Postnatal growth and function of the pre-acinar airways

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The postnatal growth of the pre-acinar or conducting airways of the lung was examined by measuring the dimensions of selected axial pathways in lungs at different stages of development. The material included both formalin-fixed specimens and bronchograms. A method of comparing the relative sizes of each part of the pathways was developed which allowed for differences between the number of branches or generations measured in each specimen. The results indicate that the pre-acinar airways of the infant may be regarded as a miniature version of those in the adult and that this relationship persists during postnatal growth. Each individual branch grows in a symmetrical fashion both in length and in diameter and bears a constant relation to the whole. The physiological function of the conducting airways during growth was investigated using published data on the breathing pattern of infants. Particular attention was given to the conditions of airflow, to the warming and humidification of inhaled air, and to the filtration of airborne dust.

The airways, alveoli, and blood vessels each follow a different pattern of growth. The pre-acinar or conducting airways are virtually complete at birth and further division of these airways does not occur (Bucher and Reid, 1961). However, alveoli arise from some of the terminal airways after birth and it has been shown that they develop by a centripetal process from the end of an airway and that this may affect up to three generations (Boyden and Tompsett, 1965). On the other hand, the respiratory region continues to grow distally after birth—alveoli increase in number until the age of 8 and in size and complexity until adulthood (Dunnill, 1962; Davies and Reid, 1970).

For many years it was thought that the pre-acinar airways also increased in number after birth (Broman, 1923). Much of the confusion arose because comparison had been made between different segments of the lung or between axial and lateral pathways. It was shown subsequently that comparison between the various segments was most effectively made between axial pathways, that is, those passing to the distal pleural surface (Hayward and Reid, 1952).

There is little information concerning the pattern of growth at different levels of the bronchial tree. Wood's metal casts of lungs at various stages of development have been used to investigate the

relative rate of growth of selected airways, e.g., the trachea, the main bronchi, and the terminal bronchioli (Engel, 1947). With increasing age, differences between the relative diameters of the main bronchi and trachea were found although these were small in comparison with the increase in linear dimensions. The size given for the diameter of the terminal bronchiolus (0.2 mm in the adult) is smaller than is generally stated and probably reflects the fact that the lungs studied were not inflated.

Detailed measurements of airways throughout the adult lung have been made and the results used for the development of models for the study of respiratory function (Weibel, 1963; Horsfield and Cumming, 1968). Since to carry out similar measurements on lungs at representative ages between birth and adulthood would be a formidable task, our attention is concentrated on selected pathways in a series of lungs to cover the growth period. The trachea, main bronchi, and segmental bronchi are easily identified and their size in different lungs can be compared precisely. In the distal airways it is more difficult because some pathways supply alveoli after a short course of only 1 cm or so with only a few side branches, while others run many centimetres and give rise to numerous side branches. From any given path-

way the side or lateral branches run a shorter course than the axial pathways—those that pass to the distal pleural surface. The axial pathways, therefore, offer a more satisfactory basis for comparison than the lateral pathways but, depending on the size of segments, even the length of the axial pathways varies. This means, for example, that in smaller segments—such as the apical segment of the lower lobes—the maximum number of generations along an axial pathway may be only 15, while in the posterior basal segment there may be as many as 25 intrasegmental branches (Hayward and Reid, 1952).

All pathways of whatever length end in a similar cluster or three to five terminal bronchioli arising approximately 2 mm apart (Reid, 1958; Reid and Simon, 1958). It is for this reason that terminal bronchioli are similar throughout the lung although the preterminal airways may vary widely. All pathways, no matter how long, can be regarded as starting as a segmental bronchus and ending with a terminal bronchiolus.

It is the purpose of this paper to examine the growth pattern of each generation along selected axial pathways from different segments of lungs at various stages of growth. Additional information concerning the pattern of breathing during childhood enabled some aspects of the physiological function of the pre-ancinar airways in infancy to be examined.

