Spirometric studies in children

THESIS

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MARGARET

SPIROMETRIC STUDIES IN CHILDREN

With Special Reference to Asthma

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PART 1

CHAPTER 1

"Man is living longer due to his escape from his acute infections only to fall prey to a wide variety of functional disturbances"

Burgess L. Gordon

Diseases of the lungs, such as chronic bronchitis and emphysema, and their circulatory complications are now responsible for an increasing amount of invalidism and mortality in the adult. Although many factors, such as air pollution, occupation and smoking, play an important role in their pathogenesis, these diseases may also represent degenerative or infective sequelae of antecedent respiratory diseases, many of which may have occurred in childhood. One can only speculate whether children really "outgrow" attacks of "asthma" or chronic respiratory infection, or whether these diseases lie dormant in a latent and subclinical form only to harass their victim in later life with unexplained episodes of dyspnoea, cough and expectoration.

"Asthma" illustrates this problem. It occurs in subjects who have an over-excitable mucosa and musculature of the bronchial tree. The condition is characterised by a recurrent cough and a wheezing type of dyspnoea in which most difficulty appears to occur during expiration. It thus represents a "non-specific" reaction occurring in a wide variety of diseases and as a reaction to many factors such as allergens, infections, reflex physical and psychic stimuli that have no effect usually on normal subjects.

The clinical course of asthma in childhood is surrounded by as much controversy and uncertainty as is its incidence (Dees, 1957) and Osler's aphorism that "the asthmatic pants on to a ripe old age" has been disproved in the United Kingdom by Williams (1953) and in the United States of America by Dees (1957).

Opinions on the natural history of the condition vary greatly, some workers believing that nearly all children can become free of asthma by about the age of 15 years (Rackemann and Edwards, 1952), others maintaining that few ever lose the affliction (Fontana, 1952; Ryssing, 1959).

The same controversy surrounds chronic respiratory infections in childhood. Furthermore, functional impairment is often only recognised when the disease processes have caused disturbances which have become extensively, even irreversibly, established.

These conditions therefore pose important problems for the clinician, both in the evaluation of disability and the immediate and longitudinal assessment of pulmonary disease.

At the present time this assessment in childhood is largely dependent on the history and physical examination, supplemented by radiological investigation of the chest. However, these methods alone are in many ways incomplete and unsatisfactory and the difficulty of assessing the severity of asthma by these three means is appreciable.

The history often covers a period of weeks or months and is based on reports given by the mother or the child. These accounts of the intensity of symptoms depend largely on memory influenced by such factors as the emotional outlook of the mother or child, the relationship between mother, child and doctor, psychological and social factors operating at home and the threshold of "wheezing" for the child; so that what may appear to be a catastrophic illness to one may be borne with Spartan indifference by another (Lowell et al., 1955). Answers to questions on the amount and effect of medication used by the patient are open to the same criticisms, and the importance attached to any answer depends largely on the physician's ability to weigh correctly the descriptive terms used by the patient and his ability to record these correctly.

Dyspnoea, the major symptom of ventilatory insufficiency, is one of the most difficult to evaluate clinically. It may arise because of true impairment of ventilatory function, or from the increased awareness of normal exercise ventilation, or from a combination of these two factors. Because of the wide variation in the threshold of onset of this symptom in different patients it is possible for a patient to have severe respiratory disability with no pulmonary insufficiency, or vice versa.

The interpretation of the physical signs may be even more difficult than that of the symptoms. The intensity and number of sibilant rhonchi heard on auscultation are not only difficult to express quantitatively, but also depend on the degree of ventilation. They are increased when ventilation is increased for any reason, including improvement in ventilatory function for example after a severe attack of asthma, and they decrease when the minute volume falls.

Whitfield et al. (1951) assessed 52 cases of emphysema radiologically. They came to the conclusion that although radiography can give evidence of the presence of emphysema and may be valuable in ascertaining its cause, it gives a less accurate assessment of the severity than clinical or spirometric examination.

The objective assessment of the disability resulting from common chest diseases of children and their reversibility, the results of treatment and the prognosis of the development of complications such as hypertrophic emphysema in later years, present therefore a problem of great practical importance. Such an objective assessment is at present rarely attempted and can only be carried out in specialised centres.

In an attempt to remedy this need for objective assessment I have applied the Forced Expiratory Volume (F.E.V.) and Forced Vital Capacity (F.V.C.) test to children.

This thesis is a report on the value and limitations of the practical application of the Forced Expiratory Volume and Forced Vital Capacity test in children aged from 7 to 16 years.

The first part deals with a review of the literature on lung function and evolution of the Forced Expiratory Volume and Forced Vital Capacity test. The method and apparatus used in the test, the establishment of "normal values", the correlation of these values and certain anthropometric data, the establishment of prediction formulae for normal values, a study of the effect of factors such as sex, "learning" and repeatability, posture, daily and day-to-day variations, and the inhalation of isoprenaline on these normal values are reported.

The second part deals with the practical application of the test in various pathological conditions affecting the cardio-respiratory system. The effect of respiratory disorders on ventilatory function is reported and an attempt is made to assess the effect of management, medical treatment and prognosis of a respiratory disorder at any given stage of that disorder acknowledging always that the complete evaluation of a patient requires more than laboratory tests.

CHAPTER 2

The function of the lungs has been defined by Donald (1953) as the maintenance in the arterial blood of normal and nearly constant oxygen and carbon-dioxide contents and tensions, under all physiological conditions, and doing so without causing any undue sensation of ventilatory discomfort or any adverse effects on the heart or other organs.

The respiratory system can be regarded as a supply channel (Dornhorst, 1952) and, from the point of view of clinical testing, this channel is divisible into three zones (Arnott, 1956; McKerrow, 1953).

1. The passage from the mouth to the alveoli, flow along which can be regarded as the Ventilatory Function or "bellows function" of the lung. It is therefore the mechanical component of lung function. The essential features of the forces that play a part in this Ventilatory Function have been summarised by McKerrow in the following Table -

I. The essential features of inspiration

- Force assisting
  - muscular component
    - chest wall
    - diaphragm
  - elastic component - chest wall elasticity

- Force opposing
  - viscous component
    - tissue resistance
    - air resistance
  - elastic component - lung elasticity

II. The essential features of expiration

- Force assisting
  - muscular component - usually absent
  - elastic component - lung elasticity

- Force opposing
  - viscous component
    - tissue resistance
    - air resistance
  - elastic component - chest wall elasticity

Under normal conditions inspiration is an active muscular movement. On the other hand, as soon as inspiration is completed active movement ceases, the thorax relaxes and drops back to its original position, not only because of the effect of gravity and relaxation of the muscles, but also because of the elasticity inherent in the pulmonary parenchyma. This elasticity tends to pull the lung back to its original size.

The calibre of the smaller bronchi and bronchioli changes during the act of breathing. In inspiration these tubes elongate and dilate. In expiration they shorten and constrict. While this action is insignificant in normal breathing, it is extremely important where there is bronchiolar narrowing due to causes such as oedema, bronchospasm and secretions.

2. The mechanisms of diffusion from the alveolar gas phase through the alveolar wall into the capillary blood stream - the Diffusion Function.
3. The haemodynamics of pulmonary capillary blood flow - the Circulatory Function.

Although the lungs must be capable of effective diffusion and be supplied with adequate pulmonary blood flow to function properly under varying conditions of stress, it has become more apparent during recent years that many respiratory diseases are disabling because they diminish the effective ventilatory capacity of the lung.

The body has only a limited number of reactive possibilities in disease and the same picture of ventilatory impairment may be caused by different clinical entities.

The principal cause of disability in asthma, and to a large extent in emphysema, is a disturbance of the ventilatory function.

Ventilatory function may also be impaired by any loss of functioning lung (e.g. in consolidation, collapse, resection and pneumothorax), pulmonary congestion (e.g. heart failure), pulmonary fibrosis, airway obstruction due to any cause, muscular weakness (e.g. poliomyelitis), rigidity of the thoracic cage (e.g. ankylosing spondylitis).

Ventilation consists of the mass movement of air from the atmosphere to the alveoli and involves the "bellows-action" of the chest and the distribution of air in the lungs. The clinical signs of ventilation, both degree of movement of the chest and rate of respiration, are frequently deceiving as an indication of the volume of air actually breathed by the subject. Furthermore, ventilation is influenced by psychic and emotional factors, and wide variations unrelated to any abnormalities of the cardio-respiratory system are encountered.

A large number of tests, both simple and complicated, have been described for the measuring of ventilatory function, some measuring overall mechanical function, others measuring its different components. This latter group includes measurement of the elastic properties of the lungs, expressed as compliance - defined as the volume change brought about by one centimetre of water pressure - and mechanical resistance (viscous component) which measures the amount of pressure necessary to obtain a certain flow rate. The overall response of the lungs can also be measured in terms of the mechanical work done per minute in moving the lungs. These tests require specialised techniques and costly equipment, confining these analyses to research laboratories and specialised centres. Gaensler (1955) reviewed the available methods for the analysis of the different components of mechanical function and McIlroy and Eldridge (1956) and Heaf and Prime (1956), the measurement of the mechanical properties of the lungs by simplified methods.

The clinician needs a test which does not require a trained staff for its application or interpretation, and which can be used on sick people. The test must give some objective indication of the relative efficiency of the diseased lungs and be of some help in evaluating the management, treatment and prognosis of the disease. The paediatrician, furthermore, needs a test which is easy to explain and demonstrate, and not too difficult or distressing for a child to perform. It must be of sufficient interest and short duration to attract and hold the child's attention and co-operation. It must show no "learning effect" in subsequent performances and comparable results must be obtained on repeated testing.

No single test used at present fulfils all these requirements or is capable of giving reliable information under all circumstances.

Of the simple tests available for the measurement of overall mechanical lung function the Forced Expiratory Volume and Forced Vital Capacity Test comes nearest to complying with these requirements. This test was developed because of the disadvantages of the Vital

Capacity Test and the Maximum Breathing Capacity Test, which are the other two simple tests available for the measurement of ventilatory function.

The multiplicity of terms which are in use has undoubtedly confused clinicians and delayed the widespread adoption of simple tests of ventilatory function in clinical practice. The terminology used in this thesis is based on a report to the Thoracic Society on the terminology for measurement of ventilatory capacity by Gandevia and Hugh-Jones (1957). The terminology has been recommended for general use in the United Kingdom.

(FIG. 1)

The Table reproduced from their article summarises the recommended terms, their abbreviations and their commonly used synonyms.

1. Forced Vital Capacity: the forced vital capacity is the maximum volume of gas which can be expired following a maximum inspiration, the expiratory phase being accomplished rapidly, and as forcibly as possible. Abbreviation : F.V.C.

2. Forced Expiratory Volume (over a stated time interval) : the forced expiratory volume is that volume of gas expired between two stated time

intervals during the performance of the forced vital capacity test. Abbreviation: F.E.V. The time intervals are indicated by a subscript. Where the first time interval is zero, only the second time is stated. Thus F.E.V.$_{0.25 - 0.75}$ and F.E.V.$_{1.0}$ refer respectively to the volume expired during a forcible expiration from the end of the first 0.25 seconds to the end of 0.75 seconds and to the volume expired during the first one second.

Two methods are available for the measurement of the F.V.C. and F.E.V. values. Gaensler (1951a) described a method using an ordinary spirometer to which was added an attachment which accurately recorded both the total F.V.C. and any volume expired during a pre-set interval of .1 to 10 seconds, thus giving the value directly on a dial. Kennedy (1953a) recorded the spirographic tracing of the F.V.C. on a fast moving kymograph. This is termed the Forced Expiratory Spirogram. Abbreviation: F.E.S. A similar tracing of the Forced Inspiratory Vital Capacity is termed the Forced Inspiratory Spirogram. Abbreviation: F.I.S. Details and the form of the F.V.C. and F.I.V.C. became then clearly visible. This method has the advantage that the F.V.C. is recorded graphically, the volume expired in any desired time interval being calculated from a single performance. The spirograms provide a permanent record which can easily be filed and compared quantitatively and qualitatively with later tracings. This method thus has several advantages over that of Gaensler, though it is perhaps more cumbersome.

3. Vital Capacity. The vital capacity is the maximum volume of gas which, following a maximum inspiration, can be measured during an expiration which is not rapid or forced. Abbreviation: V.C.

   When the forced expiratory volume is expressed as a percentage of the "vital capacity" the method of measuring the "vital capacity" is indicated by the use of F.V.C. or V.C. as defined above, to describe the denominator. Abbreviation: F.E.V. %

4. Maximum Breathing Capacity. The maximum breathing capacity is the maximum volume of air that can be breathed per minute. It can be measured directly, under various conditions, or alternatively it can be estimated indirectly by prediction from spirographic tracings and from the F.E.V. at certain

time intervals. Abbreviation: M.B.C.

(a) Maximum Voluntary Ventilation Test (M.V.V.) which gives a direct measurement of the M.B.C., is expressed in litres per minute and is the maximum volume of gas which the subject breathes when breathing as deeply and as quickly as possible or when breathing as deeply as possible at a controlled frequency, both tests being performed over a specified time.

(b) The Indirect M.B.C. expressed in litres per minute is the maximum volume of gas which the subject can breathe per minute as predicted from measurements of either the inspiratory or expiratory spirogram, or both.

For the purposes of discussion in this thesis the term M.B.C. is used where it has been determined by a direct measurement, without qualifying the type of test carried out. Abbreviations of the recommended terms are used in the remainder of the thesis.

The F.E.V. is a more reproducible value than the F.V.C. and the variability of the results of the F.E.V. in a given normal individual is small compared with the range between normal and abnormal and it thus has excellent discrimination and sensitivity.

The results of the F.E.V. and F.V.C. test are affected by changes of airflow and tissue resistances, compliance of the chest and lung, muscular force and the size of the lungs. Reduced absolute values for the F.V.C. and F.E.V. are brought about therefore by any factor which imposes a check on the speed of expiration. They are considerably reduced by a change in the "bellows-action" of the chest, whether this be due to obstruction in the airways or to restriction in the ease of movement of the chest itself. These F.V.C. and F.E.V. values do not correlate precisely with the ordinary vital capacity values, for it may be possible for those whose total lung capacity is reduced, to use their small inspiratory volume at a maximal level of ventilation. On the other hand, those with normal capacity whose airway is obstructed, may fail to yield a normal maximum value for ventilation because of the reduction in rate of airflow, particularly in expiration. Because a high residual volume of air creates a mechanical disadvantage to ventilation at speed, the existence of such a change, irrespective of obstruction, may also reduce the F.V.C. and F.E.V. values.

Because this test requires less co-operation and is less tiring than the M.B.C. test it is more suitable for use in disabled patients and children. Furthermore, if a patient has normal F.E.V. values, manifestations of impairment of mechanical function are unlikely to be found by other, more complicated, tests. It is now widely used in Chest Hospitals and by those interested in diseases of the chest in adults, as the most practical and helpful test available for the assessment of ventilatory function.

A review of the literature at the time this project was started failed to reveal any publications on "normal" values for the F.V.C. and F.E.V. in children, although Kennedy and Thursby-Pelham (1956) had reported the effect of oral cortisone on the ventilatory function of children with chronic asthma. Ventilatory function was assessed by predicting the Indirect M.B.C. from the $F.E.V._{.75}$ multiplied by 40 and termed the $E.F.R.^{40}$ by Kennedy (1953a). Kennedy et al. (1957) have subsequently published "normal" values for $E.F.R.^{40}$ ($F.E.V._{.75} \times 40$) for boys between the ages of 8 and 14 years.

CHAPTER 3

EVOLUTION OF THE F.E.V. and F.V.C. TEST AS A TEST FOR THE MEASUREMENT OF VENTILATORY FUNCTION

Hippocrates and Plato believed blood was tempered in the lungs, which were placed near the heart "to keep it cool and in exact obedience". Galen (130-200 A.D.) thought the lungs expanded with the chest and thus air was drawn into them. Boyle (1627-1691) expressed the belief that the lungs became filled with air because the chest dilated. In 1628 Harvey published his first work on the circulation of blood, and in 1667 Hooke kept a dog alive by artificial respiration performed with bellows.

The first attempt to determine the volume of air taken into the lungs as a single breath was made by Borelli in 1679. Hales (1677-1761) later carried on the work, and concluded that the greatest volume of air that could be forced from the lungs after the deepest breath was about 220 cubic inches.

No standard instrument for accurate measurement of ventilatory capacities had been devised until Hutchinson (1846) introduced the first objective and scientific method by measurement of the subject's vital capacity. He designed the first spirometer and made a large series of observations on the V.C. in approximately 3,000 people, in health and illness. He considered the standing height to be the principal factor determining the V.C. and calculated "normal" values based mainly on this measurement. He found that weight, the degree of mobility of the chest, body position, age, sex and occupation all influenced the vital capacity, but that the sitting height and the circumference of the chest did not.

Much discussion and observation took place in the following 10 years, as to what should be taken into account when determining "normal" standards and what factors influenced V.C. values. Fabius (1853) for instance noted that taking food, and constipation, diminished the V.C. and stated that the administration of 1 ounce of lenitive of electuary increased the V.C. of his assistant by 250 ml. Flack (1921) reviewed the literature on the V.C. and the principal factors which determine it, and mentioned the work of Simon (1848), Fabius (1853), Wintrich (1854), Schneevogt (1854), Arnold (1855) and later, Bohr (1907). Many others have since written on the subject - Peabody and Wentworth (1917), Dreyer (1919), West (1920) , Emerson and Green (1921), Wilson and Edwards (1921), Stewart (1922), Cripps et al. (1923), Myers (1925), Schlesinger (1934)

Robinson (1938), Wright (1946), Baldwin et al. (1948), Mills (1949), Wright et al. (1949), Bateman (1950), Whitfield et al. (1951), Moore et al. (1951), Turner and McLean (1951), Morse et al. (1952), Ferris et al. (1952), Ferris and Smith (1953), Needham et al. (1954), Wade (1954), Jones (1955), Gilson et al. (1956), Kennedy et al. (1957), Michelson and Lowell (1958), Helliesen et al. (1958).

Although the vital capacity is easily measured, and has stood the test of time, it is a measurement of static lung capacity and correlates poorly with the dynamic ventilatory function performed by the lungs. It only measures the difference between two static volumes, namely the difference between maximal inspiration and maximal expiration and can therefore only measure volume defects in disease. It is not a valid test of mechanical function of the lung and subjects with severe respiratory disability often show large or normal vital capacities, though the slow forced expiration they use shows that much of the expired volume can be of little use to them when hyperventilation is necessary during exertion (McKerrow, 1953; Gilson and Hugh-Jones, 1949).

The V.C. is of practical use only if serial readings are made, the value of a single determination having been compared to that of a single blood-sugar estimation (Wright, 1950).

In an attempt to elaborate a dynamic test of ventilatory capacity, Hermannsen (1933) introduced the Maximum Breathing Capacity test. This measurement of dynamic capacity was extensively used after its introduction. It measures the volume of air that can be breathed in one minute.

The M.B.C. values vary according to age, sex and size of subject and the method of performing the test. Individual variation is large (Cournand et al., 1939; Dripps and Comroe, 1947; Baldwin et al.,1948). The M.B.C. is reduced by restriction of, or obstruction to, air circulation, and the maintenance of a large M.B.C. depends on the integrity of the "chest bellows", the tracheobronchial airways and the pulmonary tissues and their elastic properties. It can therefore be limited by chest wall abnormalities such as gross kyphosclerosis and paralysis of the diaphragm, obstruction to the airways as in asthma and obstructive emphysema, decrease in elasticity as in fibrosis and pulmonary congestion.

The M.B.C. test is established as a useful and reliable test of pulmonary function (Comroe, 1950; Gray et al., 1950; American Trudeau Soc. 1950) and may provide even more information when it is related to the V.C. (Gaensler, 1950a; 1951a). He compared the two volumes, each expressed as the percentage of the predicted normal value. The ratio of the percentage of the predicted M.B.C. to the percentage of the predicted vital capacity is called the "air velocity index", In normal patients, and in patients with restrictive insufficiency, this index is 1.0 or larger, whereas in patients with obstructive defects it is invariably less than 1.0. The index must be regarded in the light of absolute figures because an equal reduction of both volumes is not reflected by an abnormal air velocity index. The correlation between the maximal breathing capacity and the vital capacity is poor (Cournand et al., 1939; Comroe, 1951; Gaensler et al., 1951) and the disparity between the V.C. and M.B.C. in pathological states of the lung is widely recorded in the literature (Cournand and Richards, 1941; Baldwin, 1946; Baldwin et al. 1949; Gaensler, 1950b; Matheson et al., 1950; Lukas, 1951; Beale et al. 1952; Lukas and Plum, 1952; Braun et al., 1953).

In conditions with a low grade obstruction of the pulmonary airways this disparity becomes more manifest during the performance of the M.B.C. test, and although the M.B.C. may be greatly reduced, the V.C. may be observed to be normal, or nearly normal, in such cases.

In contrast Lukas and Plum (1952) noted while assessing pulmonary function in adults following acute poliomyelitis with respiratory paralysis, that the M.B.C. was below normal but relatively better preserved than the V.C. with which it correlated poorly.

Different methods for the M.B.C. estimation have been suggested; Kaltreider and McCann (1937) used a test requiring heavy exercise and Schmidt et al.(1938) one requiring the measurement of a single rapid breath in relation to time. All these methods have severe limitations. The method of Hermannsen (1934) is the most satisfactory. The subject connected to a spirometer, performs his maximum ventilatory effort, choosing his own depth and rate of respiration. This volume is recorded on a moving drum over a period of 15 seconds.

However, the values obtained for the M.B.C. vary according to the conditions under which the test is carried out and in particular with the rate of breathing at which it is performed. Values are therefore extremely variable and the discrepancies are due not only to the difference in the technique of performing the test but also the type of instrument used, the co-operation of the subject and the experience of the observer (McKerrow, 1953; Needham et al., 1955).

Much other criticism has been directed against the test. Kennedy (1953b) found in over 2,000 assessments of the M.B.C. that the method was fatiguing, time-consuming and also that a considerable learning factor had to be overcome by the subject. Simonin (1954) and Needham et al. (1955) stated that the test may cause a further spread, or exacerbation of infection in damaged lung tissue. Herxheimer (1952) stated that sustained maximum breathing may increase bronchospasm while Leuallen and Fowler (1955) thought the principal limitation of the test was that the subject's obstructive impairment tended to be under-estimated. Gaensler (1951a) stated that it measured both resistance and defects of stroke volume.

In the search for a simple dynamic test of ventilatory function, time relationships were included in determining the V.C. on the kymographic recordings by Barach (1938), Cournand et al. (1939) and Segal (1950). Gross (1943) also introduced a time relationship in his studies of the V.C. in cardiac and pulmonary disease. He measured the time required for full maximal expiration, divided the V.C. by that time, and termed the result the "expiratory velocity". An attempt was made to predict the M.B.C. from the V.C. or the volume of the V.C. expired per unit of time (Cournand et al. 1939). Gilson and Hugh-Jones (1949) used the whole V.C. to predict the M.B.C. Schmidt and Gaubatz (1938) measured the volumes in a single rapid and deep breath in relation to time.

Other workers used the F.E.V. for their M.B.C. prediction and the Table summarises the time intervals suggested by these different workers.

Table/

TABLE I

0.5 sec.	0.6 sec.	.75 sec.
Roche) Thivollet) 1949	D'Silva) Kazantzis) 1954	Kennedy 1950 1953 a Kennedy et al. 1957 Stuart-Harris) Handley) 1957

1 sec.	3.2 sec.	2 sec.
Tiffeneau) Pinelli) 1947 Tiffeneau et al. 1949 Gaensler 1951 a Roche) Thivollet) 1949 Hirdes) Van Veen) 1952 D'Silva) Kazantzis) 1954	Gaensler 1951	Needham et al 1955

The F.E.V. is measured either by taking a tracing on a fast kymograph of the movement of the spirometer bell during a F.V.C. test, from which the time and volume can be measured with a suitable scale (Kennedy, 1950; Kennedy, 1953) or by an automatic timing device (Gaensler, 1951a, 1951b).

The close correlation between the M.B.C. and

Indirect M.B.C. has been described by Gaensler (1951b), Kennedy (1953a), Motley (1953) and McKerrow (1953).

No standard time interval over which to measure the F.E.V. for the prediction of the Indirect M.B.C. has yet been adopted. Tiffeneau's (1948) procedure consists of multiplying the $F.E.V_1$ by 30. Kennedy (1953a) multiplied the $F.E.V._{.75}$ by 40. Cara (1953) multiplied the $F.E.V_I$ by 37.5. Data suggests however that a factor of 35 for the multiplication of the $F.E.V_I$ is approximately correct (Gandevia and Hugh-Jones, 1957).

Different time intervals over which absolute values for the F.E.V. should be measured have been used. Some of these have already been mentioned and it has been pointed out that emphasis was frequently placed on the relationship between the pattern of expiratory flow and the M.B.C. Leuallen and Fowler (1955) came to the conclusion that in adult patients with chronic bronchitis or emphysema the expiratory retardation was found to be more pronounced during the expulsion of the mid-part of the F.V.C. Gaensler (1951a) found that the $F.E.V_1$ gave the greatest contrast between normal subjects and those with asthma or emphysema. Hume and Gandevia (1957a) regarded the $F.E.V_1$ as comparable to the M.B.C. in its sensitivity to the influence of broncho-dilator drugs, both being more sensitive than the F.V.C. Other suggested time intervals include the F.E.V. $_{.5}$ (Miller et al. 1954), the time taken to expel 63% of the F.V.C. (D'Silva and Kazantzis, 1954), the F.E.V.$_{3}$ (Bell and Howell, 1955 and Pinkerton and van Metre, 1958) and the F.E.V. $_{.2}$ (Bell and Howell, 1955).

No standard time interval over which the F.E.V. should be measured has been laid down, although recently there has been some agreement that the F.E.V.$_{1}$ is appropriate for clinical purposes, and it is now widely used in adults not only in England but also in the United States of America and on the Continent (Gandevia and Hugh-Jones, 1957).

Improvement in the measured values of ventilatory function in response to a broncho-dilator drug, given orally, by inhalation or injection, is now widely used to indicate the presence of reversible bronchospasm (Rossier, 1949; Gilson and Hugh-Jones, 1955; Snider et al. 1955; Kennedy and Thursby-Pelham, 1956; Hume and Gandevia, 1957a, and Gandevia and Prime, 1957).

Gandevia and Prime (1957) examined the pressure-volume relationships during a rapid forced expiration in patients with broncho-spasm, before and after the administration of broncho-dilator drugs. They used a technique for measuring intraoesphageal pressures based on that described by Dornhorst and Leathart (1952) and measured and recorded gas volumes by means of a spirometer and kymograph. They concluded that the effect of broncho-dilator drugs was manifested not only by an increase in the value of the F.E.V. but also by a lowering of the peak and mean pressures achieved during delivery.

From the pactical and clinical viewpoint, measurements of the $F.E.V._1$ and $F.E.V._2$ during the F.V.C. test are sensitive indicators of changes in tissue and airway resistance in the lungs and nothing of clinical value can be gained by adding measurements of intrathoracic pressure to this simple observation.

It is common practice to express the F.E.V. as a percentage of the V.C. or the F.V.C. (Tiffeneau et al. 1949; Gaensler, 1951a; Pemberton and Flannagan, 1956). These workers found that in normal subjects the $F.E.V._1$ is greater than 70% of the F.V.C. whereas Leaullen and Fowler (1955) found that the $F.E.V._1$ was 72% in females and 65% in males. A fairly narrow range of between 70% - 85% for the $F.E.V._1$ is now generally accepted as normal in adults.

In subjects with a purely restrictive defect of ventilation (as in ankylosing spondylitis, some cases of pulmonary fibrosis, etc.) both the $F.E.V._1$ and the V.C. are reduced proportionately so that the $F.E.V._1$ still forms more than 70% of the V.C.

In subjects with an obstructive defect of ventilation (such as in asthma and emphysema) however, the $F.E.V._1$% may fall to very low levels - in the order of 30% - 50% (Gaensler, 1951a; Drutel and Dechoux, 1952).

A reduction of the $F.E.V._1$% implies obstruction to the airways and is found in both asthma and emphysema. It is held to be of importance as an index of the severity of the obstructive element of the disease. Dulfano et al. (1953) investigated the $F.E.V._1$ % in patients with chronic bronchial asthma during two phases of their disease - while free of subjective symptoms and during acute exacerbations. They, and also Lowell and Schiller (1953), reported that at low initial levels, the $F.E.V._1$% tends to remain constant after an inhalation of a bronchodilator aerosol, although the absolute values of the F.E.V. and F.V.C. were improved. Dulfano et al. (1953) suggested that the constancy of the ratio might indicate a "fixed state" of the bronchial tree in the symptom-free group. In patients during an acute exacerbation the ratio decreased after the attack was relieved by a broncho-dilator aerosol, because of the greater improvement of the F.V.C. compared with the $F.E.V._1$. They came to the conclusion that the ratio does not represent a valuable index of the degree of improvement of the asthmatic patient undergoing treatment, and suggested that the F.V.C., although subject to some criticism, may be employed as a guide to the overall improvement in these patients.

This work was based on sigle readings and Thomson and Hugh-Jones (1958) have recently discussed the value of the F.E.V.% when serial readings afe carried out. They have pointed out that during treatment in asthma the $F.E.V._{\%}$ tends to remain comtant until the V.C. value approaches what is presumably its normal value for that patient, and only after that as the $F.E.V._1$ increases further with treatment, does the $F.E.V._1\%$ reach its normal value of about 80%. In emphysema this disproportionate increase in the $F.E.V._1$ does not occur, so that the $F.E.V._1\%$ remains low despite continued treatment and initial benefit from an increase in the absolute F.E.V.$_1$. In a patient with asthma therefore a low value for the F.E.V.$_1$% suggests insufficient treatment or the presence of concurrent emphysema. Serial readings help to distinghish these two.

Furthermore, Thomson and Hugh-Jones (1958) could not agree with Cara and Sadoul (1953) who stated that a low percentage (25% - 55%) was in itself diagnostic of emphysema when taken on a single reading. If, when the F.V.C. is within normal range, the F.E.V.$_1$ reaches its normal value, then no further benefit can be expected from treatment.

Current views on the mechanism of expiratory obstruction in emphysema (Dayman, 1951; Mead and Whittenberger, 1953; Fry et al. 1954) indicate the reasons why the F.E.V. is such a useful test. Resistance to expiratory flow, in some degree in normal persons and to a greater degree in patients with pulmonary emphysema, increases in two ways. Firstly, as the volume of the lungs decreases with an accompanying reduction in elastic pulmonary tensions and in the diameters of the airways, and secondly as voluntary expiratory effort is increased. In the second phase there is an accompanying rapid development of a high pressure gradient between the alveoli and the airways. The testing procedure of maximally rapid and deep expiration emphasises the combined effect of these two obstructive forces (Leuallen and Fowler, 1955).

The advantages of the F.E.V. and F.V.C. test can be summarised as follows:

1. The test requires less co-operation and is less tiring than the M.B.C. test. It is therefore suitable for the assessment of ventilatory function in disabled people and children.
2. It is a repeatable test.
3. If a patient has normal values for the F.E.V. it is unlikely that manifestations of impairment of ventilatory function will be found by other more complicated tests.
4. The F.E.V. is a measure of that part of the F.V.C. which is of use to the subject for hyperventilation.
5. The test has excellent discrimination - that is, the variability of results in a given normal individual is small compared with the range between normal and abnormal.

6. The F.E.V. and M.B.C. tests are comparable in sensitivity to the influence of broncho-dilator drugs.
7. The shape of the F.V.C. spirogram can supply valuable information. In emphysema and asthma the initial flow rate is low and the spirogram long and drawn out. A change in the slope and shape of the spirogram after the use of broncho-dilator drugs in a patient with an abnormal spirogram may give some information on the reversibility of the underlying pathology.
8. The serial study of the values for the F.E.V. and F.V.C. may be of some help in differentiating between emphysema and insufficiently treated asthma.
9. The F.E.V. test may also be used as a guide in the management and prognosis of other cardio-respiratory illnesses.
10. The test may be used for the objective assessment of the value of different broncho-dilator drugs in a given individual.

CHAPTER 4

APPARATUS

Bernstein and Mendel (1951) have shown that the Knipping, Benedict-Roth and Tissot spirometers possess large recording errors due primarily to inertia of their moving parts. They found an error of up to 40% using a Benedict-Roth spirometer during hyperventilation due to oscillatory movement of the water in the bell. According to McKerrow (1953) an error of over 10% may be recorded during hyperventilation using a Tissot spirometer.

The ordinary Benedict-Roth type of spirometer is thus not suitable for ventilatory capacity tests (Arnott, 1956), whereas that described by Bernstein, D'Silva and Mendel (1952) has been shown to be of great value. This type of spirometer is now widely used in most hospitals and Research Centres in the United Kingdom. Kamener and Malkin (1957) built a spirometer of the Bernstein type and tested it for accuracy. With the bell only slightly submerged the volume recordings were correct to 2% and when deeply submerged the recordings were correct to 7%.

These findings were in accordance with those of Bernstein, D'Silva and Mendel (1952).

In a critical discussion of the Forced Vital Capacity spirogram, Bernstein (1954) showed that the new spirometer gave an accurate record of the curve, and that the smoothly changing slope found by D'Silva and Kazantzis (1954) which is always concave upwards was correct. The complicated curve as described by Kennedy (1953b)which has a straight portion followed by a sudden inflexion or subsequent region of undulations, is probably due to recording artéfacts produced by oscillations of the Knipping spirometer bell. These oscillations are caused by the fast initial air entry during the performance of the Forced Vital Capacity test.

Shephard (1956) re-examined the sources of error in the spirometer method of recording the Forced Vital Capacity, by simultaneously taking pneumotachographs and forced expiratory spirograms, direct recording of pressure fluctuations in the spirometer bell and detailed study of the wave form oscillations induced under static and dynamic conditions. The sources of error he found included failure to indicate the true starting point of the test, initiation of a more rapid respiratory acceleration than is found under conditions of minimal resistance, and an obscuring of the endpoint for the F.E.V. due to oscillations of the bell. Because of these possible errors, he favoured the pneumotachographic method of recording the F.V.C. Gilson (1957) in his lecture on lung function tests pointed out that in general the measurements of volume during forced expiration are not readily falsified by the type of apparatus used and it has been shown that the volume expelled in periods of 0.5 seconds and over, is the same whether recorded on a spirometer or integrated from the record of an inertia-free pneumotachograph. A spirometer similar to that described by Bernstein ét al. (1952) has been used in the present investigation. The apparatus mounted on a stainless steel trolley in shown in FIG.2. Because of the expected wide range of volumes in the children of 6 to 16 years whom I planned to measure, two or more spirometers of different dimensions would have been ideal equipment. However, the main consideration in this project was to try to establish the F.E.V. and F.V.C. test as a simple and effective aid to the clinician, which can be used in any hospital or consulting room. Under such conditions one spirometer for use in both adults and children is a more practical and economical proposition, although the possibility of some error in the accurate measurement of small volumes cannot be eliminated. Some support for the use of one spirometer has recently been put forward by Kennedy et al. (1957). They used a large spirometer for boys aged between 11 and 14 years and a smaller one for boys between 8 and 10 years but their findings suggested that the type of spirometer had very little effect on the vital capacity readings .

