equation it appears that, under some circumstances, the child's nose would be less efficient than the adult's nose. At present, there is great uncertainty regarding the nose.

The answer to the remainder of your questions is that the data do not exist.

M. T. R. REISNER: If particle deposition in the tracheobronchial tract of children and young people is greater than in that of adolescents, will you agree with me that smaller airways serve as a better elutriator (pre-separator) for the respirable dust fraction, which then has less chance to penetrate into the alveolar range, and be deposited there?

Epidemiological studies in West German coal-mines have shown that the younger the miners have been at start of work underground (age less than 22 years), the less frequently they have contracted simple pneumoconiosis with the same dust exposure.

R. F. PHALEN: Correct. The higher tracheobronchial deposition would produce a sparing effect on the deep lung. For appropriate risk estimates for children one should consider separately materials that are hazardous when deposited in the tracheobronchial region and materials that are hazardous when deposited in the deep lung. Asthma, and perhaps other tracheobronchial diseases, are common in children.

C. P. YU: We have made similar deposition calculations for humans at different ages. We found total deposition in the lung is maximum at 2 years old and that deposition in the head region decreases as age increases.

R. F. PHALEN: Our preliminary work on the nose does not show such a maximum at age 2 years. The greater total deposition for smaller people is consistent with our work and the recent work of Thomas and Healy of Los Alamos. They have a paper which is to be presented later in this meeting. Our tracheobronchial conclusions are similar to those of Hofmann's, who considered very small particles and calculated dose in terms of mass deposited per square centimetre of airway surface.

J. N. PRITCHARD: I intend to demonstrate later in this meeting significant differences in tracheobronchial deposition between men and women, which I believe are attributable to differences in airway diameter. In view of this, were the casts measured from male or female lungs?

R. F. PHALEN: We measured male and female lungs and found no significant difference in airway dimensions when they were matched for body height.

M. T. R. REISNER: We have heard a lot of sophisticated results on the regional deposition of inhaled particles in the human respiratory tract, but what are the consequences to be drawn from these results? For instance, we are still measuring respirable dust for pneumoconiosis reasons, with samplers according to recommendations which are more than 25 years old, or have been recently made by AEC, ACGIH, ISO etc., but do not consider our present knowledge on alveolar deposition. Why?

J. HEYDER: A standard is now available for those dust samplers; one is from the ISO, and there is a more recent one from the Governmentally-appointed American Industrial Hygienists, and we have representatives from those organisations in the audience. Would anyone like to comment on Dr. REISNER's question?

R. F. PHALEN: (Chairman of the ACGIH Air Sampling Procedures Committee) there will be a paper tomorrow afternoon on the implications of particle deposition in various anatomical airway regions, to particle size sampling for hazard evaluation. Also the ACGIH has a report of our committee available for purchase from that organisation.