Lung volumes, ventilatory capacity, and transfer factor in healthy British boy and girl twins

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Cotes, J. E., Dabbs, J. M., Hall, A. M., Axford, A. T., and Laurence, K. M. (1973). *Thorax*, 28, 709–715. Lung volumes, ventilatory capacity, and transfer factor in healthy British boy and girl twins. Normal values are reported for the lung volumes, ventilatory capacity, and transfer factor of 212 healthy British twin children aged 8 to 16 years. The boys and the girls share a common relationship to height for the residual volume, peak expiratory flow rate, and Kco (transfer factor per litre of lung volume). For the inspiratory capacity and the transfer factor, also its membrane component (Dm), the values for the boys exceed those for the girls by, on average, 10%. This difference may be due, at least in part, to the boys taking more exercise.

For most clinical purposes the assessment of lung function comprises measurement of the ventilatory capacity for which normal values in healthy children are readily available. In adults, and now to an increasing extent in children, this is being supplemented by measurement of the lung volumes by the closed circuit helium dilution method and of the transfer factor (diffusing capacity) by the single breath carbon monoxide method. Regression equations on standing height for the lung volumes of healthy children are available for several countries on the continent of Europe and in North America and are in general similar (Polgar and Promadhat, 1971). The only data so far available for the lung volumes of British children suggest that the regression coefficients on height are similar to those for children of European descent living elsewhere but the residual volumes are apparently higher by about 0.5 l. (Godfrey, Kamburoff, and Nairn, 1970). There are few published data for the single breath transfer factor, and none so far from the United Kingdom. Thus there remains a need for reference values for lung function in healthy British children, which the present study may in part meet. The data were obtained for healthy twins during an investigation into the respective contributions to normal lung function

of genetic and environmental factors. This aspect and also the physiological response to exercise will be reported separately.

SUBJECTS AND METHODS

The children were identified mainly through the birth records for the area, and a few via local contacts. They were approached by an independent third party who visited the homes and explained to the twins and to their parents what would be involved and why the study was being carried out. The nature of the study was also described in the local press and to the registered general practitioners of those who were invited to participate. No pressure was put on the children to take part and it was made clear to those who attended that they were free to withdraw at any time during the study if they wished to do so. Six children withdrew, three mainly on account of breathing through a mouthpiece, one felt faint, and in two instances the cause was not apparent. Their average age was 9.3 yr (range 8–10 yr). The results which are reported relate to the children's first attendance at the laboratory, except in the case of nine children who attended a second time because the first result was technically unsatisfactory; this was usually on account of a leak from the mouthpiece during the measurement of the residual volume. In addition, six children attended a second time on account of their having respiratory symptoms on the first attendance, including one pair of identical twins. The results for these children are not included in the analysis. Also excluded are the results for six children of

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ethnic groups other than European. The present results relate to children of European descent who had never had a notable chest illness and were free from respiratory symptoms at the time of the study. In addition, data for reproducibility were

TABLE I
DETAILS OF THE SUBJECTS: MEAN VALUES AND RANGES

	Number	Age (yr)	Height (m)	Weight (kg)
Boys				
Identical twins ..	48 ¹	11.6 (8-16)	1.46 (1.21-1.80)	37.8 (22.5-60.0)
Non-identical twins	48	11.46 (8-15)	1.46 (1.22-1.75)	37.4 (21.5-75.5)
From boy/girl pairs	32	10.7 (8-16)	1.42 (1.19-1.79)	32.9 (22.5-63.5)
Girls				
Identical twins ..	56 ¹	11.4 (8-16)	1.44 (1.18-1.62)	37.0 (19.0-56.5)
Non-identical twins	48	11.0 (8-15)	1.42 (1.15-1.67)	35.6 (19.5-65.0)
From girl/boy pairs	32	10.7 (8-16)	1.41 (1.23-1.69)	32.9 (20.5-61.0)

¹ For the main analysis in order not to underestimate the extent of normal variation the data for the second born of the identical twins were omitted.

FIG. 1. Distribution of subjects with respect to stature.

obtained on 13 children who were asymptomatic twin brothers or sisters of those who attended twice for one of the reasons given above. Details of the subjects are listed in Table I and their distributions with respect to height in Figure 1.