In the Bernstein type of spirometer the following measures are used to reduce the inertia of the moving parts and the tendency of the water column to resonate (FIG. 3) :

TO REDUCE THE INERTIA OF THE MOVING PARTS -

1. By reducing the mass of the bell. In order to do this the bell is made of aluminium sheeting which is very light yet strong, and its proportions are altered to give a better ratio between contained volume and surface area.
2. By reducing the velocity and acceleration of the bell. Because the cross-sectional area of the bell is large it does not have to move far to accommodate the respired air. Therefore

for any specified rate of airflow the velocity of the bell is reduced, as are also the acceleration and deceleration at the turnover points at the top and the bottom of the excursion of the bell.

3. By substituting thin cord for compensated chain suspension. This results in a considerable reduction in weight.

4. By using two very light pulleys of small diameter carried on ball-races in place of a single, large, heavy one. This change reduces the inertia and the frictional resistance to movement.

TO REDUCE THE TENDENCY OF THE WATER COLUMN TO RESONATE -

1. Reduction of the length of the bell necessarily reduces the length of the water column and this raises its resonant frequency.

2. The annular radius of the water jacket inside the bell is made as small as possible and the outer annular radius is made as large as possible. These measures damp the oscillatory movements of the water.

The use of the wider bell decreases the accuracy with which the measurements of volume are made. When the spirometer was calibrated the thickness of the pen marking represented 25 ml. and the usable capacity was 9.0 litres.

Rubber tubing 2" in diameter and 30" in length connected the altered anaesthetic mask to the inlet of the spirometer. The increase in "dead-space" in the apparatus and the wide diameter of the tubing were advantageous when the F.V.C. and F.E.V. were measured, as both tended to make the pressure changes within the apparatus smaller.

Experiments with various face-masks and mouthpieces showed that a modified anaesthetic mask of suitable size and shape gave the best results. The only objection to it was that a few children associated it with gas anaesthesia, but their fears were dispelled after a few breaths from it. It had the advantage that the child could apply it to his face himself and secure an airtight fit relatively easily. Nose-clips and mouth-pieces were found either to irritate or amuse some of the children so that it was difficult to obtain their full concentration and co-operation during the test.

The waterjacket of the spirometer was mounted by three pins on a trolley. The inlet of the spirometer was connected to the rubber tubing by an air-tight joint which was easily disconnected for emptying and cleaning of the waterjacket. Two spirit levels were mounted on the sides of the waterjacket to ensure that the apparatus was level before readings were taken.

Distilled water was used in the jacket to prevent corrosion of the aluminium bell.

The standing and stem heights were measured with the accurately calibrated (in inches) metal measure attached to the side of the trolley. The same seat (12" high and without a back) was used in the determination of the stem height.

A Super Ten Electric Recording Drum with a cylinder 12" in diameter and 12" high was used. Only the fastest speed was used for recording purposes. The drum speed was checked by means of a time marker. It was constant after 0.2 seconds of engaging the clutch, and remained so over any given interval of time at a speed of 1.67 cm/sec. which was used throughout the investigation in every test. A check at regular intervals was made on the accuracy of the speed of the drum. Any variation in the speed would obviously make all readings invalid. Superfine, smooth, white, glazed paper was used in all recordings. This permitted smooth writing and minimum friction between the pen and paper.

The spirometer was calibrated by the following method (FIG. 4). The air in the flask was replaced by accurately measured volumes of water (Temp. 20°C).

The water was warmed to this temperature to approximate the thermal conditions under which the spirometer was to be used. These were as follows -

Room temperature = 20°C
Temperature of the water in the water jacket = 19.5°C
Temperature of the air in the spirometer system = 19.5°C
Barometric pressure was not measured.

The movement of the bell caused by the displacement of air in the flask was recorded on the cylinder. The procedure was repeated four times and the final displacement over 5.5 litres never varied by more than 100 ml. (Range 5.450 - 5.550 litres).

Using this data, a transparent scale was constructed, graduated horizontally in 0.05 litres (50 ml.) and vertically in 0.25 seconds.

The danger of cross infection was considered. On the advice of the bacteriologist it was decided that in order to combat this the air in the system was exchanged after each test by moving the bell up and down 4 or 5 times and at frequent intervals the face-mask was washed with soap and water or Cetavalon.

Before each test the spirometer was checked to ensure that all its parts were moving freely. Little else was required in the maintenance of the apparatus - a favourable point in any apparatus to be used by the clinician.

CHAPTER 5

METHOD OF CONDUCTING TEST

When this investigation was started, no values were available for the F.E.V. and F.V.C. in healthy children, as measured by a Bernstein spirometer. Kennedy et al. (1957) published results for the V.C. and the E.F.R. $_{40}$ (F.E.V. $_{.75}$ x 40) in a group of 175 healthy school boys between the ages of 8 and 14 years. He used a spirometer similar to that described by Gilson and Hugh-Jones (1949) for the boys between 11 and 14 years, and a smaller spirometer for the younger boys. No other series of measurements for boys and none for healthy girls are at present available.

Wright (1946) stated that normal values of pulmonary function are dependant not only on the section of population studied but also on the method of assessment and on the apparatus used. D'Silva and Kazantzis (1954) made a strong plea that each laboratory should determine its own values for "normals", because the F.V.C. test is not performed entirely independently of the observer.

A large number of healthy children were studied at the Bristol Central Health Clinic. Children belonging to all sections of the community, from varying social classes and schools, attend the Clinic for routine medical examinations, dental treatment, first-aid, eye tests, inoculations, etc.

Children were examined and the test carried out whenever it was convenient and therefore not under basal conditions. The nursing staff gave valuable and voluntary help in interviewing parents and children and enquiring whether they would take part in the investigation.

The child with his parent was brought into the room by the sister who introduced them to me. After a preliminary talk to put both at ease, some explanation of the investigation was given. A general history, with special reference to respiratory and cardiac conditions was taken from the parent. The child's age to the nearest 3 months was recorded. The apparatus was then shown and demonstrated to the child. A physical examination of the respiratory and cardiovascular systems was then carried out, and during this examination a point was made of gaining the child's confidence. The criteria on which the child was accepted as "normal" for the investigation were:

1. A healthy, active child taking part in all normal school activities
2. No history of any disease of the respiratory system, apart from minor coughs and colds
3. No history suggestive of hayfever, eczema, asthma or "wheeziness"
4. No history of cardiac disease
5. No abnormal physical signs in the respiratory or cardiovascular system

The general nutritional state and the build of the child were noted. All anthropometric measurements were made with the children without shoes, the boys stripped to the waist and the girls stripped of all heavy outer clothing.

In measuring the standing height, the routine as advised by Krogman (1948) and Sutcliffe and Canham (1950) was followed, viz. -

1. The child stood with heels together and equal weight on both feet
2. The back was flattened against the upright until the back of the head was touching the upright, and the arms were free and hanging loosely at the sides with the palms facing the thighs.
3. The child looked straight ahead and was encouraged to stretch upwards to the maximum without raising the heels off the ground

4. The chest was not to be thrown out or the back curved
5. The triangle was lowered until the horisontal part touched the highest point of the head
6. The height was noted to the nearest ½ inch.

For measurement of the sitting height, the child sat against the upright, on a square box which was 12 inches high, and the same routine as for measuring the standing height was then followed.

The weight was measured and noted to the nearest pound, the child standing quite still on the platform of the scales. Samples of the excess clothing which the girls were wearing when measured were found to weigh, on an average, 2 lbs. This amount was subtracted from the measured weight of each girl, making the weights for boys and girls comparable.

By the time these measurements and examinations had been carried out a friendly relationship with the child had usually been established.

The time lapse between first showing the child the apparatus and actually carrying out the test seemed to increase his eagerness to perform it. Another method of obtaining his fullest co-operation was to ask another child who had already performed the test, to demonstrate it. To introduce some element of competition into their performances, two or three children were often taken in at the same time. The child was also encouraged to compete against his previous efforts and was shown the resulting curve after each attempt.

Before performing the test, the apparatus was again explained to the child. Boys showed a much greater interest and understanding and more keenness to try the test than girls. A necessary assurance was that the apparatus did not contain gas and did not smell. The child was encouraged to try the face-mask and to apply it himself.

All recordings were made in the standing position with the child stripped of all heavy outer clothing, jackets, jerseys, etc., but not skirts.

The drum was set in motion a few seconds before recording any test.

Suitable instruction and demonstration was given, the following points being stressed to the child:-

1. He must breathe in as deeply as possible through his open mouth
2. He must then apply the mask firmly to his face, if necessary with the help of the observer
3. He must then blow out through his open mouth as "fast and far" as possible. (The experience of the observer was of some importance here in judging whether the child had in fact blown a maximum forced expiration).

Throughout the performance the observer encouraged the child to blow "quicker and harder" and observed the recording all the time. Once the maximum volume had been expelled, as judged from the tracing, the child was asked to breathe in as quickly and as deeply as possible.

The tracing was then shown to the child and discussed with him, and he was asked to try again and do better. Throughout the test the emphasis was on the words "hard", "fast" and "see how steep you can make the curve" rather than on "see how far you can blow it". The same procedure was followed in discussion on the inspiratory curve.

Experience showed that the children developed a quicker and better understanding of the test when their first attempts were recorded and they could see the tracings than when they merely made a few attempts with no resultant tracing to see.

Two sources of error were:-

1. The child sometimes started to blow before the mask was firmly applied to his face. This excessive keenness on the part of the child was sometimes difficult to control.
2. The child sometimes pursed his lips instead of blowing through the widely opened mouth. Gross pursing of the lips was easily detected from the slope of the curve, but slight pursing was difficult to detect. The child was reminded before each test to blow through his open mouth.

My experience suggests that, for children, the F.E.V. results are largely dependent on the child's co-operation, contrary to the findings of McDermott and McKerrow (1956), who found that in adults, provided a full inspiration was taken, the results were largely independent of the subject's further co-operation.

Four to six tracings were recorded for each child, an interval of 2 - 3 minutes being allowed between each attempt.

All the gas volumes were measured at ambient pressure in a centrally heated (thermostatically controlled) room, the observed range being 19°C - 20°C. Gas volumes were not adjusted to body temperature and ambient pressure conditions and saturated with water vapour at 37°C (B.T.P.S.) for several reasons. Conditions of testing did not vary very much and it was unlikely that the volume of air ventilated in a single forced expiration would reach 37°C fully saturated. Furthermore, according to Whitfield et al. (1950) the procedure of correcting the vital capacity to uniform temperature and vapour to obtain maximum accuracy, involves dubious assumptions. The same views were expressed by Needham et al. (1954). Gandevia et al. (1957) did not use any correction for temperature or pressure when they assessed outpatient broncho-dilator therapy using the

F.E.V. test.

According to Ferris and Smith (1953) corrections to B.T.P.S. on the average increase volumes by 7% - 9%.

Atmospheric conditions during this present series varied from clear, dry days to days of "smog" or rain.

MATERIAL USED:

A total of 133 boys were interviewed and examined; 122 of these were healthy, fully co-operative and interested in the test. 7 of the 133 were unco-operative and no amount of explanation or demonstration could persuade them to blow. (Of these, 4 were scared of the mask and tubing and said it reminded them of previous gas anaesthesia). 4 of the 133 were not tested, because they had colds.

All 122 boys tested were able to perform the expiratory part of the curve satisfactorily, but two of the younger ones were unable to carry out the inspiratory part successfully. All the younger children had some difficulty in carrying out this part of the test. However, rather than confuse them and so impair their expiratory curves, no additional attempts were made to obtain a better inspiratory curve.

Of the 58 girls interviewed and examined, 3 refused to co-operate and the remaining 55 were able to perform the expiratory curve satisfactorily, although 4 of the younger ones were unable to perform the inspiratory part.

Most of the children wanted to keep repeating the test in an attempt to better their own or a friend's previous effort. The test became popular amongst the children in the neighbourhood of the Clinic, and quite a few brought their friends along, or were willing to blow again and again when the experiments to determine the effect of "learning" were carried out.

The children attended the Central Health Clinic for the following reasons:-

School Medical Treatment Room........ (cuts, bruises, etc.)	26
Dental Clinic..........................	35
School Medical Examination............	87
Eye Clinic............................	7
Foot Clinic...........................	8
Eneuretic Clinic......................	2
For Poliomyelitis inoculation........	3
Accompanying a friend................	9
	177

The age distribution of the children tested is shown in the accompanying Table. The age range for boys was 4.5 years to 16.25 years and for girls 4.5 years to 15.25 years.

TABLE II

No. of Boys	Age in Years (nearest 3 months)	No. of Girls
3	7	3
11	7 - 7.75	2
3	8 - 8.75	6
7	9 - 9.75	3
11	10 - 10.75	5
20	11 - 11.75	9
7	12 - 12.75	9
21	13 - 13.75	8
23	14 - 14.75	5
12	15 - 15.75	5
4	16	-

FIGS. 5 and 6 show the comparison of heights and weights with age. These results are similar to those of Sutcliffe and Canham (1950).

As a group, the children showed the now recognised trend in the United Kingdom of being taller and heavier than their predecessors.

<u>METHOD OF MEASURING TRACINGS</u>

FIG. 7 shows a typical tracing

The forced expiratory and inspiratory spirograms were measured with the transparent scale. In most of the spirograms the beginning of expiration was sharply defined and in these, a vertical line to the horizontal was projected from this point, and the zero point of the time and litre scale placed on it with the vertical zero line on the projected vertical line. The total volume and the volume expired in any particular time interval could then be read directly off the scale.

In those spirograms where the start of expiration was not so sharply defined, the steepest part of the curve was projected backwards and the zero point was taken as the intersection of this line with the horizontal. This procedure was suggested by D'Silva and Kazantzis (1954).

FIG. 8

In some of the spirograms, difficulty was experienced in determining the exact point of intersection of the vertical line on the scale with the spirogram and in those cases an approximate reading was taken to the nearest 50 ml. All other readings were taken to the nearest 25 ml..

Analysis of the spirograms showed that the whole F.V.C. was expelled in under 1 second in 10 children (6 boys and 4 girls) and in under 0.75 second in 3 children (2 boys and 1 girl).

A standard time interval of .75 second over which to measure the F.E.V. seemed therefore most appropriate for clinical purposes in children and this time interval for the F.E.V. has been used throughout this work.

For each child examined, the spirogram with the largest $F.E.V._{.75}$ was then taken as representing that child's maximum attempt. The measurements recorded from these expiratory and inspiratory vital spirograms were then recorded as the "normal" values for that particular child.

Kennedy et al. (1957) took the mean of four readings for their determination of the $E.F.R._{40}$ ($F.E.V._{.75} \times 40$).

Gaensler (1951a) used the three efforts which resulted in the highest total V.C. to obtain the timed volumes.

Thomson and Hugh-Jones (1958) took the mean of three readings to record the $F.E.V._1$

Leuallen and Fowler (1955) used the largest volume of three or more maximal expirations.

Gandevia, Hume and Prime (1957) used the highest value for the $F.E.V_1$ from three tracings.

The reasons for measuring in this investigation the spirograms with the largest $F.E.V_{.75}$ were as follows:-

1. By definition the Forced Vital Capacity is the maximum volume of gas which can be expired following a maximum inspiration, the expiratory phase being accomplished as rapidly and forcibly as possible (Gandevia and Hugh-Jones, 1957). The value of the $F.E.V_{.75}$ and the slope of the upper half of the spirogram are measures of these criteria.

2. When the vital spirograms (4 - 6 for each individual) of the 122 boys and 55 girls were analysed, the maximum value for $F.E.V_{.75}$ and F.V.C. for each usually occurred in one spirogram. This was so for 86 boys and 44 girls.
   Further analysis of the spirograms of the remaining 47 children (36 boys and 11 girls) where the largest $F.E.V_{.75}$ and F.V.C. values for each occurred in

different spirograms, showed that the variations between the readings in these different spirograms, when expressed in absolute values, was considerable.(TABLE III.) These observations in children are, therefore, not in agreement with the views of Thomson and Hugh-Jones (1958), McDermott and McKerrow (1956) and D'Silva and Kazantzis (1954) who stated that in adults the variations between F.E.V. readings were small for any given individual during performance of the test.

3. The F.E.V.$_{.75}$ expressed as a percentage of the F.V.C. is a measure of the patency of the airways. A study of Table III shows the wide range in the F.E.V.$_{.75}$/FVC % depending on which of a particular child's spirograms was measured.

The variations in the F.E.V.$_{.75}$ and F.V.C. readings in different spirograms as shown in Table III may be due to a number of factors:

1. The most important, perhaps, is that children like to watch the spirometer bell and movement of the pen and are more interested in blowing the bell as high as possible than in blowing it as fast as possible. It is interesting to note that on the whole the children making this error were in the older age group, where the competitive sense is keen.

2. Poor application of the mask to the face.
3. Blowing through pursed lips and not through the open mouth.
4. Failure of the observer during the performance of the test to exhort the child to blow as fast as possible.

Most of these mistakes, if particularly looked for, can be eliminated. One cannot stress too much that the observer must be alert and must concentrate as much as the child throughout the performance of the test.

(i)

TABLE III

$F.E.V_{.75}$ F.V.C. and F.E.V% VALUES OBTAINED BY MEASUREMENT OF (i) THE SPIROGRAM WITH THE LARGEST F.V.C. (ii) THE SPIROGRAM WITH THE LARGEST $F.E.V_{.75}$ OF THE SPIROGRAMS RECORDED ON ONE OCCASION

		(i) Spirogram with largest F.V.C. Litre		(ii) Spirogram with largest $F.E.V_{.75}$ Litre		Difference between F.V.C. in (i) and (ii) Litre	Difference between $F.E.V._{75}$ in (i) and (ii) Litre	F.E.V%	
Sex	Age	$F.E.V_{.75}$	F.V.C.	$F.E.V_{.75}$	F.V.C.			(i)	(ii)
M	11.75	0.900	2.400	1,600	2.250	0.150	0.700	37	71
M	12.5	1.300	2.500	1.825	2.325	0.175	0.525	52	78
M	13.5	1.450	3.150	2.250	3.075	0.075	0.800	46	73
M	16.25	1,500	4.250	2.350	4.100	0.150	0.850	35	57
M	14	2.100	4.300	2.600	3.800	0.500	0.500	49	68
M	13.75	3.350	3.800	3.375	3.700	0.100	0.025	88	91
F	13.25	0.850	2.950	1.800	2.550	0.400	0.950	29	71
F	10.25	0.750	1.750	1.300	1.600	0.150	0.550	43	50
F	14.25	1.850	3.300	2.350	2.900	0.400	0.500	56	81

(ii)

		(i) Spirogram with largest F.V.C. Litre		(ii) Spirogram with largest $F.E.V_{.75}$ Litre		Difference between F.V.C. in (i) and (ii) Litre	Difference between $F.E.V_{.75}$ in (i) and (ii) Litre	F.E.V.%	
Sex	Age	$F.E.V_{.75}$	F.V.C.	$F.E.V_{.75}$	F.V.C.			(i)	(ii)
F	11.5	1.250	2.350	1.825	2.250	0.100	0.575	53	81
M	11.75	1.300	2.400	1.650	2.250	0.150	0.350	54	73
F	10.75	1.350	1.900	1.700	1.825	0.075	0.350	71	93
M	13.25	1.350	2.500	1.800	2.450	0.050	0.450	54	73
M	11.00	1.600	2.950	2.200	2.650	0.300	0.600	54	83
M	15.75	2.000	3.750	2.950	3.500	0.250	0.950	53	84
F	15.00	1.500	3.350	1.900	3.200	0.150	0.400	45	59
M	14.50	1.400	4.075	2.450	3.400	0.675	1.050	34	72
F	15.25	1.375	3.050	2.250	2.850	0.200	0.875	45	79
F	14.5	1.050	2.700	1.450	2.550	0.150	0.400	39	57
M	13.00	1.150	2.750	2.250	2.600	0.150	1.100	42	87
M	14.75	2.000	3.350	2.250	3.325	0.025	0.250	60	68
M	15.00	2.000	2.650	2.250	2.625	0.025	0.250	75	86

(iii)

		(i) Spirogram with largest F.V.C. Litre		(ii) Spirogram with largest $F.E.V_{.75}$ Litre		Difference between F.V.C. in (i) and (ii) Litre	Difference between $F.E.V_{.75}$ in (i) and (ii) Litre	F.E.V.%	
Sex	Age	$F.E.V_{.75}$	F.V.C.	$F.E.V_{.75}$	F.V.C.			(i)	(ii)
M	13.25	1.550	3.200	2.000	3.050	0.150	0.450	48	66
M	10.25	1.400	1.900	1.550	1.750	0.150	0.150	74	89
M	13.5	2.000	4.000	3.250	3.850	0.150	1.250	50	84
M	13.5	1.850	2.650	2.100	2.500	0.150	0.250	70	84
M	14.75	1.750	4.100	3.250	4.000	0.100	1.500	43	81
M	15.25	3.250	4.600	3.350	4.250	0.350	0.100	71	79
F	11.50	1.150	2.275	1.600	2.250	0.025	0.450	51	71
M	14.5	1.250	3.200	2.000	2.800	0.400	0.750	39	71
F	15.0	1.050	2.750	2.350	2.700	0.050	1.300	38	87
M	10.25	2.000	2.550	2.050	2.500	0.050	0.050	78	82
M	14.75	1.750	3.700	2.250	3.500	0.200	0.500	47	64
F	12.50	0.800	2.200	2.050	2.100	0.100	1.250	36	98
F	11.00	1.500	2.900	2.300	2.750	0.150	0.800	52	84

(iv)

Sex	Age	(i) Spirogram with largest F.V.C. Litre		(ii) Spirogram with largest $F.E.V._{.75}$ Litre		Difference between F.V.C. in (i) and (ii) Litre	Difference between $F.E.V._{.75}$ in (i) and (ii) Litre	F.E.V.%	
		$F.E.V_{.75}$	F.V.C.	$F.E.V_{.75}$	F.V.C.			(i)	(ii)
M	13.00	1.750	2.750	2.000	2.500	0.250	0.250	64	80
M	12.00	1.100	2.000	1.150	1.950	0.050	0.050	55	59
M	12.25	1.750	2.750	2.300	2.550	0.200	0.550	64	90
M	7.75	0.400	1.300	0.850	1.200	0.100	0.450	31	71
M	9.00	1.750	2.300	1.900	2.150	0.150	0.150	76	88
M	15.25	1.850	3.500	2.300	3.350	0.150	0.450	53	69
M	11.25	1.150	2.700	2.000	2.600	0.100	0.850	43	77
M	13.50	1.950	3.100	2.300	2.850	0.250	0.350	63	81
M	15.75	1.350	3.200	2.400	3.000	0.200	1.050	42	80
M	13.75	1.650	2.800	1.800	2.650	0.150	0.150	59	68
M	11.00	1.000	1.500	1.300	1.400	0.100	0.300	67	93
M	11.25	1.750	2.400	1.950	2.275	0.125	0.200	73	86

CHAPTER 6

A. THE FORCED EXPIRATORY SPIROGRAM AND THE FORCED INSPIRATORY SPIROGRAM

B. ANTHROPOMETRIC AND SPIROMETRIC MEASUREMENTS

The spirograms (Forced Expiratory Spirogram and Forced Inspiratory Spirogram) and the spirometric values obtained from these for every child examined were analysed and the results and findings are discussed in the following four chapters.

A. THE FORCED EXPIRATORY SPIROGRAM AND THE FORCED INSPIRATORY SPIROGRAM

The forced expiratory spirogram (F.E.S.) has been defined as the spirogram of a complete forced expiration, and the forced inspiratory spirogram (F.I.S.) as the spirogram of a complete forced inspiration. These spirograms trace the rate of flow for expiration and inspiration at maximal speed and amplitude.

(i) The Forced Expiratory Spirogram

A variety of descriptions has been given of the shape of the pattern of expiratory flow as recorded by a spirometer. The F.E.S. has been said to be a straight line followed by a curve, the two parts being demarcated by a critical point, which is sometimes difficult to establish. (Tiffeneau and Drutel, 1952; Olivier and Drutel, 1949; Hirdes and van Veen, 1952; Leuallen and Fowler, 1955).

A straight line on a spirometric record implies that the rate of flow is constant. However, pneumotachographic records of patients who showed a straight line on the spirometric records have not shown an initial period of sustained constant rate of flow (Leuallen and Fowler, 1955).

Other workers have described the curve as one with a smoothly changing slope, always concave upwards, and not having an initial straight portion followed by a sudden inflexion at a critical point or the subsequent region of small undulations (Kazantzis, 1953; D'Silva and Kazantzis, 1954).

In a critical discussion of the shape of the F.E.S., Bernstein (1954) found the record to be a smooth curve, concave upwards, and that the more complicated curves described by Kennedy (1953a) and others were due to recording artefacts. These can be eliminated by a well designed spirometer such as the one described by Bernstein, D'Silva and Mendel (1952).

A study of the forced expiratory spirograms obtained from the normal children investigated shows the curve to be characterized by two different phases. The first phase of the expiration is always recorded as an almost straight line. As the speed of expiration lessens the curve deviates more and more from this initial straightness (Fig. 7) and becomes horizontal when the forced expiration is completed. The curve is always smooth and any undulations can be traced to varying effort during expiration, coughing or attempts to obtain additional air by a quick, short inspiration. The angle at which the second phase begins (Fig. 7, $F.E.V._A$) may be sharply defined, but more often than not, the deviation away from the straight line is so gradual that an accurate measurement of the expired volume at this point may be difficult.

The spirograms recorded were found, in general, to be remarkably uniform in shape and almost specific at any particular occasion for a given individual. The shape of the curve is only of importance for the validation of any predictions, such as the Indirect M.B.C., which are to be made from such spirograms. Since, however, throughout this study the absolute values for the F.E.V.$_{.75}$ and F.V.C. are used as a measurement of ventilatory function and no theoretical implications are involved, the two fractions of the curve are unimportant.

The time taken for the delivery of the whole of the F.V.C. (F.V.C.$_T$) is of some practical importance (page 142). This value was measured in the normal children, and although the results varied considerably, the following average values were obtained: -

Under 9 years	1.5 sec.	(range 0.6 - 2.6 sec.)
9 - 12 years	1.7 sec.	(range 1.1 - 2.7 sec.)
Over 12 years	1.9 sec.	(range 1.1 - 2.6 sec.)

(ii) <u>The Forced Inspiratory Spirogram</u>

The F.I.S. is, in general, steeper than the F.E.S. and is linear throughout its length, with the exception of the initial and terminal fractions (Kennedy, 1953a). A study of the forced inspiratory spirograms obtained in normal children showed a wide variation. Spirograms obtained from a child aged 13.25 years and a child aged 7.5 years are given in Fig. 7 to illustrate this variation. In the older children the spirogram approximated to the adult shape but in the smaller children a wide variation in the shape was observed. Only 2 of the 122 boys and 4 of the 55 girls were unable to complete a full inspiration following the forced expiration. This failure was probably due to the difficulty on the part of the smaller child in mastering the technique. Rather than confuse these children unduly, stress was laid on the expiratory aspect which they readily understood and carried out. On the whole, the children had no particular difficulty in performing the test.

The time taken for the completion of the F.I.S. (F.I.V.C.$_T$) was measured and the average values obtained were as follows:-

Under 9 years	.95 sec.	(range 0.6 - 1.7 sec.)
9 - 12 years	.9 sec.	(range 0.6 - 1.4 sec.)
Over 12 years	1.0 sec.	(range 0.8 - 1.2 sec.)

B. ANTHROPOMETRIC AND SPIROMETRIC MEASUREMENTS

The abbreviations used throughout the remainder of this thesis need a word of explanation. F.E.V.%

TABLE IV

(1)

TABLE OF ANTHROPOMETRIC AND SPIROMETRIC MEASUREMENTS

GIRLS:

	Age (yrs)	Standing Ht. (ins)	Sitting Ht. (ins)	Wt. (lbs)	F.E.V .75	F.V.C.	F.E.V%	F.I.V .75	F.I.V.C.	F.IV. %
1.	13.00	59.50	32.00	116	2.325	2.775	84	1.350	2.750	49
2	15.00	62.25	33.75	98	1.900	3.200	59	1.500	3.025	50
3	15.00	62.25	34.75	120	2.600	3.250	80	1.800	3.200	56
4	15.25	62.25	32.50	102	2.250	2.850	79	2.050	3.200	64
5	14.50	60.00	32.25	96	1.450	2.550	57	0.800	2.550	31
6	8.25	50.50	26.50	47	1.450	1.500	97	-	-	-
7	10.25	58.50	30.50	99	2.175	2.700	81	1.700	2.700	63
8	4.50	44.75	24.50	55	0.900	1.200	75	0.850	1.200	71
9	13.25	60.25	32.00	82	2.450	2.675	92	1.700	2.600	65
10	9.75	53.50	28.25	75	1.750	1.950	90	1.750	2.000	88
11	13.25	58.25	30.50	91	1.800	2.550	71	1.500	2.650	57
12	11.50	54.50	28.75	65	1.725	2.100	82	1.625	2.075	78
13	14.00	60.50	31.75	99	2.200	2.600	85	1.600	2.550	63
14	10.25	52.75	28.50	71	1.300	1.600	81	1.000	1.700	59
15	13.25	60.50	33.00	124	2.250	3.150	72	1.200	2.900	41
16	11.50	60.00	31.50	110	1.825	2.250	81	1.600	2.200	73
17	12.25	63.00	33.75	110	2.350	3.025	78	1.450	2.600	56
18	8.50	48.50	27.00	50	1.100	1.175	94	1.000	1.200	83
19	7.75	48.50	26.50	57	1.250	1.400	89	1.150	1.200	96
20	10.75	57.75	30.00	78	1.700	1.825	93	1.300	1.850	70
21	9.25	50.75	27.75	54	1.500	1.700	88	1.200	1.650	73
22	11.25	52.75	28.00	64	1.400	1.500	94	0.700	1.300	54
23	14.75	66.25	34.50	163	2.750	3.300	83	2.600	3.200	81
24	14.50	62.50	33.50	153	2.500	2.700	93	1.800	2.450	73
25	11.50	56.00	28.50	85	1.600	2.250	71	1.600	2.250	71
26	15.25	63.00	34.50	117	3.100	3.350	93	2.250	3.225	70
27	15.00	61.50	32.00	96	2.350	2.700	87	2.600	2.775	94

TABLE IV

(ii)

Girls

	Age (yrs)	Standing Ht. (ins)	Sitting Ht. (ins)	Wt. (lbs)	F.E.V .75	F.V.C. In litres	F.E.V %	F.I.V .75	F.I.V.C.	F.I.V. %
28	13.75	52.50	35.00	129	2.500	2.850	88	1.500	2.200	68
29	12.50	56.50	29.00	73	2.050	2.100	98	1.000	1.750	57
30	11.25	59.00	32.75	113	1.750	2.450	72	1.600	2.350	68
31	10.75	57.00	31.50	95	1.750	2.300	76	1.750	2.300	76
32	11.00	60.00	32.00	110	2.300	2.750	84	1.650	2.900	57
33	11.00	59.50	30.00	80	2.250	2.350	96	2.200	2.250	98
34	13.00	60.75	31.75	87	2.100	2.350	89	1.250	2.275	55
35	9.50	48.5	26.50	51	1.300	1.500	87	1.050	1.400	75
36	11.00	55.00	29.00	76	1.650	2.000	83	1.600	1.950	82
37	8.75	50.50	27.00	57	1.350	1.600	84	0.950	1.600	59
38	10.25	57.50	29.50	81	1.650	1.900	87	1.000	1.775	56
39	11.50	57.00	30.00	74	1.750	2.000	88	1.700	1.900	89
40	13.00	62.00	31.00	82	1.950	2.450	80	1.000	2.450	41
41	12.75	61.00	32.50	106	2.900	3.250	89	2.150	2.800	77
42	14.50	67.75	33.25	117	2.650	2.900	92	2.250	2.850	79
43	13.25	61.00	31.25	92	2.650	3.100	86	1.750	2.900	60
44	12.00	57.00	29.75	100	1.600	1.925	83	1.000	1.550	65
45	12.00	64.00	34.25	92	2.150	2.500	86	1.650	2.500	66
46	12.25	59.00	30.50	85	2.100	2.725	77	1.950	2.750	71
47	12.25	52.50	29.00	65	1.650	1.650	100	0.975	1.375	71
48	12.00	56.50	29.00	69	1.625	2.225	73	1.750	2.200	80
49	12.00	58.50	30.00	83	2.300	2.850	81	2.050	2.700	76
50	8.00	47.00	26.00	43	1.350	1.525	89	-	-	-
51	7.75	48.00	26.00	51	1.300	1.700	76	1.525	1.675	91
52	8.00	52.00	28.00	56	1.500	1.700	88	1.150	1.475	78
53	6.00	46.00	25.00	46	2.200	0.950	84	-	-	-
54	6.50	46.00	26.00	46	0.850	1.375	89	-	-	-
55	8.00	55.00	30.50	59	1.150	2.625	84	1.000	2.450	41

(i)

TABLE IV

TABLE OF ANTHROPOMETRIC AND SPIROMETRIC MEASUREMENTS
BOYS:

	Age (yrs)	Standing Ht. (ins)	Sitting Ht. (ins)	Wt. (lbs)	F.E.V .75	F.V.C.	F.E.V%	F.I.V .75	F.I.V.C.	F.I.N%
					In Litres					
1	14.00	55.50	29.75	77	1.950	2.300	85	1.800	2.050	88
2	14.25	63.75	32.25	98	2.250	3.000	75	1.100	3.000	37
3	14.00	58.75	29.00	76	1.700	2.250	76	1.400	2.250	62
4	11.00	60.75	31.75	101	2.200	2.650	83	2.250	2.700	83
5	7.00	47.50	27.50	56	1.300	1.650	79	0.575	1.700	34
6	13.50	60.00	31.75	83	2.350	2.825	83	2.175	2.825	76
7	14.50	62.75	33.75	108	2.250	3.500	64	2.250	3.500	64
8	15.00	63.25	33.00	104	2.800	3.350	84	2.750	3.450	80
9	12.75	60.00	32.00	85	2.100	2.500	84	1.275	2.300	55
10	11.25	55.50	29.00	70	1.950	2.275	86	1.300	2.300	57
11	11.25	55.50	29.50	77	1.600	2.200	73	0.950	1.800	53
12	15.75	63.75	34.25	120	2.950	3.500	84	2.150	3.350	64
13	10.00	50.50	28.50	63	1.400	1.725	81	1.500	1.550	97
14	14.00	58.50	30.00	79	2.250	2.675	84	1.850	2.550	73
15	14.25	62.00	32.00	104	2.250	3.450	65	1.500	2.450	61
16	14.50	63.50	33.50	102	2.450	3.400	72	2.250	3.450	65
17	13.25	50.00	28.00	65	1.600	1.950	82	1.350	1.900	71
18	13.25	60.50	29.50	94	2.400	2.775	87	1.900	2.800	68
19	9.75	52.50	29.00	62	1.500	1.875	80	1.300	2.050	63
20	13.00	60.50	30.50	92	2.250	2.600	87	1.450	2.450	59
21	15.75	69.50	33.50	150	2.800	5.300	53	1.750	5.100	34
22	14.75	61.50	32.50	100	2.250	3.325	68	1.750	3.300	53
23	15.00	61.75	32.50	94	2.250	2.625	86	1.800	2.625	69
24	13.25	64.00	32.50	102	2.000	3.050	66	1.600	3.150	51
25	10.25	54.25	28.00	63	1.550	1.750	89	1.250	1.700	74
26	14.00	58.75	30.00	76	1.850	2.425	76	2.000	2.200	91
27	14.50	64.75	34.50	124	3.300	3.950	84	1.550	4.000	39
28	14.50	57.25	29.25	84	2.025	2.300	88	1.150	2.200	52

TABLE IV

(ii)

