

# Dead space ventilation in normal children and children with obstructive airways disease

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**Kerr, A. A. (1976). *Thorax*, 31, 63–69. Dead space ventilation in normal children and children with obstructive airways disease.** Anatomical dead space was measured in 72 normal children aged from 5 to 16 years, using the single breath method. There was a linear increase in this measurement with height, weight, and end-inspiratory lung volume.

Physiological dead space was measured in 52 normal children using the Bohr equation and substituting a rebreathing  $PCO_2$  for alveolar  $PCO_2$ . There was a parallel increase in this measurement with height, weight, and end-inspiratory lung volume. The difference between the two dead space measurements constitutes the alveolar dead space and was constant over the whole age range at  $45 \pm 22$  ml.

The ratio of physiological dead space to tidal volume was  $33.6 \pm 4.6\%$  and was unaltered by age or change in lung volume.

The effect of airways obstruction on the dead space volumes was studied in 36 children with asthma and 28 with cystic fibrosis. Physiological dead space increased with increasing airways obstruction. Anatomical dead space remained constant in spite of marked increases in lung volume associated with the airways obstruction.

There is little published information on the various dead space volumes in children (Polgar and Promadhat, 1971). Hart, Orzalesi, and Cook (1963) measured the anatomical dead space in 73 normal subjects aged 4 to 42 years. No information is obtained from these data from both children and adults about the changes throughout childhood which might occur with lung growth. The commonly used nomogram values for this age range (Radford, 1955) are based on derived data from eight boys only (Robinson, 1938).

Similarly, there is little information on the physiological dead space in normal children and on the ratio of this to tidal volume (Beaudry, Wise, and Seely, 1967; Levison, Featherby, and Weng, 1970).

The following studies were undertaken to collect more normal data and, in particular, to compare anatomical and physiological dead space.

A study was also made of the changes in dead space volumes with airways obstruction due to asthma and cystic fibrosis.

All measurements were made with the child sitting on a laboratory stool under resting conditions.

Anatomical dead space ( $V_{D \text{ anat}}$ ) was measured by a modification of the single breath method (Fowler, 1948). The electronically integrated expired volume from a Fleisch No. 1 pneumotachograph and the expired  $CO_2$  concentration from a VG Micromass 1 mass spectrometer were recorded on a U-V recorder for at least three breaths. The dead space was measured from the point where the  $CO_2$  concentration had risen halfway to the initial alveolar level (Young, 1955). Allowance of 150 ms was made for the delay in gas analysis, and a further 15 ml was subtracted for apparatus dead space. The pneumotachograph was calibrated by injecting through it 500 ml from a large syringe.

The accuracy of this method of analysis was checked in 10 normal children, 10 children with asthma, and 10 with cystic fibrosis. This was done by drawing a perpendicular through the halfway point on the  $CO_2$  trace and measuring the areas A and B on the trace as shown in Figure 1. Ideally, these areas should be equal. They were cut out and weighed, and the error in placing the perpendicular was estimated in terms of displacement to either side of ideal. There was an overall mean shift of 0.14 mm to the left for this perpendicular. Even with the greatest

## METHODS AND MATERIAL

Studies were performed on 72 normal healthy children aged 5 to 16 years. They were all from the inner London area and were well at the time of study.