The measurements were made during normal working hours. They included a short questionnaire on respiratory symptoms, past illnesses, and habitual activity, which was answered by the children and in most instances also by the parents. A brief medical examination was carried out including inspection of the fauces, the eliciting of the loose cough sign (Gandevia, 1969), and clinical examination of the

chest. In all but one instance a sample of venous blood was taken for measurement of the haemoglobin concentration: in the remaining child this quantity was assumed to be the same as for her twin. Stature and sitting height were measured using a Harpenden stadiometer; during the measurement the posture was checked carefully and gentle traction was applied to the head (Weiner and Lourie, 1969).

The peak expiratory flow rate was measured using a Wright peak flow meter (Wright and McKerrow, 1959) and the forced expiratory volume (FEV) and vital capacity (FVC) using a low resistance spirometer (McKerrow, McDermott, and Gilson, 1960). The spirometer was fitted with two pointers and timing devices which permitted the concurrent measurement of the volumes expired up to 1.0 s and 0.75 s (FEV_{1.0} and FEV_{0.75} respectively). The data which were used for the analysis comprised the means of three technically satisfactory results. These were obtained after, in most instances, two practice attempts.

The measurements of the lung volumes and the transfer factor were made in an upright seated posture, the former by the closed circuit helium dilution method and the latter by the single breath carbon monoxide method using a Resparameter. The transfer factor was measured twice, on the first occasion after breathing oxygen for 5 min and then after breathing air. The data were used for the calculation of the diffusing capacity of the alveolar membrane (*D_m*) and the volume of blood in the lung capillaries (*V_c*). Full details of the procedures including the values taken for the reaction rate of carbon monoxide with oxyhaemoglobin are described elsewhere (Cotes, 1968). The result was related to the subject's own haemoglobin concentration (Cotes *et al.*, 1972) but no allowance was made for any carbon monoxide present in the blood at the start of the study. As in the whole series only two of the children admitted to smoking cigarettes, this quantity was assumed to be zero.

The data were analysed by multiple regression analysis on age, height, and weight. This was done for the data both as calculated and after logarithmic transformation. The analysis was applied to each subgroup separately and combined in the manner indicated below. Proportional values for one index of function with respect to another were obtained individually in the case of the forced expiratory volume (FEV_{1.0}) as a percentage of the vital capacity (FEV%) and of the residual volume as a percentage of total lung capacity (RV%). Other ratios were calculated using the data in their logarithmic form after first obtaining the common regression coefficient on height.

RESULTS

The primary indices of lung function were all related to body size. This was described best in terms of the regression on stature; no significant reduction in variability about the regression line

FIG. 2. Relationship to stature of lung function indices in boys and girls. (a) Total lung capacity, functional capacity, and residual volume. (b) Vital capacity, forced expiratory volume (FEV_{1.0}), inspiratory capacity, and expiratory reserve volume. (c) Peak expiratory flow rate and forced expiratory volume (FEV_{0.75}). (d) Transfer factor Kco (transfer factor per unit of lung volume), diffusing capacity of alveolar capillary membrane, and volume of blood in the lung capillaries.

was effected by also including weight and/or age in the regression. The indices which were the ratios of volumes were independent of height, age, and weight. When the results were considered by subgroups for the boys and girls separately similar relationships on height were found for the identical twins, the non-identical twins, and the appropriate members of the boy-girl twin pairs. In addition, within each twin pair, where

both twins were of the same sex, there was no average difference with respect to any of the indices measured as between the twin who was born first and the twin who was born second. Accordingly, the data were pooled for the boys and girls separately including both members of non-identical twin pairs, the appropriate member of the boy-girl twin pairs, and the first-born of the identical twin pairs. The second member of each identical twin pair was omitted to avoid the possibility of attributing to the estimated regression lines on height more precision than was justified. This aspect is considered elsewhere (Cotes *et al.*, in preparation). The mean results are summarized in Table II. A comparison was then made across the sexes. It showed that for three of the indices the boys and girls shared a common relationship to height; this was the case for the residual volume, the peak expiratory flow rate, and the transfer factor per unit of lung volume K_{co} . In the case of the other primary indices, after height was taken into account the values for the boys were on average significantly higher than those for the girls; the difference was approximately 11% in the case of the inspiratory capacity, the transfer factor, and the diffusing capacity of the alveolar membrane and approximately 6% in the case of the other primary indices. These differences are indicated in Table III. In the case of the ratio indices $FEV\%$ of forced vital capacity and $FEV_{0.75}/FEV_{1.0}$, the values for the girls are significantly different from those for the boys ($P < 0.01$ and < 0.05). These results are included in Table II.