Boys

	Age (yrs)	Standing Ht. (ins)	Sitting (Ht. (ins))	Wt. (lbs)	F.E.V .75 In litres	F.V.C.	F.E.V%	F.I.V .75	F.I.V.C.	F.I.V%
29	9.25	52.00	29.00	63	1.600	1.875	85	0.850	1.775	48
30	6.00	47.25	27.50	54	1.375	1.500	92	0.875	1.500	58
31	7.00	50.75	28.75	59	1.250	1.625	77	0.700	1.800	39
32	13.50	66.00	34.25	161	3.250	3.850	85	2.000	3.750	53
33	13.25	57.00	29.75	80	2.000	2.725	72	1.500	2.700	56
34	14.50	63.00	32.50	112	3.450	4.400	78	1.600	4.350	37
35	9.00	53.50	29.00	72	1.900	2.150	89	1.350	2.250	60
36	15.25	68.75	34.75	121	2.300	3.350	69	2.450	3.400	72
37	15.00	72.00	36.00	146	3.250	5.350	61	3.000	5.250	57
38	14.25	66.00	33.00	119	2.300	4.150	56	2.500	3.650	68
39	14.25	65.00	34.50	121	2.650	3.250	82	1.750	3.300	53
40	11.50	54.50	29.00	73	1.450	2.175	67	0.600	2.200	27
41	7.75	50.50	27.00	57	1.050	1.750	60	-	-	-
42	14.00	63.75	32.75	119	2.600	3.800	69	2.850	3.500	81
43	13.75	65.25	33.75	125	3.375	3.700	92	2.250	3.650	62
44	15.00	65.75	34.75	126	3.250	4.475	73	2.500	4.575	54
45	11.50	52.75	28.75	80	1.300	1.500	87	0.900	1.350	67
46	14.25	62.00	32.25	112	2.350	2.900	81	1.650	3.175	51
47	14.75	59.75	31.00	103	2.500	3.050	82	1.625	3.100	52
48	11.50	55.75	30.25	87	2.250	2.600	87	0.750	2.050	37
49	11.00	51.75	27.00	80	1.250	2.150	58	0.650	1.850	35
50	10.00	53.75	29.50	72	2.200	2.300	96	2.100	2.225	94
51	11.75	57.50	30.50	77	1.650	2.250	74	1.600	2.275	70
52	15.00	67.50	34.00	119	3.000	3.900	77	1.550	3.825	41
53	16.00	68.50	35.25	143	3.700	4.250	87	1.950	4.000	49
54	11.25	57.00	29.50	61	2.000	2.150	93	2.000	2.150	93
55	11.00	58.75	30.50	90	1.500	2.325	65	1.800	2.200	82
56	9.00	52.50	28.75	70	1.950	2.275	86	1.700	2.400	71
57	12.00	55.75	28.75	70	1.625	2.000	82	1.050	2.000	53
58	9.50	50.50	27.50	60	0.950	1.200	79	0.800	1.175	68

TABLE IV

(iii)

Boys

	Age (yrs)	Standing Ht. (ins)	Sitting Ht. (ins)	Wt. (lbs)	F.E.V .75	F.V.C	F.E.V %	F.I.V .75	F.I.V.C	F.I.V. %
					In litres					
59	11.25	57.00	30.00	112	1.750	2.500	70	1.200	2.550	47
60	7.75	50.00	26.50	63	1.150	1.150	100	1.000	1.025	98
61	12.25	54.50	29.00	65	1.200	2.200	55	1.450	1.825	79
62	8.75	52.25	28.50	57	1.500	1.600	94	0.600	1.600	38
63	10.25	54.25	29.50	70	1.500	2.000	75	1.500	1.900	79
64	7.75	49.00	27.00	53	1.200	1.425	84	0.850	1.600	53
65	13.25	56.00	29.75	70	1.800	2.450	74	1.500	2.500	60
66	13.50	59.00	30.50	77	2.100	2.500	84	1.450	2.600	58
67	11.75	57.50	30.75	84	2.200	2.825	78	2.150	2.800	77
68	10.00	56.00	29.75	70	1.600	2.300	70	0.800	2.175	37
69	14.75	68.00	35.50	122	3.250	4.000	82	2.350	3.600	65
70	15.25	68.25	36.00	126	3.350	4.250	79	1.600	4.200	38
71	13.25	61.00	31.00	92	2.150	3.350	64	1.750	3.250	54
72	10.75	54.25	28.50	72	1.850	2.100	83	1.650	2.000	83
73	13.25	67.50	34.00	126	2.800	3.850	73	2.300	3.550	65
74	15.00	67.50	35.00	131	3.400	4.300	79	2.400	4.200	57
75	14.50	61.00	33.50	98	2.250	3.250	70	2.350	3.175	74
76	14.50	60.50	32.00	97	2.000	2.800	71	1.750	2.700	65
77	14.75	61.00	30.25	113	2.000	2.850	70	2.650	2.850	93
78	13.50	58.00	29.50	82	2.200	2.500	88	1.400	2.350	60
79	10.25	58.50	29.50	84	2.050	2.500	82	1.700	2.550	68
80	14.75	64.50	33.25	113	2.250	3.500	65	1.400	3.400	41
81	13.75	56.50	29.00	73	2.000	2.500	80	1.350	2.500	54
82	16.00	60.25	31.50	98	2.500	3.250	77	1.800	3.100	58
83	12.00	55.50	30.00	71	1.150	1.950	59	0.850	1.950	44
84	16.00	63.25	33.25	112	2.000	4.000	50	2.000	4.000	50
85	11.75	63.50	32.75	131	2.100	3.100	68	2.200	2.850	77
86	12.25	62.50	32.50	103	2.300	2.550	90	2.400	2.650	91
87	10.00	47.25	26.75	50	0.850	1.200	71	0.850	1.300	65

TABLE IV

(iv)

Boys

	Age (yrs)	Standing Ht. (ins)	Sitting Ht. (ins)	Wt. (lbs)	F.E.V .75	F.V.C.	F.E.V %	F.I.V .75	F.I.V.C	F.I.V. %
					In litres					
88	7.75	47.00	26.50	56	1.050	1.350	78	0.600	1.250	48
89	12.25	55.50	29.50	75	2.150	2.500	86	1.800	2.150	84
90	11.00	54.00	28.00	76	1.850	2.200	84	1.050	2.200	48
91	15.25	63.50	31.50	103	2.500	3.700	68	1.900	3.350	57
92	11.25	57.00	29.00	72	2.000	2.600	77	1.600	2.650	60
93	13.75	57.50	30.75	91	2.200	2.800	79	1.750	2.750	64
94	13.50	56.50	29.25	65	1.800	2.100	86	1.550	1.650	94
95	11.25	54.50	28.00	69	1.650	2.200	75	2.000	2.150	93
96	13.50	60.75	31.00	90	2.300	2.850	63	2.000	3.150	63
97	10.50	49.00	26.50	46	0.900	1.250	72	0.700	1.100	64
98	7.50	46.00	25.75	49	1.200	1.425	84	1.150	1.400	82
99	15.75	62.00	33.50	103	2.400	3.000	80	2.300	3.100	74
100	13.75	57.75	30.00	89	1.800	2.650	68	1.700	2.800	61
101	10.50	51.50	28.00	62	1.000	1.150	87	1.000	1.000	100
102	11.00	47.75	26.50	50	1.300	1.400	93	1.000	1.000	100
103	11.00	53.00	27.75	66	1.150	1.400	82	0.750	1.200	63
104	10.50	58.50	30.00	74	2.200	2.550	86	1.100	2.350	47
105	11.75	55.25	29.00	74	1.600	2.250	71	1.350	2.100	64
106	12.50	59.25	30.25	83	1.700	2.500	68	1.050	2.150	49
107	13.25	56.75	27.75	77	1.825	2.325	78	1.700	2.275	75
108	13.50	61.75	31.00	120	2.250	3.075	73	1.600	3.200	50
109	14.50	58.75	31.00	85	2.050	2.650	77	1.350	2.350	57
110	16.25	66.50	33.50	127	2.350	4.100	57	2.350	4.100	57
111	9.75	52.50	28.75	68	1.500	2.500	60	0.900	2.300	39
112	6.00	47.00	26.00	49	1.400	1.750	80	1.150	1.375	84
113	7.50	50.00	26.50	50	1.650	1.850	89	1.200	1.700	71
114	7.50	48.00	26.00	46	1.275	1.250	96	0.950	1.250	76

TABLE IV

(v)

Boys

	Age (yrs)	Standing Ht. (ins)	Sitting Ht. (ins)	Wt. (lbs)	F.E.V .75	F.V.C.	F.E.V %	F.I.V .75	F.I.V.C.	F.I.V. %
					In litres					
115	11.75	58.00	30.00	87	1.650	2.025	82	1.800	1.975	91
116	13.25	59.00	30.00	112	2.550	3.000	78	2.900	2.950	98
117	9.50	51.50	29.00	56	1.700	2.100	81	0.925	2.000	46
118	4.50	46.00	26.00	47	0.850	0.750	100	0.700	0.700	100
119	7.00	46.50	25.00	47	1.050	1.450	72	0.900	1.375	65
120	7.50	48.00	26.00	49	1.500	1.650	91	-	-	-
121	8.00	53.50	29.00	53	1.675	2.125	79	1.475	1.850	80
122	8.00	48.00	25.00	50	1.000	1.350	73	0.450	1.300	35

indicates the F.E.V.$_{.75}$ expressed as a percentage of the F.V.C. F.I.V.% simply shows the F.I.V.$_{.75}$ as a percentage of the F.I.V.C.

The F.E.V.$_{.75}$ and F.V.C. were measured in 122 boys and 55 girls, and the F.I.V.$_{.75}$ and F.I.V.C. in 120 boys and 51 girls. From these figures the F.E.V.% and the F.I.V.% were calculated. The data obtained from these children on age, sex, standing height, sitting height and weight and the corresponding values for the F.E.V.$_{.75}$, F.V.C., F.E.V.%, F.I.V.$_{.75}$, F.I.V.C. and F.I.V.% are given in Table IV. The average values for the variable were as follows:-

TABLE V

Average Values for the Anthropometric and Spirometric Measurements

	BOYS		GIRLS	
No. of Cases	122	120	55	51
Average Age (years)	12.09	12.16	11.41	11.75
Av. Standing Height (inches)	57.58	57.72	56.69	57.42
Av. Sitting Height (inches)	30.27	30.34	30.23	30.58
Av. Weight (pounds)	85.82	86.37	85.22	88.33
F.E.V.$_{.75}$:(Litres)	1.985		1.895	
F.V.C. (Litres)	2.60		2.280	
F.I.V.$_{.75}$:(Litres)		1.556		1.512
F.I.V.C. (Litres)		2.522		2.261
F.E.V.%	76.2%		83%	
F.I.V.%		61.5%		66.8%

The values for the F.E.V.$_{.75}$, F.V.C., F.I.V.$_{.75}$ and F.I.V.C. were plotted against the anthropometric measurements of age, standing height, sitting height and weight.

The scatterdiagrams are given in FIGS.10-25. Some of these scatterdiagrams show a definite, and others an approximate, linear trend having an increase in the values for expiration and inspiration with an increase in the values of the anthropometric variable. The data obtained on these measurements was statistically analysed and is reported on in Chapter 7.

The calculated F.E.V.% and F.I.V.% values for the normal children were plotted against age and sitting height. The resulting scatterdiagrams are shown in FIGS. 26, 27, 28A and 28B. The statistical analyses were carried out on the F.E.V.% and F.I.V.%. From inspection of the scatterdiagrams a slight linear trend showing a fall in the F.E.V.% with an increase of age or sitting height could be deduced in the case of boys. This is a reflection of the relatively higher F.V.C. values obtained from the older boys and a shorter duration of the forced expiration in the younger boys. No similar trend is obvious in the girls.

By using, to illustrate this trend, the graphical procedure of drawing free-hand a line through the scatter of points, it is observed that the average F.E.V.% in boys varies from approximately 85% in the 7-year old to approximately 70% in the 16-year old. The scatter of points around this line is, however, large and the lower limits in normal boys are estimated at approximately 60 - 65%, depending on age. In girls, the values for the F.E.V.% are higher, reflecting their smaller F.V.C. values. The average value for the F.E.V.% in girls is approximately 80%, with the lower limit in normal girls in the region of 70%.

The scatter of points for the F.I.V% is so large that it excludes it from having any value in ventilatory assessment.

CHAPTER 7

A. STATISTICAL METHOD AND ANALYSIS OF RESULTS

B. PREDICTION FORMULAE

A. STATISTICAL METHOD AND ANALYSIS OF RESULTS

The aim of this study was to obtain prediction formulae, so that the $F.E.V_{.75}$, F.V.C., $F.I.V_{.75}$ and F.I.V.C. of any child could be predicted from his or her anthropometric measurements (age, standing height, sitting height and weight). The data was statistically analysed by Regression and Correlation Analysis. Lines of regression (best fitting lines through the scatter of points) were fitted for the different volumes and anthropometric measurements by the method of the least squares. In the first instance, regression lines for expiratory or inspiratory volumes as a function of a single anthropometric characteristic were calculated. The method and formulae used are discussed in (a) hereunder. Subsequently, multiple regression lines were fitted, i.e. the expiratory or inspiratory volumes were considered as a function of the multiple variables, age, standing height, sitting height and weight. The procedure is discussed in (b) hereunder.

(a)

The problem is to observe the change of the expiratory and inspiratory values as a function of the changes in the spirometric characteristics of the children.

The expiratory or inspiratory volume is denoted by the symbol Y and is regarded as the dependent variable.

The anthropometric characteristic is denoted by the symbol X and is the independent variable.

The corresponding averages are denoted by the symbols $\bar{Y}$ and $\bar{X}$.

The direction of the regression line is epitomised by the tangent of the angle of inclination, called the co-efficient of regression and denoted by b_{YX}.

a represents the intercept on the Y axis by the regression line and is a constant in the equation.

The equation of the straight line is, then, for the co-ordinate system in general, $Y = a + b_{YX}(X)$.

In order to make the straight line the best fitting line for the scatter of points, the constants a and b (where $b = b_{YX}$) were calculated as follows:

$$a = \bar{Y} - b_{YX}\bar{X}$$

$$b_{YX} = \frac{\varepsilon(X - \bar{X})(Y - \bar{Y})}{(X - \bar{X})^2} \qquad (\varepsilon = \text{sum of})$$

From the graphs (FIGS. 10 - 25), the regression lines constructed show satisfactory linear trends.

The relationship between the expiratory and inspiratory values and the anthropometric measurements is expressed by the correlation coefficient. The correlation coefficients (r) were calculated from the formula

$$r = \frac{\Sigma (X - \bar{X})(Y - \bar{Y})}{\sqrt{\Sigma (X - \bar{X})^2 \, \Sigma (Y - \bar{Y})^2}}$$

and the different values for r are given in the statistical table (Table VI).

The standard deviation (S.D.) of the points around the regression line was determined by calculating the standard error of estimate from the formula

$$\sigma_z = \sigma_y \sqrt{1 - r^2}$$

(σ_z = error of estimate)

and is given in the statistical table (Table VI).

Twice σ_z on either side of the regression line, represents the space within which approximately 95 out of 100 observations should lie on the assumption that the data is approximately normally distributed about the regression line. The data is of such a nature that this assumption of normality is valid. Each graph has two lines drawn parallel to the regression line at that distance and, on the whole, the scatter of points is confined within these limits.

(b)

To fit the multiple regression lines (by the method of least squares) the dependent variable $F.E.V._{.75}$ or F.V.C., denoted by Y, was considered as a linear function of four independent variables, X_1, X_2, X_3 and X_4 where X_1 = age, X_2 = standing height, X_3 = sitting height and X_4 = weight. The mathematical formula used was

$$Y = a + b_1X_1 + b_2X_2 + b_3X_3 + b_4X_4$$

Well known statistical methods were employed to find the numerical values of a , b_1, b_2, b_3, and b_4 in both cases where Y was taken to be the $F.E.V._{.75}$ variable, and also where Y was taken to be the F.V.C. variable. This was done for boys and girls, resulting in four multiple regression equations.

The multiple correlation coefficients

$R_{Y.X_1,X_2,X_3,X_4}$ were calculated. This is a measure of relationship similar to r (see (a) above), and indicates the degree of association between Y and all four independent variables X_1, X_2, X_3 and X_4. Furthermore, multiple standard errors of estimate (σ_z) were calculated, using the appropriate formulae. The multiple correlation coefficients and multiple standard errors of estimate are shown in the statistical table (Table VI).

The method of calculation used in this section is the standard one given in statistical texts such as:

Herdan, G: Statistics of Therapeutic Trials. (Elsevier, Amsterdam, 1955)

Kendall, M.G: The Advanced Theory of Statistics Vol. I. Chapter 15 (Charles Griffin, London)

Weatherburn, C: Mathematical Statistics Chapter 12. (University Press, Cambridge).

B. PREDICTION FORMULAE

Table VI shows that age, standing height, sitting height and weight are all positively correlated with the spirometric measurements and that the degree of correlation is high. The positive correlation between age and the spirometric measurements differs from the negative correlation in adults, first noted

TABLE VI

STATISTICAL TABLE

GIRLS		Age	Standing Ht.	Sitting Ht.	Weight
	a	+0.240	-2.470	-2.702	+0.531
$F.E.V_{.75}$	b	0.145	0.077	0.152	0.016
(55 subjects)	σ_z	0.361	0.308	0.316	0.297
	r	0.726	0.809	0.797	0.822
	a	+0.154	-3.219	-3.438	+0.584
F.V.C.	b	0.186	0.097	0.189	0.020
(55 subjects)	σ_z	0.404	0.345	0.341	0.352
	r	0.771	0.839	0.843	0.837
	a	+0.423	-1.531	-1.656	+0.673
$F.I.V_{.75}$	b	0.093	0.053	0.104	0.010
(51 subjects)	σ_z	0.412	0.375	0.372	0.395
	r	0.452	0.582	0.590	0.516
	a	+0.211	-3.194	-3.025	+0.721
F.I.V.C.	b	0.174	0.095	0.173	0.017
(51 subjects)	σ_z	0.417	0.348	0.381	0.397
	r	0.710	0.810	0.766	0.742

$F.E.V._{75}$ $\sigma_z = .233$ R= .895

F.V.C. $\sigma_z = .286$ R= .892

TABLE VI

STATISTICAL TABLE

BOYS		Age	Standing Ht.	Sitting Ht.	Weight
	a	−0.01	−3.140	−3.706	+0.183
$F.E.V_{.75}$	b	0.165	0.089	0.188	0.021
(122 subjects)	σ_z	0.450	0.325	0.365	0.334
	r	0.708	0.860	0.819	0.852
	a	−0.386	−4.770	−4.937	+0.060
F.V.C.	b	0.247	0.128	0.249	0.031
(122 subjects)	σ_z	0.592	0.439	0.577	0.387
	r	0.752	0.873	0.767	0.902
	a	−0.061	−2.450	−2.874	+0.291
$F.I.V_{.75}$	b	0.133	0.069	0.146	0.016
(120 subjects)	σ_z	0.458	0.374	0.257	0.420
	r	0.620	0.719	0.688	0.695
	a	−0.384	−3.885	−6.186	−0.190
F.I.V.C.	b	0.239	0.111	0.286	0.031
(120 subjects)	σ_z	0.555	0.526	0.376	0.262
	r	0.761	0.789	0.898	0.952

$F.E.V._{75}$ $\sigma_z = .192$ R=.881

F.V.C. $\sigma_z = .328$ R=.914

by Hutchinson (1846) and later confirmed by other workers (Baldwin et al., 1948; Gilson et al. 1955).

Because of this high correlation between all four anthropometric measurements and the spirometric values, any one or more, or all four in combination, may be used for the prediction of normal expected values. The basic prediction formula is

$$\text{Spirometric Volume in litres} = a + b\,(\text{anthropometric measurement} \pm 2\sigma_z)$$

This gives the most probable spirometric value, viz. a + b (anthropometric measurement) and the bounds about this "most probable" value, within which 95% of all normal cases should lie.

The values for a, b and σ_z for the spirometric measurement (F.E.V $_{.75}$, F.V.C., F.I.V $_{.75}$ and F.I.V.C.) and the anthropometric measurements (age, standing height, sitting height and weight) for boys and girls are given in Table VI. The following example illustrates the use of this formula in the prediction of the expected normal F.E.V $_{.75}$ and F.V.C. values in a boy with a standing height of 55".

F.E.V $_{.75}$ in litres = $-3.140 + 0.089\,(55)$ $(\sigma_z = .325)$
= $1.755 \pm .650$

with the "most probable" value = 1.755 and the limits 1.105 and 2.405

F.V.C. in litres = $-4.770 + 0.128\,(55)$ $(\sigma_z = .439)$
= $2.270 \pm .878$

with the "most probable" value = 2.270 and the limits 1.392 and 3.148

Whitfield et al. (1950) suggested that a number of physical attributes should be used for the prediction of the normal vital capacity. Multiple regression equations for the $F.E.V._{.75}$ and F.V.C., and their dependence upon age, standing height, sitting height and weight, were calculated for boys and girls independently.

Where X_1 = age, X_2 = standing height,
X_3 = sitting height, X_4 = weight

GIRLS

$$F.E.V._{.75} \text{ in litres} = 1.2875 + .0098X_1 + .0357X_2 + .0106X_3 + .00855X_4 \quad (\sigma_z = .233)$$

Multiple correlation coefficient R = .895

$$F.V.C. \text{ in litres} = -2.2379 + .0232X_1 + .0404X_2 + .0441X_3 + .0074X_4 \quad (\sigma_z = .286)$$

Multiple correlation coefficient R = .892

BOYS

$$F.E.V._{.75} \text{ in litres} = -2.4080 + .0044X_1 + .0371X_2 + .0504X_3 + .0079X_4 \quad (\sigma_z = .192)$$

Multiple correlation coefficient R = .881

$$F.V.C. \text{ in litres} = -.9118 + .0413X_1 + .0396X_2 - .0413X_3 + .0231X_4 \quad (\sigma_z = .328)$$

Multiple correlation coefficient R = .914

It is interesting to observe that in both boys and girls the contributions of sitting height and standing height to the F.E.V.$_{.75}$ values are the greatest and those of age and weight are much smaller when measurements are made in the units employed here. The same is true for the F.V.C. in girls, although the contribution of age is much greater. In boys age makes the largest contribution to the F.V.C. value, followed closely by standing height and, to a lesser extent, by weight. The contribution of sitting height, however, is negative.

The question arises as to whether the multiple correlation formulae, using all four anthropometric measurements, have any advantage in practical clinical work over formulae using a single index. The calculations using the multiple correlation formulae for the F.E.V.$_{.75}$ and F.V.C. are more complicated and more time consuming.

In the past, authors have differed on which is the most important single anthropometric measurement for the prediction of spirometric values. Moore and Gibson-Williams (1951) and Ferris et al. (1952) used body surface area whereas others follow Hutchinson (1846) and regard standing height as the main index. Jones (1955) measured the vital capacities of boys and girls and plotted height, weight and surface area against vital capacity. The findings were in agreement with those of Baldwin et al. (1948) that the most smoothly rising curve in each sex was that recording vital capacity against height. Engstrom et al. (1956), Kennedy et al. (1957) and Helliesen et al. (1958) used standing height in their prediction formulae for the V.C.

From the statistical table (Table VI) it would appear that standing height and weight are the two most important indices for prediction formulae using a single anthropometric index. Of the two, standing height is probably the most important. The prediction of expected normal values for sick children may be fallacious if the indices, such as weight, used for the prediction are altered by the disease process. To determine whether, in fact, the disease processes in the patients investigated and reported on in Part 2 of this study, have altered their standing heights and weights, these were plotted against age and compared with the normal percentile lines. From the FIGS. 37 and 38 it would appear that the distribution for standing height is within the normal range. The distribution for weight shows a tendency to be lower than the normal distribution.(These assumptions were not statistically investigated. Four of the high values for weight were actually found in very obese children who were being investigated because of their obesity.

When the results for predicted normal values for a normal boy or girl, calculated from the multiple regression formulae, are compared with those calculated from formulae using standing height alone, the differences are seen to be very small.

For example, with the measurements of, age = 12 years, standing height = 57", sitting height = 30.25", and weight = 86 lbs, the following results are obtained:

TABLE VII

	GIRLS		BOYS	
	Using 4 Anthrop. Measures	Using Standing Height Only	Using 4 Anthrop. Measures	Using Standing Height Only
$F.E.V_{.75}$ in Litres	1.921	1.919	1.964	1.933
	(σ_z = .233)	(σ_z = .308)	(σ_z = .192)	(σ_z = .325)
F.V.C. in Litres	2.314	2.310	2.578	2.526
	(σ_z = .236)	(σ_z = .345)	(σ_z = .328)	(σ_z = .439)

In Table VIII, the actual values obtained for the F.E.V$_{.75}$ and F.V.C. in the normal children and in some of the patients investigated (asthmatics, congenital heart disease, etc.) who had low F.E.V$_{.75}$ and F.V.C. values, are compared with their expected values calculated from a) formulae using standing height only,

and b) the multiple regression formulae.

In normal children the differences obtained by calculating the F.E.V$_{.75}$ and F.V.C. values from the two different formulae tend to be small. The values for the F.E.V$_{.75}$ and F.V.C. in boys and for the F.V.C. in girls obtained from the multiple regression equation tend to be larger than those obtained from standing height only. The F.E.V$_{.75}$ values in girls show the opposite trend.

In those cases of congenital heart disease and, to a lesser extent the asthmatics and the case of "funnel chest", where the children are below the weight expected for their age and height, the values obtained from the multiple regression equation are much smaller than those from the standing height equation.

In the obese children the values for both the F.E.V$_{.75}$ and F.V.C. are much larger when calculated from the multiple regression equation.

Depending on the relative values obtained for the $F.E.V_{.75}$ and F.V.C. from the two formulae, the differences may be further accentuated when the lower or upper limits of normal of these values are determined by subtracting or adding $2 \times$ S.D. The standard errors of estimate for the multiple regression equation, for both the $F.E.V_{.75}$ and F.V.C. in boys and girls, are significantly smaller than those for the standing height equation.

Because of the small differences in values obtained from the two prediction formulae in normal children, and on account of the simplicity of using standing height alone as an index in the prediction of expected normal values, the latter method is the method of choice for routine work. This is especially so in children suffering from conditions such as chronic chest disease or congenital heart disease where weight may be altered to a larger extent than standing height by the disease process.

TABLE VIII

COMPARISON OF PREDICTION FORMULAE RESULTS

	Sex	Age (years)	Standing Ht. (ins.)	Sitting Ht. (ins.)	Weight (lbs.)	OBSERVED F.E.V .75	OBSERVED F.V.C.	OBSERVED F.E.V. %	Standing H eight Regression Formula F.E.V .75	Standing H eight Regression Formula F.V.C.	Multiple Regression Formula F.E.V .75	Multiple Regression Formula F.V.C.
NORMAL CHILDREN	M	7	48	27.5	56	1.300	1.650	79	1.132	1.374	1.240	1.436
	M	10	51	28.5	63	1.400	1.725	81	1.399	1.748	1.462	1.799
	M	12	57	30.25	86	1.850	2.450	75.5	1.933	2.526	1.964	2.578
	M	15	63	33	104	2.800	3.350	84	2.467	3.294	2.480	3.242
NORMAL CHILDREN	F	8.7	48.5	27	59	1.100	1.175	93.5	1.265	1.436	1.258	1.494
	F	11.5	54.5	29	67	1.725	2.100	82	1.727	2.068	1.651	2.005
	F	12	57	30.25	86	1.800	2.200	82	1.919	2.310	1.921	2.314
	F	14	60.5	32	93	2.200	2.600	85	2.189	2.650	2.144	2.631

All Volumes in Litres

TABLE VIII (Continued)

COMPARISON OF PREDICTION FORMULAE RESULTS

DIAGNOSIS			Standing Ht. (ins.)	Sitting Ht. (ins.)	Weight (lbs.)	OBSERVED F.E.V. .75	OBSERVED F.V.C.	OBSERVED F.E.V. %	Standing Height Regression Formula F.E.V .75	Standing Height Regression Formula F.V.C.	Multiple Regression Formula F.E.V .75	Multiple Regression Formula F.V.C.
ASTHMA	M	15	62.5	33	120	1.350	2.950	45.7	2.423	3.230	2.588	3.592
	F	7.75	46	25	41	0.600	1.300	46	1.072	1.243	1.046	1.206
	M	14.5	53	29	60	1.000	1.550	64.5	1.577	2.014	1.558	1.974
CONGENITAL HEART DISEASE	F	10	54.5	28.5	52	1.075	1.400	76.7	1.727	2.068	1.503	1.837
	F	13	59	30	70	1.175	1.950	60	2.073	2.504	1.863	2.288
	F	11	52	28	56	0.900	1.525	59	1.534	1.825	1.452	1.767
OBESITY	F	12	60	31.5	144	2.100	2.700	78	2.150	2.601	2.537	2.919
	M	13	61.5	32	147	2.325	2.300	78	2.334	3.102	2.705	4.135
FUNNEL CHEST	F	11.5	60	32	77	1.800	2.225	81	2.150	2.601	1.965	2.434
								Girls σ_z	.308	.345 σ_z	.233	.286
								Boys σ_z	.325	.439 σ_z	.192	.328

All Volumes in Litres

CHAPTER 8

DISCUSSION OF FINDINGS

A. DIFFERENCES IN THE SPIROMETRIC MEASUREMENTS IN THE SEXES

B. INTER-RELATION OF SPIROMETRIC AND ANTHROPOMETRIC MEASUREMENTS

C. COMPARISON OF SPIROMETRIC VALUES OF THE PRESENT SERIES WITH THOSE BY OTHER WORKERS

(i) The F.V.C.
(ii) The $F.E.V_{.75}$
(iii) The $F.I.V_{.75}$
(iv) The F.I.V.C.

A. DIFFERENCES IN THE SPIROMETRIC MEASUREMENTS IN THE SEXES

When the $F.E.V_{.75}$ and F.V.C. are calculated, using the multiple regression formulae (p. 73) for a girl and a boy with the following anthropometric measurements: age 12 years, standing height 57", sitting height 30.25" and weight 86 lbs, the results obtained were:-

TABLE IX

	GIRL	BOY
$F.E.V_{.75}$ in litres	1.921 (σ_z = .233)	1.964 (σ_z = .192)
F.V.C. in litres	2.314 (σ_z = .286)	2.578 (σ_z = .328)
F.E.V%	83	76.2

The values calculated for a girl and boy of standing height 57" from the prediction formulae using standing height only (p.72), are as follows:-

TABLE X

	GIRL	BOY
$F.E.V_{.75}$ in litres	1.919 (σ_z= .308)	1.933 (σ_z= .325)
F.V.C. in litres	2.310 (σ_z= .345)	2.526 (σ_z= .439)
F.E.V. %	83	76.4
$F.I.V_{.75}$ in litres	1.490 (σ_z= .375)	1.483 (σ_z= .374)
F.I.V.C. in litres	2.221 (σ_z= .348)	2.442 (σ_z= .526)
F.I.V.%	67.1	60.7

Although the differences in the V.C. values of the two sexes have been compared, no similar studies are available on the $F.E.V_{.75}$, F.V.C., $F.I.V_{.75}$ or F.I.V.C. The F.V.C. is, however, comparable to the V.C. A tendency for the V.C. to be smaller in girls has been recorded, but on the whole, the V.C. values in boys and girls of the same height are very similar (Ferris et al., 1952; Ferris and Smith, 1953; and Jones, 1955).

Engstrom et al. (1956) noticed a tendency for the V.C. values for girls to be lower than those for boys.

However, they regarded this difference as too small to be of practical clinical importance. Helliesen et al., (1958) in their study did not differentiate between the sexes and Kennedy et al. (1957) examined only boys.

In the present series the F.V.C. and F.I.V.C. are 11.3% and 9.9% larger respectively in boys than in girls when these values are calculated from prediction formulae using standing height. This difference is large enough to be of practical clinical significance and it justifies the employment of separate prediction formulae for boys and girls. The differences in the $F.E.V_{.75}$ and $F.I.V_{.75}$ in the two sexes are insignificant.

The linear trend in the scatterdiagrams (Figs. 10-25) has already been mentioned. This linearity is not definite in all the cases. For boys older than 14 years, with a standing height of 64" or more, and a sitting height above 33", the values for the $F.E.V_{.75}$ and F.V.C. tend to be higher than for the other boys, with the scatter of points lying mostly above the regression line. The number of girls examined is too small for any definite conclusions to be formed, but a similar trend seems to be present in those over the age of 11 years above a standing height of 58"-59" and above a sitting height of 30". The values for the F.I.V.C.

tend to be higher in those boys over 14 years, with a standing height above 64" and a sitting height above 33". This trend is not seen for the $F.I.V_{.75}$ values. In girls, the linear trend for the $F.I.V_{.75}$ and F.I.V.C. values seems to be definite.

These findings are in agreement with those of other workers, who found an increase in the V.C. and the M.B.C. in boys during the adolescent growth spurt but very little, if any, increase in girls (Astrand, 1952; Ferris et al., 1952; Ferris and Smith, 1953, and Kennedy et al., 1957). These findings for the $F.E.V_{.75}$, F.V.C. and F.I.V.C. in boys can be correlated with the adolescent growth spurt. The number of girls investigated is too small for any definite conclusions to be formed. This growth spurt is a constant phenomenon and occurs in all children, although it varies in intensity in different individuals. In boys it usually takes place from the age of 13 to 15½ years. In girls the spurt usually begins about two years earlier, lasts from 11 to 13½ years of age, and is smaller in magnitude than that seen in boys (Tanner, 1955).

The increases found in the V.C. values in boys are greater than would be expected simply from the greater increase in body size (Tanner, 1955). Not only do the boys have a very definite adolescent spurt, but at the same time, they acquire a greater V.C. per unit of surface area than they had earlier. Probably this reflects a greater growth of the lungs in boys (Morse et al., 1952).

B. INTER-RELATION OF ANTHROPOMETRIC AND SPIROMETRIC MEASUREMENTS

Comparing the results for girls and boys in Table VI, it appears that the corresponding values of "b", the regression coefficients, are always greater for boys. This "b" measures the change in the inspiration or expiration value per unit change in the anthropometric measurements. The greater "b" for boys means a greater effect from a change in the biological characteristics on the breathing values than for girls. When similar comparisons are made for "r", the correlation coefficients, it seems that all but 4 are greater for boys than for girls (Table XI). The correlation coefficient is an overall measure of the relationship between the variables and this greater "r" for boys means that their breathing values are, on the whole, accounted for to a greater extent by their physical build.

TABLE XI

TABLE OF CORRELATION CO-EFFICIENTS

		Standing Height	Sitting Height	Age	Weight
$F.E.V_{.75}$	GIRLS	0.809	0.797	0.726	0.822
	BOYS	0.860	0.819	0.708	0.852
F.V.C.	GIRLS	0.839	0.843	0.771	0.837
	BOYS	0.873	0.767	0.752	0.902
$F.I.V_{.75}$	GIRLS	0.582	0.590	0.452	0.516
	BOYS	0.719	0.688	0.620	0.695
F.I.V.C.	GIRLS	0.810	0.766	0.710	0.742
	BOYS	0.789	0.898	0.761	0.952

Of the anthropometric measurements, the standing height, sitting height and weight all show close correlation with the $F.E.V_{.75}$ and F.V.C. values in boys and girls, and with the F.I.V.C. in boys and to a lesser extent in girls. Age shows less correlation with these spirometric measurements. The correlation between the $F.I.V_{.75}$ and the anthropometric measurements is much lower.