MATERIAL AND METHODS

The material studied and the method used are listed in Table I.

TABLE I
MATERIAL EXAMINED

Age	Specimen	Pathway Examined	Path No.
Newborn	Formalin-fixed lung	Post Basal RLL	1
18 mth	" " "	Post Basal LLL	2A
		Lat Basal LLL	2B
19 mth	Bronchogram	Post Basal LLL	3
22 mth	Formalin-fixed lung	Post Basal RLL	4
4 yr	" " "	Post Basal LLL	5A
		Lat Basal LLL	5B
5 yr	Bronchogram	Post Basal RLL	6
8 yr	"	Post Basal RLL	7
11 yr	"	Post Basal RLL	8
Adult	"	Post Basal RLL	9A
		Post Basal LLL	9B
		Post Basal RLL	10A
		Axial RML	10B
		Post Basal RLL	11
		Post Basal RLL	12A
		Axial RUL	12B
		Axial RUL	12C

Measurement of the dimensions of an axial pathway and its side branches was made in three ways:

- (1) examination of bronchograms from four adults and from four children, the latter aged 19 months, 5, 8, and 11 years;
- (2) dissection of various axial pathways in formalin-fixed lungs from three children aged 18 months, 22 months, and 4 years; and
- (3) examination of serial sections of the posterior basal segment of a newborn lung.

(1) **BRONCHOGRAMS** In a series of normal bronchograms from children and adults a suitable axial pathway was traced (by A.H. and G.S.) towards the diaphragm in either the posterior or anterior segment. In addition, in the adult, an axial pathway to the right middle and upper lobe was studied (Table I).

The bronchograms were examined by transmitted light, and a dissecting microscope was used to measure the peripheral airways. Along the selected pathway, the diameter midway between branches was taken and the distance between carinae was measured, from which the total length of the pathway could be estimated. When possible these measurements started with the trachea. The diameter of each side branch was also recorded. Only those pathways in which a millimetre pattern could be identified on the bronchograms were traced (Reid and Simon, 1958). It would be unlikely that all side branches are filled at bronchography and this was confirmed by the lower numbers that were counted by this method than by the other two methods used. However, these errors in the estimation of the numbers of generations in a pathway did not affect the accuracy of the measurement of its total length. Measurements on the bronchogram had the advantage that the lung was at its normal volume. Because the bronchogram films are taken with the patient close to the cassette, any distortion would be slight and was ignored.

(2) **DISSECTION** Starting from the main bronchus of an axial pathway, the airway to the posterior basal segment was traced by naked-eye dissection with the help of a magnifying glass where necessary.

In all lung specimens examined the pulmonary artery had been injected with Micropaque barium suspension before inflation and fixation with formalin. Both these procedures helped the lung to maintain its form. A transparent scale was used to measure the diameter of the airway and also the distance between successive carinae. It was possible by this method to include every airway, certainly to within the region of the millimetre pattern. Even here, the small airways could be identified, but particularly in the smallest lungs, the ultimate one or two airways were probably missed. It seems that full inflation gives lung volumes similar to those found in life (Heard, 1960). Using 10% formol saline as a fixative we found that the volume of any inflated lung falls by approximately one-third during fixation. Linear measurements were therefore multiplied by 1.5 to correct for this shrinkage ($1 \cdot 5^3 = 1 \cdot 5$).

(3) **SERIAL SECTIONS** Microscopic serial sections of a newborn right lung were used to trace and measure the length of each generation along an axial pathway

to the posterior basal segment starting with the lobar bronchus. The main bronchus was measured from the specimen. Since we found that the effect of processing reduces alveolus but not airway size, no correction for processing was used in this study. During reconstruction of the airway branching pattern, measurements were made of the diameters of each of the side branches as well as of the axial airway midway between its divisions.

