STUDIES OF LUNG FUNCTION IN CHILDREN

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During recent years research in pulmonary physiology has increased our knowledge of pulmonary function and improved methods of measurement to the point where they can be employed in elucidating the problems of pulmonary disease.

Yet very few studies have been performed in children. One of the main reasons put forward is that the necessary co-operation for tests of this kind cannot be obtained. In our experience this is untrue in the majority of children of seven years and over; below this age special methods require to be developed and little progress has been made except in the case of newborn infants in whom the whole body plethysmograph designed by Cross⁵ has been used to measure ventilation. Another reason is that obvious examples of pulmonary insufficiency are thought to be rare in children; yet during an asthmatic attack a child is frequently cyanosed and has severe ventilatory difficulty, and infants with pneumonia often show signs of marked pulmonary insufficiency. Oxygen tents are in everyday use in the medical treatment of children but little is known about the blood gases in the conditions concerned. Yet this information is likely to be at least as important as knowledge of the blood urea in renal disease. Morrison¹⁷ estimated the capillary blood oxygen content of babies with 'bronchiolitis' but there is no corresponding work on carbon-dioxide tensions.

A number of investigators, however, are making contributions to our knowledge of lung function in children. Kennedy *et al.*^{13, 14, 15} have studied the ventilatory capacity of normal children and of children with asthma; Engstrom *et al.*⁷ the static lung volumes, and Helliesen *et al.*¹² the mechanical properties of the lungs of normal children.

It is against this background we have attempted certain simple functional measurements in children. Our interest has first centred on normal children and on children with asthma and bronchiectasis and the work considered in this paper deals with this. In the future we hope to deepen

this field and to extend our studies to younger children and infants, especially to the states of acute pulmonary insufficiency which they may develop.

Methods of Study

It is convenient to consider the function of the lungs in two main ways—ventilation and gas exchange. Ventilation is the process by which alveolar gas is exchanged with the atmosphere so that gradients are maintained for oxygen and carbon dioxide between alveolar gas and pulmonary capillary blood. Gas exchange is a process which is dependent on the diffusion of oxygen and carbon dioxide across the alveolar capillary membrane.

Ventilation is dependent on the neuromuscular apparatus which expands the chest and the mechanical properties of the chest wall, the lungs and the airways. Gas exchange depends on the size, thickness, and possibly the composition of the alveolar-capillary membrane, and also on the relative distributions of ventilation and blood flow in the lungs. Inequalities in this distribution (ventilation-perfusion ratios) in different parts of the lung result in arterial desaturation even when other functions are normal.

In these initial studies it was decided to choose methods which would indicate abnormalities of either 'ventilation' or 'gas exchange', further studies being necessary to define the exact nature of these abnormalities.

Ventilatory Capacity

The measurement of the maximum volume of gas which an individual can ventilate in a fixed time has been employed as a measurement of ventilatory function for many years. This is termed the Maximum Breathing Capacity and it can be measured by requesting the subject to breathe as hard as possible through a valve box into a Douglas bag for 15 seconds. The result is expressed in litres per min. This is an exhausting procedure and the results are very dependent on the co-operation of the patient and on the rate of

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breathing which he chooses or which is chosen for him when the test is performed to a metronome.

During the past ten years this test has been gradually replaced by a single breath test in which a timed portion of the forced vital capacity is used to express the ventilatory function^{23, 10}. The original justification for this procedure was that the fraction of the forced vital capacity expelled in the first second represented that part of it which was actually used (or the tidal volume) during the performance of the maximum breathing capacity at a rate of 30 per minute. The volume after 0.75 seconds would be the tidal volume at the rate of 40 per minute and so on. In fact, the relationships are more complex than this as the times taken for inspiration and expiration are different and the position of the chest on inspiration varies at different rates of breathing.³ Nevertheless, a very good correlation exists between the direct maximum breathing capacity and the timed fraction of a forced expiration.¹⁰ For the reasons stated the factor by which the timed fraction must be multiplied in order to predict the maximum breathing capacity is different from that originally envisaged. For example, the one second volume should be multiplied by 37.5⁴ for prediction of M.B.C. There is, of course, no special merit in multiplying these results by any factor except that the normal values for maximum breathing capacity are better known in adults. In children this does not apply and we have avoided the practice.