These findings for "r" are in agreement with those of Kennedy et al. (1957) who also found the correlation co-efficient between the $I.F.R^{40}$ and anthropometric measurements to be lower than that for the $E.F.R^{40}$.

The values for "r" in boys for the $F.E.V_{.75}$ and $F.I.V_{.75}$ are compared with those for the $E.F.R^{40}$ and $I.F.R^{40}$ (Kennedy et al., 1957) in Table XII.

TABLE XII

	Standing Height	Sitting Height	Age	Weight
$E.F.R^{40}$ (Kennedy et al.)	0.768	0.772	0.620	0.702
$F.E.V_{.75}$ (Present series)	0.860	0.819	0.708	0.852
$I.F.R^{40}$ (Kennedy et al.)	0.588	0.507	0.418	0.468
$F.I.V_{.75}$ (Present series)	0.719	0.688	0.620	0.695

The correlation co-efficient values obtained by Kennedy et al. (1957) are smaller than those obtained here. However, the correlation co-efficients for $E.F.R^{40}$ and $F.E.V_{.75}$ do not differ significantly (in a statistical sense) except in the case of weight. The correlation co-efficients for

$I.F.R^{40}$ and $F.I.V_{.75}$ differ significantly. No explanation of these differences is put forward, although it may lie in the techniques of measurement. The important point is that in both Kennedy's and the present series the correlation co-efficients obtained for the expiratory measurements are much higher than those obtained for the inspiratory measurements.

The correlation co-efficient values obtained by Kennedy et al. (1957) and Helliesen et al. (1958) between the V.C. and the anthropometric measurements are compared in Table XIII with those for the F.V.C. and the anthropometric measurements in the present series.

TABLE XIII

			Standing Height	Sitting Height	Age	Weight
Kennedy et al. (1957)		r	0.847	0.812	0.602	0.801
Helliesen et al. (1958)		r	0.930	-	-	-
Present Series	Boys	r	0.873	0.767	0.752	0.902
	Girls	r	0.839	0.843	0.771	0.837

Because of the low correlation co-efficients between the $F.I.V_{.75}$ and F.I.V.C. and the anthropometric measurements, and the difficulty some of the children had in performing a satisfactory forced inspiratory spirogram, the $F.E.V_{.75}$, F.V.C. and F.E.V.% must be regarded as more suitable values for the evaluation of ventilatory function in children.

C. COMPARISON OF SPIROMETRIC VALUES OF PRESENT SERIES WITH THOSE BY OTHER WORKERS

(i) F.V.C.

The values obtained for the F.V.C. may not be strictly comparable with the V.C. values obtained from a full, unhurried and steady expiration. No work has been done on normal children to ascertain what effect, if any, the speed of maximum expiration after a maximum inspiration has on the total volume expired. Scarrone et al. (1955) reported only a slight variation between the F.V.C. and V.C. in three out of forty normal adults. The difference in the other 37 was in the range of - 5% to + 5%.

No series has been published for the V.C. in children where the Bernstein spirometer was used

TABLE XIV

COMPARISON OF VITAL CAPACITIES

AUTHOR	PREDICTION FORMULA	STANDING HT.	PREDICTED VALUE FOR V.C. or F.V.C. Litres	S.D.	VALUES CORRECTED TO B.T.P.S.	SPIROMETER
PRESENT SERIES 55 Girls	F.V.C. = −3.219 + .097 (Standing Height)	55"	2.116	σ_s = .345	No.	Bernstein Type
PRESENT SERIES 122 Boys	F.V.C. = −4.770 + 0.128 (Standing Height)	55"	2.270	σ_s = .439	No.	Child Standing
FERRIS AND SMITH (1953) - 233 Girls	Table	139.7 cm (55")	2.190	0.27	Yes	Benedict - Roth Type
FERRIS ET AL. (1952) - 161 Boys	Table	139.7 cm (55")	2.270	0.45	Yes	Child Standing
KENNEDY ET AL. (1957) - 175 Boys	V.C. (ml.) = 115.93 Standing Height - 4348	55"	2.028	.290	Corrected 37°C and sat. with water	Gilson and Hugh-Jones Child sitting
ENGSTROM ET AL. (1956) - 50 Boys + 43 Girls	V.C. = 2.87 x 10^{-6} x Standing Height$^{2.75}$	139.7 cm (55")	2.276	± 12.6%	Yes	Benedict - Roth Type Child Sitting
HELLIESEN ET AL. (1958)- 52 Boys + 33 Girls	V.C. = 1.63 x Standing Height x 2.87 x 10^{-3}	55"	2.573	-	Yes	Child Sitting

for the measurements. Furthermore, the present series differs from most others in that the results were not corrected to B.T.P.S. and the test was performed in the standing position.

In spite of these objections, it is interesting to compare the values obtained for the F.V.C. in the present series with values for the V.C. in recent publications (Table XIV). The findings of Needham et al. (1954) are not included in this comparison because the values they published are for older subjects (11 to 19 years).

It is interesting to note that the values for the F.V.C. for both boys and girls is almost identical with the V.C. in boys (Ferris et al., 1952; Engstrom et al., 1956) and girls (Ferris and Smith, 1953). From the description by Ferris et al. (1952) and Ferris and Smith (1953) of the method they used in their tests, they may well have measured the F.V.C. values. The V.C. recorded was the largest of 3 or more maximal expirations following a maximal inspiration. The younger children were encouraged to "blow out all the candles on your birthday cake".

(ii) $F.E.V_{.75}$

The only other comparable series for $F.E.V_{.75}$

values has been published by Kennedy et al. (1957). By dividing their E.F.R ^{40} values by 40, the F.E.V $_{.75}$ values were obtained. They measured 175 normal schoolboys between the ages of 8 and 14 years. The values were measured in the sitting position and all values were corrected to 37°C and saturated with water vapour. The E.F.R ^{40} was taken as the mean of 4 readings and expressed in litres/minute. The authors considered height and age to be the most relevant indices for calculating the expected normal E.F.R ^{40} value and used the following regression equation :

E.F.R ^{40} = $(3.23 \times x_1) + (2.41 \times x_2) - 135$
in litres
where x_1 = height in inches
x_2 = age in years
(S.D. = 10.7 litres/min.)

For convenience in clinical work they also published a nomogram. From this nomogram the predicted E.F.R^{40} is given for height in inches and age in years. Using their prediction formula and nomogram, the predicted E.F.R ^{40} for a boy aged 12 with a standing height of 57" is approximately 78.03 litres (± 10.7 litres) per minute. This figure corresponds to a F.E.V $_{.75}$ level of 1.950 litres (± .268).

When the F.E.V $_{.75}$ is calculated on the basis of the present work for a boy aged 12 years, with a standing height of 57", a sitting height of 30.25" and weighing 86 lbs, from the present multiple regression equation, a value of 1.964 ($\pm$ 0.192) is obtained. For practical purposes this value is the same as that predicted from Kennedy's nomogram.

Kennedy and his co-workers used a spirometer similar to that described by Gilson and Hugh-Jones (1949). In the present series a spirometer of the type described by Bernstein, D'Silva and Mendel (1952) was used. The similarity, almost identity, of the predictions by different workers using different apparatus and technique suggests that these F.E.V $_{.75}$ values could probably be accepted as standard normal.

(iii) F.I.V $_{.75}$

The only other comparable series for the F.I.V $_{.75}$ in children is again that of Kennedy et al. (1957). By dividing their I.F.R ^{40} values by 40 the F.I.V $_{.75}$ value can be obtained. The same group of boys, technique and correction of volumes to 37°C and saturated with water were used. They gave the following regression equation:

$$\text{I.F.R}^{40} = 3.06x_1 - 97.4 \text{ litres/min.}$$

(S.D. = 15.7 litres/min.)

where x_1 = standing height in inches.

Calculations for a boy with a standing height of 55", according to that formula shows

$$I.F.R^{40} = 70.90\ (\pm\ 15.7)\ \text{litres/min.}$$

$$F.I.V_{.75} = 1.773\ (\pm\ .393).$$

This gives a value considerably higher than the value for a corresponding child in the present series

$$F.I.V_{.75} = 1.345$$
$$(S.D. = 0.374)$$

The discrepancy is not surprising. The difficulty of obtaining an adequate F.I.S. in the present series has already been discussed and may well account for the low $F.I.V_{.75}$ values obtained. It may equally apply to Kennedy's figures.

(iv) F.I.V.C

No literature on the F.I.V.C. is available on children for purposes of comparison.

CHAPTER 9

FACTORS WHICH MAY INFLUENCE THE $F.E.V_{.75}$ AND F.V.C. TEST IN CHILDREN

A. LEARNING
DAY TO DAY VARIATION

B. EFFECT OF POSTURE - Standing
Sitting
Supine

C. ISOPRENALINE INHALATION

D. ATMOSPHERIC CONDITIONS

A review of the literature did not reveal any reports on the following aspects of the $F.E.V_{.75}$ and F.V.C. test in normal children.

(a) The effect of learning on the $F.E.V_{.75}$ and F.V.C. levels

(aa) The day to day variation of these values in a given individual

(b) The effect of posture on the $F.E.V_{.75}$ and F.V.C. values

(c) The effect of isoprenaline inhalation on the $F.E.V_{.75}$ and F.V.C. values in normal children.

(d) The effect of atmospheric conditions on the $F.E.V_{.75}$ and F.V.C. values.

These aspects were therefore investigated in several different groups of normal children. The effects of learning on the F.E.V $_{.75}$ and F.V.C. values, and the day to day variation of these values, were studied in a group of children seen either at the Central Health Clinic or in the Outpatient Department of the Royal Hospital for Sick Children, Bristol. The effects of posture and isoprenaline inhalation on the F.E.V $_{.75}$ and F.V.C. values were studied in a group of hospital in-patients and children who visited them in hospital. The in-patients used in these tests were all admitted with conditions unrelated to their respiratory systems. They were all ambulant and active in the ward and none gave a history or showed clinical or radiological evidence of past or present chest disease.

The same technique was used for taking anthropometric and spirometric measurements as has already been described. The recorded F.E.V $_{.75}$ and F.V.C. values are those measured from the spirogram showing the highest F.E.V $_{.75}$ value of the 4-6 taken at the particular occasion. The values obtained for the "normal" hospital in-patients were all well within the normal range and it seems reasonable to assume that they were actually, and not only nominally, normal subjects.

A. LEARNING
DAY TO DAY VARIATION

The effect of learning was studied, that is, whether any significant improvement occurred in the $F.E.V_{.75}$ and F.V.C. values on repetition of the test

(a) after an interval of 30 minutes
(b) after a number of days.

This investigation provided the opportunity to study also the normal day to day variations in the values.

(a) The test was carried out as described and then repeated after an interval of 30 minutes by 21 boys and 4 girls. (Table XV). The volumes by which the $F.E.V_{.75}$ and F.V.C. levels differed in the two readings were recorded as positive or negative figures. Changes of volume in the range of $\pm$ 100 ml. occurred for the $F.E.V_{.75}$ in 80% of the cases and for the F.V.C. in 88% of the cases. The largest increase in the $F.E.V_{.75}$ was 225 ml. (11.8%) and the largest decrease was 275 ml. (17.7%). The largest increase in the F.V.C. was 150 ml. (5.7%) and the largest decrease was 150 ml. (5.8%). All the other differences were within the $\pm$ 10% range.

Differences (increases or decreases) of 10% or more on the initial $F.E.V_{.75}$ or F.V.C. level are regarded as being "medically significant" in this study. This is in accordance with the practice of Gandevia et al. (1957) and Thomson and Hugh-Jones (1958) who regarded as being significant any

TABLE XV

LEARNING EFFECT ON REPEATING THE TEST AFTER 30 MIN.

FIRST READING			SECOND READING		
F.E.V .75 In	F.V.C. Litres	F.E.V%	F.E.V .75 In	F.V.C. Litres	F.E.V%
1.650	2.375	70	1.625	2.325	70
1.475	1.725	86	1.475	1.700	87
1.250	1.675	75	1.350	1.700	79
1.400	1.675	84	1.425	1.700	84
2.275	2.900	78.5	2.350	2.825	83
1.550	1.975	78.5	1.275	1.950	65
1.600	1.725	93	1.625	1.800	90
1.650	1.875	88	1.550	1.775	87
2.150	2.500	86	2.000	2.600	77
2.100	2.700	78	2.100	2.725	77
1.800	2.600	69	1.750	2.450	71
1.875	2.200	85	1.875	2.100	89
1.900	2.100	90	1.975	2.175	91
1.800	2.600	69	1.750	2.475	71
1.675	2.125	79	1.650	2.175	76
1.225	1.525	80	1.075	1.550	69
1.450	2.050	71	1.500	2.100	72
2,300	2.700	85	2.350	2.800	84
1.900	2.200	86	1.950	2.100	93
1.650	2.000	82.5	1.600	1.900	84
1.875	2.350	80	1.700	2.250	75.5
1.100	1.350	81.5	1.025	1.300	79
1.150	1.375	84	1.150	1.425	81
1.900	2.650	71.5	2.125	2.800	76
1.250	1.675	75	1.350	1.725	78

improvement of 10% or more in either the V.C. or in the volume of air expired in the first second of forced expiration, following the inhalation of a 1% isoprenaline aerosol.

Statistical analysis showed that the differences between the volumes of the first and second readings of both the $F.E.V_{.75}$ and F.V.C. were not statistically significant. t-tests were made to test the hypothesis of no differences between first and second readings. The following values of t were obtained:-

$F.E.V_{.75}$: t = 1.396 with 24 degrees of freedom, and
F.V.C. : t = 1.094 also with 24 degrees of freedom.

These t values are less than 2.06, the critical value at the 5% level of significance.

Therefore no appreciable learning effect could be demonstrated on repeating the test after 30 minutes. Although considerable differences were recorded between the $F.E.V_{.75}$ and F.V.C. values of the first and second readings, these were (with two exceptions for the $F.E.V_{.75}$) always within the ± 10% range. Furthermore, the average $F.E.V_{.75}$ and F.V.C. values at the second reading were lower than at the first. The corollary to this conclusion is that changes in the $F.E.V_{.75}$ or F.V.C. values of 10% or more after, for instance, bronchodilator drugs, may fairly be attributed to the effects of the drugs.

(b) The test was carried out repeatedly, as described, over a period of days in 28 normal boys and 6 normal girls. The test was repeated on a total of 112 occasions (variation 2 - 8) in the boys and 19 times (variation 2 - 9) in the girls.

The daily variations of the $F.E.V_{.75}$ and F.V.C. values in some of these children are compared in Fig.29 along with two cases of congenital heart disease (coarctation of the aorta and pulmonary stenosis) and an asthmatic. The variation in the normals and the congenital heart disease cases is very much the same and differs from the large variation seen from day to day in the asthmatic.

For purposes of statistical analysis, the first and last available readings for each child were used. The time interval between these two readings was usually less than 2 weeks and never more than 3 weeks (Table XVI).

The changes in $F.E.V._{.75}$ values in 20 of the boys and in 2 of the girls were in the $\pm$ 100 ml. range. In the remaining cases the differences were

TABLE XVI

(i)

DAY TO DAY VARIATION AND LEARNING EFFECT

FIRST READING			LAST READING			
F.E.V .75 In Litres	F.V.C.	F.E.V %	F.E.V .75 In Litres	F.V.C.	F.E.V. %	Interval between readings (days)
GIRLS						
2.900	3.250	89	2.700	2.725	99	18
1.950	2.100	93	1.750	2.250	78	7
1.750	2.450	71.5	1.750	2.250	78	7
2.200	2.700	81.6	2.500	2.700	93	14
2.250	3.150	71.5	2.450	2.875	85	8
1.300	1.700	76.5	1.250	1.675	75	21
BOYS						
2.350	3.000	78	2.550	2.950	86	3
1.700	2.100	81	1.700	2.150	79	14
1.925	2.175	88.5	1.800	2.000	90	19
2.150	2.500	86	2.000	2.600	77	1
1.550	1.750	88.7	1.300	1.800	72	1
1.400	1.750	80	1.300	1.675	78	1
1.650	1.850	89	1.575	1.825	86	21
1.200	1.250	96	1.150	1.275	90	7
1.650	2.025	81	1.625	2.300	71	10
1.700	2.250	75.5	1.600	2.075	77.5	7
2.000	2.550	78.5	2.100	2.700	78	4
2.500	3.250	77	2.450	3.250	75.5	5
3.250	4.000	81	3.350	3.750	89.5	14
1.625	2.000	81.2	1.800	2.200	82	2
3.000	3.800	79	2.800	3.850	73	4
3.250	4.475	73	3.800	4.425	86	7
2.225	2.650	84.	2.250	2.600	86.	13
2.100	2.500	84.2	2.100	2,400	87.7	15

(ii)	F.E.V .75 In Litres	F.V.C.	F.E.V %	F.E.V .75 In Litres	F.V.C.	F.E.V %	Interval between readings (days)
BOYB							
	2.300	2.850	81	2.300	3.100	74	21
	2.250	3.500	64.5	2.250	3.400	66	4
	1.950	2.300	85	1.950	2.300	85	21
	2.350	2.825	83	2.350	2.700	87	14
	2.200	2.775	79	2.050	2.750	74.5	1
	1.650	2.100	78.5	1.650	2.000	82.5	4
	2.250	2.650	85	2.300	2.800	82	5
	1.750	2.100	83	1.600	2.025	79	2
	2.300	2.800	82	2.300	2.900	79	1
	2.600	3.000	87	2.650	3.150	84	3

considerable. The range of variation in the minority group of boys was between + 550 ml. (a 17% increase) and - 250 ml. (a 16% decrease) and in the girls it was between + 300 ml. (a 13.5% increase) and - 200 ml. (a 10% decrease). The corresponding range for the F.V.C. in the minority group of boys was between + 275 ml. (13.5% increase) and - 250 ml. (6.25% decrease) and for girls between + 150 ml. (7.2% increase) and - 525 ml. (19.4% decrease). The changes in the F.V.C. values in 17 of the boys and in two girls were in the ± 100 ml. range.

The average $F.E.V_{.75}$ and F.V.C. values at the last reading were lower than at the first. These variations are not statistically significant.

t-tests were made and the following values for t obtained:

GIRLS

$F.E.V_{.75}$: t = 0.21 with 18 degrees of freedom, and
F.V.C. : t = 0.515 also with 18 degrees of freedom.
These t values are less than 2.45, the critical value at the 5% level of significance.

BOYS

$F.E.V_{.75}$: t = 1.917 with 111 degrees of freedom, and
F.V.C. : t = 1.886 also with 111 degrees of freedom.
These t values are less than 2.05, the critical value at the 5% level of significance.

The day to day variations of the $F.E.V_{.75}$ and F.V.C. expressed as a percentage of the initial value, in the majority of cases, varied within the ± 10% range. However, the larger variations that may occur in certain "normal" individuals from day to day must be taken into consideration when the test is being used in the assessment of daily improvement or deterioration in pathological cases.

From this investigation it is clear that no learning effect could be demonstrated on the $F.E.V_{.75}$ and F.V.C. values on repetition of the test over, or after, a period of days.

B. THE EFFECT OF POSTURE

Hutchinson (1849) showed that the V.C. decreased with a change from the erect to the supine position. This has been confirmed by Christie and Beams (1922), Wilson (1927), Hamilton and Morgan (1932), Hurtado and Fray (1933), Wade and Gilson (1951), Whitfield et al. (1950) and Michelson and Lowell (1958), but the last named also compared values for the $F.E.V_{1\ sec.}$ measured in the erect and recumbent positions and could demonstrate no significant change.

Bohr (1907) suggested that a period of 40 minutes or longer was necessary before the alterations in the lung produced by postural change become maximal. Livingstone (1928) and Whitfield et al. (1950) suggested that the maximal changes occurred within the space of two to five breaths.

Attinger et al. (1956) studied the mechanics of breathing in the sitting, supine, and prone positions. Mechanical resistance, including the resistance to air-flow per se and the resistance to tissue deformation, was usually highest in the supine position and lowest in the sitting position. Expiratory resistance was somewhat higher than inspiratory resistance in all the positions studied.

Standing and Sitting: The effect on the $F.E.V_{.75}$ and F.V.C. values of changing from a standing to a sitting position was studied in 20 children (15 boys and 5 girls). The test was carried out on 43 occasions (variation 1 - 5) in the usual way in the standing position and then repeated in the sitting position after an interval of 15 minutes. The differences in the $F.E.V_{.75}$ and F.V.C. values in the two readings were recorded and analysed. (Table XVII).

The volumes for the $F.E.V_{.75}$ were smaller in the sitting position on 21 occasions (49%), without

TABLE XVII

(i)

THE EFFECT OF POSTURE

	F.E.V. .75 In Litres	F.V.C.	F.E.V. %	F.E.V. .75 In Litres	F.V.C.	F.E.V. %
	1.650	1.800	91.5	1.500	1.800	83
P.A.	1.650	1.850	89	1.675	1.875	89
	1.650	1.825	90	1.625	1.850	88
	1.575	1.825	86	1.650	1.800	91.5
	1.925	2.125	90.5	1.925	2.050	94
E.W.	2.000	2.200	91	2.000	2.250	89
	1.900	2.100	90.5	1.925	2.100	92
	1.800	2.000	90	1.825	2.025	89
	1.650	2.050	80.5	1.725	2.150	80
R.C.	1.750	2.200	79.5	1.750	2.150	81
	1.700	2.150	79	1.750	2.175	80.5
P.D.	1.075	1.125	95	0.950	1.075	88.5
	1.050	1.450	72	1.050	1.300	81
	0.950	1.350	70	0.925	1.300	71
A.T.	0.950	1.200	79	0.900	1.200	75
J.C.	2.200	2.625	84	2.150	2.575	83
D.S.	0.825	1.000	82.5	0.800	1.075	74.5
S.T.	1.675	2.125	79	1.650	2.150	77
	1.225	1.525	80	1.225	1.600	77
K.L.	1.350	1.525	88.5	1.250	1.550	81
A.L.	1.400	2.000	70	1.400	1.950	72
P.K.	1.000	1.350	74	1.000	1.300	77
S.J.	1.150	1.375	84	1.175	1.350	87
P.E.	1.750	2.550	69	1.900	2.850	67
	1.900	2.800	68	2.100	2.950	71
C.S.	2.100	2.700	78	1.875	2.450	76.5

(ii)

	F.E.V .75	F.V.C. In litres	F.E.V %	F.E.V. .75	F.V.C. In litres	F.E.V. %
D.S.	1.500	1.900	79	1.500	1.700	88
	1.525	1.750	87	1.525	1.800	84.5
D.C.	1.450	1.750	83	1.300	1.700	76.5
	1.500	1.625	92	1.425	1.550	92
	1.525	1.825	83.5	1.500	1.725	87
	1.475	1.725	85.5	1.475	1.700	87
D.B.	2.550	3.050	83.5	2.500	3.000	83
R.C.	1.500	2.200	68	1.325	2.125	62
	1.650	2.375	69	1.600	2.250	71
	1.725	2.450	70	1.300	2.100	62
	1.625	2.300	71	1.575	2.400	66
P.C.	0.475	0.650	73	0.700	0.725	97
P.E.	1.250	1.675	75	1.250	1.600	78
	1.400	1.675	83.5	1.275	1.625	78.5
	1.325	1.500	88	1.075	1.550	69.5
	1.350	1.650	82	1.300	1.625	80
	1.350	1.625	83	1.350	1.625	83

change on 12 occasions (28%) and larger on 10 occasions (23%); for the F.V.C. the volumes were smaller on 23 occasions (53.5%), unchanged on 4 occasions (9.5%) and larger on 16 occasions (37%). In the statistical check on the volume changes t-tests were made and the following values for t obtained:-

$F.E.V_{.75}$: t = 2.53 with 42 degrees of freedom, and
F.V.C. : t = 2.19 also with 42 degrees of freedom.

These values for t are significant (being larger than 2.02, the critical value at the 5% level of significance). The inference is that there was a definite decrease in the volume expired when the posture was changed from standing to sitting. When the average decrease is expressed as a percentage of the average initial volume in the standing position, it is found to be very small - $F.E.V_{.75}$ = 2.08% : F.V.C. = 1.04%. From the scientific point of view a decrease in expiration occurs on this postural change but it is so small that it cannot be regarded as other than "medically insignificant". From the practical point of view it is negligible.

<u>Standing and Supine</u>: The effect on the $F.E.V_{.75}$ and F.V.C. values of changing from the standing to the supine position was studied in 18 children (14 boys and 4 girls). The test was carried out in the usual

TABLE XVIII

(i)

THE EFFECT OF POSTURE ON THE F.E.V.$_{.75}$ AND THE F.V.C. VALUES

	STANDING			SUPINE		
	F.E.V.$_{.75}$ In	F.V.C. Litres	F.E.V%	F.E.V.$_{.75}$ In	F.V.C. Litres	F.E.V.%
P.E.	1.350	1.650	82	1.300	1.575	82.5
	1.350	1.625	83	1.300	1.550	84
	1.250	1.550	81	1.275	1.575	81
	1.400	1.675	84	1.200	1.575	76
	1.250	1.675	75	1.350	1.700	79
E.W.	2.000	2.200	91	1.900	2.150	88
	1.900	2.100	90	1.850	2.100	88
	1.950	2.125	92	1.650	1.950	85
	1.800	2.000	90	1.775	2.000	89
P.A.	1.650	1.825	90	1.575	1.775	89
	1.650	1.850	89	1.500	1.750	86
R.C.	1.700	2.150	79	1.675	2.050	82
	1.750	2.200	80	1.700	2.150	79
A.T.	1.050	1.450	72.5	0.900	1.300	69
	0.950	1.350	70	0.650	1.300	50
	0.950	1.200	79	0.750	1.200	62.5
D.C.	1.525	1.825	84	1.375	1.575	87
	1.475	1.725	85.5	1.350	1.625	83
R.C.	1.625	2.300	71	1.400	2.350	60
D.S.	0.825	1.000	82.5	0.700	0.925	76
P.B.	1.575	1.825	86	1.500	1.775	84.5
K.L.	1.225	1.525	88.5	1.075	1.550	69
	1.350	1.525	88.5	1.150	1.450	79
A.L.	1.400	2.000	70	1.275	1.750	73
P.K.	1.000	1.350	74	0.600	1.150	52
S.J.	1.150	1.375	84	1.100	1.175	94

(ii)

	STANDING			SUPINE		
	F.E.V. .75	F.V.C.	F.E.V %	F.E.V .75	F.V.C.	F.E.V%
	In Litres			In Litres		
A.L.	1.900	2.325	82	1.150	2.000	57.5
P.E.	1.750	2.550	69	1.900	2.850	67
	1.900	2.800	68	1.950	2.775	70
D.S.	1.500	1.900	79	1.450	1.750	83
C.S.	2.100	2.600	81	1.950	2.450	80
	1.850	2.600	71	1.750	2.350	74.5
	2.100	2.700	78	1.875	2.450	76.5
S.M.	1.500	2.450	61	1.650	2.050	80.5
	1.950	2.300	85	1.850	2.200	84

way in the standing position and repeated 15 minutes later when lying supine without a pillow. The test was repeated a total of 35 times (variation 1 - 5). The volumes by which the $F.E.V_{.75}$ and F.V.C. in the supine position differed from those in the standing position, were recorded and analysed (Table XVIII). The $F.E.V_{.75}$ and the F.V.C. values were smaller in the supine position on 30 occasions (86.7%) and larger on 5 occasions (13.3%).

When statistically analysed, the values for the supine position were seen to be significantly lower than those for the standing position. t-tests were made and the following values for t obtained:

$F.E.V_{.75}$: t = 5.362 with 34 degrees of freedom
F.V.C. : t = 5.625 also with 34 degrees of freedom

These values for t are significant, being higher than 2.03, the critical value at the 5% level of significance.

The average values for the $F.E.V_{.75}$ and F.V.C. in the standing position were 1.533 litres and 1.923 litres. The lowering of these values in the supine position represented 8.7% of the standing $F.E.V_{.75}$ value and 5% of the standing F.V.C. value. This lowering is large enough to warrant consideration when the test is carried out in the supine position.

C. THE EFFECT OF ISOPRENALINE INHALATION

20 normal children (15 boys and 5 girls) were seen on 32 occasions (variation 1 - 4) and the test was carried out before and after the inhalation of isoprenaline from a Medihaler. The interval between tests was 5 - 10 minutes. The pre- and post-isoprenaline values for the $F.E.V_{.75}$ and F.V.C. were measured. The volumes by which the post-isoprenaline values differed from the pre-inhalation values were recorded and analysed. (Table XIX). The increases and decreases after iso-prenaline were expressed as percentages of the pre-inhalation values.

All the changes in the $F.E.V_{.75}$ values were within $\pm$ 10% range, with the exception of one child who showed an increase of 11.8%. The F.V.C. changes were also within the $\pm$ 10% range, with one exception which showed a decrease of 12.3%. The volumes obtained for the post-isoprenaline $F.E.V_{.75}$ were, in 10 cases, larger than the pre-isoprenaline value; in 4 cases they remained the same, and in 18 cases they were smaller. The post-isoprenaline values for the F.V.C. had increased in 15 cases, remained unchanged in 1 case and decreased in 16 cases.

When statistically analysed, the post -

TABLE XIX

THE EFFECT OF ISOPRENALINE INHALATION ON NORMAL CHILDREN

	PRE - INHALATION			POST - INHALATION			Increase in F.E.V as % 1st Reading	Increase in F.V.C. as % 1st Reading
	$F.E.V_{.75}$ In Litres	F.V.C. In Litres	F.E.V%	$F.E.V_{.75}$ In Litres	F.V.C. In Litres	F.E.V%		
	1.650	2.375	70	1.625	2.325	70	- 1.5	- 2.1
1	1.725	2.450	70	1.600	2.300	69.5	- 7.2	- 6.1
	1.625	2.300	71	1.500	2.175	69	-7.7	-5 .4
	1.500	1.625	92	1.500	1.750	86	-	+ 7.7
2	1.525	1.825	84	1.375	1.600	86	- 9.8	-12.3
	1.475	1.725	85.5	1.475	1.675	88	-	- 2.9
3	2.750	3.200	86	2.775	3.200	87	+ .9	-
4	1.750	2.200	79.5	1.700	2.100	81	- 2.8	- 4.6
5	1.650	1.850	89	1.650	1.800	92	-	- 2.7
	1.575	1.825	86	1.550	1.750	89	- 1.6	- 4.2
	1.250	1.675	75	1.350	1.700	79	+ 8	+ 1.5
	1.350	1.625	83	1.400	1.650	85	+ 3.7	+ 1.5
6	1.250	1.550	81	1.175	1.575	75	- 6.0	+ 1.6
	1.400	1.675	84	1.425	1.700	84	+ 1.8	+ 1.5
7	2.200	2.625	84	2.000	2.475	81	- 9.1	- 5.7

	PRE - INHALATION			POST - INHALATION			Increase in F.E.V as % 1st Reading	Increase in F.V.C. as % 1st Reading
	$F.E.V_{.75}$ In Litres	F.V.C.	F.E.V%	$F.E.V_{.75}$ In Litres	F.V.C.	F.E.V%		
8	0.950	1.350	70	0.925	1.300	71	- 2.6	- 3.7
9	1.525	1.750	87	1.500	1.800	83	- 1.6	+ 2.8
	1.900	2.100	90	1.975	2.175	91	+ 3.9	+ 3.6
10	1.950	2.125	92	1.900	2.100	90.5	- 2.6	- 1.2
	1.800	2.000	90	1.900	2.050	93	+ 5.5	+ 2.5
11	1.800	2.600	69	1.750	2.475	71	- 2.8	- 4.8
12	0.950	1.200	79	0.975	1.250	78	+ 2.6	+ 4.2
13	0.750	0.925	81	0.800	0.975	82	+ 6.7	+ 5.4
14	1.675	2.125	79	1.650	2.175	76	- 1.5	+ 2.4
15	1.225	1.525	80	1.075	1.550	69	- 1.2	+ 1.6
	1.350	1.525	88	1.300	1.600	81	- 3.7	+ 4.9
16	1.400	2.000	70	1.300	1.900	68.5	- 7.1	- 5.0
17	1.000	1.350	74	0.925	1.450	64	- 7.5	+ 7.4
18	1.150	1.375	84	1.150	1.400	82	-	+ 1.8
19	1.900	2.325	82	1.800	2.175	83	- 5.3	- 6.5
20	1.900	2.650	72	2.125	2.800	76	+ 1.8	+ 5.7
	1.950	2.800	70	2.000	2.650	76	+ 2.6	- 5.4

isoprenaline values obtained for the $F.E.V_{.75}$ were found to be significantly lower than the pre-isoprenaline levels. No significant changes were observed for the F.V.C. values although the average values were lower after isoprenaline. t-tests were made and the following t values obtained:

$F.E.V_{.75}$: t = 2.827 with 31 degrees of freedom, and
F.V.C. : t = 2.008 also with 31 degrees of freedom.
The critical value at the 5% level of significance is 2.04.

This is a rather unexpected result since the average lowering in the $F.E.V_{.75}$ expressed as a percentage of the average initial $F.E.V_{.75}$ value was only 1.41. The explanation for this statistical finding is not readily found. It may have been a psychological effect. These "non-asthmatics" usually objected to the inhalations and this may have had an upsetting effect on the subsequent spirogram. Or it may be due to a hitherto unsuspected effect of the drug on the normal bronchial tree. The response is so different from that obtained from asthmatic subjects that the bronchodilator effect and the resulting ventilatory improvement in the latter become even more significant than it appeared when the asthmatics alone were under consideration. It would almost certainly exclude any possibility that the benefit in the asthmatic was of a psychological nature, i.e. a "functional" benefit due to the application of a piece of special apparatus of slightly dramatic type. Any increase in the $F.E.V_{.75}$ or the F.V.C. of more than 10% after the inhalation of isoprenaline (and presumably other bronchodilator drugs) can be regarded as significant.

The effect of drugs on the pulmonary ventilation in normal children as judged by this kind of spirometry obviously needs further study.

D. THE EFFECT OF ATMOSPHERIC CONDITIONS

To assess what effects atmospheric conditions may have on the $F.E.V_{.75}$ and F.V.C. test, the following comparisons were made: -

1. During the period when measurements were being carried out on normal children, 5 days of severe "smog" conditions prevailed. Eight of the children seen on more than one occasion (see experiments on "learning effect" and "day to day variation") were tested on a day of smog and on a clear day. When the values for the $F.E.V_{.75}$ and F.V.C. for the two days are compared no consistent differences are found. Any increase or

decrease can be accounted for by the normal day to day variation. t-tests were made. No statistically significant differences could be demonstrated between the clear and smog days. (Table XX).

2. Ten children who were seen on more than one occasion were paired so that the results of any two who attended on the same days could be compared. The values for the $F.E.V_{.75}$ and F.V.C. are given in Table XXI. No consistent increase or decrease for any of the five pairs is found, and any change can again be accounted for by normal day to day variation.

Although 1. and 2. were not "planned" experiments but rather incidental observations and no definite conclusions can be drawn, the results suggest that atmospheric conditions, in general, have no effect on the ventilatory function of normal children.