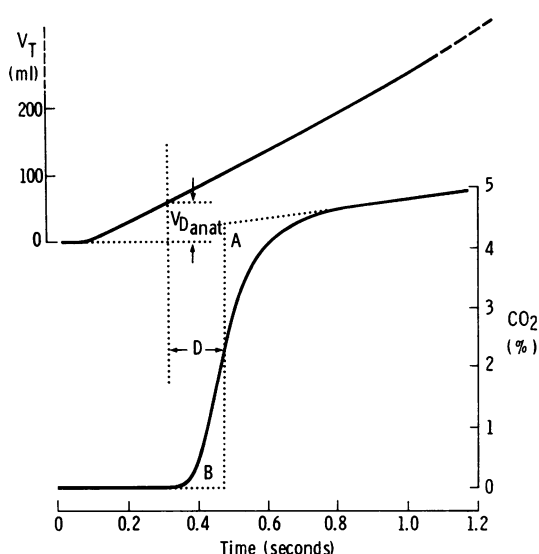


FIG. 1. Tidal volume trace ( $V_T$ , above) and expired  $\text{CO}_2$  trace (below) showing the method used to measure anatomical dead space ( $V_{D \text{ anat}}$ ). Ideally, the triangular areas A and B should be equal. In this study the perpendicular between the two areas was drawn so that it crossed the  $\text{CO}_2$  trace halfway between 0%  $\text{CO}_2$  and the initial alveolar  $\text{CO}_2$  concentration. Using this method there was no significant difference in the areas. D is the delay due to the sampling time of the  $\text{CO}_2$  analyser.

displacement, however, there was no measurable underestimation of the volume of  $V_{D \text{ anat}}$ . The method was further checked by injecting a  $\text{CO}_2$  mixture through an added dead space and comparing the recorded  $V_D$  of this with the actual added volume measured by filling it with water. There was a 1% overestimate for an added dead space of 95 ml and a 9% overestimate for a 64 ml dead space. The mean coefficient of variation for  $V_{D \text{ anat}}$  measurement in 12 children who had five or more breaths analysed was 10.1%.

The physiological dead space ( $V_{D \text{ phys}}$ ) was measured using the Bohr equation (Comroe *et al.*, 1962). An accurately timed mixed expired gas collection was made over at least 3 minutes. The volume was measured by the pneumotachograph. This was calibrated immediately after the collection by taking a second collection through it into a wet spirometer (C. F. Palmer Ltd, London), the volume of which was measured and corrected to BTPS. The  $\text{CO}_2$  and  $\text{O}_2$  content of the final mixed expired gas collection was measured with the mass spectrometer. The end-tidal  $\text{PCO}_2$  was recorded during the collection, and if this varied by more than 5%, the collection was discarded. Alveolar  $\text{PCO}_2$  was measured indirectly

by a rebreathing method using mixtures of  $\text{CO}_2$  in air (Collier, 1956). Tracings were accepted only if a true  $\text{CO}_2$  equilibration plateau was obtained between 10 and 20 seconds from the start of rebreathing. Duplicate estimates were made, and from these the mixed venous  $\text{PCO}_2$  was obtained; 6 mmHg was subtracted to give the arterial  $\text{PCO}_2$ , which was assumed to equal alveolar  $\text{PCO}_2$ . The mean arterial  $\text{PCO}_2$  measured by this method in 52 normal children was 39.3 mmHg with a standard deviation of 3.1 mmHg. The coefficient of variation for  $V_{D \text{ phys}}$  measurement was 6.0% in one adult tested four times.

During the 3 minute collection for the measurement of  $V_{D \text{ phys}}$ , minute ventilation ( $\dot{V}_E$ ), tidal volume ( $V_T$ ), and breathing frequency ( $f$ ) were recorded. From these, alveolar minute ventilation ( $\dot{V}_A = \dot{V}_E - \dot{V}_{D \text{ anat}}$ ) and alveolar dead space ( $V_{DA} = V_{D \text{ phys}} - V_{D \text{ anat}}$ ) were calculated.

Thoracic gas volume (TGV) was measured by the plethysmographic method of Dubois *et al.* (1956). End-inspiratory lung volume (EILV) was taken as the sum of TGV and  $V_T$ .

## RESULTS

Anatomical dead space ( $V_{D \text{ anat}}$ ) measurements were obtained in 72 normal children and the results are illustrated in Figure 2.