RESULTS

COMPARISON OF RESULTS FROM BRONCHOGRAPHY AND DISSECTION Measurements by both methods were compared from two cases of similar age; in the 19-month-old child they were made on a bronchogram, in the 18-month-old child by lung dissection. The measurements for all generations studied in each case are plotted in Fig. 1 and it can be seen that the results from the two methods are similar.

FIG. 1. Comparison of measurements of airway diameter along one pathway obtained by dissection (●) in a child aged 18 months and from a bronchogram (○) in a child aged 19 months.

VARIATION IN LENGTH AND DIAMETER OF AIRWAY GENERATIONS The total length of an axial pathway increases steadily with age although the distance between successive branches of an airway varies widely (Hayward and Reid, 1952). This variability is particularly obvious in its more proximal part, but it might be expected that a more consistent pattern would be apparent in the distal airways where the pattern of branching seems more regular. However, even for the terminal bronchiolus (Fig. 2) for a given age, the lengths varied so widely at any age that no pattern of growth emerged. By contrast, the diameter of the terminal bronchiolus (Fig. 3) is seen to increase steadily

FIG. 2. Length of terminal bronchiole at different ages (each point represents one measurement).

FIG. 3. Diameter of terminal bronchiole at different ages (each point represents one measurement).

with age but, as with most other aspects of lung growth, the increase is greatest in the early years.

COMPARISON OF AIRWAY DIMENSIONS AT DIFFERENT AGES: THE PATTERN OF GROWTH The problem of making valid comparison between different lungs is illustrated by two examples plotted in Fig. 4; one refers to measurements from the serial sections of the newborn lung, the other from an adult bronchogram. In dissections of the infant lung 25 generations were measured, whereas in the adult bronchogram only 18 airways were identified along the corresponding pathway although the terminal bronchiolus was reached in each case. If the diameter of each airway is plotted against its respective generation as counted, the terminal bronchiolus in the adult is compared with a much more proximal generation in the child. As a result it is not possible to draw conclusions about the growth of different regions of the pathway from these curves. However, the difficulty is resolved if each of these two pathways is taken to represent 100 units of length and the diameter of the airway is plotted against its position expressed as a per-

FIG. 4. Diameter of each generation along a corresponding axial pathway in an adult and in the newborn lung. Generation $\circ$ represents the trachea.

centage of the total path length from the bifurcation of the trachea to the end of the terminal bronchiolus (see Fig. 5). The extent to which the two

FIG. 5. Diameter of the airway at different percentage points along the two pathways shown in Fig. 4. The pathway begins at the bifurcation of the trachea, and the distal end of the terminal bronchiolus corresponds to the 100% point.

curves have the same slope and shape is the measure of the symmetry of growth of each

region of each part of the bronchial tree, in both length and diameter. The measurements of each pathway were analysed in detail in this way to establish the nature of the growth pattern.

The details of the statistical analysis are shown in Appendix A. It was concluded from the analysis that the average calibre of the pre-acinar airways at various percentage distances along their length could be described by an empirical mathematical expression. The curves obtained by application of the expression to measurements of individual pathways from the lungs of subjects of different ages were remarkably similar in shape (Fig. 6). The

FIG. 6. Computed curves showing the diameter of the airways at different percentage points along the pathways. Each curve is based on the grouped data specified in Table II.

similarity indicates that these pathways increase in size during postnatal growth in a uniform manner. The length and diameter of each branch or generation appear to grow proportionately and to retain a constant relationship to the whole. Assuming that other pathways develop in a similar fashion, the results suggest that the pre-acinar region of the infant bronchial tree may be regarded as a miniature version of the adult pattern and that this pattern persists during postnatal growth.

PHYSIOLOGICAL IMPLICATIONS OF THE RESULTS The pre-acinar airways modify the inspired air, making it warm, moist, and relatively free of dust before it reaches the alveoli. This and other physiological functions are closely related to the form and size of the airways and to the rate of flow within them. The present study indicates that the pre-acinar airways have a similar form in the infant and in the adult. By making use of this information, together with published data on the pattern of breathing in the adult and in the infant, it was possible to analyse the physiological function of the bronchial tree during postnatal growth. This function must vary at different ages because some activity varies in proportion to the characteristic linear measurements of the body (L), others vary with the area (proportional to L^2) and yet others with the volume (proportional to L^3).