Comparison of the linear and the logarithmic versions of the regression equations on stature showed that for the present subjects these did not differ materially. However, in both sexes for

TABLE II
MEAN VALUES AND STANDARD DEVIATIONS FOR DATA USED IN THE ANALYSIS

No.	Boys		Girls	
	Mean	SD	Mean	SD
	104		108	
Age (yr)	11.3	2.4	11.0	2.3
Height (m)	1.45	0.15	1.42	0.12
Weight (kg)	36.2	11.8	35.2	9.9
Haemoglobin conc. (g%)	13.2	1.1	13.0	0.8
Forced expiratory volume ($FEV_{0.75}$, l.)	2.16	0.68	1.95	0.51
Forced expiratory volume ($FEV_{1.0}$, l.)	2.34	0.75	2.08	0.55
Forced vital capacity (FVC, l.)	2.78	0.86	2.39	0.59
$FEV_{0.75} \times 100 \div FVC$ ($FEV_{0.75}\%$)	77.9	5.2	81.2 ¹	4.9
$FEV_{1.0} \times 100 \div FVC$ ($FEV_{1.0}\%$)	84.0	4.4	86.9 ¹	4.2
$FEV_{0.75}/FEV_{1.0}$ (%)	92.7	2.5	93.5 ¹	2.8
Peak expiratory flow rate (PEFR, l min ⁻¹)	327.5	78.4	317.0	70.6
Total lung capacity (TLC, l.)	3.57	1.13	3.08	0.79
Vital capacity (VC, l.)	2.83	0.89	2.43	0.62
Inspiratory capacity (IC, l.)	1.91	0.59	1.61	0.42
Expiratory reserve volume (ERV, l.)	0.95	0.40	0.82	0.26
Functional residual capacity (FRC, l.)	1.66	0.63	1.47	0.45
Residual volume (RV, l.)	0.72	0.30	0.65	0.24
$RV \times 100 \div TLC$ ($RV\%$)	20.0	4.5	21.0	4.6
Transfer factor (Tl, ml min ⁻¹ torr ⁻¹)	20.6	6.5	17.6	4.4
Transfer factor $\div$ lung volume (K_{co} , min ⁻¹ torr ⁻¹)	6.15	0.80	6.15	0.68
Diffusing capacity of alv. membrane (D_m , ml min ⁻¹ torr ⁻¹)	34.3	11.0	29.2	8.8
Volume of blood in alveolar capillaries (Vc, ml)	54.9	22.3	48.2	15.9

* For conversion to SI units (mmol min⁻¹ kPa⁻¹) the numbers should be divided by 2.99.

¹ For significance see text.

TABLE III
REGRESSION RELATIONSHIPS FOR PREDICTION OF INDICES OF LUNG FUNCTION FROM STANDING HEIGHT (m) IN NORMAL BOYS AND GIRLS OF EUROPEAN DESCENT

Index	Relationship for Each Index in Boys and Girls Separately		Girl/Boy ¹ Difference %	Coefficient Term for Height ²⁻⁴⁸	
	Boys	Girls		Boys	Girls
TLC	1.227 ht ^{2.80}	1.189 ht ^{2.64}	9	1.281	1.171
VC	1.004 ht ^{2.72}	0.946 ht ^{2.61}	10	1.081	0.924
IC	0.720 ht ^{2.55}	0.657 ht ^{2.47}	11	0.685	0.611
ERV	0.264 ht ^{2.37}	0.283 ht ^{2.80}	6	0.327	0.306
FRC	0.500 ht ^{2.12}	0.528 ht ^{2.81}	4	0.586	0.553
RV		0.237 ht ^{2.77}	Nil		0.245
$FEV_{0.75}$	0.780 ht ^{2.67}	0.744 ht ^{2.66}	5	0.778	0.743
$FEV_{1.0}$	0.812 ht ^{2.77}	0.788 ht ^{2.73}	6	0.840	0.791
PEFR		455.7 ht-332	Nil		—
Tl	8.059 ht ^{2.46}	7.584 ht ^{2.33}	10	7.431	6.717
D_m	15.43 ht ^{2.07}	12.03 ht ^{2.41}	12	12.33	10.96
Vc	17.69 ht ^{2.81}	19.89 ht ^{2.40}	7	19.27	18.00
K_{co}		7.054 ht-0.4	Nil		—

For symbols and units see Table II.