TABLE XX

EFFECT OF "SMOG" ON NORMALS

Name	CLEAR DAYS Date	F.E.V $_{.75}$ (In Litres)	F.V.C. (In Litres)	F.E.V%	"SMOG" DAYS Date	F.E.V $_{.75}$ (In Litres)	F.V.C. (In Litres)	F.E.V%
A.G.	18/12	1.900	2.250	85	11/12	1.950	2.100	93.0
M.B.	18/12	1.750	2.250	78	11/12	1.750	2.450	71.5
J.M.	20/12	2.200	2.700	81.6	6/12	2.500	2.700	92.4
D.C.	25/11	1.950	2.300	85	11/12	1.900	2.000	95
O.K.	26/11	2.350	2.825	83	6/12	2.500	2.875	87.4
S.W.	26/11	2.250	3.500	64.5	29/11	2.250	3.400	66.4
K.S.	13/12	2.100	2.700	78	11/12	2.100	2.450	85.7
B.B.	16/12	2.450	3.250	75.5	6/12	2.250	3.400	75

TABLE XXI

PAIRED NORMALS

Name	Date	$F.E.V_{.75}$ In Litres	F.V.C.	F.E.V%	Date	$F.E.V_{.75}$ In Litres	F.V.C.	F.E.V%
R.C.	19/3	1.700	2.100	81	21/3	1.650	2.000	82
D.B.	19/3	2.550	3.050	84	21/3	2.550	2.950	87
R.C.	19/3	1.700	2.100	81	4/4	1.700	2.150	79
E.W.	19/3	1.925	2.175	89	4/4	1.950	2.125	92
A.G.	11/12	2.050	2.100	93.5	18/12	1.900	2.250	84
M.B.	11/12	1.750	2.450	71.5	18/12	1.750	2.250	78
P.E.	14/3	1.300	1.700	77	17/3	1.150	1.750	66
P.D.	14/3	1.200	1.250	96	17/3	1.275	1.375	93
D.D.	6/12	3.250	4.000	81.3	20/12	3.350	3.750	89.5
J.M.	6/12	2.500	2.700	92.4	20/12	2.200	2.700	81

SUMMARY

1. Anthropometric and spirometric investigations were carried out on 122 "normal" boys and 55 "normal" girls. The anthropometric measurements recorded were age, standing height, sitting height, and weight. The spirometric recordings consisted of Forced Expiratory (F.E.S.) and Forced Inspiratory Spirograms (F.I.S.). Characteristics of the shapes of the F.E.S. and F.I.S. were investigated. The $F.E.V_{.75}$ and F.V.C. were measured from the F.E.S. in 122 boys and 55 girls. The $F.I.V._{.75}$ and F.I.V.C. were measured in 120 boys and 51 girls. The corresponding F.E.V% and F.I.V% values were calculated for each child.

2. The shapes of the F.E.S. and F.I.S. in children have been discussed. The F.E.S's were found, in general, to be remarkably uniform in shape and almost specific at any particular occasion for a given individual. The average time taken for the delivery of the F.V.C. varies from 1.5 secs. to 1.9 secs. depending on the age of the child. The average time taken for the completion of the F.I.S. varies from .95 sec. to 1 sec. depending on age.

3. The values obtained for the $F.E.V._{.75}$, F.V.C., $F.I.V._{.75}$ and F.I.V.C. were statistically analysed. Regression lines for the expiratory or inspiratory volumes, as a function of a single anthropometric characteristic were calculated. Expiratory and inspiratory volumes were also considered as a function of the multiple variables, age, standing height, sitting height and weight.

4. A high degree of correlation was found between each of the four anthropometric measurements and the spirometric measurements. Because of this, any one or more, or all four of the anthropometric measurements in combination may be used for the prediction of expected normal spirometric values.

5. The basic prediction formula is:

   Spirometric volume in litres = a + b (anthropometric measurement) $\pm\ 2\sigma_z$

   This gives the "most probable" spirometric value viz: a + b (anthropometric measurement), and the bounds about this "most probable" value within which 95% of all normal cases should lie. These bounds ($\pm\ 2\sigma_z$) are quite large for all the spirometric measurements. This constitutes one of the disadvantages of spirometric investigation.

Multiple regression prediction formulae were also calculated for the $F.E.V_{.75}$ and F.V.C. independently for girls and boys:

x_1 = age, x_2 = Standing Height, x_3 = Sitting Height
x_4 = Weight.

GIRLS:

$$F.E.V_{.75} = -1.2875 + .0098x_1 + .0357x_2 + .0106x_3 + .00855x_4$$

$$\sigma_z = .233$$

$$F.V.C. = -2.2379 + .0232x_1 + .0404x_2 + .0441x_3 + .0074x_4$$

$$\sigma_z = .286$$

BOYS:

$$F.E.V_{.75} = -2.4080 + .0044x_1 + .0371x_2 + .0504x_3 + .0079x_4$$

$$\sigma_z = .192$$

$$F.V.C. = -.9118 + .0413x_1 + .0396x_2 - .0413x_3 + .0231x_4$$

$$\sigma_z = .328$$

6. The prediction formulae using standing height alone, as an index in the prediction of expected normal spirometric values, is considered to be the method of choice for routine work. The values for "a", "b" and σ_z

in the basic prediction formula for the $F.E.V_{.75}$, F.V.C. $F.I.V_{.75}$ and F.I.V.C. in girls and boys are:-

TABLE XXII

		GIRLS	BOYS
$F.E.V_{.75}$	a	-2.470	-3.140
	b	0.077	0.089
	σ_z	0.308	0.325
F.V.C.	a	-3.219	-4.770
	b	0.097	0.128
	σ_z	0.345	0.439
$F.I.V_{.75}$	a	-1.531	-2.450
	b	0.053	0.069
	σ_z	0.375	0.374
F.I.V.C.	a	-3.194	-3.885
	b	0.095	0.111
	σ_z	0.348	0.526

7. The average F.E.V% in normal boys varies from approximately 70% - 85% depending on age, with the lower limit at approximately 60% - 65%. The value for the F.E.V.% is higher in normal girls and is approximately 80%, with the lower limit in the region of 70%.
The scatter of points for the F.I.V.% is so large that it excludes this index from having any value in ventilatory assessment.

8. The $F.E.V_{.75}$, F.V.C. and F.E.V% are more suitable values for the evaluation of ventilatory function in children than the $F.I.V_{.75}$ F.I.V.C. and F.I.V.%.

9. Values obtained for the $F.E.V_{.75}$ in boys have been compared and are in agreement with those of Kennedy et al. (1957), the only other comparable figures. The values obtained for the $F.I.V_{.75}$ in boys, although lower than Kennedy's, are in general in agreement. The values for the F.V.C. in girls and boys are in close agreement with the corresponding values obtained by Ferris and Smith (1953) and Ferris et al. (1952) for the V.C. No figures other than those of the present series are available for the F.I.V.C. in girls and boys or for the $F.E.V_{.75}$ and $F.I.V_{.75}$ in girls.

10. The F.V.C. and F.I.V.C. values are 11.3% and 9.9% larger, respectively, in boys than in girls. This difference is large enough to be of practical clinical significance and justifies the use of separate prediction formulae for these values in the two sexes. The differences in the $F.E.V_{.75}$ and $F.I.V._{.75}$ values in the two sexes are insignificant.

11. No appreciable learning effect could be demonstrated in the $F.E.V_{.75}$ and F.V.C. values on repeating the

test (a) after 30 minutes and (b) over a period of days.

12. The $F.E.V_{.75}$ and F.V.C. values vary from day to day. This variation, expressed as a percentage of the initial value is in the majority of cases within the $\pm$ 10% range.

13. A statistically significant decrease for both the $F.E.V_{.75}$ and F.V.C. values has been demonstrated in (a) changing from the standing to the sitting position and in (b) changing from the standing to the supine position.

The decrease seen in (a) is so small that it can be considered as "medically insignificant" and ignored in practical clinical work. The lowering of the $F.E.V_{.75}$ and F.V.C. in (b) however, is large enough to warrant consideration when the test is carried out in the supine position.

14. The investigation into the effect of isoprenaline inhalation on the $F.E.V_{.75}$ and F.V.C. values in normal children produced unexpected results in that the $F.E.V_{.75}$ values were found to be significantly lower after the isoprenaline inhalation. The average decrease in the $F.E.V_{.75}$ expressed as a percentage of the initial level is actually very small. Further investigations should be carried out to confirm or elucidate these findings.

15. Consequently, any increase in the $F.E.V_{.75}$ or F.V.C.

of more than 10% after the inhalation of isoprenaline (and presumably other broncho-dilator drugs) in children with asthma or any condition associated with bronchospasm can be regarded as significant.

16. Changes in atmospheric conditions have no effect on the $F.E.V_{.75}$ and F.V.C. values in normal children.

The Forced Expiratory Volume and Forced Vital Capacity Test has been found to be suitable for the assessment of ventilatory function in children over the age of 6 years. It is a simple, interesting, easily performed and repeatable test.

Description	Recommended Term	Abbreviation
Spirogram of a forced, complete inspiration or expiration	Forced inspiratory/expiratory spirogram	F.I.S./F.E.S.
Volume of gas exhaled over a given time interval during a complete forced expiration*	Forced expiratory volume, qualified by time interval used	$F.E.V._T$
Volume of gas expired after full inspiration; expiration being as rapid and complete as possible (that is, forced)*	Forced vital capacity	F.V.C.
$F.E.V._T$ expressed as percentage of vital capacity	Percentage expired (in T sec.)	F.E.V.%
Maximum volume of air which subject can breathe per min.	Maximum breating capacity	M.B.C.
Volume of air which subject can breathe on voluntary maximum hyperventilation for a given time (direct measurement of the "M.B.C.," usually made during 15 sec.) (a) frequency controlled (b) frequency uncontrolled	Maximum voluntary ventilation (a) no specific qualification (b) qualified by "free" (Frequency to be indicated in both cases)	(a) M.V.V. (b) $M.V.V._F$ (Frequency as subscript, e.g., $M.V.V._{60}$, $M.V.V._{F60}$)
Volume of air which subject can breathe in one minute (as predicted from $F.E.V._T$)	Indirect maximum breathing capacity	Ind. M.B.C.

FIG. 1.

FIG. 2.

PHYSICAL CHARACTERISTICS OF SPIROMETER

BELL	ALUMINIUM
WALL THICKNESS	0·30mm.
LENGTH	28·8 mm.
DIAMETER	23·1 mm.
WEIGHT	250 g.
COUNTERPOISE	200g.
CORD WEIGHT	NEGLIGIBLE
TOTAL WT. OF MOVING PARTS	450g.
TWO PULLEYS	PERSPEX
DIAMETER	6·0 cm.
THICKNESS	3·0 mm.
WEIGHT	22·5 g. each
MOMENT OF INERTIA	314 g. cm^2 total for two pulleys

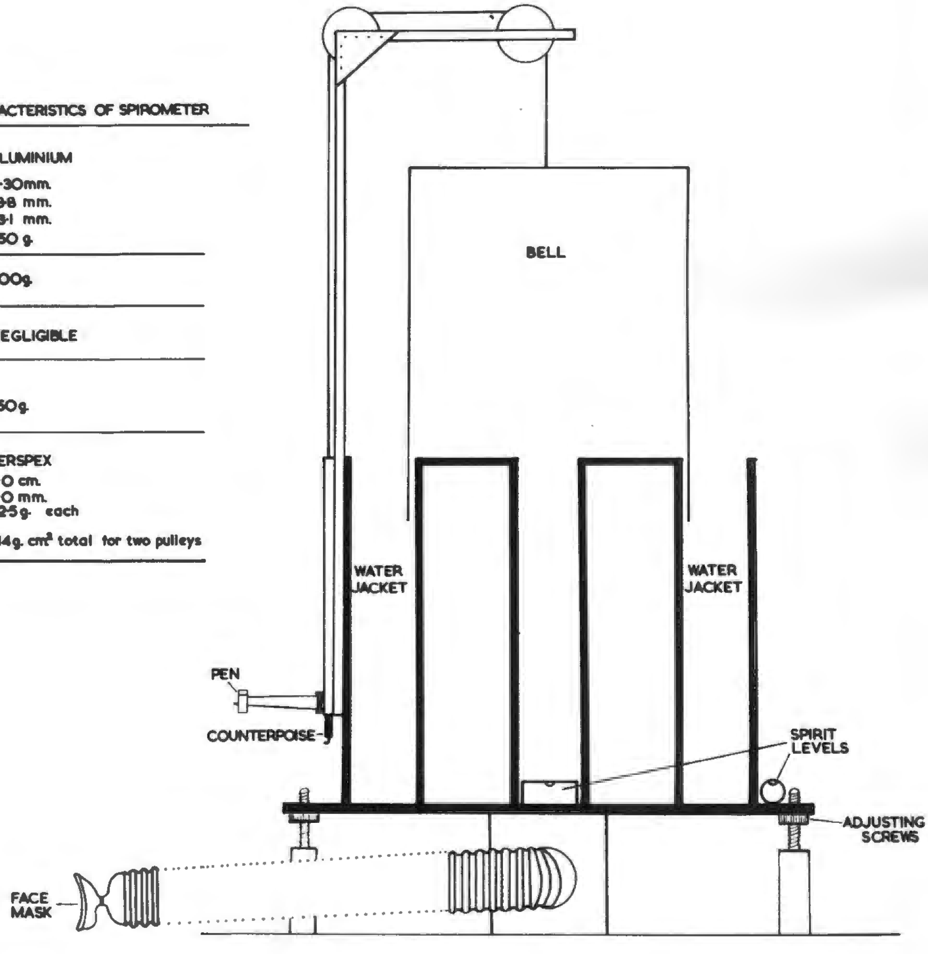


FIG 3

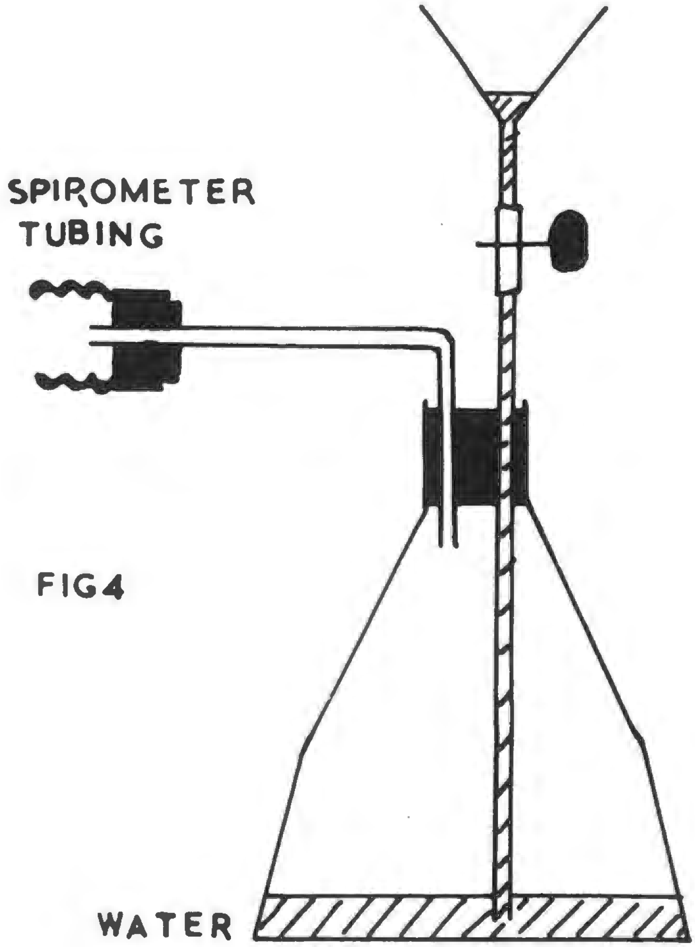
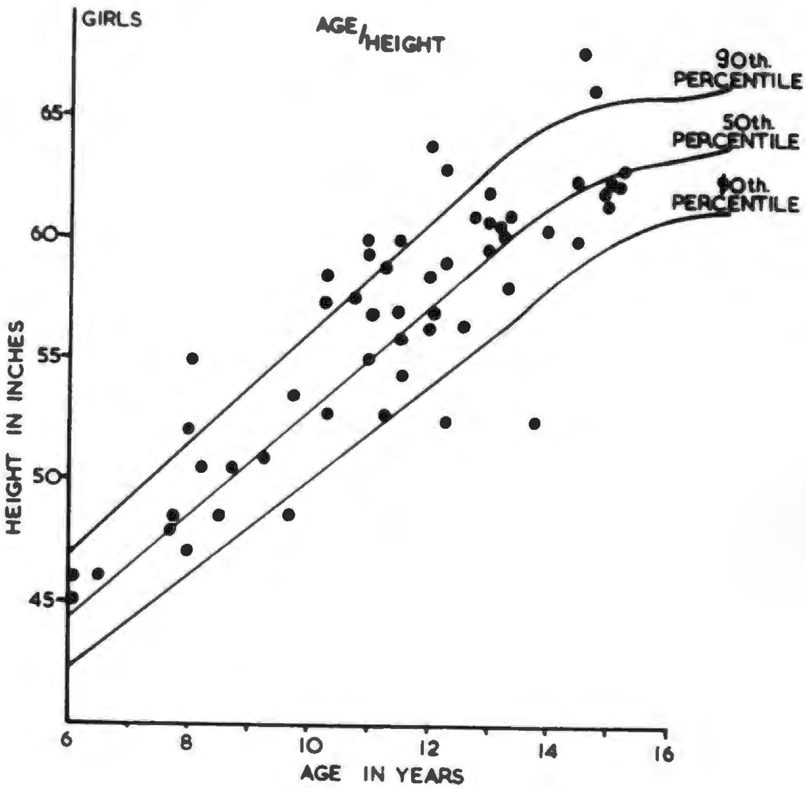


FIG4


GIRLS
AGE/HEIGHT
HEIGHT IN INCHES
AGE IN YEARS
90th. PERCENTILE
50th. PERCENTILE
10th. PERCENTILE
45
50
55
60
65
6
8
10
12
14
16

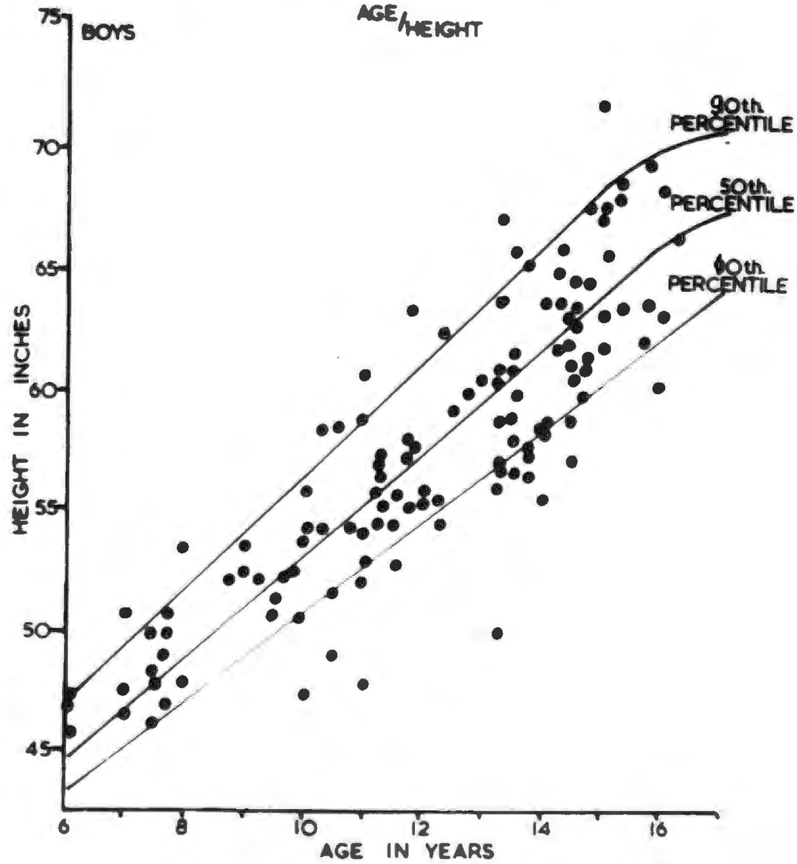
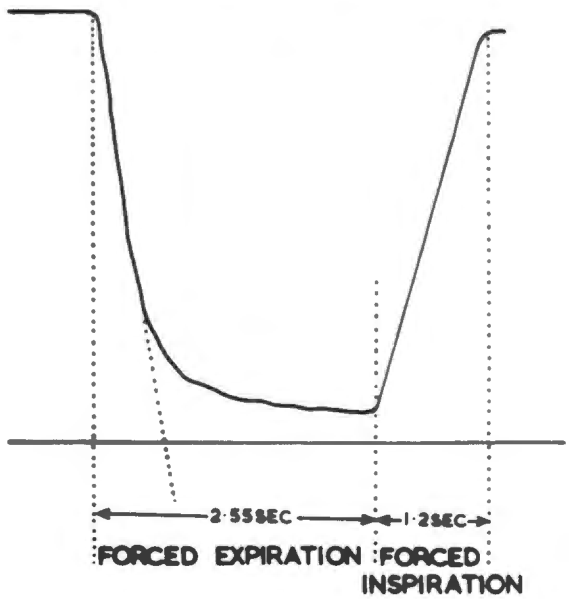

BOYS
AGE/HEIGHT
HEIGHT IN INCHES
AGE IN YEARS
90th. PERCENTILE
50th. PERCENTILE
10th. PERCENTILE
45
50
55
60
65
70
75
6
8
10
12
14
16

FIG 6

L.P. ♀ AGE 13YRS. 3MTHS. "NORMAL"

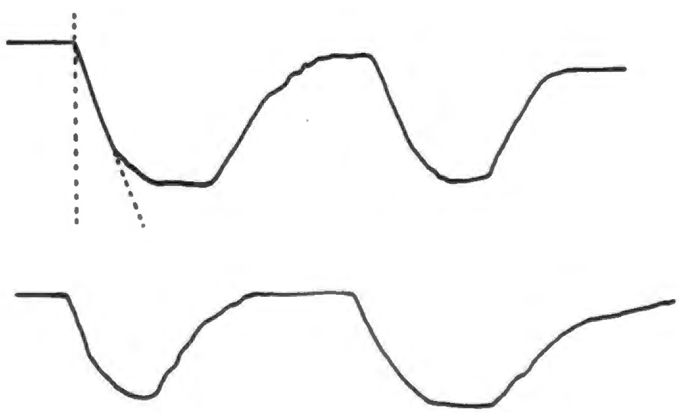
WEIGHT: 94LBS. HEIGHT: 61" SIT'G HEIGHT: 31⅛"



$FEV_{.25sec.}$	=	1·50 Litres
$FEV_{.75sec.}$	=	2·65
$FEV_{.25-.75sec.}$	=	1·15
$FEV_{1sec.}$	=	2·85
FEV_{A}	=	2·1
FVC	=	2·9
$FEV_{.75}/FVC$	=	91·4%
$FIV_{.25sec.}$	=	·50 Litres
$FIV_{.75sec.}$	=	2·25
$FIV_{.25-.75sec.}$	=	1·75
$FIV_{1sec.}$	=	2·775
FIVC	=	2·85
FIV_{A}	=	2·80
$FIV_{.75}/FIVC\%$	=	79%

P.D. AGE: 7YRS. 6MTHS.

WEIGHT: 46LBS. HEIGHT: 48" SIT'G HEIGHT: 26"



$FEV_{.75sec.}$	=	1·075
FVC	=	1·125
$FEV_{.75}/FVC$	=	95%

FIG. 7

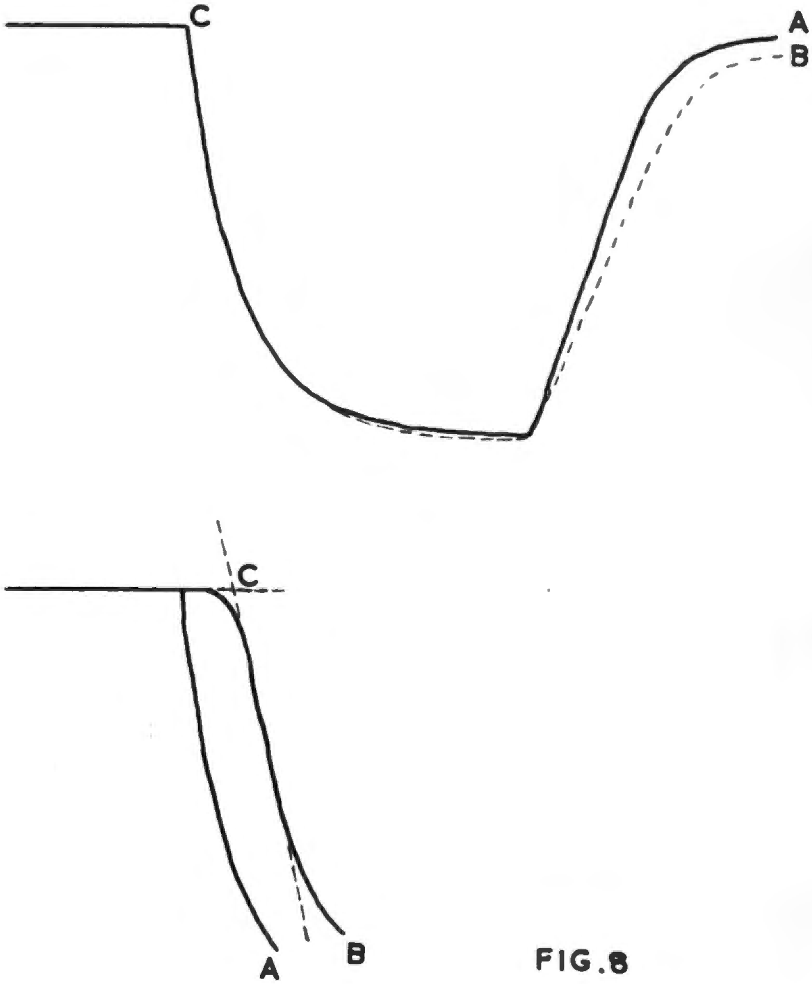
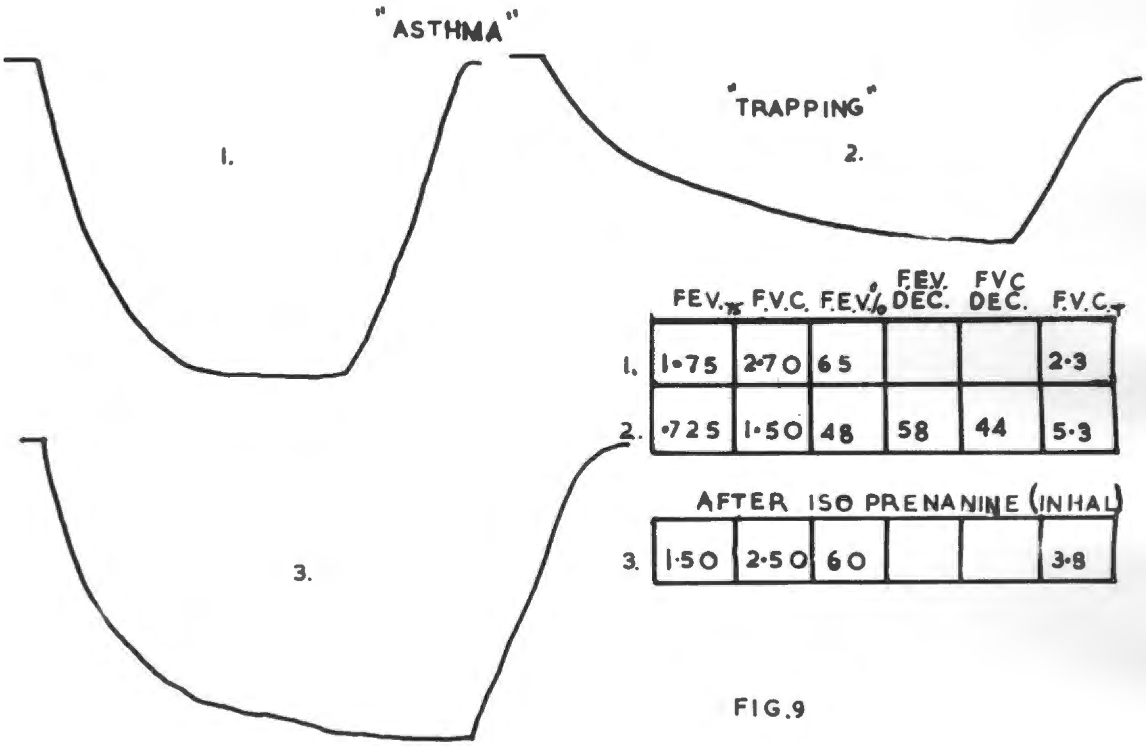


FIG. 8



	F.E.V.$_{.75}$	F.V.C.	F.E.V.%	F.E.V. DEC.	F.V.C. DEC.	F.V.C.$_T$
1.	1·75	2·70	65			2·3
2.	·725	1·50	48	58	44	5·3

AFTER ISO PRENANINE (INHAL)

3.	1·50	2·50	60			3·8

FIG.9

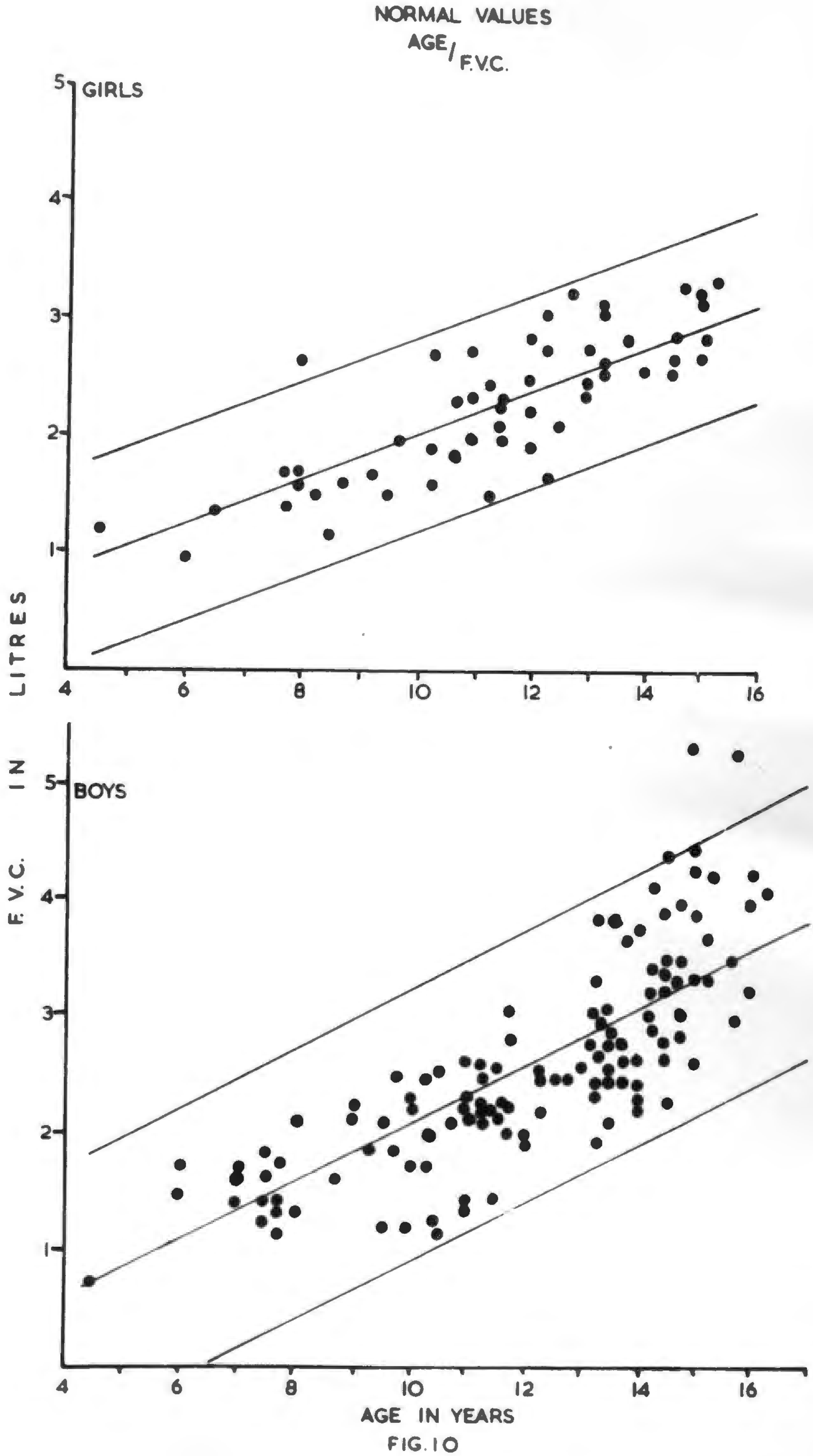

NORMAL VALUES
AGE/F.V.C.
GIRLS
BOYS
F. V. C. IN LITRES
AGE IN YEARS
1
2
3
4
5
4
6
8
10
12
14
16

FIG. 10

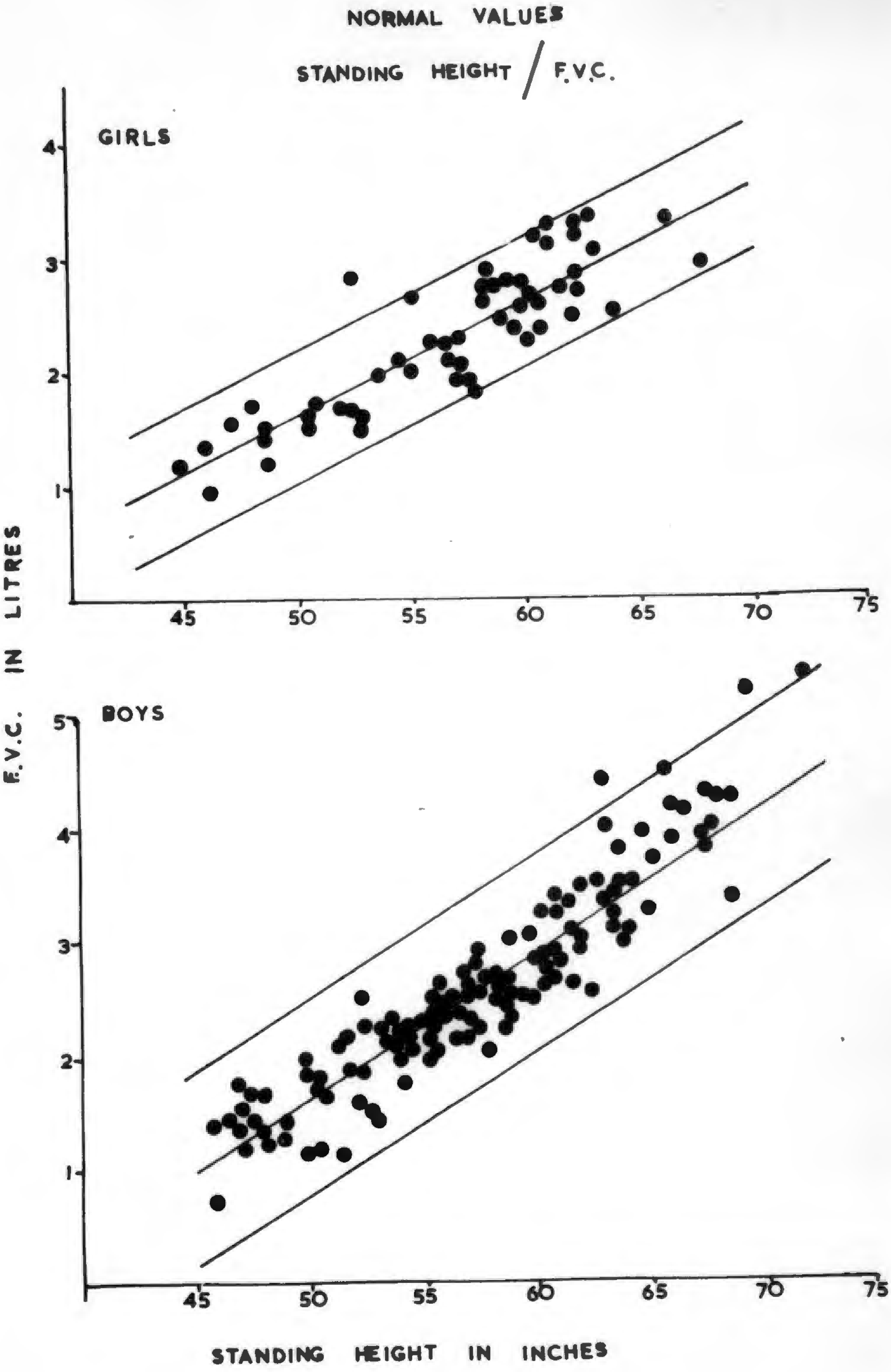
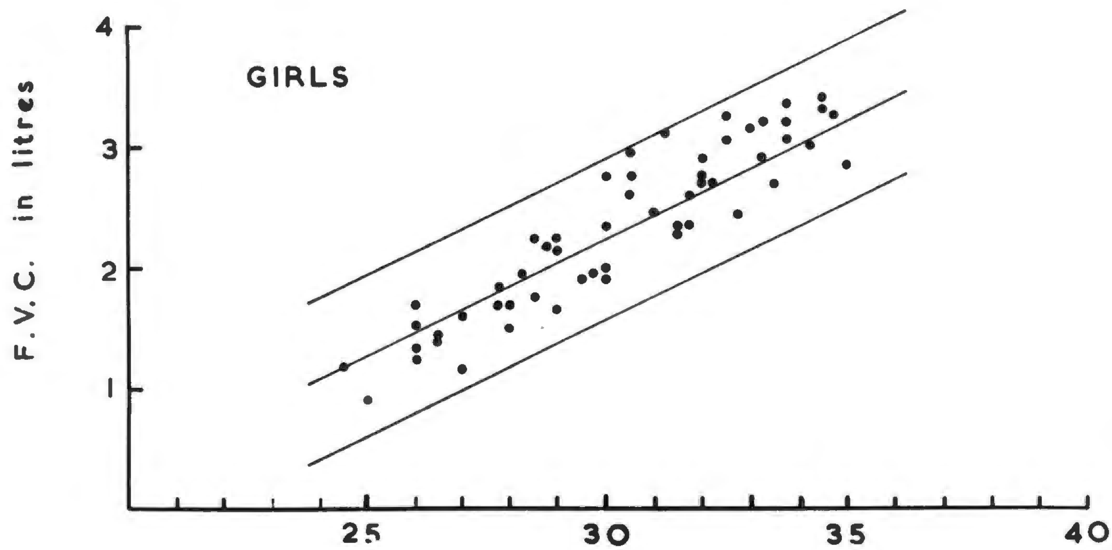

NORMAL VALUES
STANDING HEIGHT / F.V.C.
GIRLS
BOYS
F.V.C. IN LITRES
STANDING HEIGHT IN INCHES
1
2
3
4
5
45
50
55
60
65
70
75

FIG. 11.