To compare function in the infant lung with that in the adult, it is necessary to know the rate of breathing and the volume of each breath relative to the volume of the pre-acinar airways. While the figures for the latter are available in the adult, they have not yet been measured in the infant, and indirect evidence must be used. Cook and his colleagues (1955) showed that the ratio between tidal volume and physiological dead space was nearly identical in the infant and the adult. In health the physiological dead space is roughly the same as the anatomical dead space, that is, the volume of the conducting or pre-acinar airways. For a similar ratio between tidal volume and the dead space to be found in the infant as well as in the adult, it seems that the tidal volume in the infant must be scaled down to the same degree as the volume of the airways.

A representative value for the tidal volume of the adult is 500 ml and that of the infant about 15 ml, giving a ratio of $500/15=33.3/1$. From the above reasoning it is suggested that the ratio between the volumes of the conducting airways is also about $33.3/1$. Because of their geometrical similarity it follows that the ratio between any corresponding linear measurements, such as the length or diameter of a particular airway, must be equal to $33.3^{1/3}/1$, i.e., $3.2/1$ and the cross-sectional area, or surface area, to $(3.2/1)^2$, i.e., $10.2/1$.

A resting adult breathes at about 12 breaths per minute, while the newborn infant has a breathing rate of about 34 per minute. The ratio between the duration (T) of each breath in the adult and in the infant is thus about $2.8/1$. As noted above, the ratio between the characteristic linear measurements (L) of the airways is about $3.2/1$. The comparison of the physiological functions of the pre-

acinar airways given below was made by using these ratios. The viscosity and density of the air were assumed to be constant, the only variables being L and T. Each was assigned a nominal value of unity in the infant, the corresponding values in the adult being 3.2 and 2.8. The basic data are shown in Table II and the derived information in Table III.

TABLE II

RELATION BETWEEN SOME MEASUREMENTS TYPICAL OF THE INFANT AND OF THE ADULT (FROM COOK *et al.* (1955))

	Adult	Infant	Adult/Infant Ratio
Body weight (kg)	70	2.5	28/1
Oxygen consumption (ml min^{-1})	232	17	14/1
Tidal volume (ml)	500	15	33/1
Frequency of breathing (min^{-1})	12	34	1/2.8
Alveolar ventilation (ml min^{-1})	4,140	355	12/1
Dead space/total volume ratio	0.31	0.32	

TABLE III

COMPARISON BETWEEN PHYSIOLOGICAL FUNCTIONS OF THE PRE-ACINAR AIRWAYS IN THE INFANT AND IN THE ADULT

	Relationship to T and L	Interpretation
Duration of each breath (T)	—	Adult > infant (2.8/1)
Characteristic linear dimension (L)	—	Adult > infant (3.2/1)
Velocity of airflow	$\alpha L T^{-1}$	Adult = infant (1.1/1)
Transit time	αT	Adult > infant (2.8/1)
Reynolds number	$\alpha L^2 T^{-1}$	Adult > infant (3.7/1)
Pressure drop	αT^{-1}	Adult < infant (0.36/1)
Aerosol deposition (diffusion)	$\propto (T/L)^{-1}$	More effective in infant
Aerosol deposition (sedimentation)	$\propto (T/L)^{-1}$	Adult similar to infant
Aerosol deposition (impaction)	$\propto (T)^{-1}$	More effective in infant
Humidification	$\propto (T/L)^{-1}$	More effective in infant

MINUTE VENTILATION The oxygen consumption and minute ventilation of the newborn infant are, as in the adult, closely related to the body surface area or square of the linear measurements (Cook *et al.*, 1955). The minute ventilation of the adult is about 6,000 ml/min and of the infant 500 ml/min. The ratio between these two is 12/1 which is, as expected, close to $(3.2/1)^2$. On the other hand, the ratio between the volume of their pre-acinar airways (each being proportional to L^3) is of the order $(3.2/1)^3=33/1$, and it is apparent that these airways must conduct a greater volume of air each minute relative to their size in the infant than in the adult. The infant obtains the extra ventilation by breathing more rapidly and not by breathing more deeply.