The timed fraction of the forced vital capacity is now termed the Forced Expiratory Volume (F.E.V.) and the time referred to is indicated in seconds as a suffix, e.g. (F.E.V. 1.0, F.E.V. 0.75, etc.).¹¹ There is also fairly general agreement that the one second value (F.E.V. 1.0) is a satisfactory simple and valid measurement.

Procedure for Measurement of F.E.V. 1.0

A number of methods are available. We have used a spirometer with a light aluminium bell similar to that described by Bernstein, D'Silva and Mendel² recording on a drum moving at 2 cms. per second. The child's nose was obstructed with a clip and he was asked to take in a maximum breath and then, applying his lips around a straight plastic tube, to breathe out as far and as fast as possible. This produced a tracing of expired volume on time on the kymograph similar to that in Fig. 1. A competitive spirit was easily aroused and after a number of practice attempts, very consistent readings were obtained, 95% of individual readings of the F.E.V. 1.0 being within 4% of the individual mean values. The tracing was analysed into the F.E.V. 1.0 marked by a bar in Fig. 1, and the Forced Vital Capacity (F.V.C.) which is the full height of the tracing. The shape

Spirogram of NORMAL CHILD. A.R.
height 53 inches

FIG. 1.—The Forced Vital Capacity is represented by the total height of the tracing and the Forced Expiratory Volume in one second as the vertical distance between the upper base line and the mark at one second.

of the tracing also is significant and this can be expressed as a ratio of the F.E.V. 1.0 to the F.V.C.

$$\text{or F.E.V. \% , i.e. } \frac{\text{F.E.V.}}{\text{F.V.C.}} \times 100.$$

Diffusing Capacity

The uptake of oxygen by the lungs is dependent on the diffusing capacity and on the distribution of ventilation-perfusion ratios of the lungs. Complex methods which analyse these factors have been devised by Riley and his co-workers.^{6, 19, 20} These require a knowledge of mixed venous and arterial oxygen tensions with the subject breathing two different oxygen mixtures. West *et al*²⁴ have devised a single breath method for measuring inequalities of ventilation perfusion ratios but this requires a mass spectrometer for the rapid simultaneous analysis of expired gas tensions of oxygen and carbon dioxide.

A simpler approach to the gas exchange function can be achieved by the measurement of the diffusing capacity for carbon monoxide although there are many inherent difficulties in the interpretations of this measurement. Since the early work of the Kroghs,¹⁶ a number of workers have employed low concentrations of this gas for the measurement of pulmonary diffusing capacity. Carbon monoxide has a marked affinity for haemoglobin (210 times that of oxygen), so that in low

concentrations it is taken up avidly by red cells in the pulmonary capillary blood. For this reason the tension of this gas remains virtually zero in the pulmonary capillary plasma and may be ignored in computing the partial pressure difference of the gas between alveoli and blood. Carbon monoxide has the advantage that it can be simply and accurately measured by modern physical methods. The requirements for the measurements are, therefore, reduced to a knowledge of the uptake of carbon monoxide over a fixed time interval and the mean partial pressure of alveolar carbon monoxide. The main difficulty arises in arriving at a valid figure for mean alveolar carbon monoxide tension. Filley *et al.*⁸ arrived at this by measuring the physiological dead-space using arterial CO_2 tension as representing mean alveolar CO_2 tension. Ogilvie *et al.*¹⁸ have devised a timed breath-holding method which enables a more exact estimate of the mean alveolar carbon monoxide tension. This requires preliminary estimation of the functional residual capacity (F.R.C.) and an accurately timed period of breath-holding. The simplest available method is one of those described by Bates¹ which relies on an end-tidal sample as representative of alveolar gas, carbon monoxide uptake being measured during a steady state. This has the disadvantage that when inequalities of ventilation exist the end-tidal sample will not be truly representative of the mean alveolar gas tensions, the underventilated areas being poorly represented in the sample. In spite of this disadvantage, the method has the great merit of simplicity and is easily applicable to children since it requires neither timed breath-holding nor arterial puncture. For these reasons this method was used in our studies.