NORMAL VALUES

Sitting height / F.V.C.



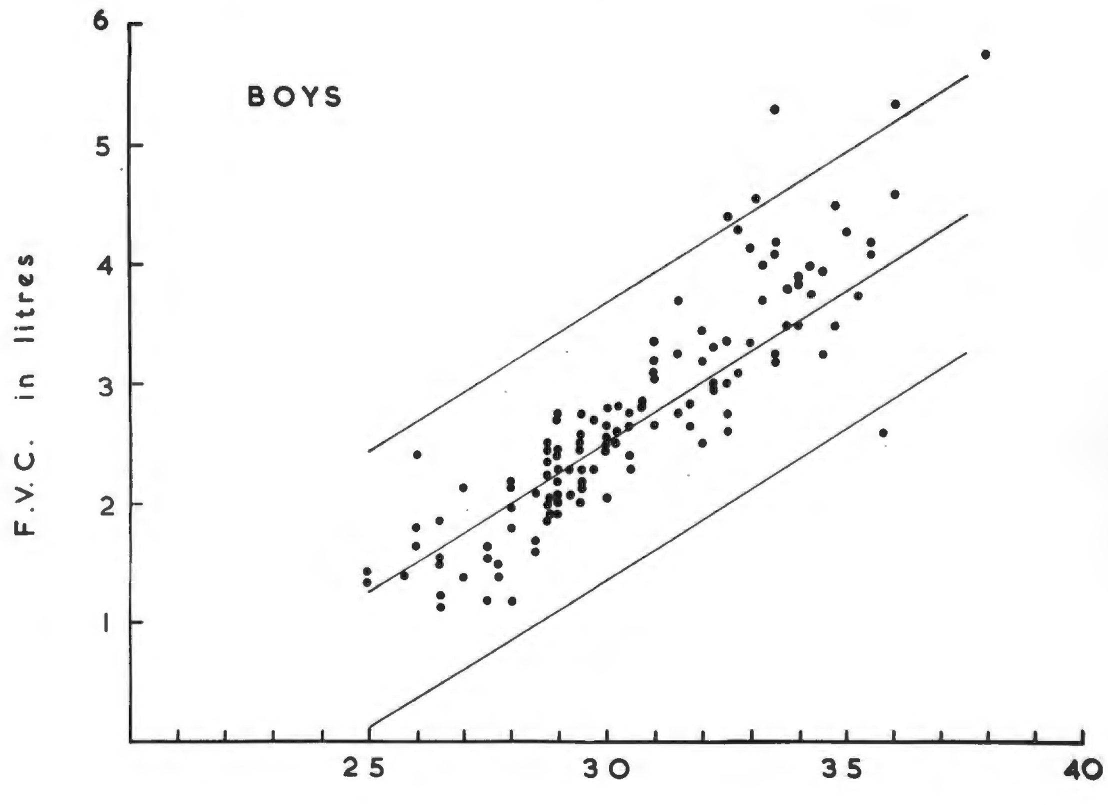


FIG.12

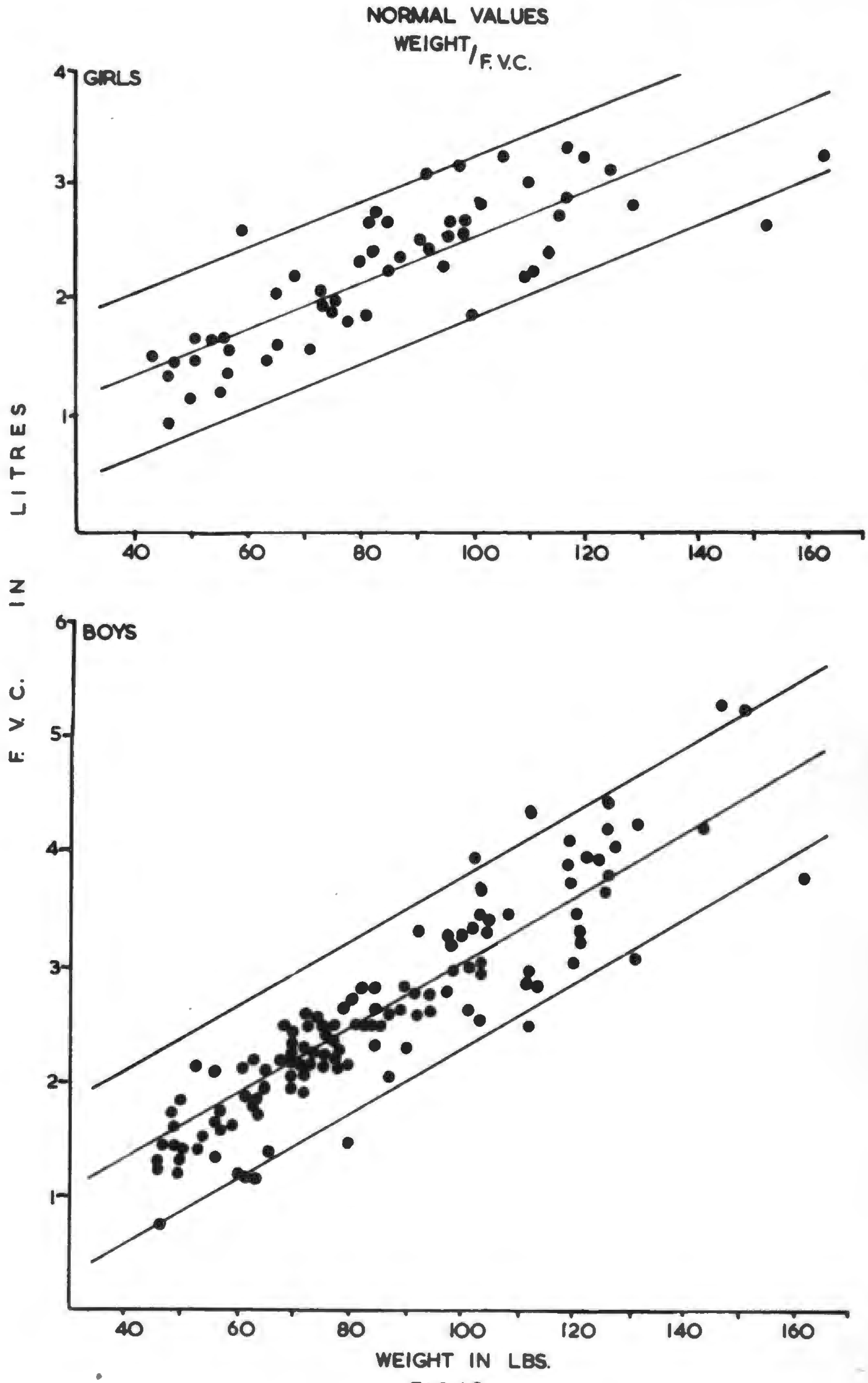

NORMAL VALUES
WEIGHT/F.V.C.
GIRLS
BOYS
F.V.C. IN LITRES
1
2
3
4
5
6
40
60
80
100
120
140
160
WEIGHT IN LBS.

FIG. 13

NORMAL VALUES

AGE / F.E.V. $_{\cdot 75}$

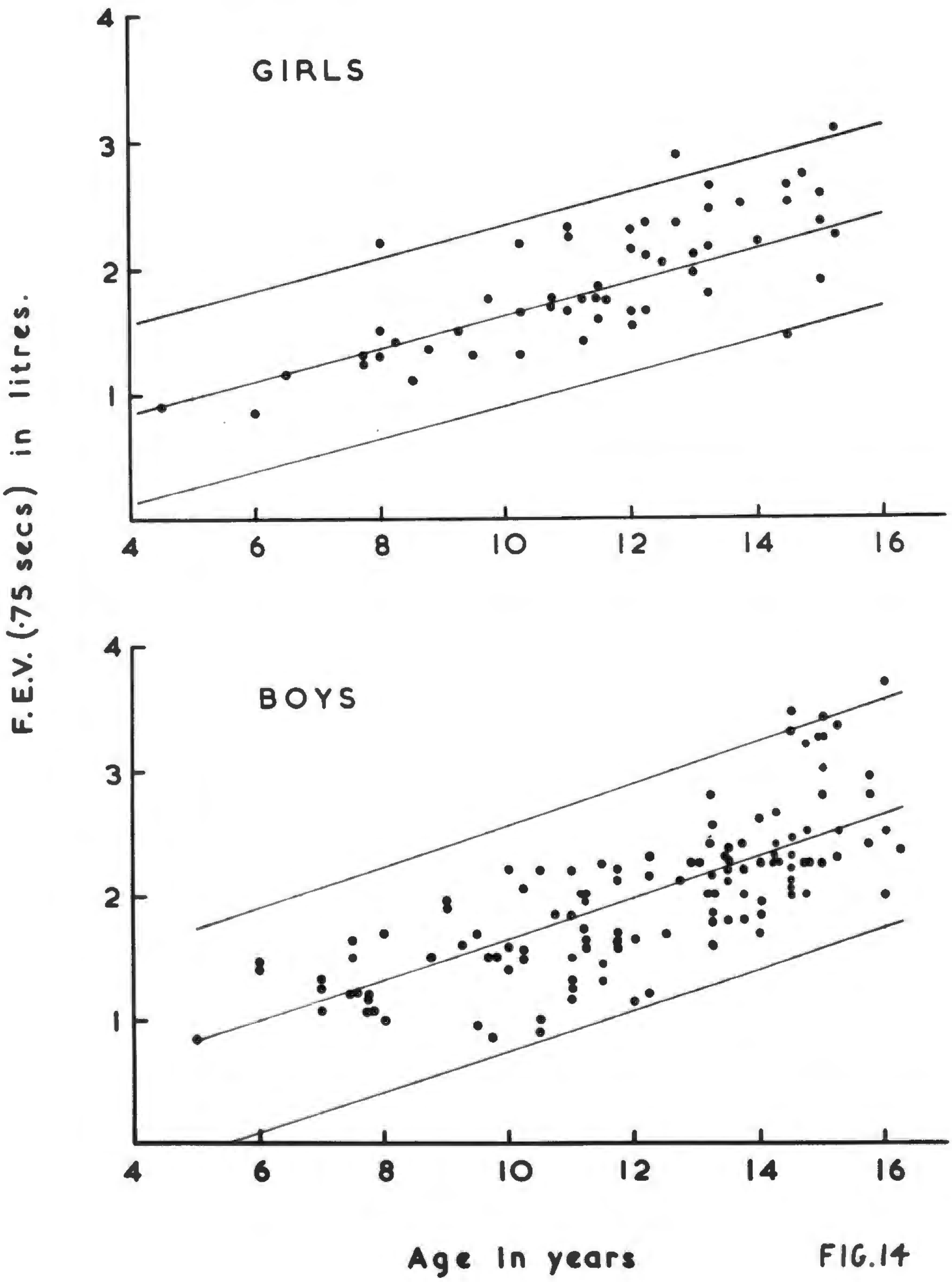


FIG. 14

NORMAL VALUES

STANDING HEIGHT / F.E.V.$_{.75}$

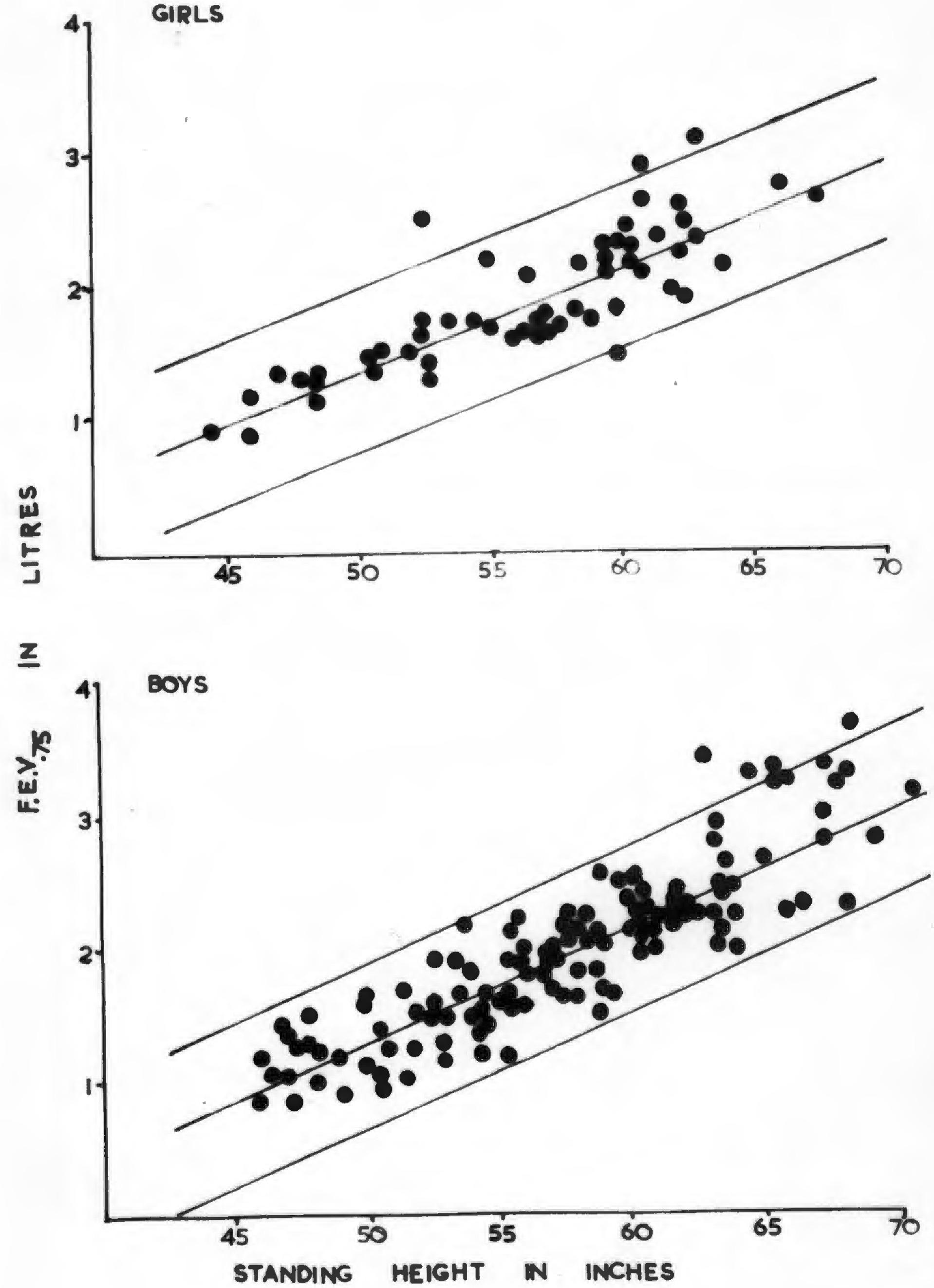


FIG. 15

NORMAL VALUES.

Sitting height. / F.E.V. .75

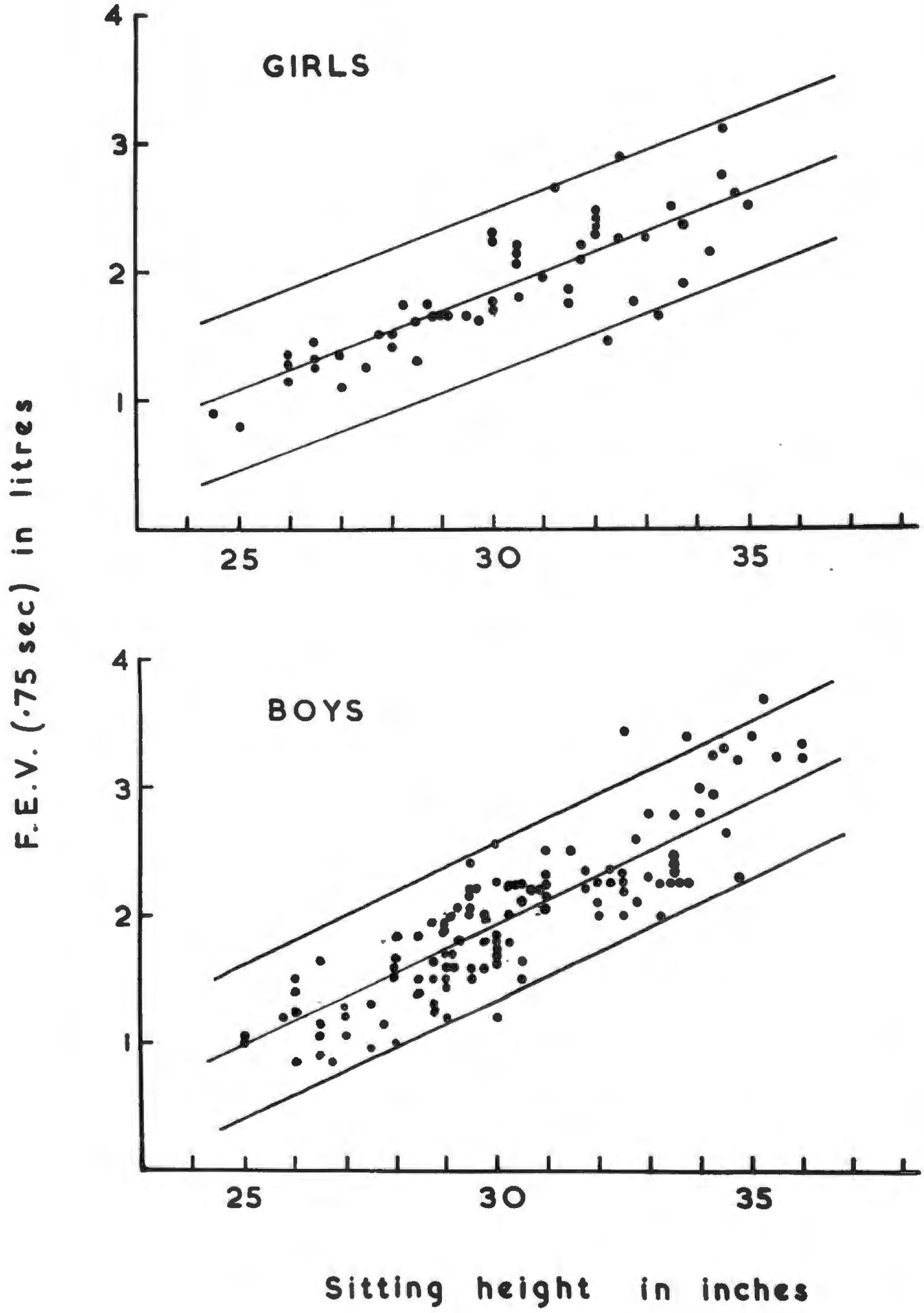


FIG 16

NORMAL VALUES

Weight / F.E.V. ·75

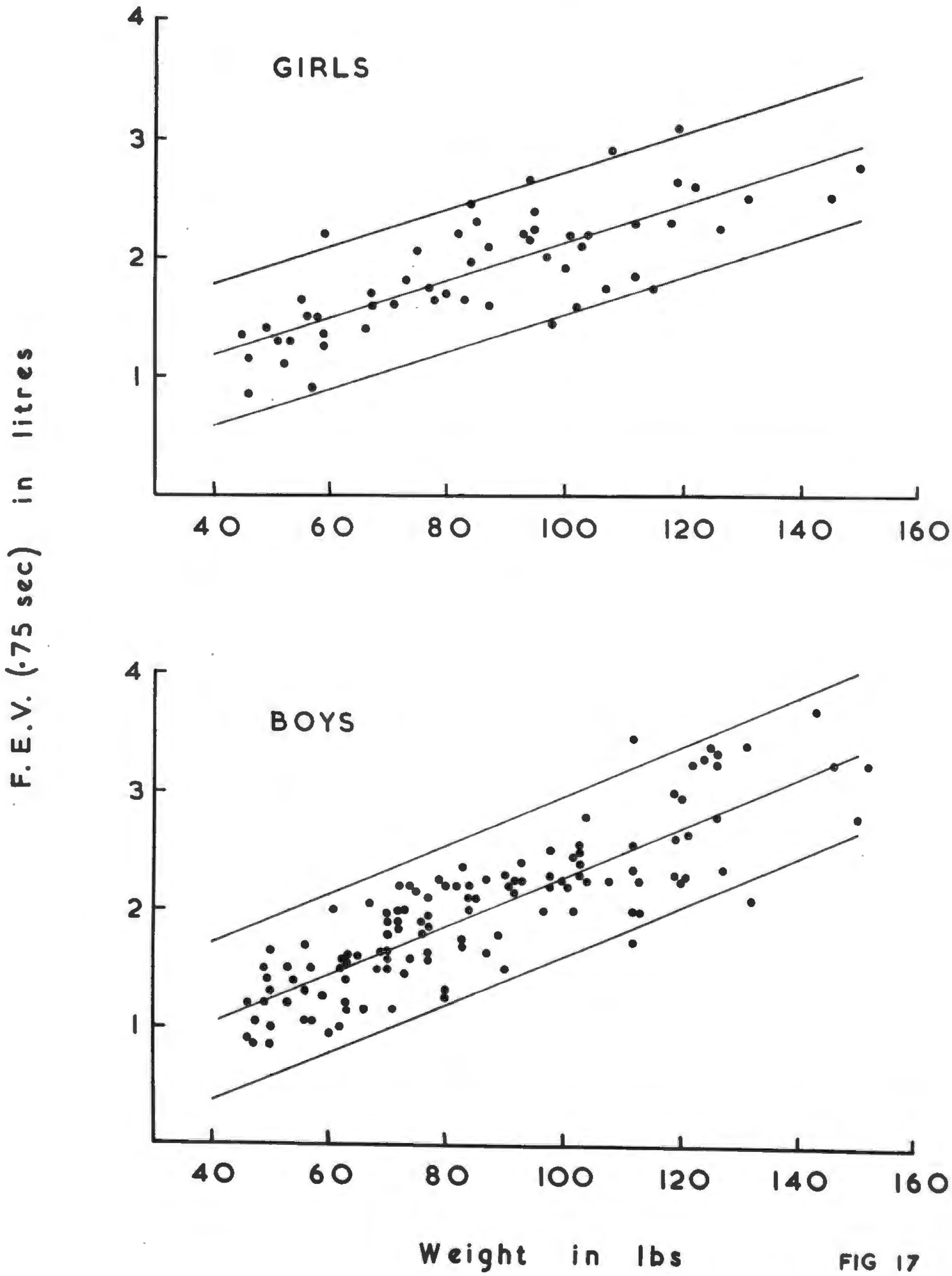


FIG 17

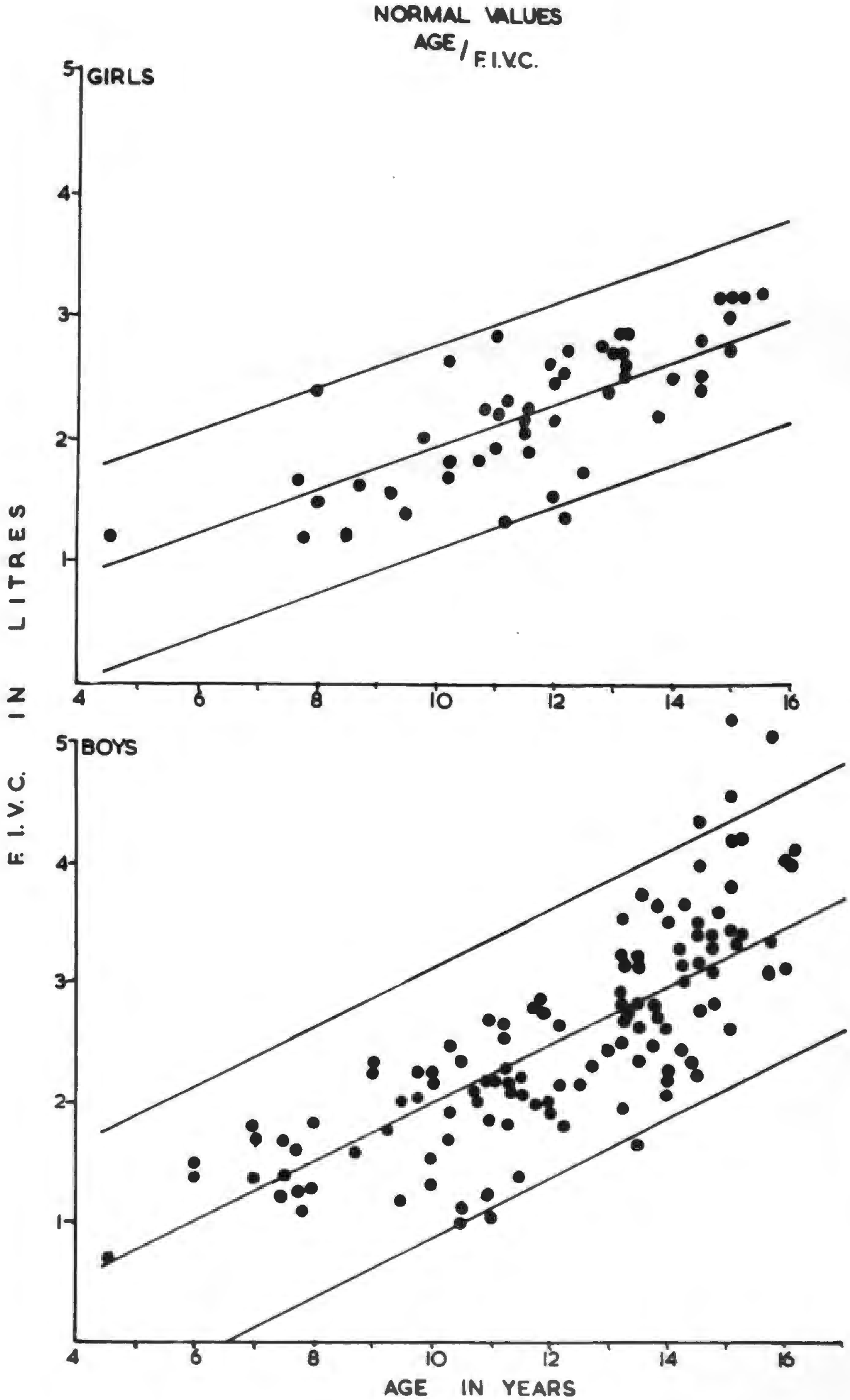

NORMAL VALUES
AGE / F.I.V.C.
GIRLS
BOYS
F.I.V.C. IN LITRES
AGE IN YEARS
1
2
3
4
5
4
6
8
10
12
14
16

FIG. 18

NORMAL VALUES
STANDING HEIGHT / F.I.V.C.

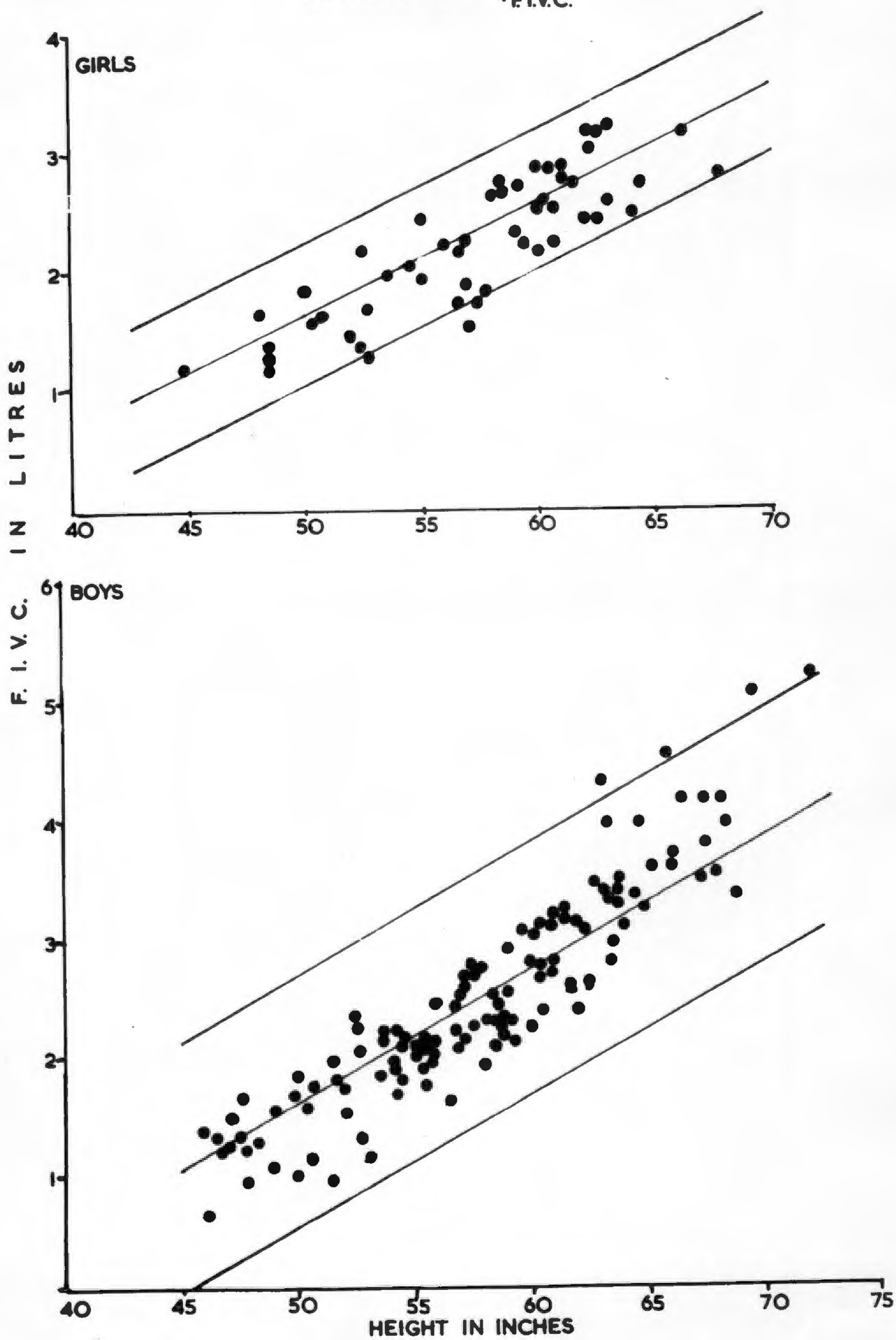


FIG. 19

NORMAL VALUES

SITTING HEIGHT / F.I.V.C.