VELOCITY OF AIRFLOW The velocity of airflow within any given airway is calculated by dividing the airflow measured at the mouth by the total cross-sectional area of the airways in that generation. The airflow at the mouth is obtained by dividing the tidal volume by the duration of each breath. Since the tidal volume is proportional to L^3 , the cross-sectional area of an airway to L^2 , and the duration of a breath equal to T , the velocity of airflow must be proportional to $L^3/TL^2=L/T$. Substitution gives values of 1/1 in the infant and $3.2/2.8=1.1$ in the adult. This thus implies that the ratio of airflow velocity in the adult and infant is 1.1/1 and that the velocity is virtually the same in both. The individual airways are, of course, longer in the adult and the time taken for air to pass through an airway, or transit time, is greater than in the infant.

REYNOLDS NUMBER The Reynolds number (Re) of fluid flow is a dimensionless quantity expressing the probability that turbulent flow will develop in the system.

For a round tube:

$$Re = VD\rho/\eta$$

where V is the velocity of flow (cm/sec), D is the diameter of the tube (cm), ρ is the density of the fluid, and η its coefficient of viscosity. Turbulence depends on the other factors, such as the length of the tube, but is generally likely to develop if Re exceeds about 2,300. The value of Re clearly differs in each region of the respiratory tract, depending on the size of each airway and on the rate of airflow within them. However ρ and η are constant and the effect of growth on the value of Re in a particular airway may be examined by its relationship to V and D , which in turn depend on the two variables L and T . As noted above, the velocity of airflow is proportional to L/T and the linear size of the airways to L . The numerical value of Re thus changes in proportion to L^2/T if L and T are the only variables. This applies only to the special case under discussion and cannot imply a general mathematical proportionality since Re is dimensionless while L and T are, by definition, the dimensions of the system.

Substituting for L and T gives a relative value of Re of 1/1 in the infant and $10.2/2.8=3.7$ in the adult. The value of Re in any airway of the infant is thus lower than its equivalent value in the adult. The propensity to turbulence is diminished and there is less convective mixing between tidal air and lung air.

PRESSURE DROP The pressure drop across a particular airway or across the whole bronchial tree

may be examined in a similar manner. If the airflow is assumed to be predominantly lamina, then the pressure drop across a round tube is given by $P=8\eta LV/R^4$ where η is the coefficient of viscosity of the air, L the length of the airway (cm), V the volume flow of air (cm^3/sec), and R the radius of the airway (cm). In terms of the two variables L and T , the rate of airflow (tidal volume divided by duration of each breath) is proportional to L^3/T whether measured at the mouth or, since the geometry of the model is fixed, in any given airway. Because η is constant and both L and R are linear measurements of size, the numerical value of the pressure drop is proportional to the value of $L \times L^3/T \times 1/L^4 = 1/T$. This again does not imply a general mathematical relationship but does describe the way in which the conditions of airflow change during the growth of the pre-acinar airways. It indicates that the pressure swing from the mouth to the terminal bronchiole is greater in the infant than in the adult.