For a full discussion of the factors involved in measuring diffusing capacity for carbon monoxide the reader is referred to the paper by Forster, Fowler, Bates and Van Lingen.⁹

From the measurement of diffusing capacity for carbon monoxide (D.CO) a figure can be derived for the diffusing capacity for oxygen (D.O_2) which is the gas of physiological interest. The diffusion velocities of two gases are related directly to the ratio of their solubilities and inversely to the ratio of the square roots of their molecular weights. The diffusing capacity of the lung for these gases can be regarded as similarly related so that $\text{D.O}_2 = \text{D.CO} \times 1.23$.¹⁶

Method for Measuring D.CO .

In our studies the following modification of Bates's¹ method was used. The child sat at a table and breathed through a valve box from a polythene bag containing a prepared mixture of 0.1% CO in air. After a settling-down period

REGRESSION of $\text{FEV}_{1.0}$ on HEIGHT CUBED with confidence intervals of two standard deviations
 $\text{FEV}_{1.0} = 0.000116 \text{ Ht}^3 + 0.11$

FIG. 2.—Results of F.E.V. 1.0 in 418 healthy school children.

to allow for equilibration in the lungs and for clearing the dead space of the apparatus, the expired gas was collected in a second bag for a period of one minute by a stop-watch. Simultaneously, the last portion of each expirate was removed by an Otis-Rahn end-tidal sampler to a third small bag. At the end of the procedure, the concentrations of CO in the expired and end-tidal samples were measured using an infra-red gas analyser, and the volume of the expired gas measured by passing it through a gas meter. The minute ventilation was this volume plus the volume of the samples passed into the analyser. The diffusing capacity for CO was calculated as the uptake of CO in one minute per mm. Hg. of alveolar CO tension according to $V (\text{FI}-\text{FE})$

the expression $\frac{\text{FET} (\text{B}-47)}{\text{FET} (\text{B}-47)}$ where V is minute ventilation and FI, FE and FET are fractions of CO in inspired, expired, and end-tidal gas, and B is barometric pressure. Each child was tested twice and the results expressed as a mean of the two readings.

Results—Ventilatory Capacity
 Normal Values

The F.E.V. 1.0 and F.V.C. of 418 healthy school children between 7 and 18 years were measured.²¹ There were equal numbers of girls and boys. F.E.V. 1.0 was correlated better with the standing height than with the weight, surface

FIG. 3.—Superimposed spirogram tracings of 4 children of equal height, demonstrating types of abnormal patterns (see text).

area, or age, and the results were presented as a regression on the height cubed when the relationship was linear, and the coefficient of variation between individuals was 9% (Fig. 2). The height is a satisfactory standard for comparison between normals and children with chest disease because this is much less frequently abnormal, in these conditions, than weight or surface area, and also less variable from time to time. Nor is there any difference between the F.E.V. 1.0 of normal boys and girls when the height is used as a reference. The F.V.C. was presented in tabular form for height. The shape of the spirometers obtained at different ages was very consistent, in children of differing size the mean F.E.V.% in boys being 84.6% and in girls 88.6%. The higher F.E.V.% in girls was due to their having consistently slightly lower values of F.V.C. than the boys and this was thought to be due to the unwillingness of girls to expel the last part of their vital capacity. This slight difference in co-operation did not affect the results for F.E.V. 1.0.