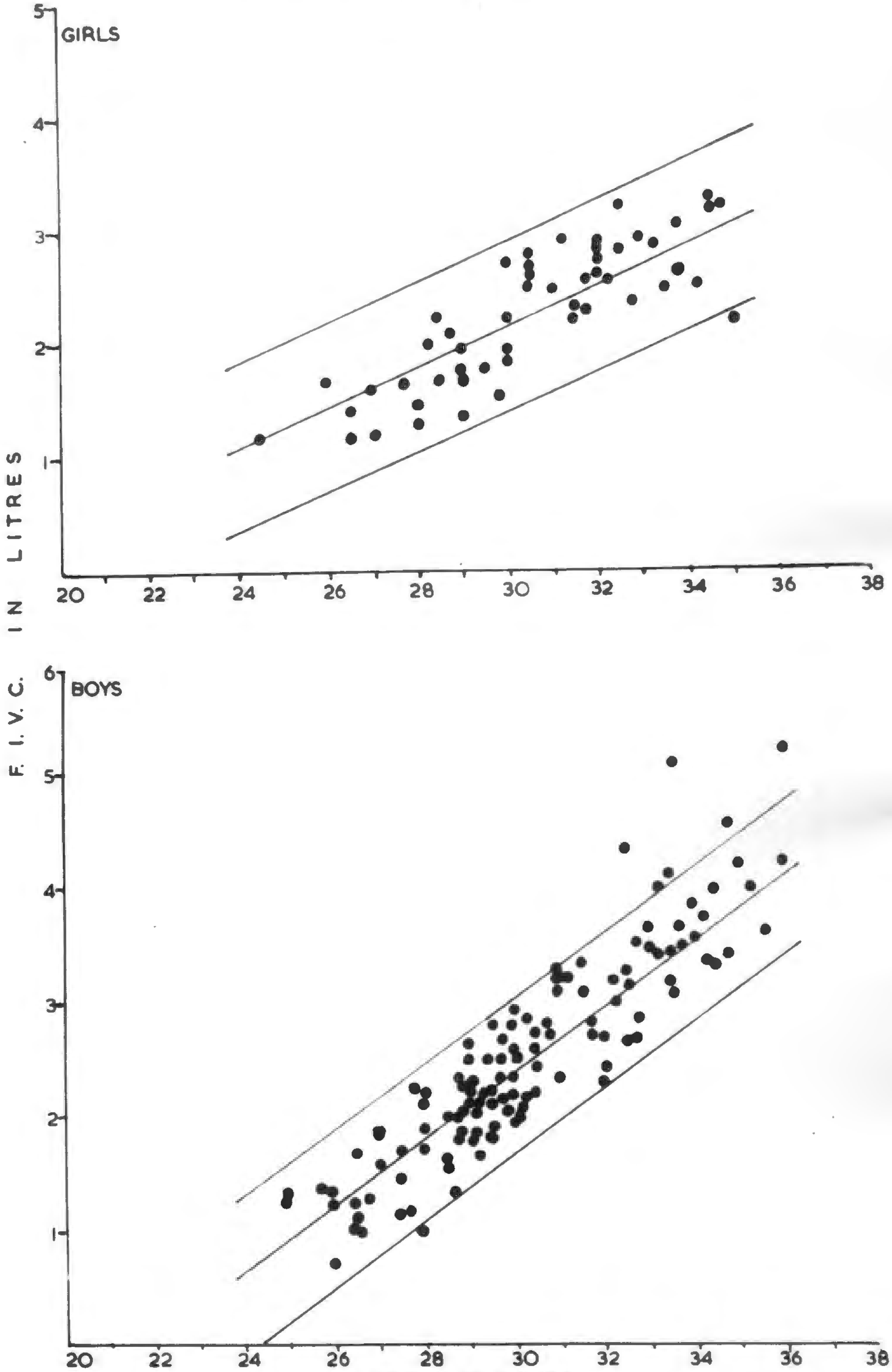


FIG. 20

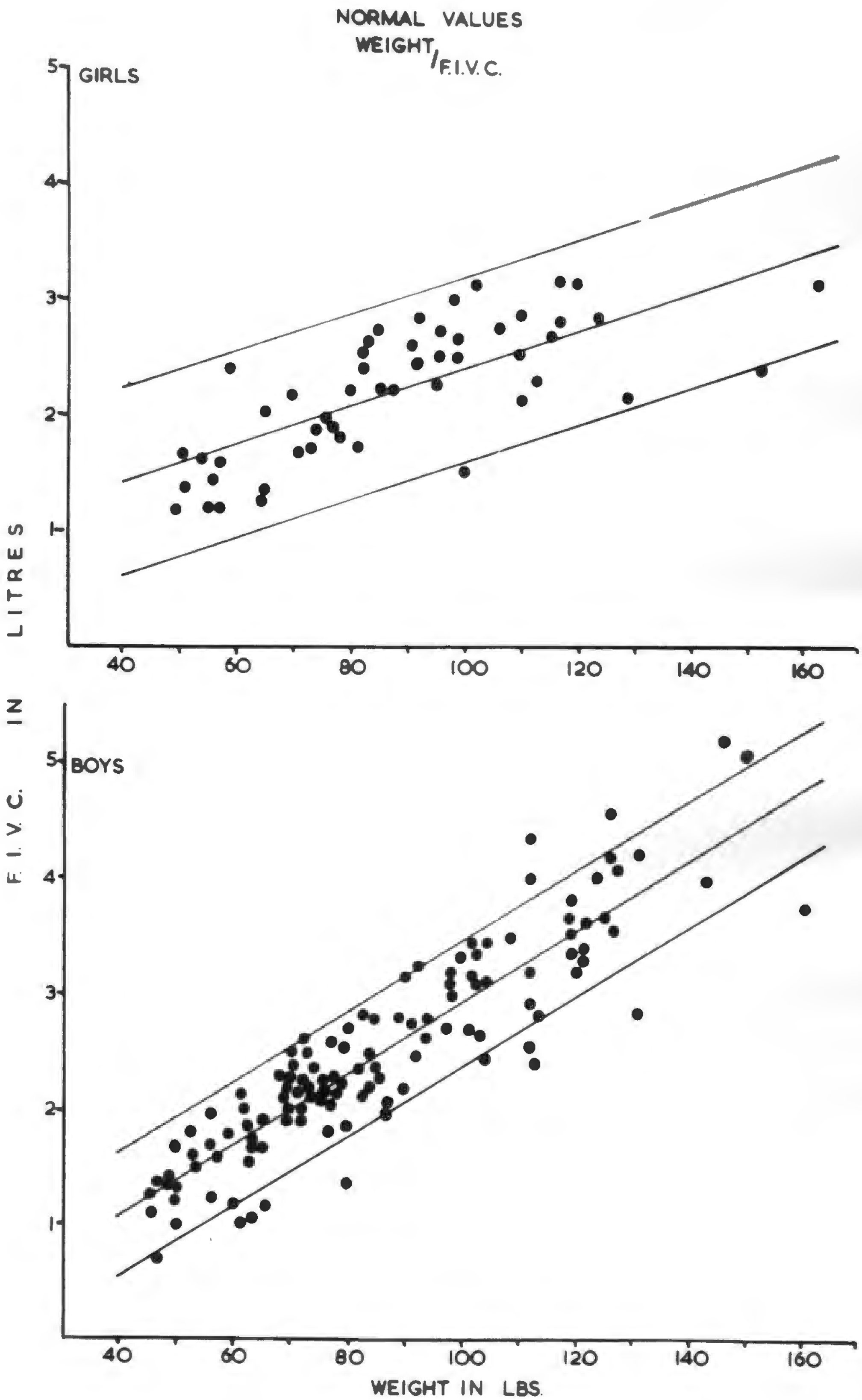

NORMAL VALUES
WEIGHT/F.I.V.C.
GIRLS
BOYS
F. I. V. C. IN LITRES
WEIGHT IN LBS.
1
2
3
4
5
40
60
80
100
120
140
160

FIG. 21

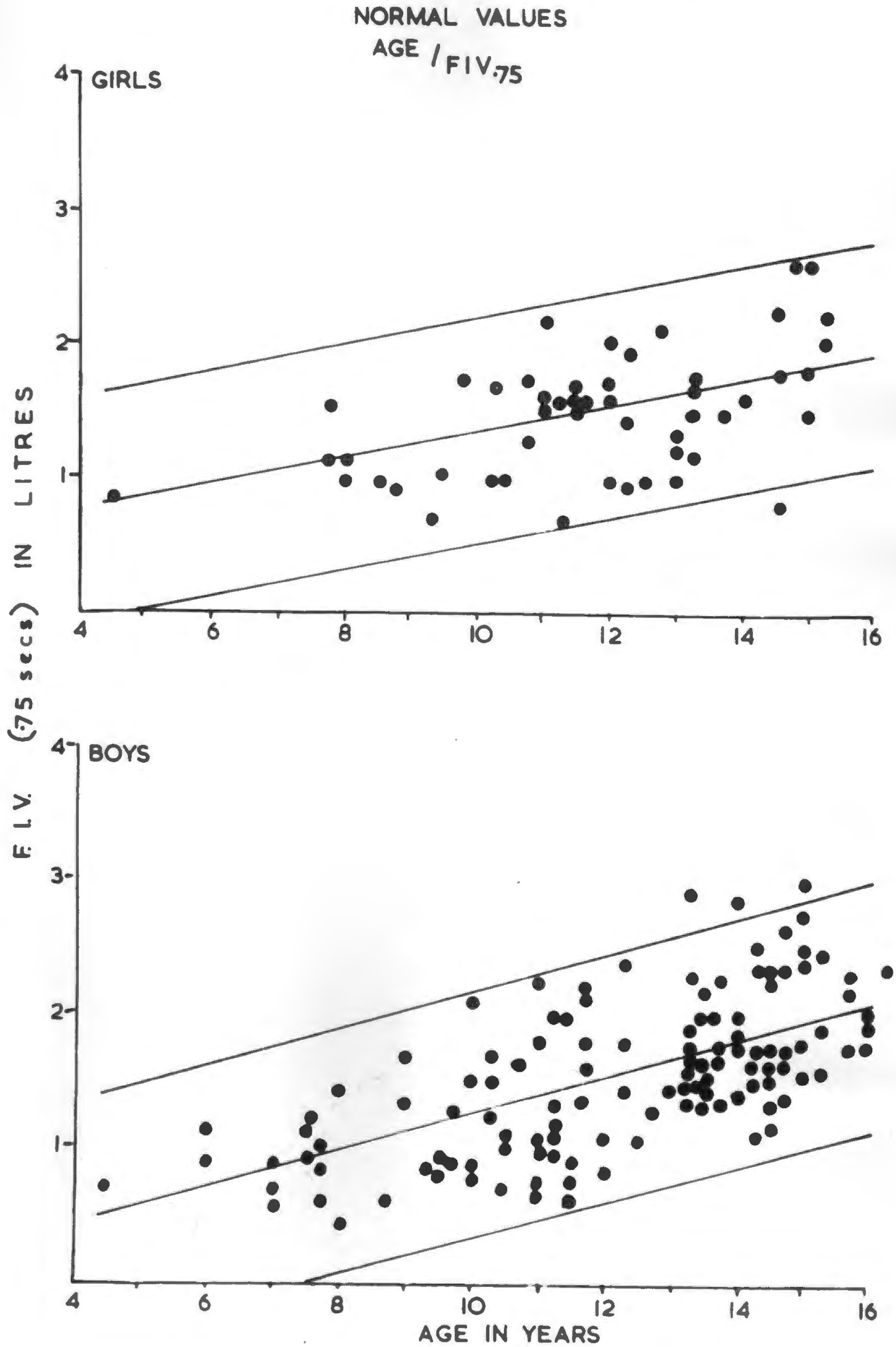

NORMAL VALUES
AGE / FIV.75
GIRLS
BOYS
F.I.V. (·75 secs) IN LITRES
4
3
2
1
4
6
8
10
12
14
16
AGE IN YEARS

FIG.22

NORMAL VALUES
STANDING HEIGHT / F.I.V. .75

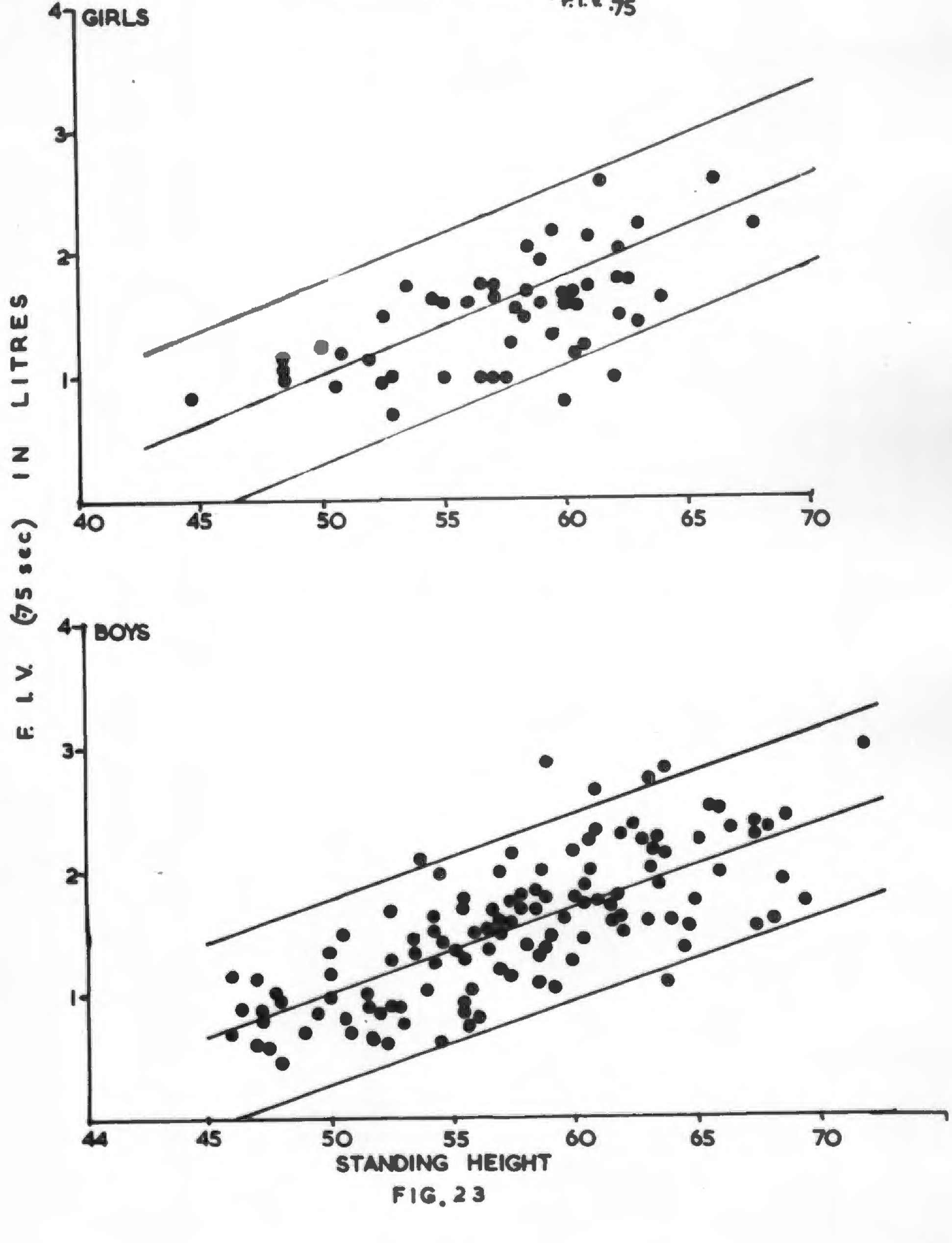


FIG. 23

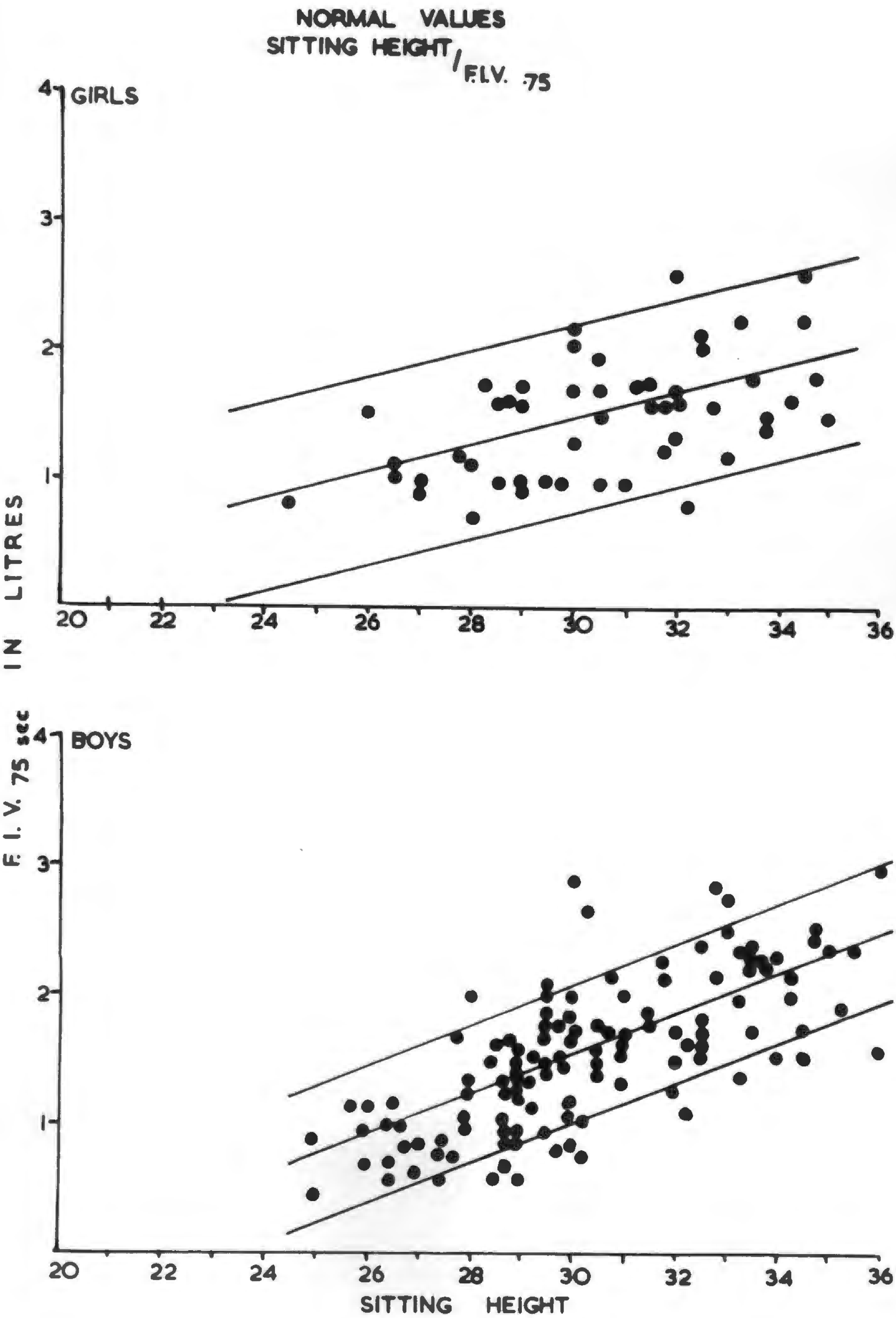

NORMAL VALUES
SITTING HEIGHT/F.I.V. ·75
GIRLS
BOYS
F. I. V. 75 sec IN LITRES
4
3
2
1
20
22
24
26
28
30
32
34
36
SITTING HEIGHT

FIG. 24

NORMAL VALUES
WEIGHT / F.I.V. 75

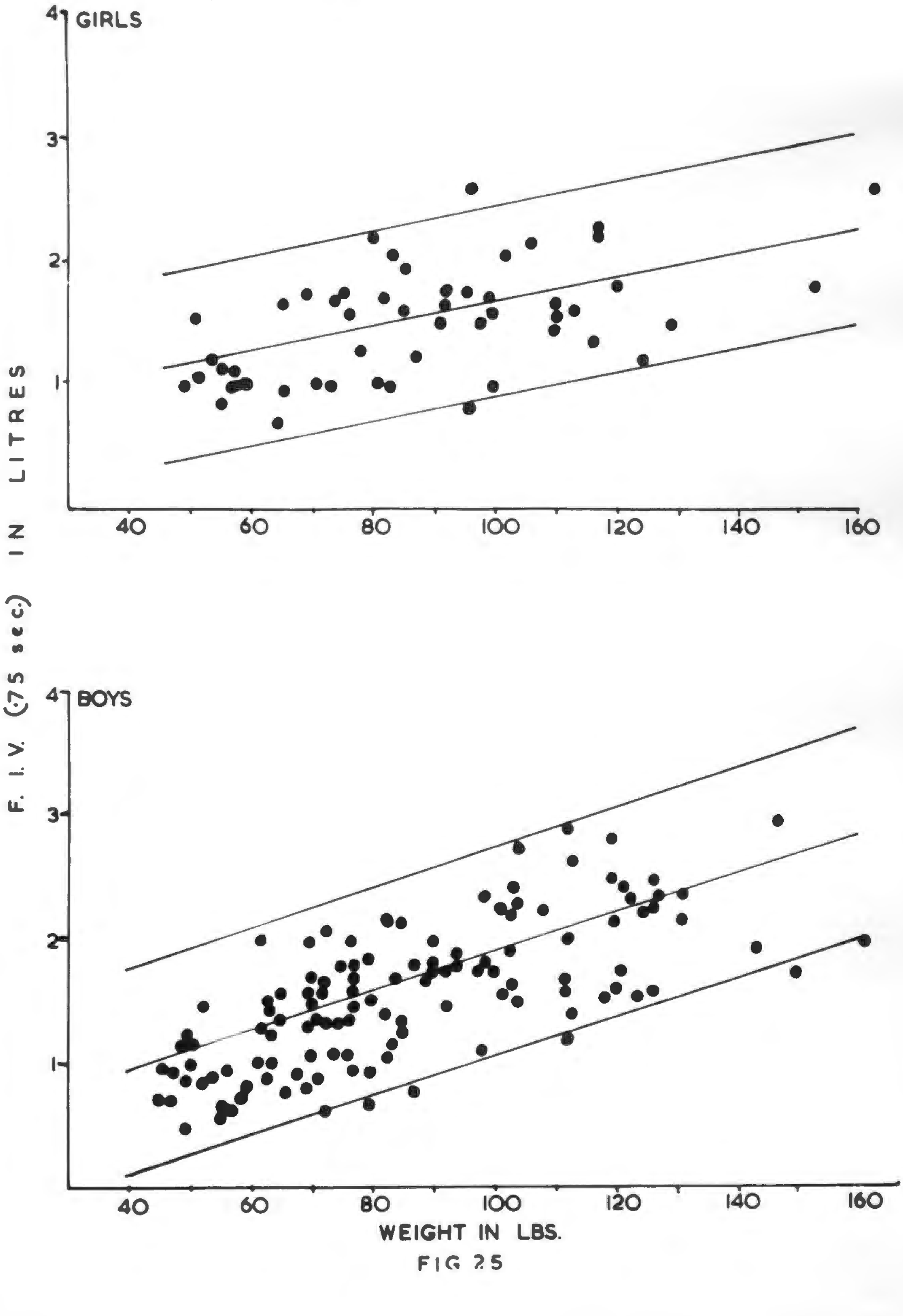


FIG 25

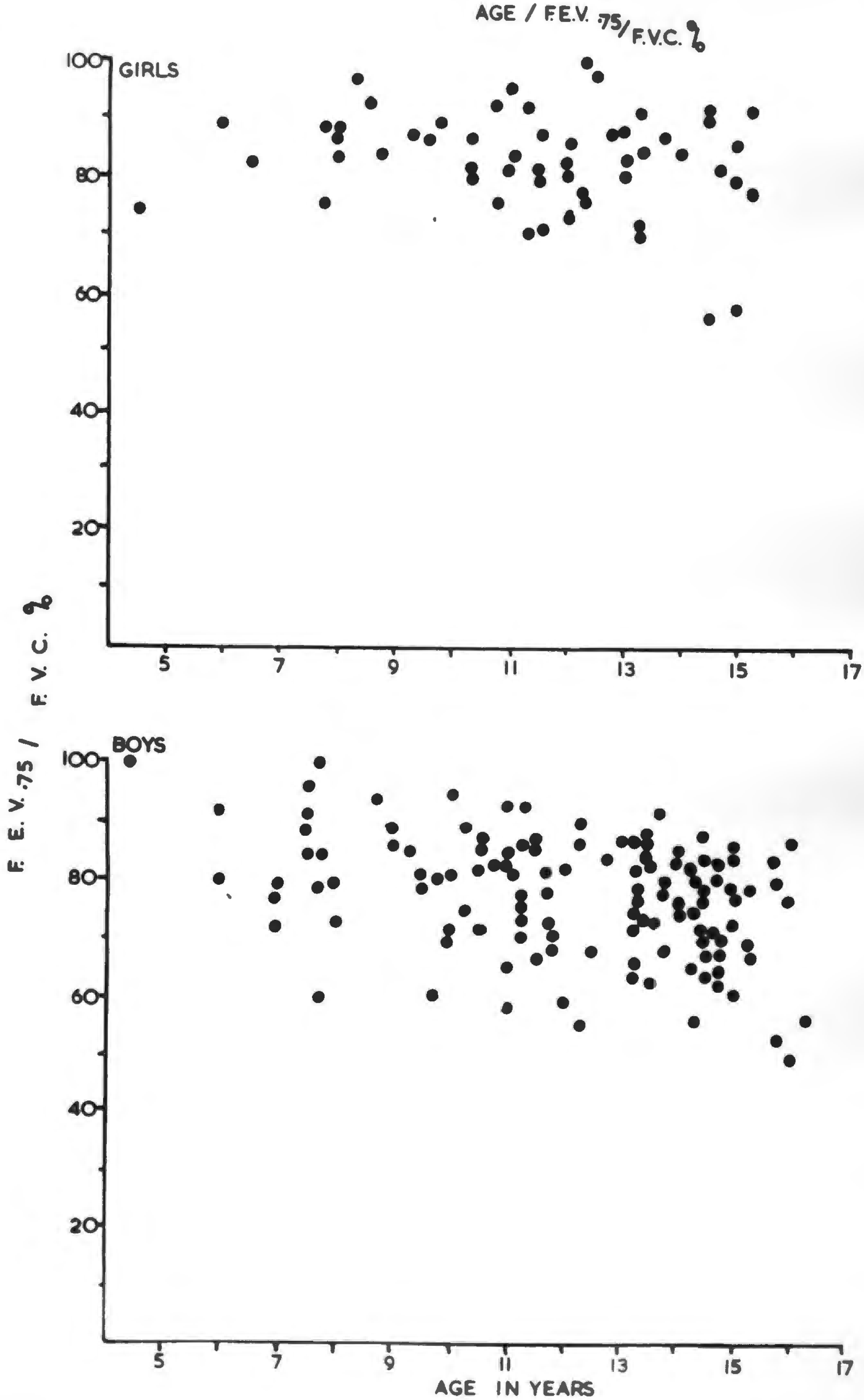

AGE / F.E.V. ·75/F.V.C. %
GIRLS
BOYS
F. E. V. ·75 / F. V. C. %
100
80
60
40
20
5
7
9
11
13
15
17
AGE IN YEARS

FIG.26

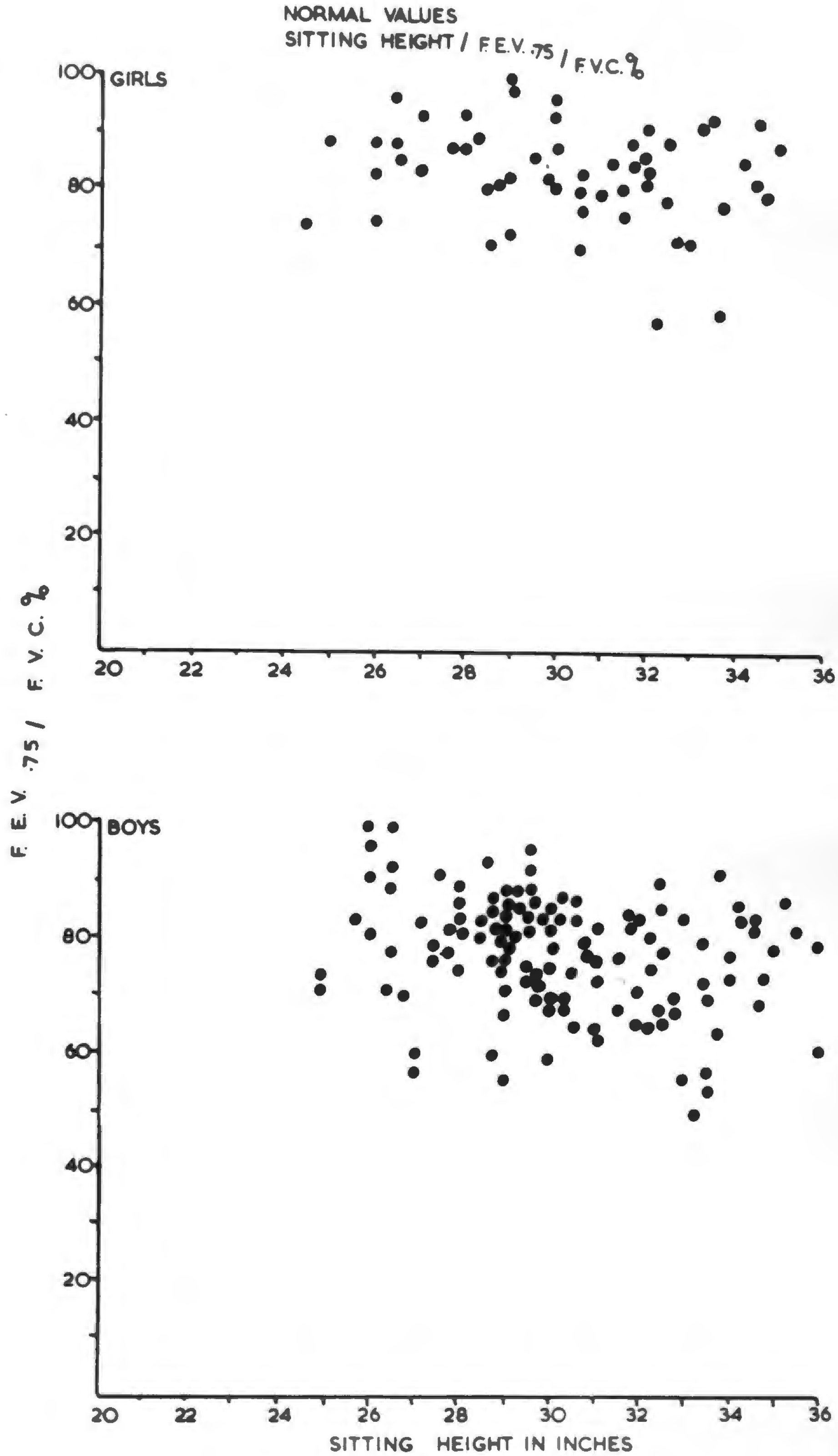

NORMAL VALUES
SITTING HEIGHT / F.E.V. .75 / F.V.C. %
GIRLS
BOYS
F.E.V. .75 / F.V.C. %
100
80
60
40
20
20 22 24 26 28 30 32 34 36
SITTING HEIGHT IN INCHES

FIG. 2 7

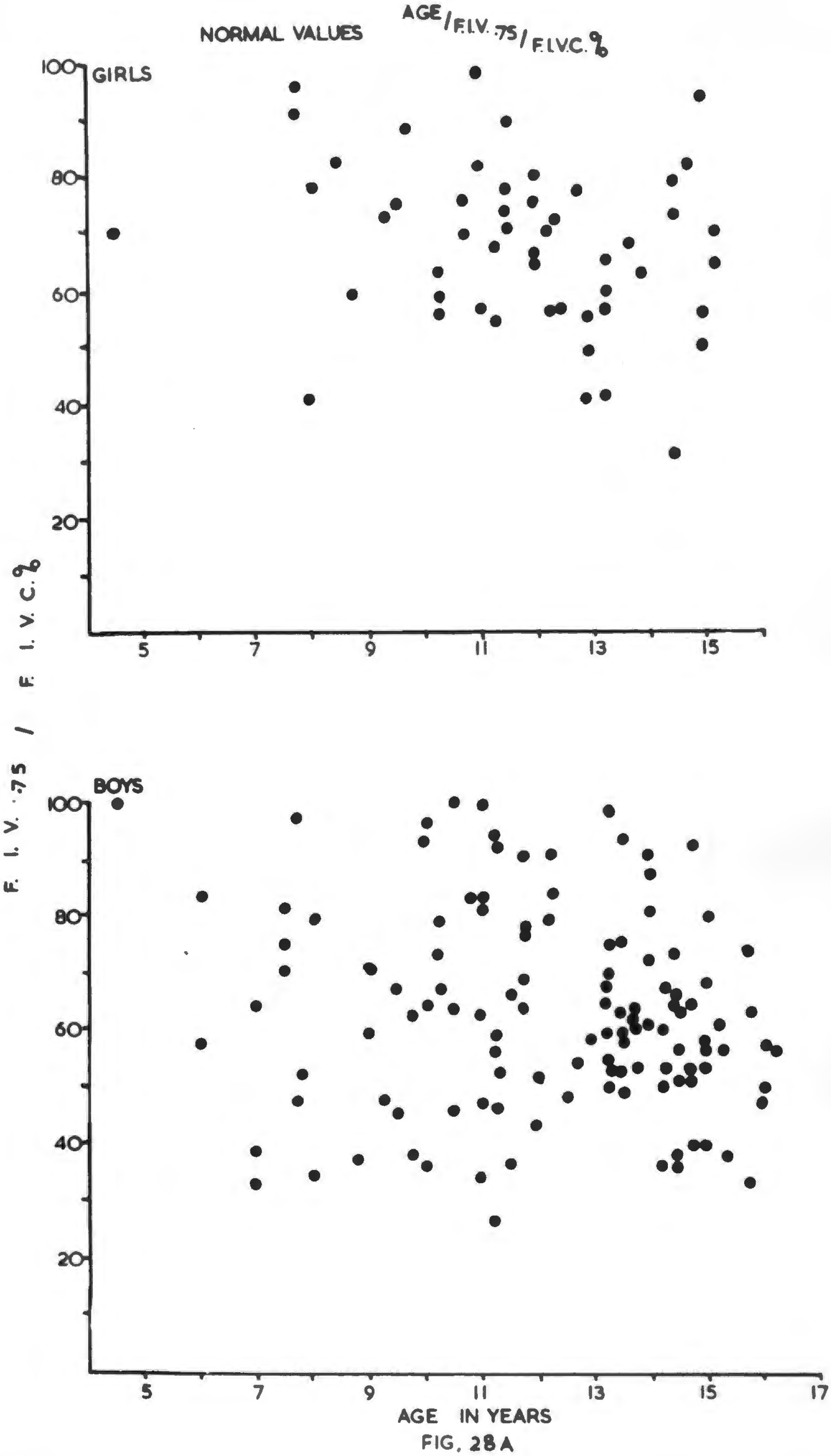
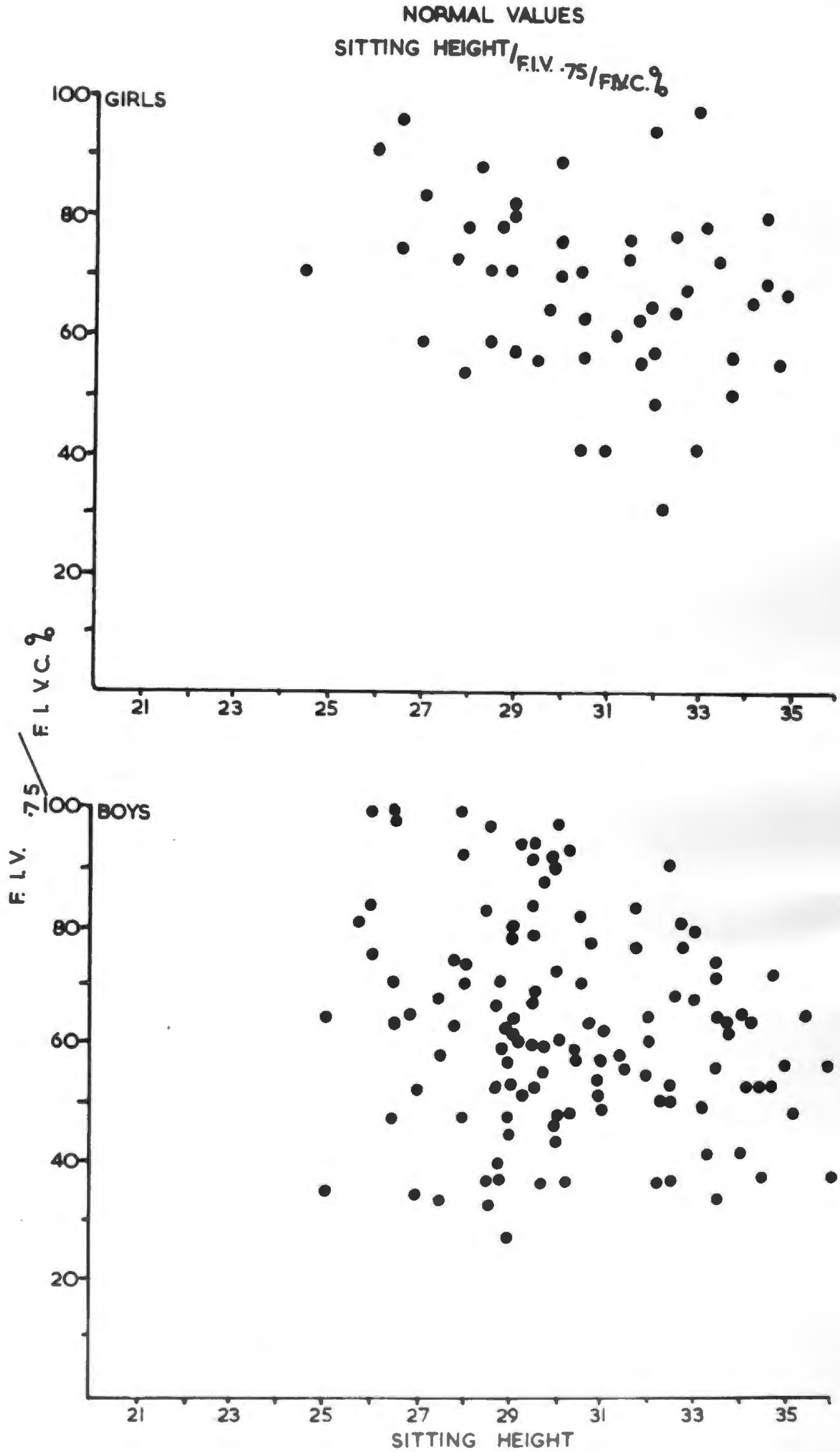