DUST DEPOSITION The conducting airways may be regarded as a protective filter which prevents large particles penetrating to the alveoli. The filtration of individual particles is determined by the mechanisms of diffusion, sedimentation, and impaction. These depend on the size of the particles and of the airways and on the pattern of breathing. The different factors have been investigated by Landahl (1950) who obtained expressions whereby the regional filtration of particles in the lung can be calculated. The analysis indicates that particle deposition due to diffusion is a function of T^1/L sedimentation of T/L , and impaction of $1/T$. The relative effects of impaction and diffusion for a given size of particle are more effective in the infant but the sedimentation of particles on to the surface of the mucosa due to gravity has

FIG. 7. Percentage of inhaled particles which penetrate beyond the terminal bronchiolus. The calculations refer only to particles contained in that fraction of the tidal air which reaches the alveolar region of the lung.

about the same effect as in the adult. The overall protective efficiency of the ciliated airways was calculated. The method of doing this is described in Appendix B and the results are illustrated in Figure 7. It can be seen that the conducting airways of the infant do form a more efficient protective mechanism than in the adult but the overall change in the size distribution of particles penetrating to the alveolus is surprisingly small.

HUMIDIFICATION AND TEMPERATURE CONTROL Diffusion of water vapour and of heat from the surface of the mucosa are functions of $T^{1/2}/L$ and are more effective as this ratio increases in value. The ratio is almost twice as large in the infant as in the adult and indicates that inhaled air is warmed and humidified at a relatively higher point in the respiratory tract of the former.

DISCUSSION

The anatomical specimens and bronchograms were obtained from adults and children whose lungs were normally developed. Only a few specimens were available at any one age, however, and their absolute dimensions varied too widely to be used to estimate the rate of growth of the lung at different ages. The analysis was concerned solely with the relative growth of each generation of the pre-acinar airways. The results show that the axial pathways maintain their relative proportions during postnatal development and that each generation grows at the same rate. It seems most unlikely that the axial pathways alone have a special pattern of development and it is therefore reasonable to suppose that other airways grow in the same way. The conclusion that the non-respiratory zone of the infant lung is a miniature version of the adult pattern indicates that its development is very different from that of the alveoli which after birth multiply as well as increase in size (Dunnill, 1962).

A previous investigation into the growth of the bronchial tree (Hogg *et al.*, 1970) used measurements of the diameter, but not the length of each branch in pathways from the lungs of adults and children. Their statistical analysis made use of the linear relationship relating the log of the airway diameter to the airway generation (Weibel, 1963). They reported that growth was uniform throughout most of the bronchial tree but that the airways beyond the eighteenth generation appeared to be disproportionately narrow in young children. The discrepancy is probably because they were able to measure only one airway (Hogg, 1971).

There are limitations to our analysis of the physiological function of the infant bronchi. The tidal volume and rate of breathing vary continuously in the young child and the aerosol filtration calculations refer only to mouth breathing. Despite these reservations the results give a reasonable indication of the effects of the considerable disproportion in size between the adult and infant lungs.

The airflow is evidently less turbulent in the infant lung than in the adult, and convective mixing between the inhaled and lung air in the infant is presumably reduced in comparison with the adult. The overall pressure swing between the mouth and the terminal bronchiolus should be greater in the infant. This is consistent with the slightly greater oesophageal pressure swing found in the infant compared to that in the adult (Cook *et al.*, 1955). The resistance of the airways in children has been measured directly by a retrograde catheter technique (Hogg *et al.*, 1970). The results were expressed as the airway conductance (the inverse of resistance) divided by the predicted normal lung weight. It was found to be constant for the first 12 to 15 generations and was independent of age. However, the peripheral airways had a relatively greater resistance in young children and this supported their suggestion that the airways distal to the eighteenth generation were disproportionately narrow in young children. Our findings suggest that the airway conductance per gramme of lung tissue should be constant throughout the pre-acinar conducting region of the bronchial tree and not only in the first 12 to 15 generations. However, the resistance of the airways is proportional to the radius raised to the fourth power (Hogg *et al.*, 1970), and it is therefore unlikely that anatomical measurements can make a reliable contribution to any estimate of the resistance of the peripheral zone.