¹ For each index this is based on the regression with the same exponent for boys and girls.

almost all the indices the mean data for the shortest and the tallest height groups were found to deviate slightly (but not significantly) from the linear regression lines. These deviations were not apparent when the logarithmic version of the data was used. The latter are displayed in Figs. 2(a)–2(b). The regression equations are listed in Table III both in the form in which they were derived for boys and girls separately and using the average exponent on height of 2.68 which gives effectively the same result; the latter in conjunction with a table of values for height^{2.68} (Appendix 1) simplifies the calculation of reference values.

DISCUSSION

The present data relate to healthy children of European descent living in or near to Cardiff which is a commercial and industrial city of population approximately 280,000; the rainfall is on average 100 cm per year and the atmosphere is relatively free of harmful pollution (Ministry of Technology, Warren Spring Laboratory, 1965–67). The heights of the children relative to their ages approximated very closely the mean values observed for healthy British children (Tanner, Whitehouse, and Takaishi, 1966) and in other respects the children did not appear to differ from single children of the same age.

The between day reproducibility of the individual measurements was assessed for the 13 children who accompanied their twin sibling on a second visit to the laboratory. The reproducibility expressed as a coefficient of variation (i.e., standard deviation of a single observation divided by the mean value) was 4% for the forced expiratory volume and vital capacity and 2% for the peak expiratory flow rate. For these indices the mean values were significantly higher on the second occasion than on the first; however, the differences were very small (<5%). The remaining indices showed rather greater day-to-day variability (range 8% to 16%) but, with the exception of the KCO which was decreased on average by 10%, the mean values were very similar on the two occasions. The lower values for the KCO were associated with a slightly higher value for the alveolar volumes, so the transfer factor, for which the mean values were 17.4 and 16.4 ml min⁻¹ torr⁻¹, was not reduced significantly. This difference is similar to that observed in adults. Thus the data for reproducibility suggest that the results used for the analysis are stable and representative of the subjects.

The regression relationships for indices of lung

function on stature agree closely with those from a number of sources outside the United Kingdom which are summarized by Polgar and Promadhat (1971), including the forced expiratory volume (FEV_{1.0}), peak expiratory flow rate, total lung capacity, vital capacity, functional residual capacity, and residual volume. The vital capacities are also very similar to those reported from the UK, e.g., by Strang (1959) and by Godfrey and his colleagues (1970). However, the values found by the latter authors for the residual volume and for the indices which are dependent on residual volume are all larger than those reported in the present paper and are also larger than the average values reported by Polgar and Promadhat (1971). The higher values may possibly be due to the thoracic gas volume at functional residual capacity and the expiratory reserve volumes being measured separately by Godfrey and others (1970). No comparable data appear to be available elsewhere for the inspiratory capacity and the expiratory reserve volume and there are few data reported for the FEV_{0.75}.

The data for the transfer factor by the single breath method are similar to those reported by Bucci, Cook, and Barrie (1961), who used the same method and posture, and slightly higher than those found for the single breath method by Baran and Englert (1968) and for the rebreathing method by DeMuth and Howatt (1965). The volume of blood in the lung capillaries in relation to height is also similar to that observed by Bucci and his colleagues but the calculated values for the diffusing capacity of the alveolar membrane in the present series are on average lower. The discrepancy, which is of the order of 30%, is almost exactly accounted for by the different values assumed in the two studies for the partition coefficient (λ) which is one of the components of the reaction rate of carbon monoxide with oxyhaemoglobin (respectively infinity and 2.5).

The present results support the use of an exponential and not a linear relationship on stature for expressing lung function data in children, but the evidence is inconclusive. The exponential method has the advantage of avoiding the need for an additional term to accommodate the changes in adolescence suggested by Dickman, Schmidt, and Gardner (1971). However, neither approach is adequate for describing the transition between adolescence and early adult life, for which there is need for serial data.