Abnormal Patterns in Chest Disease

Fig. 3 shows the types of abnormal tracings obtained. There were obviously marked reductions of F.E.V. 1.0 in these patients and also marked differences in the shapes of the curves obtained. The child with pulmonary haemosiderosis had a lesion of a restrictive type which limited the extent of movement of the lungs but not the rate of movement so that the spirogram is very small, but of a normal shape and the F.E.V.% is normal. The children with asthma had a lesion which restricted the rate of movement of the chest so that the F.V.C. was reduced much less than the F.E.V. 1.0. This lesion was presumably due to bronchial obstruction and in these children the F.E.V.% was much lower than normal. These patterns have been described by Thompson and

FIG. 4.—Pooled results of F.E.V. 1.0, as a percentage of mean normal value for height, compared with physical signs on auscultation: 15 patients 202 readings. The circles are mean values and the vertical lines represent two standard deviations. The differences between the means are all significant at the 5% level.

Hugh-Jones.²² They are adequately expressed in terms of F.E.V.% and they give an indication of the cause of ventilatory impairment.

Asthma

Twenty children with asthma were examined at regular intervals (14 of them every fortnight) for six months. Serious abnormalities of ventilatory capacity were found, the tracings obtained being similar to C and D in Fig. 3. When the results were pooled, expressed as a percentage of normal for height and compared with simultaneously recorded clinical factors such as physical signs on auscultation, dyspnoea, and days since the last asthmatic attack, a satisfactory discrimination on the basis of F.E.V. 1.0 was observed between these categories. Fig. 4 demonstrates this for physical signs. At the same time, there was a marked overlap so that individual readings were not predictable from clinical signs. This was due to the fact that marked differences existed between the results in individual children with asthma and that in most of the seriously affected children ventilatory abnormalities persisted between the episodes of overt illness. Typical examples of this state are shown in Fig. 5. The value of measuring F.E.V. 1.0 in asthma was greatest in detecting these subclinical states of ventilatory impairment. It was also found that during the successful treatment of an asthmatic child a degree of ventilatory impairment frequently persisted after the child was free from symptoms and signs. Even when the normal range of F.E.V. 1.0 was

FIG. 5.—Serial records of F.E.V. 1.0 in 3 children (with asthma). The top record is a child who was normal most of the time and the other two records show different degrees of persistent ventilatory impairment.

reached, the F.E.V.% tended to remain low. The child could not be regarded as entirely normal until the F.E.V. 1.0 and the F.E.V.% were normal, this being regarded as the point where the child had reached his individual normal values. We have found that a number of asthmatic children even at their best have some persisting bronchial obstruction.

Resulting in Bronchiectasis

Thirty-nine children with bronchiectasis were examined on a number of occasions. The results in this group are shown in Fig. 6 and compared with the normal range. Some impairment of ventilatory capacity was frequent in these children and in most of them the abnormality was persistent. As might be expected, there was less variation from time to time than in asthma and very severe ventilatory impairment was less common. In general, the pattern of the spirometry was of the type suggesting the presence of bronchial obstruction but in a few children there was a restrictive pattern or a mixed restrictive-obstructive pattern.

FIG. 6.—Results of F.E.V. 1.0 in 39 children with bronchiectasis. The mean and two standard deviations of the normal are shown as in Fig. 2. Each child with bronchiectasis is represented as a vertical line and each reading of the F.E.V. 1.0 as a horizontal mark on the lines.

The clinical signs in bronchiectasis, the child's general condition, his weight, and the radiological extent of the condition were all uncorrelated with the results for ventilatory capacity. The only obvious correlation found was that children with very diffuse signs on auscultation tended to have lower F.E.V. 1.0's.

It was concluded that the ventilatory impairment in bronchiectasis was usually due to an associated diffuse bronchitis which caused obstruction to bronchial air flow and that the presence or absence of this bronchitis was not usually obvious on clinical grounds.

Results—Diffusing Capacity

Normals

Seventy-nine normal children were examined. These were 'ward' normals in whom pulmonary and cardiac disease had been excluded on clinical grounds. A satisfactory correlation with height was obtained and the results are presented as a regression on height (Fig. 7). The coefficient of variation between children was 19%. In individual children the coefficient of variation between readings was 9%.