The effect of the change in lung size on the filtration of aerosols is surprisingly small. It has usually been assumed that the bronchial tree of the infant lung is a much more effective barrier to airborne dust than that of the adult because the airways are so much smaller and should trap dust that much more easily. The individual airways are certainly narrower but they are also shorter, and the time available for sedimentation or diffusion is reduced by the higher rate of breathing. From the practical point of view it appears that the alveoli of the infant are 'protected' to about the same degree as those in the adult. However, it should be remembered that, during a given interval of time, infants absorb a greater dose of any air-

borne material per kilogramme of body weight or per unit of lung volume than does the adult because of their increased ventilation. It has been claimed (Dautrebande, 1962) that the size of the particles in therapeutic aerosols is a dominant factor in their effectiveness. The present research suggests that there is no indication for using smaller particles for the treatment of infants since the distribution of inhaled material is virtually unchanged.

The more efficient humidification of the tidal air in the infant lung is noteworthy. This may be a comparative feature of real importance in preventing dying of the mucosa during prolonged crying.

Our thanks are due to Mr. W. H. Walton for his helpful comments.

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APPENDIX A

STATISTICAL ANALYSIS The anatomical data consisted of measurements of the dimensions of axial pathways to both lower lobes and to the right upper and middle lobes. The trachea was common to each and comparisons were therefore made of pathways considered to originate at the bifurcation of the trachea.

Previous data (Weibel, 1963) for the mean dimensions of the whole of the bronchial tree were also examined. They are modified so that the fifteenth generation was identified as the terminal bronchiolus (Horsfield and Cumming, 1968). Averaged pathways of this type have fewer generations than an axial pathway as measured in this study but nevertheless serve as a reference model with which experimental data may be compared. When the diameter of any airway in the average model (Weibel, 1963) was related to its percentage distance along the whole path length, a smooth curve was obtained which could be described algebraically by an equation of the form:

$$-Bx^2$$

$$D=Ae$$

where D=diameter of the airway (mm)
and x=distance of the measurement from the bifurcation of the trachea, expressed as a percentage of the total path length.

A and B are regression coefficients which were estimated, using the method of least squares, as

$$A=10.86 \text{ (mm)}$$

$$B=2.80 \times 10^{-4}$$

This simple equation described the data from Weibel (1963) remarkably well, the correlation coefficient reaching -0.998. Similar relationships were fitted, therefore, to all 18 sets of the experimental data derived from single pathways, and in each case the modulus of the correlation coefficient exceeded 0.9. Estimated values of the coefficients A and B are shown in the Appendix Table where the results are grouped according to the age of the case. Group 6 is made up of pathways other than those to the basal segment.

APPENDIX TABLE
RESULTS FROM FITTING $D = Ae^{-Bx^2}$

Group	Path Nos.	Estimates of		Correlation Coefficient	Residual Degrees of Freedom	Standardized Ratio ¹
		A (mm)	B $\times 10^{-4}$			
I	1	2.29	2.74	-0.953	23	0.30
	2A	8.78	2.85	-0.963	14	-0.66
	2B	8.60	3.32	-0.957	11	-1.69
	3	5.26	2.49	-0.962	14	1.30
II	4	7.84	2.83	-0.963	17	-0.14
	5A	6.42	2.37	-0.946	13	1.86
	5B	5.26	2.05	-0.914	12	2.89
III	6	7.58	2.53	-0.945	21	1.38
	7	9.62	3.09	-0.983	14	-1.92
IV	8	8.93	3.27	-0.984	26	-3.98
	9A	12.68	2.90	-0.981	16	-0.61
V	9B	11.62	2.90	-0.972	16	-0.52
	10A	10.39	3.02	-0.984	18	-1.64
	11	12.30	2.74	-0.956	16	0.28
	12A	15.84	2.97	-0.982	15	-1.19
VI	10B	9.61	2.99	-0.966	14	-0.83
	12B	12.18	3.34	-0.979	13	-2.74
	12C	11.68	2.83	-0.955	15	-0.16
VII		10.86	2.80	-0.998	13	—

¹ Standardized ratio = $(B_{\text{Weibel}} - B_i) / (\text{standard error of } B_i)$.