The present results show more clearly than most the differences in lung function between boys and girls. In the case of the lung volumes, the findings are similar to those of Geubelle and

Breny (1969), who also observed a sex difference for the vital capacity but not for the residual volume. In the present study, the difference extends to the forced expiratory volume but not to the peak expiratory flow rate, and to the transfer factor with its subdivisions but not to the K_{CO} . These findings may reflect the greater dependence on lung volume of the FEV than of the peak expiratory flow rate but additional factors are involved since, for example, the ratio FEV/VC and the ratio $FEV_{0.75}/FEV_{1.0}$ are both significantly higher in the girls than in the boys. The difference is consistent with the observation of Godfrey and his colleagues (1970) that the girls have the higher specific conductance. The information which is available is insufficient to identify the cause. The similarity for K_{CO} between the boys and girls shows that the difference in transfer factor and its subdivisions reflects the difference in size of the lungs in the two sexes (assuming that the proportion of the alveolar wall occupied by alveolar capillaries is the same for both). In addition, the ratio Dm/Vc is the same in boys and girls and not materially different from the value found in adults. This finding is evidence that the relationship of the diameters of the alveolar capillaries to the thickness of their walls is unaffected by growth. By contrast, the K_{CO} decreases during childhood which suggests that growth takes place in the interstices between the capillaries to a greater extent than in the gas-exchanging portion of the membrane.

The sex difference in lung function, with the possible partial exception of the expiratory reserve volume (see Fig. 2b), is apparent at the age of 8 years and, on a proportional basis, is relatively unaffected by growth. This sex difference is greatest for vital capacity, which is also determined in part by the extent to which the subject engages in active physical pursuits (Andrew, Becklake, Guleria, and Bates, 1972; Cotes *et al.*, 1973a; Weibel, 1972). In this respect the present children, who were mainly city dwellers, were not particularly athletic. But it was conspicuous from their responses to the questions that the boys appeared to be more active than the girls. In addition, their cardiac frequency during exercise at the oxygen uptake of 0.5 l min^{-1} , after standardizing for body muscle (Cotes *et al.*, 1973b), was significantly lower in the boys than in the girls (paper in preparation). This finding may possibly be due to psychological factors; alternatively, it lends support to the view that the boys were the more active and hence that their greater pulmonary capacity was to some extent culturally determined. Whether or not this is the full

explanation for the differences in lung function between boys and girls is an open question.

Meanwhile, the present data provide reference values, in healthy urban children in the UK, for those indices of lung function which are commonly measured in a routine lung function laboratory.

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APPENDIX 1

NUMERICAL VALUES FOR HEIGHT^{1,2}

Height	Height ^{1,2}	Height	Height ^{1,2}	Height	Height ^{1,2}
1·10	1·291	1·34	2·192	1·58	3·408
1·11	1·322	1·35	2·235	1·59	3·466
1·12	1·355	1·36	2·279	1·60	3·524
1·13	1·388	1·37	2·325	1·61	3·583
1·14	1·421	1·38	2·371	1·62	3·643
1·15	1·454	1·39	2·416	1·63	3·704
1·16	1·489	1·40	2·463	1·64	3·764
1·17	1·524	1·41	2·511	1·65	3·827
1·18	1·559	1·42	2·560	1·66	3·890
1·19	1·593	1·43	2·607	1·67	3·952
1·20	1·630	1·44	2·658	1·68	4·017
1·21	1·666	1·45	2·708	1·69	4·082
1·22	1·704	1·46	2·758	1·70	4·145
1·23	1·742	1·47	2·808	1·71	4·211
1·24	1·779	1·48	2·861	1·72	4·277
1·25	1·819	1·49	2·912	1·73	4·343
1·26	1·858	1·50	2·964	1·74	4·411
1·27	1·898	1·51	3·018	1·75	4·479
1·28	1·937	1·52	3·070	1·76	4·548
1·29	1·979	1·53	3·126	1·77	4·619
1·30	2·019	1·54	3·179	1·78	4·689
1·31	2·063	1·55	3·236	1·79	4·762
1·32	2·105	1·56	3·293	1·80	4·833
1·33	2·148	1·57	3·350		