There were 52 children in whom a satisfactory steady-state gas collection with constant end-tidal  $\text{PCO}_2$  was obtained. Data from these children only were included in results of  $V_{D \text{ phys}}$  and ventilation

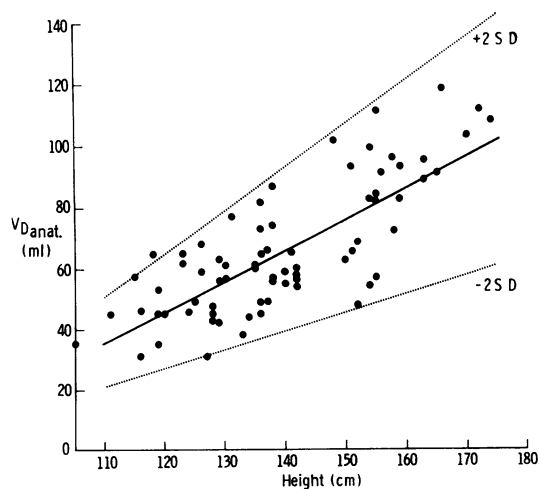


FIG. 2. Anatomical dead space ( $V_{D \text{ anat}}$ ) plotted against height for 72 healthy children. The regression line and 2 standard deviations from the regression are shown.

measurements. The results of  $V_{D \text{ phys}}$  measurement in this group of children are shown in Figure 3.

EILV is the most appropriate lung volume to which to relate  $V_{D \text{ anat}}$ , as it represents the actual lung volume from which  $V_{D \text{ anat}}$  is measured. The regression equations and correlation coefficients for all these data are given in Table I.

There was no significant difference in the slopes of the regression lines for  $V_{D \text{ anat}}$  and  $V_{D \text{ phys}}$  ( $P > 0.05$ ), and the mean difference between them was 44.5 ml.

Table II shows the mean values for  $f$ ,  $\text{PaCO}_2$ ,  $R$ ,  $V_{D \text{ anat}}/V_T$ ,  $V_{D \text{ phys}}/V_T$ ,  $V_{DA}$  and  $V_{DA}/V_A$ . None of these varied significantly with age.

Tidal volume ( $V_T$ ) showed a linear relationship to height:

$$V_T(\text{ml}) = 4.19 \times \text{Height (cm)} - 206.6 \quad (r = 0.596)$$

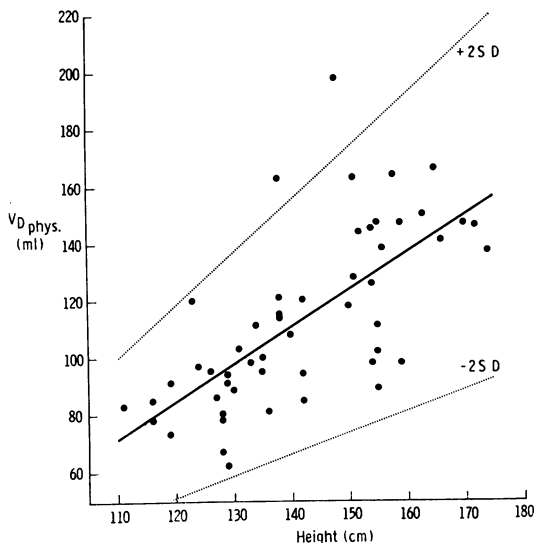


FIG. 3. Physiological dead space ( $V_{D \text{ phys}}$ ) plotted against height for 52 healthy children. The regression line and 2 standard deviations from the regression are shown.

TABLE I

RELATIONSHIPS BETWEEN RESPIRATORY DEAD SPACE VOLUMES AND HEIGHT, WEIGHT, AGE, AND END-INSPIRATORY LUNG VOLUME IN NORMAL CHILDREN

Regression Equation	r	Co-efficient of Variation of Regression
$V_{D \text{ anat}} \text{ (ml)} = 1.018 \times \text{Height (cm)} - 76.2$	0.774	20.4%
$V_{D \text{ anat}} \text{ (ml)} = 3.716 \times \text{Age (years)} + 27.0$	0.552	26.7%
$V_{D \text{ anat}} \text{ (ml)} = 1.374 \times \text{Weight (kg)} + 16.5$	0.755	21.3%
$V_{D \text{ anat}} \text{ (ml)} = 0.028 \times \text{EILV (ml)} + 7.3$	0.800	20.3%
$V_{D \text{ phys}} \text{ (ml)} = 1.307 \times \text{Height (cm)} - 72.5$	0.687	19.7%
$V_{D \text{ phys}} \text{ (ml)} = 1.660 \times \text{Weight (kg)} + 51.1$	0.672	20.1%
$V_{D \text{ phys}} \text{ (ml)} = 0.031 \times \text{EILV (ml)} + 45.1$	0.671	20.1%