Group 1 Newborn

- II Mean age of group—19 months
- III Mean age of group—4 years 4 months
- IV Mean age of group—9 years 6 months
- V Adult lungs (pathways to lower lobes)
- VI Adult lungs (pathways to RML and RUL)
- VII Mean data from adult lung (Weibel, 1963).

The results are illustrated in Fig. 6 where curves based on the appropriate regression coefficients are shown for each of the groups. The close similarity in curvature is obvious. The intercept values correspond to the mean of the absolute size of the airways in each group.

A statistical analysis was made in order to investigate the significance of differences between the 18 estimated values of B shown in the table. It was found that residual variability about the individual regression lines was not quite significant at the 10% level ($\chi^2_{17} = 23.52$). This suggestion of some heterogeneity of variance made interpretation of results from an analysis of covariance difficult. A formal test of significance indicated that there were some real differences in the values of B for the 18 sets of data ($F_{17,174} = 2.5$).

Each of the 18 estimated values of B were, therefore, compared with the average data for the adult lung (Weibel, 1963). The ratios of these differences to the standard errors of the relevant regression coefficients are shown in the last column of the table. It is evident from these results that in most

cases the way in which the diameter of an airway decreased with respect to the percentage length of the pathway is indistinguishable from the pattern demonstrated by the mean adult data. Furthermore, no trend associated with the age of the lung is apparent, neither in the estimated values of B nor in the significance of the difference between these values and that calculated from the latter. In only three cases (5B, 8, and 12B) were the estimated B values significantly different from that calculated from the mean adult data. These were interpreted as reflecting individual differences between the particular three pathways concerned and the average growth pattern for the whole lung. Much more remarkable is the similarity between the curvature representing the data from a single pathway in the newborn lung and the curvature based on many pathways for the adult.

APPENDIX B

CALCULATION OF AEROSOL DEPOSITION IN CONDUCTING AIRWAYS (METHOD OF LANDAHL (1950)) Each fraction of inspirate is considered to pass through successive generations of airways in series. In each generation, or region, an airborne particle may be deposited by three different mechanisms which act independently but which depend on the dimensions and speed of airflow in that generation and on the size of the particle. The airways thus form a system of filters. Successive fractions of the aerosol are removed in each generation and the final concentration passing the terminal bronchiolus is obtained from the product of the whole series. It is necessary to calculate the mean rate of airflow and the time spent by a fraction of air in each generation.

The deposition probabilities are:

- (1) probability (S_a) of particle deposition in an airway (α) due to sedimentation

$$S_a = 1 - e^{-0.8 V_s \cos \theta T_a / R_a}$$

- (2) probability (D_a) of particle deposition in an airway (α) due to diffusion

$$D_a = 1 - e^{-0.58 \sqrt{2} \overline{DT}_a / R_a}$$

- (3) probability (I_a) of particle deposition in an airway (α) due to impaction

$$I_a = \frac{P}{1 + P}$$

$$\text{where } P = V_s U_{a-1} \sin \theta / gR$$

- (4) combined probability (P_a) of particle deposition in an airway (α).

$$P_a = S_a + D_a + I_a - S_a D_a - S_a I_a - D_a I_a + I_a S_a D_a$$

T_a = transit time in airway α (sec)
 V_s = terminal velocity of aerosol particle (cm sec⁻¹)
 D = coefficient of diffusion of aerosol particle (cm² sec⁻¹)
 R = radius of airway (cm)
 V = mean airflow velocity in airway (cm sec⁻¹)
 θ = average inclination of the airways from the horizontal (degrees)

The terminal velocity and diffusion coefficient of an airborne particle depend on its size, shape, and density. The values used are those appertaining to spheres of unit density. The results shown in Fig. 7 express the probability that a given particle will penetrate beyond the terminal bronchiole and thus have access to the alveoli. The calculations refer only to particles contained in that fraction of the tidal air which reaches the alveolar region of the lung.