Asthma

The results were almost all within the normal

FIG. 7.—Results of Diffusing Capacity for CO in 79 normal children, 35 girls and 44 boys. $D.CO (ml/min/mm.Hg.) = 0.39 \times Ht. (inches) - 9.1$. Coefficient of variation between children = 19%.

FIG. 8.—Results of Diffusing Capacity for CO in 37 children with bronchiectasis compared with normal limits.

● idiopathic pulmonary haemosiderosis
□ fibrocystic disease of pancreas

FIG. 9.—Results of Diffusing Capacity for CO in two children with diffuse pulmonary conditions.

range, irrespective of the presence or absence of obvious bronchial obstruction at the time of testing.

Bronchiectasis

The results in 37 children are shown in Fig. 9. Most of them were within the normal range but there were a few slightly below it and the mean of the readings was significantly lower than normal. No definite correlation was found between low readings for diffusing capacity and the child's clinical condition.

Diffuse Pulmonary Lesions

Only two children with the diffuse pulmonary lesions classically associated with impaired diffusion in adults were examined (Fig. 10). One child with fibrocystic disease of the pancreas and severe pulmonary involvement had a normal diffusing capacity. One child with idiopathic pulmonary haemosiderosis had a severe impairment of diffusing capacity. Both of these findings were very consistent when tested on three separate occasions.

Discussion

Ventilatory Capacity

Measurements of ventilatory capacity have a bearing on our understanding and treatment of the conditions considered above. In asthmatics the most interesting observation is that abnormalities associated with obstruction to bronchial air-flow persist between attacks of overt wheezing. In many of these children the attacks can be regarded as exacerbations of a subacute state and not as isolated events. Under these circumstances treatment is likely to be most effective when

administered continuously over long periods and it is false to imagine that all is well when the individual asthmatic attack is over. The treatment can be regarded as fully successful only when the F.E.V. 1.0, the F.V.C. and the F.E.V.% are normal for the child's size. The fate of children who have prolonged periods of bronchial obstruction is unknown but it is obviously possible that some of them may develop permanent pulmonary damage from this. It will require prolonged observation to investigate this possibility.

In bronchiectasis, ventilatory impairment must be due to diffuse disease associated either with bronchial obstruction or with pulmonary fibrosis or both. Probably bronchial obstruction is mainly responsible and it is an important fact that these changes are unlikely to be caused by localized disease and they may be taken therefore, as an indication of the diffuseness of the condition. This may be an important factor in deciding suitability for surgical treatment. Whitwell²⁵ has shown

that areas of lung which appear normal on bronchography are frequently as seriously damaged as areas with dilated bronchi, so that the bronchogram can prove an unreliable guide to the extent of the condition. Most of the poorer results of surgery can certainly be attributed to the persistence of abnormal areas and it is doubtful if surgery is justified at the present time unless the whole of the diseased lung can be excised.

Diffusing Capacity

Our experience shows that a simple method of measuring diffusing capacity is practicable in children, and the normal limits have been defined. At least one example of a severe diffusion defect has been detected and there will doubtless prove to be some others. These, however, are likely to be rare and because of this, the measurement of diffusing capacity will have only a very limited application in children. The finding of lower than normal values in bronchiectasis is not particularly helpful as the defects are slight. They may be, in fact, due to inequalities of ventilation and blood-flow, rather than to impairment of diffusion as usually understood. Any steady state method for measuring diffusing capacity will be affected by this even when no obstacle to diffusion exists in any individual part of the lung.⁹ Bronchiectasis is often diffuse and patchy and might be expected to be associated with these inequalities. An investigation of this possibility might be rewarding.

Conclusions

Measurements of ventilatory capacity are useful and practicable in children. Measurements of pulmonary diffusing capacity are practicable but

of limited usefulness. A great deal of work still remains to be done in extending these investigations to states of pulmonary insufficiency in acute respiratory disease in young children.

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