TABLE II

DATA ON VENTILATION IN 52 NORMAL CHILDREN

	Mean	Standard Deviation
$f$ (breaths/minute)	17	3.9
$\text{PaCO}_2$ (mmHg)	39.3	3.1
$R$	0.751	0.076
$V_{D \text{ anat}}/V_T$ (%)	18.0	5.0
$V_{D \text{ phys}}/V_T$ (%)	33.6	4.6
$V_{DA}$ (ml)	44.7	22.4
$V_{DA}/V_A$ (%)	14.0	5.7

Alveolar ventilation also had a significant correlation with height:

$$\dot{V}_A(\text{l/min}) = 0.034 \times \text{Height} + 0.395 \quad (r = 0.548)$$

Satisfactory data were obtained in 36 children with bronchial asthma, in eight of whom second measurements were obtained at a time when the degree of airways obstruction had altered. In the total group of asthmatic children,  $V_{D \text{ anat}}$  remained at the volume expected for height but was diminished in relation to EILV (Fig. 4). The diminution relative to lung volume was greater with more severe degrees of hyperinflation. These findings were consistent with those in the eight children in whom serial studies were performed. In spite of a mean increase in EILV of  $604 \pm 348$  ml (1SD), there was an increase in  $V_{D \text{ anat}}$  of only  $0.63 \pm 11.2$  ml (1 SD). By contrast, the rise in  $V_{D \text{ phys}}$  was either in proportion to the rise in lung volume or greater than would be expected (Fig. 5).

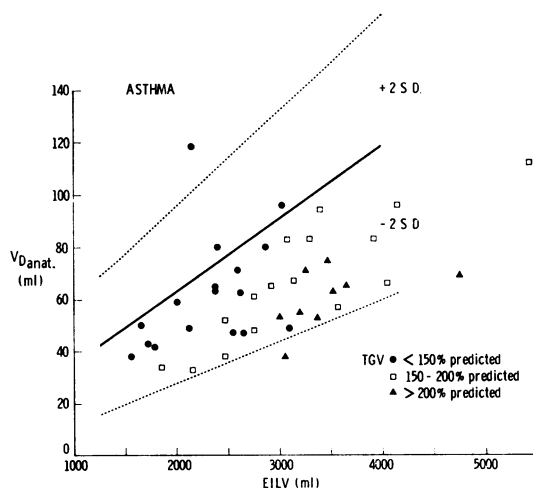


FIG. 4. Anatomical dead space ( $V_{D \text{ anat}}$ ) plotted against end-inspiratory lung volume (EILV) in 42 asthmatic children. The degree of hyperinflation is indicated by the increase in thoracic gas volume (TGV), which is shown as a percentage of that predicted for height. The mean  $\pm 2$  SD lines are shown for the regression of  $V_{D \text{ anat}}$  against EILV in healthy children.

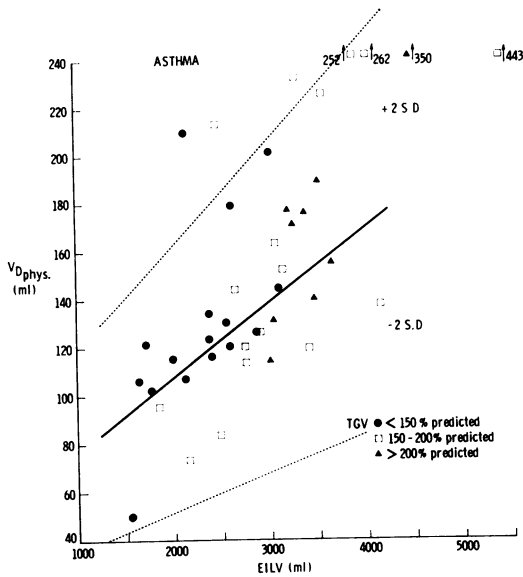


FIG. 5. Physiological dead space ( $V_{D \text{ phys}}$ ) plotted against end-inspiratory lung volume (EILV) in 42 asthmatic children. The degree of hyperinflation is indicated by the increase in thoracic gas volume (TGV), which is shown as a percentage of that predicted for height. The mean  $\pm 2$  SD lines are shown for the regression of  $V_{D \text{ phys}}$  against EILV in healthy children.

The results of  $V_D$  measurement in 28 children with cystic fibrosis are shown in Figures 6 and 7. The relative decrease in  $V_{D \text{ anat}}$  with increase in EILV was less apparent, but most values did lie in the lower half of the normal range. There were large increases in  $V_{D \text{ phys}}$  with increasing severity of disease as indicated by increase in lung volume.

#### DISCUSSION

It has been shown that the respiratory dead space measured by relating expired gas concentration changes to expired volume ( $V_{D \text{ anat}}$ ) is the same for all respiratory gases (Bartels *et al.*, 1954). It is, therefore, reasonable to compare the values of  $V_{D \text{ anat}}$  obtained in the present study with earlier data using the original nitrogen technique (Fowler, 1948). The only data available over a similar age range are from studies by Hart *et al.* (1963) and Beaudry *et al.* (1967). These results are shown in Figure 8. The data on adult males from Fowler (1948) are also shown for comparison. The results from other studies tend to fall between the regressions for the two different measurements of  $V_D$  in the present study. An apparent decrease in  $V_{D \text{ anat}}$  can occur with breath-holding (Bartels *et al.*, 1954; Shepard, Campbell,

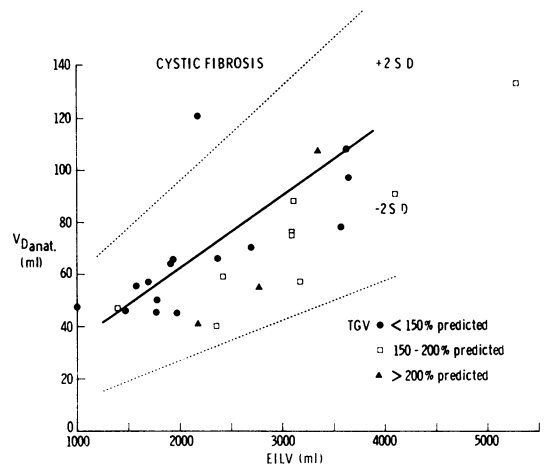


FIG. 6. Anatomical dead space ( $V_{D \text{ anat}}$ ) plotted against end-inspiratory lung volume (EILV) in 28 children with cystic fibrosis. The degree of hyperinflation is indicated by the increase in thoracic gas volume (TGV), which is shown as a percentage of that predicted for height. The mean  $\pm 2$  SD lines are shown for the regression of  $V_{D \text{ anat}}$  against EILV in healthy children.

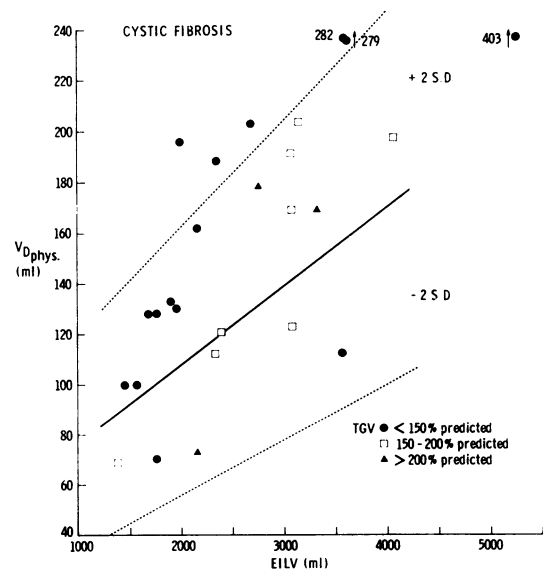


FIG. 7. Physiological dead space ( $V_{D \text{ phys}}$ ) plotted against end-inspiratory lung volume (EILV) in 28 children with cystic fibrosis. The degree of hyperinflation is indicated by the increase in thoracic gas volume (TGV), which is shown as a percentage of that predicted for height. The mean  $\pm 2$  SD lines are shown for the regression of  $V_{D \text{ phys}}$  against EILV in healthy children.

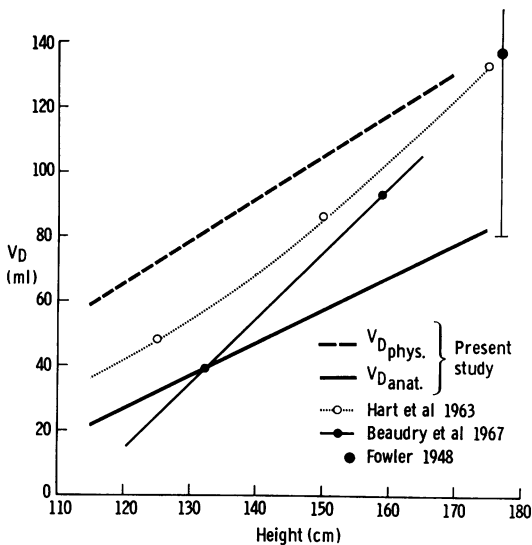


FIG. 8. Comparison of dead space ( $V_D$ ) measurement in healthy subjects. The values from Fowler (1948) are the mean and 2 SD for 45 adult males using the  $N_2$  single breath method. The other data are from Beaudry et al. (1967), using the Bohr equation in children, and from Hart et al. (1963), using the  $N_2$  single breath method in children and adults.

Martin, and Enns, 1957). Alternatively, increasing the breathing frequency may cause an apparent increase in  $V_{D\text{anat}}$ , and a real increase in  $V_{D\text{anat}}$  occurs with increased lung volume (Shepard et al., 1957; Lifshay, Fast, and Glazier, 1971). From the data available, none of these factors appears to contribute significantly to the variation in  $V_D$  results between the present study and earlier work.

It is accepted in adults that  $V_{D\text{anat}}$  and  $V_{D\text{phys}}$  are virtually identical in normal lungs (Comroe et al., 1962). That a similar relationship holds for children has been assumed (Polgar and Promadhat, 1971), but no direct measurement of both types of dead space in the same children has previously been made. The present study shows a mean difference of 44.5 ml between the regression lines for  $V_{D\text{anat}}$  and  $V_{D\text{phys}}$ . This difference ( $V_{D\text{A}}$ ) remains constant with age, and it might be expected to become a smaller proportion of  $V_A$  in older children. This does not appear to be so.  $V_{D\text{A}}/V_A$  shows no correlation with age, height or lung volume, presumably because there is a wide variation in  $V_{D\text{A}}$  measurement.

The use of 6 mmHg as the  $a-\bar{v}$  difference for  $PCO_2$  has recently been questioned by McEvoy, Jones, and Campbell (1974). They found that 10 mmHg was a more appropriate figure in adults with normal  $PCO_2$  and when the blood was fully oxygenated. The Collier method for rebreathing  $PCO_2$ , as used in the present

study, uses a mixture of  $CO_2$  in air. At equilibration the  $O_2$  content of the bag was about 16% so that Hb would not be fully saturated. In these circumstances the  $PCO_2$  would be lower than if it were saturated, provided the  $CO_2$  content remains constant. Accordingly, the  $a-\bar{v}$  difference for  $PCO_2$  would be expected to be lower in the present study than in the work of McEvoy et al. (1974). This is borne out by the fact that the range of  $Paco_2$  in these normal children, as estimated by the rebreathing method, is the same as is generally accepted for direct measurement. However, in children with airways obstruction, the  $a-\bar{v}$  difference may have been greater than 6 mmHg and, if so, this would result in an overestimate in estimated  $Paco_2$  and  $V_{D\text{phys}}$  in this group.

The ratio of wasted ventilation to tidal volume ( $V_{D\text{phys}}/V_T$ ) has been cited as a useful index in intensive respiratory management (Downes, Fulgencio, and Raphaely, 1972) and as a sensitive index of early changes with disease, especially during exercise challenge (Levine et al., 1970). A normal value of 30% is usually quoted for this ratio (Polgar and Promadhat, 1971). The values obtained in the present study show a wide range, which is comparable to data reported in studies on normal infants, older children, and adults (Table III).

Recently, Harris et al. (1973) pointed out the inapplicability of relating  $V_{D\text{phys}}$  to  $V_T$  only. In their study in adults, they defined a multiple regression of  $V_D$  on age, height,  $V_T$  and the reciprocal of respiratory frequency which gave the best prediction of  $V_{D\text{phys}}$ . In the present study a similarly improved correlation was obtained by using simple regressions of  $V_{D\text{phys}}$  on height, weight, and lung volume (EILV) rather than the ratio of  $V_{D\text{phys}}$  to  $V_T$ .

There is a significant correlation between  $V_T$  and height, and these data agree with those of Levison et al. (1970). The estimated figures given by Cook and Motoyama (1968) are too low. The alveolar ventilation data ( $\dot{V}_A$ ) from this study are significantly higher than the measurements of Levison et al. (1970) and the estimates of Cook and Motoyama (1968). Both  $V_T$  and  $\dot{V}_A$  are increased if not taken under basal conditions, and this probably accounts for the discrepancies. The normal values for the respiratory quotient (R, Table II) indicate that this increase in ventilation was appropriate to the increase in oxygen consumption above the basal state.

The changes in  $V_D$  with disease are of considerable interest. It is well established that  $V_{D\text{phys}}$  is increased in both asthma and cystic fibrosis (Downes et al., 1972). Comparison of Figs. 5 and 7 shows that in cystic fibrosis the  $V_{D\text{phys}}$  increase is less dependent on the degree of hyperinflation (as shown by the rise in EILV) than it is in asthma. This is presumably

TABLE III  
COMPARISON OF  $V_D$  phys/ $V_T$  IN NORMAL SUBJECTS IN THE SITTING POSITION

Study	Age Range	Number	Mean	Standard Deviation
Mellemsgaard (1966)	15-40 years	40	29.1	7.2
Mellemsgaard (1966)	40-77 years	40	33.7	7.1
Fowler (1948)	19-38 years	45	25.9	7.6
Raine and Bishop (1963)	17-40 years	32	23.8	6.2
Raine and Bishop (1963)	40-66 years	17	26.1	6.4
Present study	7-16 years	52	33.6	4.6
Beaudry <i>et al.</i> (1967)	11-55 years (mean)	18	26.1	7.3
Levison <i>et al.</i> (1970)	7-19 years	42	29	not given
Strang (1961)	0-8 days	9	57	8
Nelson <i>et al.</i> (1962)	0-42 days	25	25	7
Cook <i>et al.</i> (1955)	0-7 days	16	32	12

because cystic fibrosis is a patchy disease (Bodian, 1952), and consequently there is a localized increase in the ventilation:perfusion ratio which results in increased  $V_D$  phys. In asthma, on the other hand, there is more diffuse airways obstruction, resulting in diminished  $\dot{V}_A$  without gross ventilation:perfusion inequality until hyperinflation is severe (TGV more than 150% predicted, in Fig. 5).

The changes in  $V_D$  anat are different. In asthma, the individual  $V_D$  anat values are all within the normal range for height but are low in relation to EILV. In normal lungs, increased lung volume causes an increase in  $V_D$  anat (Shepard *et al.*, 1957; Lifshay *et al.*, 1971). This did not occur in those patients in whom the increased lung volume was due to airways obstruction. There are two possible explanations for this:

(1) In asthma, narrowing of the small airways produces poor alveolar emptying during expiration. This results in air trapping at alveolar level with increase in the total lung volume. Such an increase in lung volume is not associated with reduced intrapleural pressure and increased radial traction on the large airways, as occurs when a person with normal lung mechanics increases his lung volume. Consequently, the asthmatic with hyperinflated lungs will tend not to have increased large airway volume.

(2) During attacks of asthma, the smooth muscle in the tracheal and bronchial walls also contracts. Olsen, Stevens, and McIlroy (1967) showed in cats that this results in reduced airway wall compliance. This would reduce the effect that breathing at a higher lung volume has on  $V_D$  anat by preventing the expansion of the large airways that normally occurs with increase in lung volume. From the present data it is not apparent which of these factors is the more important.

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