NORMAL VALUES
AGE/F.I.V. .75/F.I.V.C.%
GIRLS
BOYS
F. I. V. .75 / F. I. V. C. %
100
80
60
40
20
5
7
9
11
13
15
17
AGE IN YEARS

FIG. 28A


NORMAL VALUES
SITTING HEIGHT/F.I.V. ·75/F.I.V.C.%
GIRLS
BOYS
F. I.V. ·75/F. I. V.C. %
100
80
60
40
20
21
23
25
27
29
31
33
35
SITTING HEIGHT
FIG 28B

DAY TO DAY VARIATION

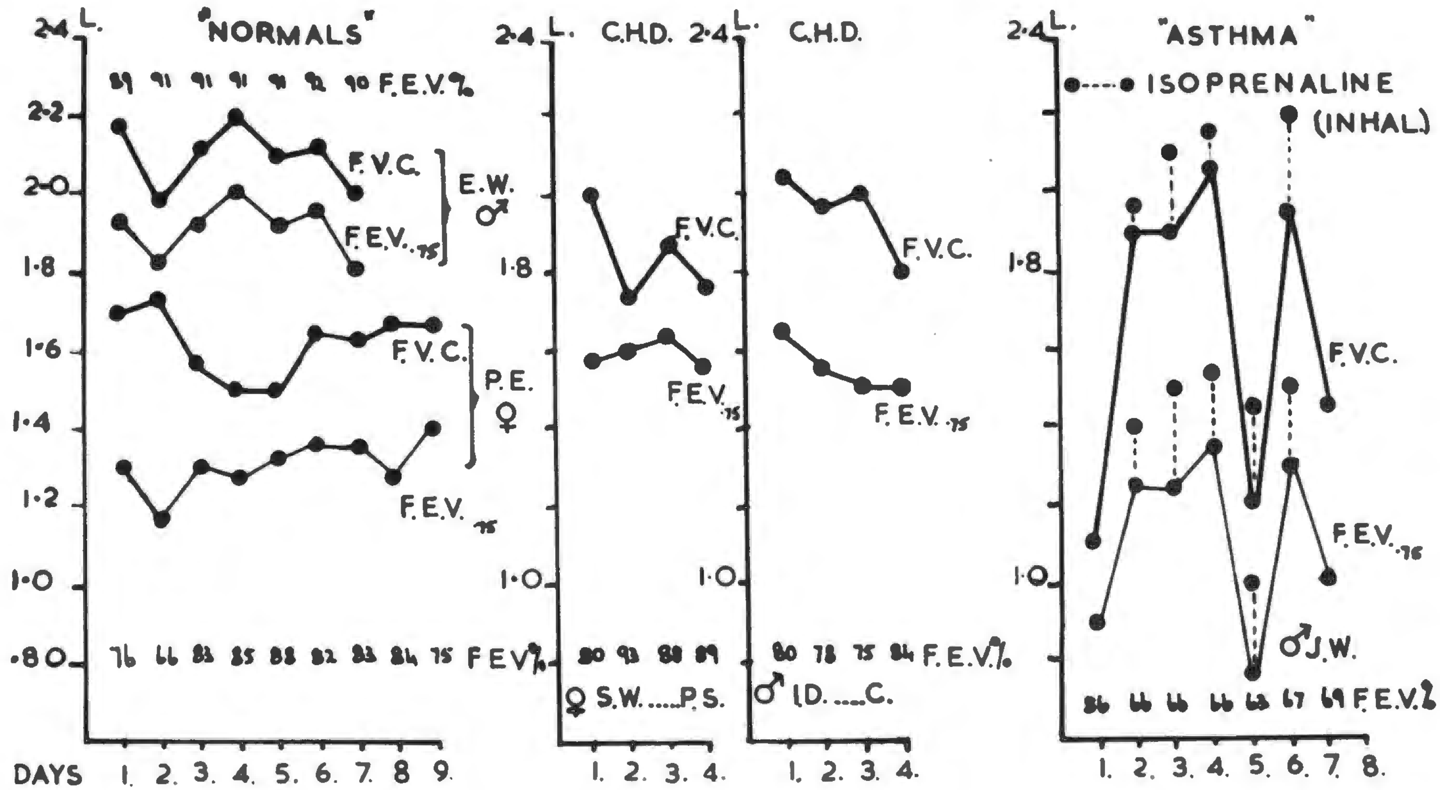


FIG. 29

"ASTHMA"

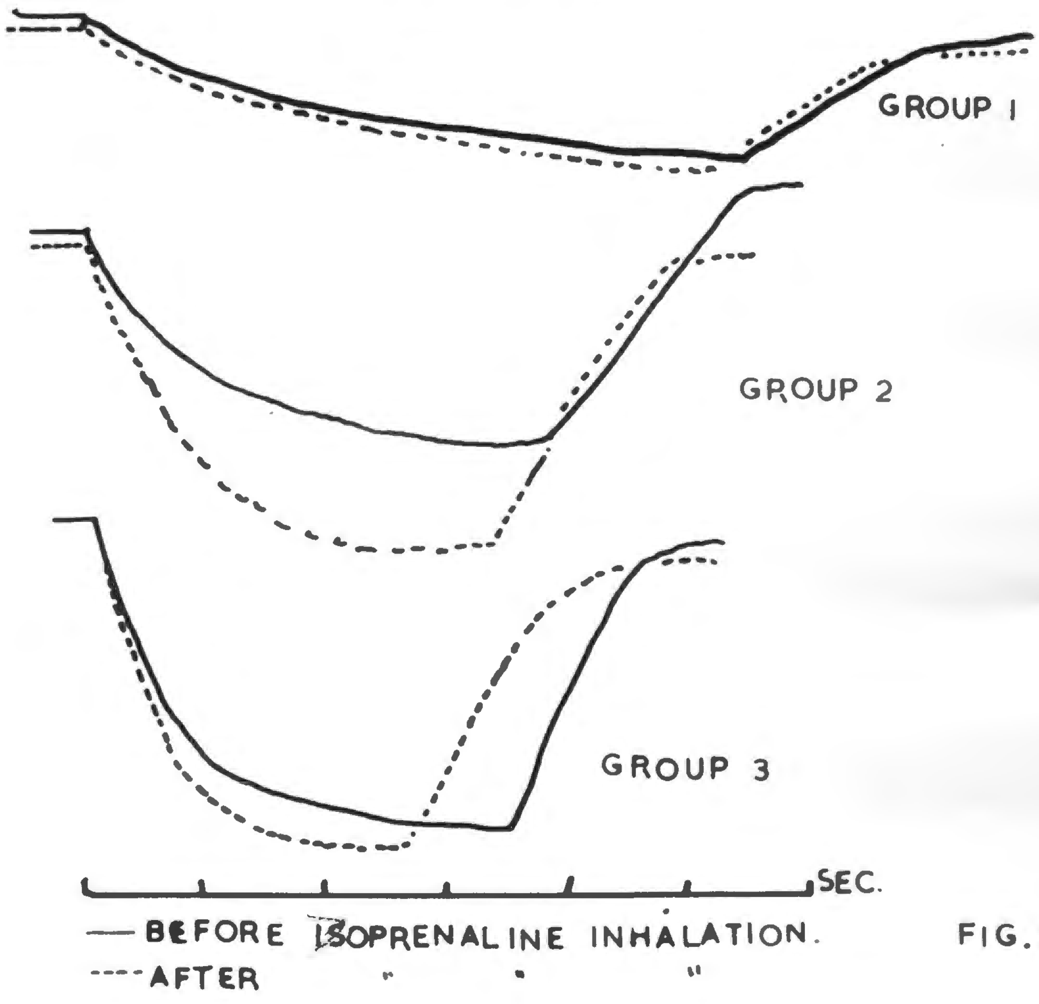
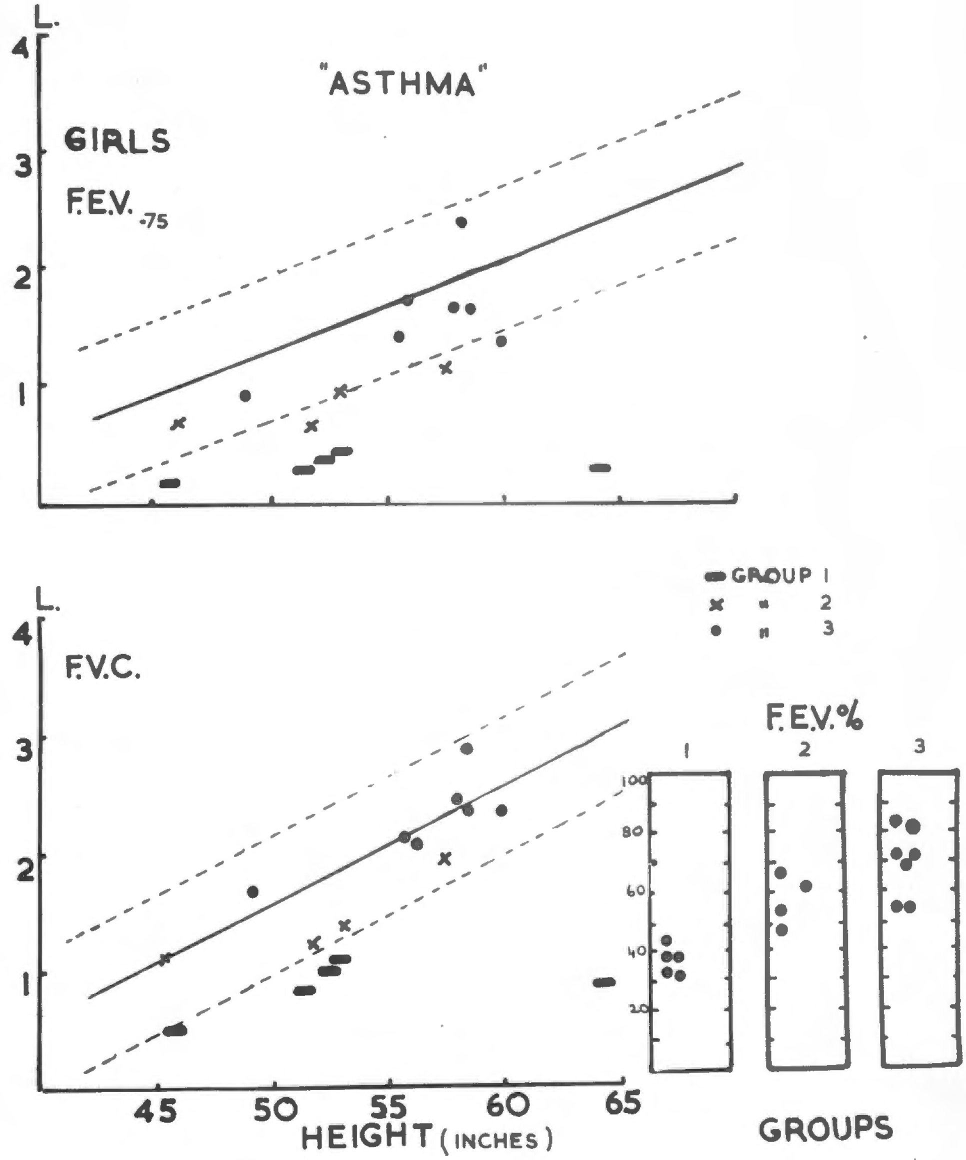


FIG. 30



L.
"ASTHMA"
GIRLS
F.E.V.·75
4
3
2
1
L.
F.V.C.
GROUP 1
2
3
F.E.V.%
1
2
3
100
80
60
40
20
45
50
55
60
65
HEIGHT (INCHES)
GROUPS

FIG.31

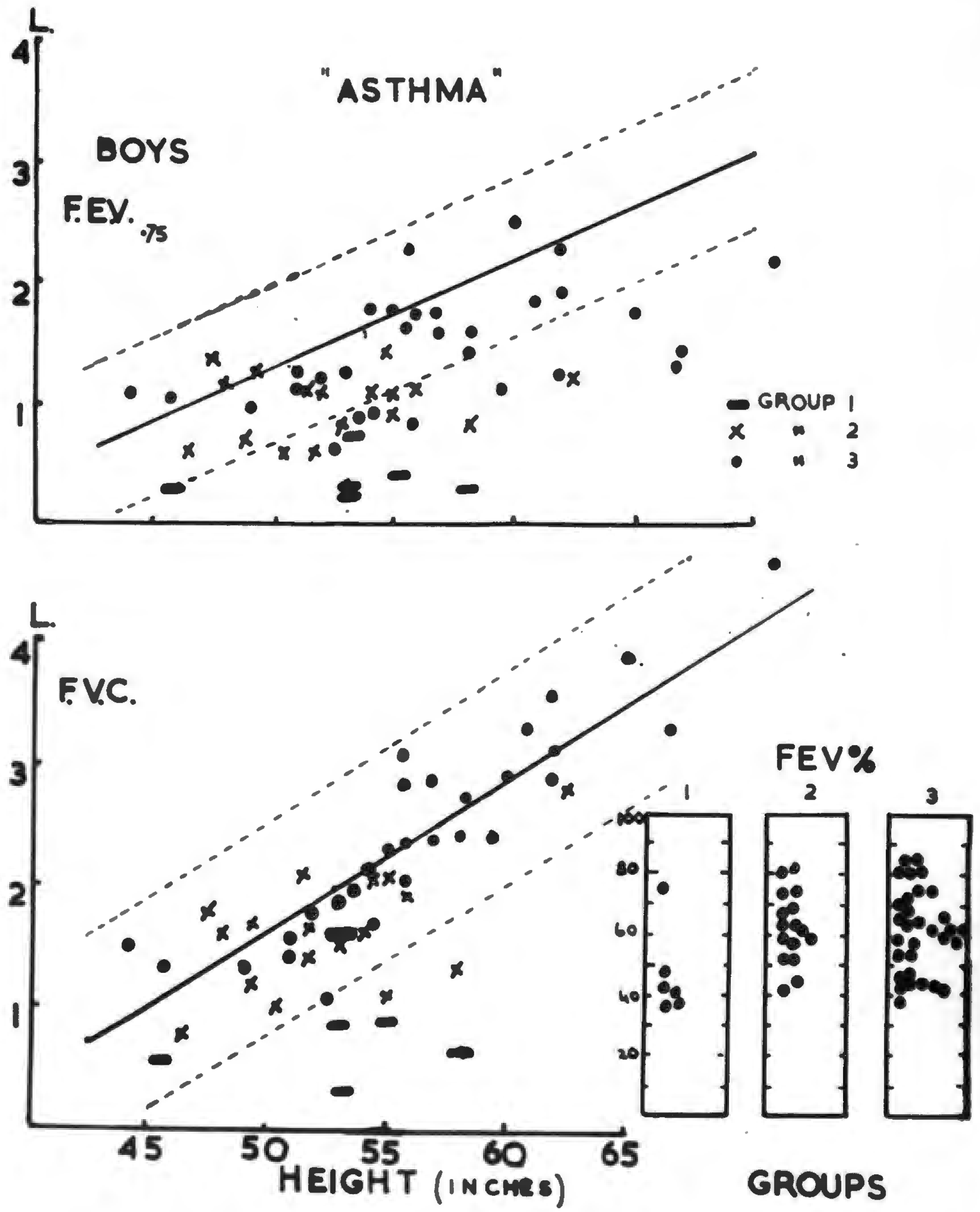

"ASTHMA"
BOYS
F.E.V. ·75
L.
4
3
2
1
GROUP 1
" 2
" 3
F.V.C.
FEV%
1
2
3
100
80
60
40
20
45
50
55
60
65
HEIGHT (INCHES)
GROUPS

FIG.32

'ASTHMA'

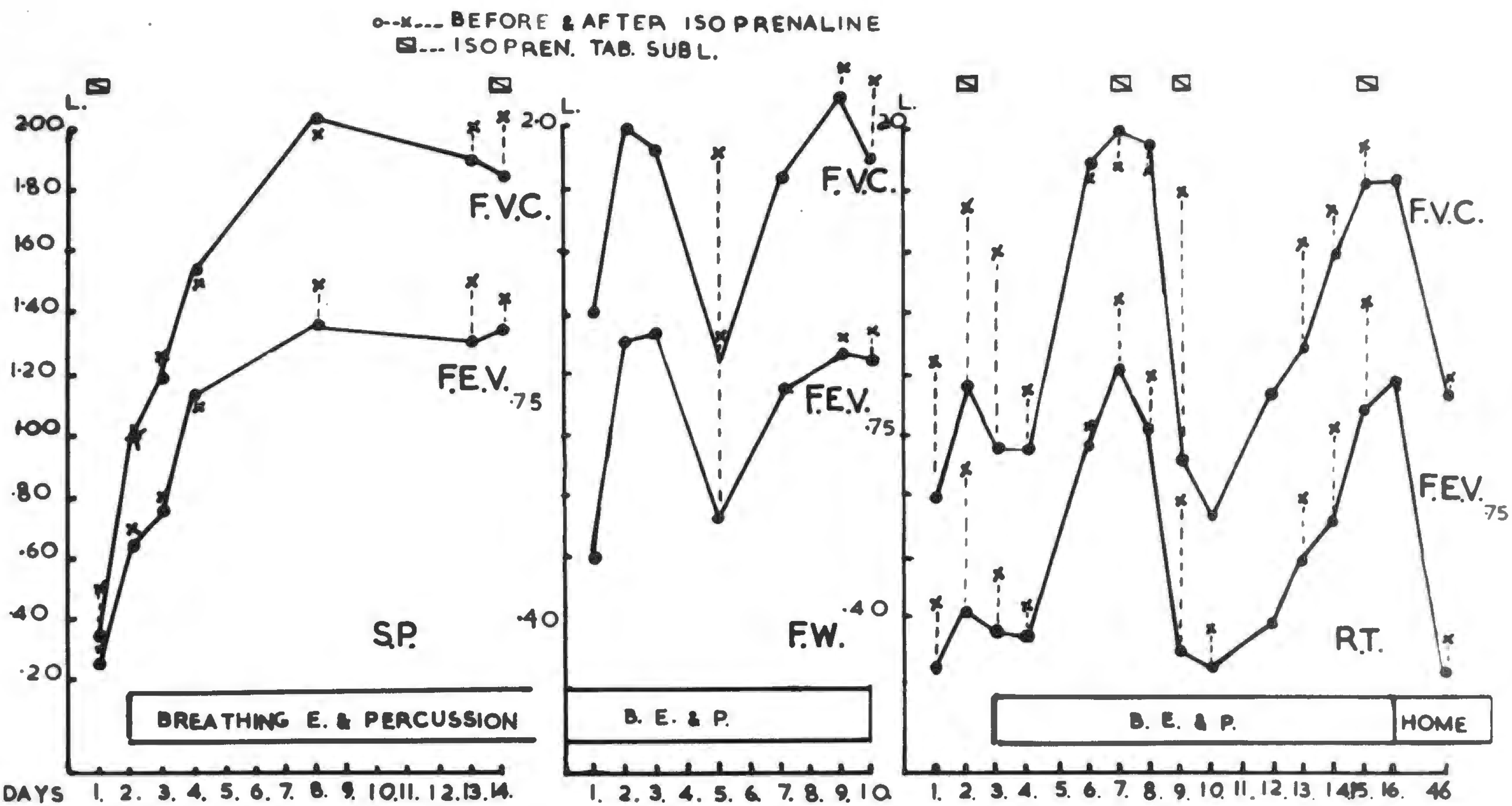


FIG. 33

ASTHMA

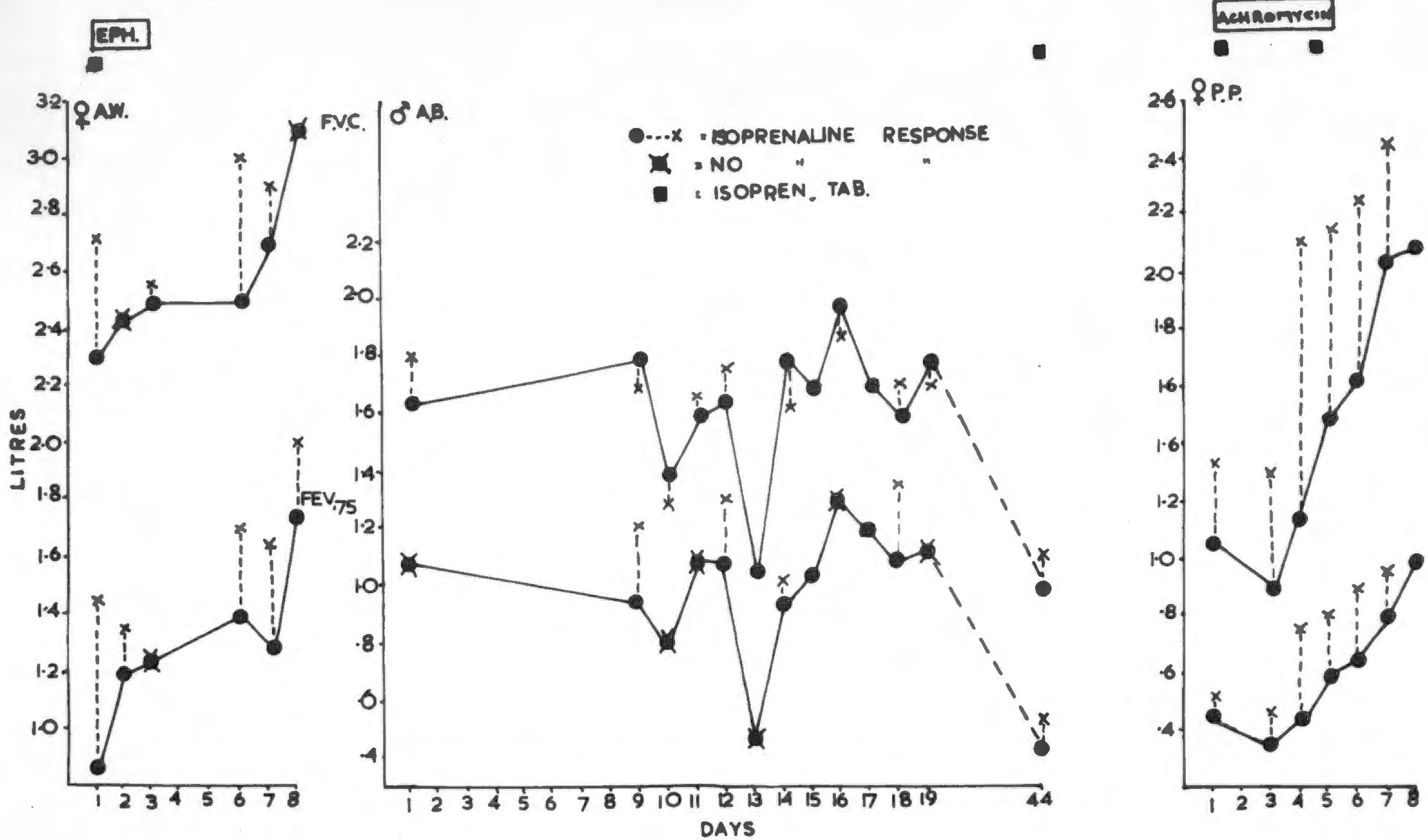


FIG. 33A

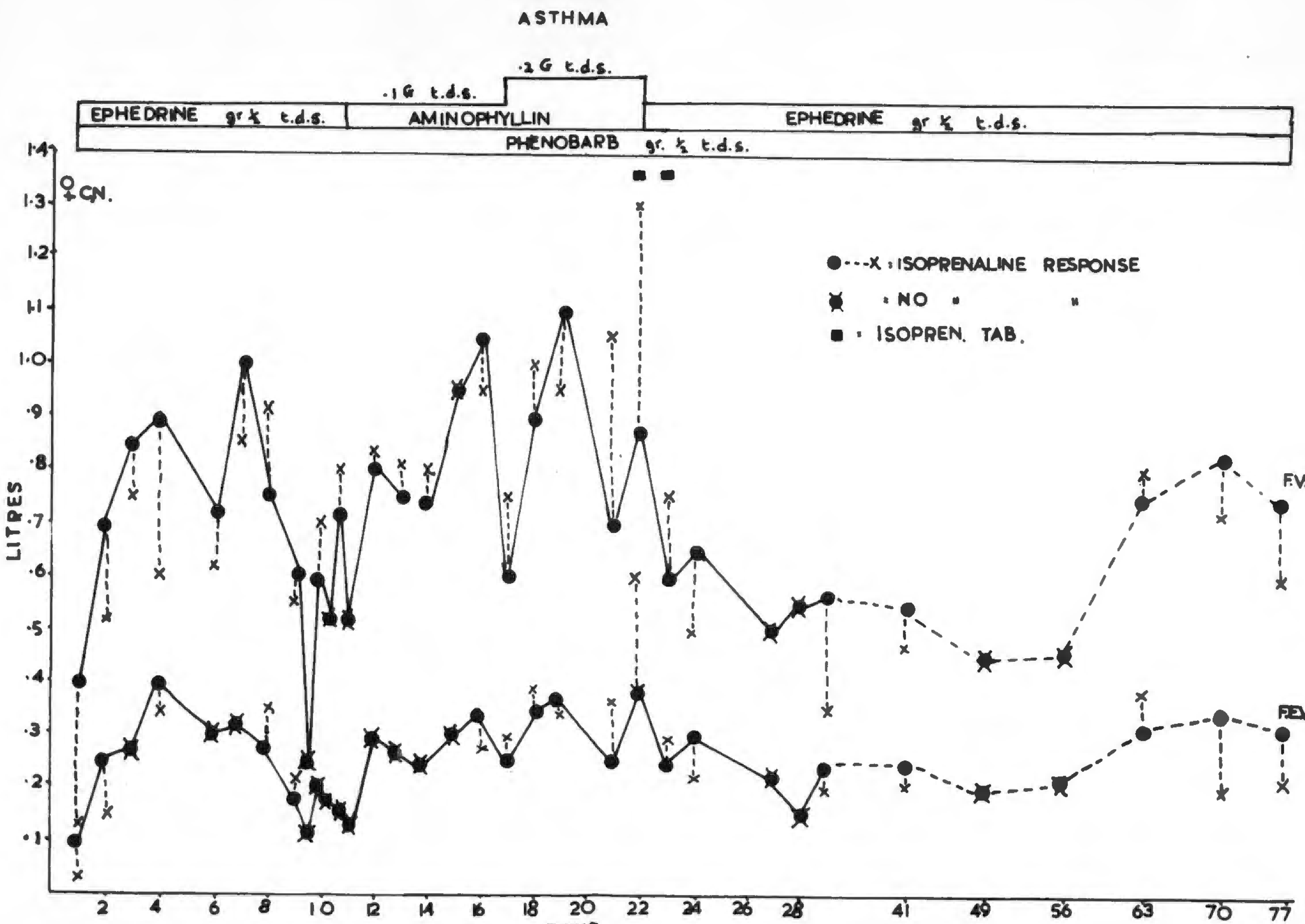
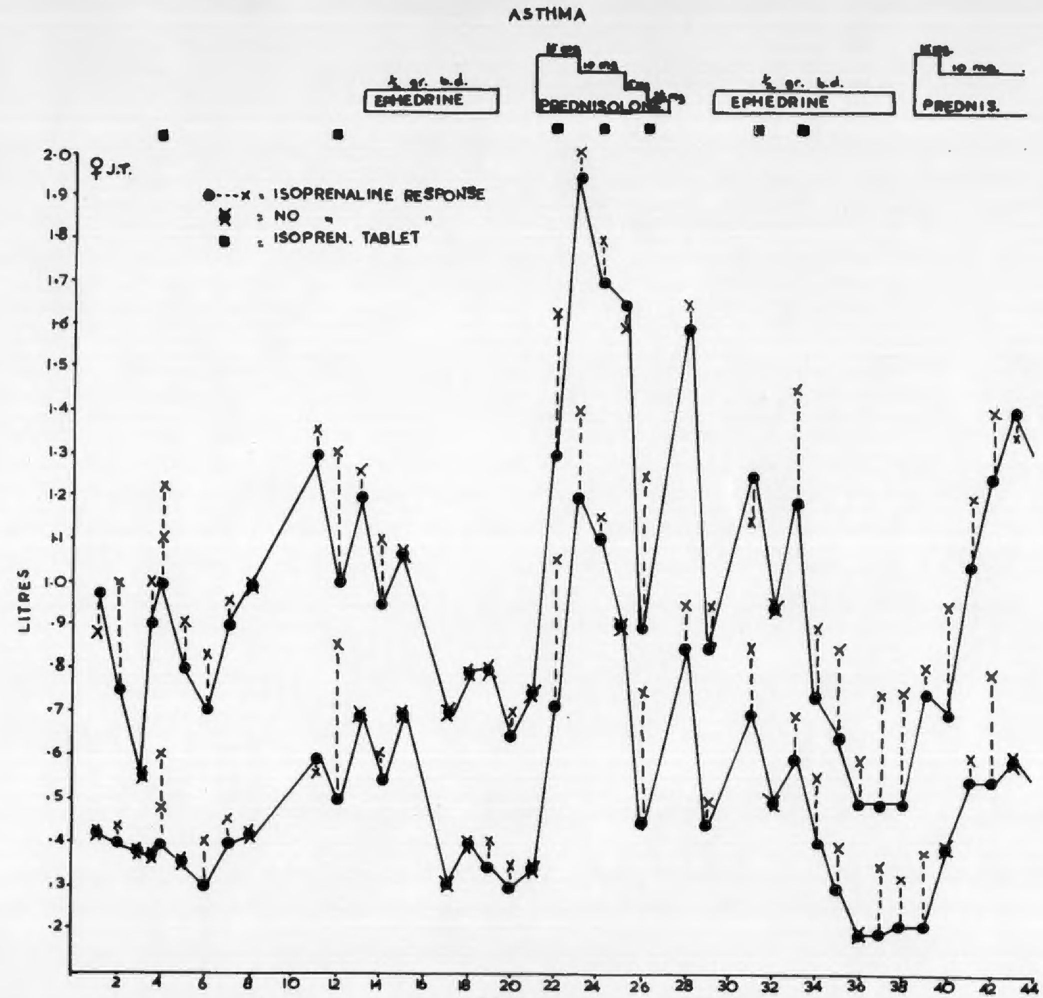
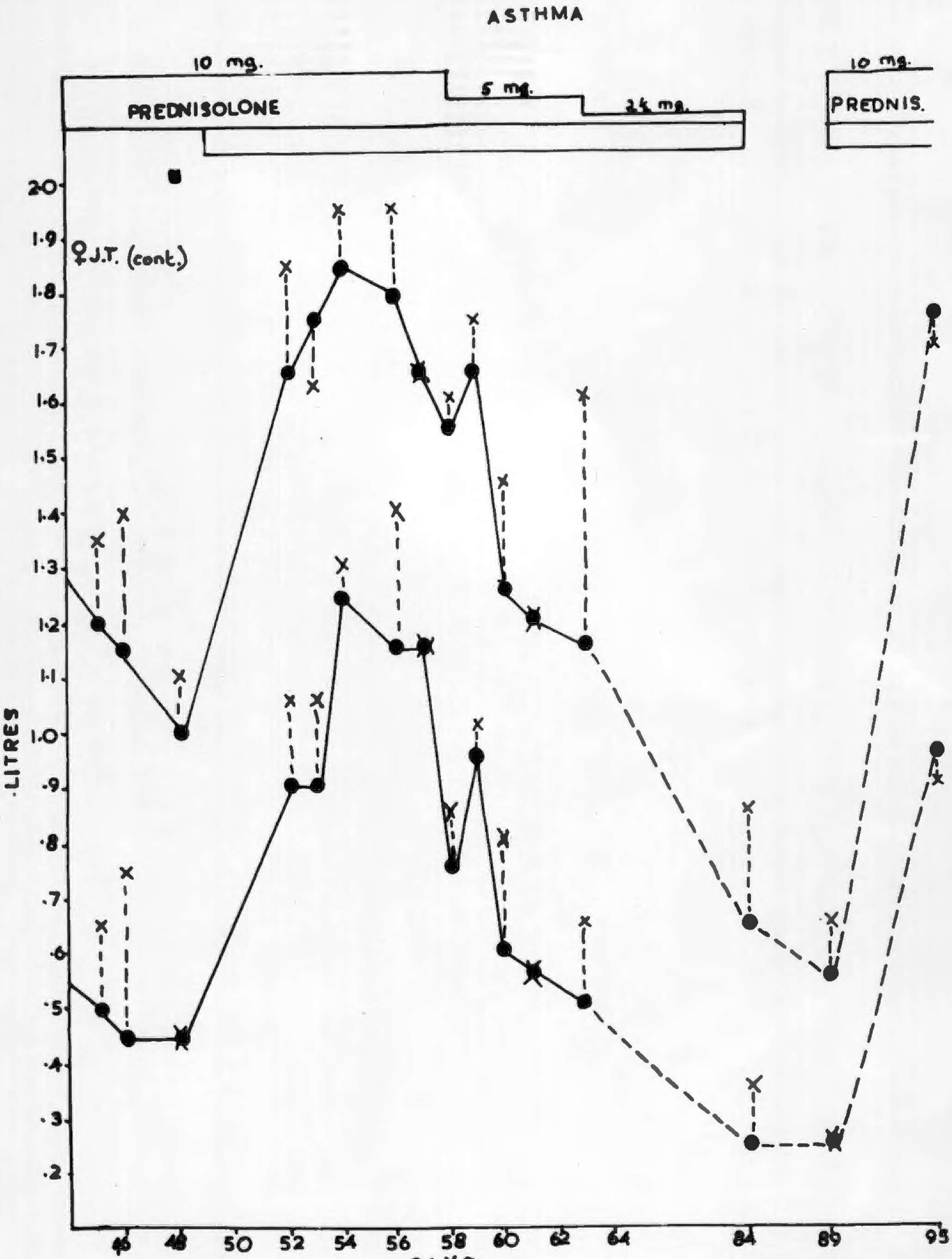

ASTHMA
·1 G t.d.s.
·2 G t.d.s.
EPHEDRINE gr ½ t.d.s.
AMINOPHYLLIN
EPHEDRINE gr ½ t.d.s.
PHENOBARB gr. ½ t.d.s.
♀ C.N.
LITRES
●---X : ISOPRENALINE RESPONSE
: NO " "
■ : ISOPREN. TAB.
F.V.C.
F.E.V.·75
DAYS

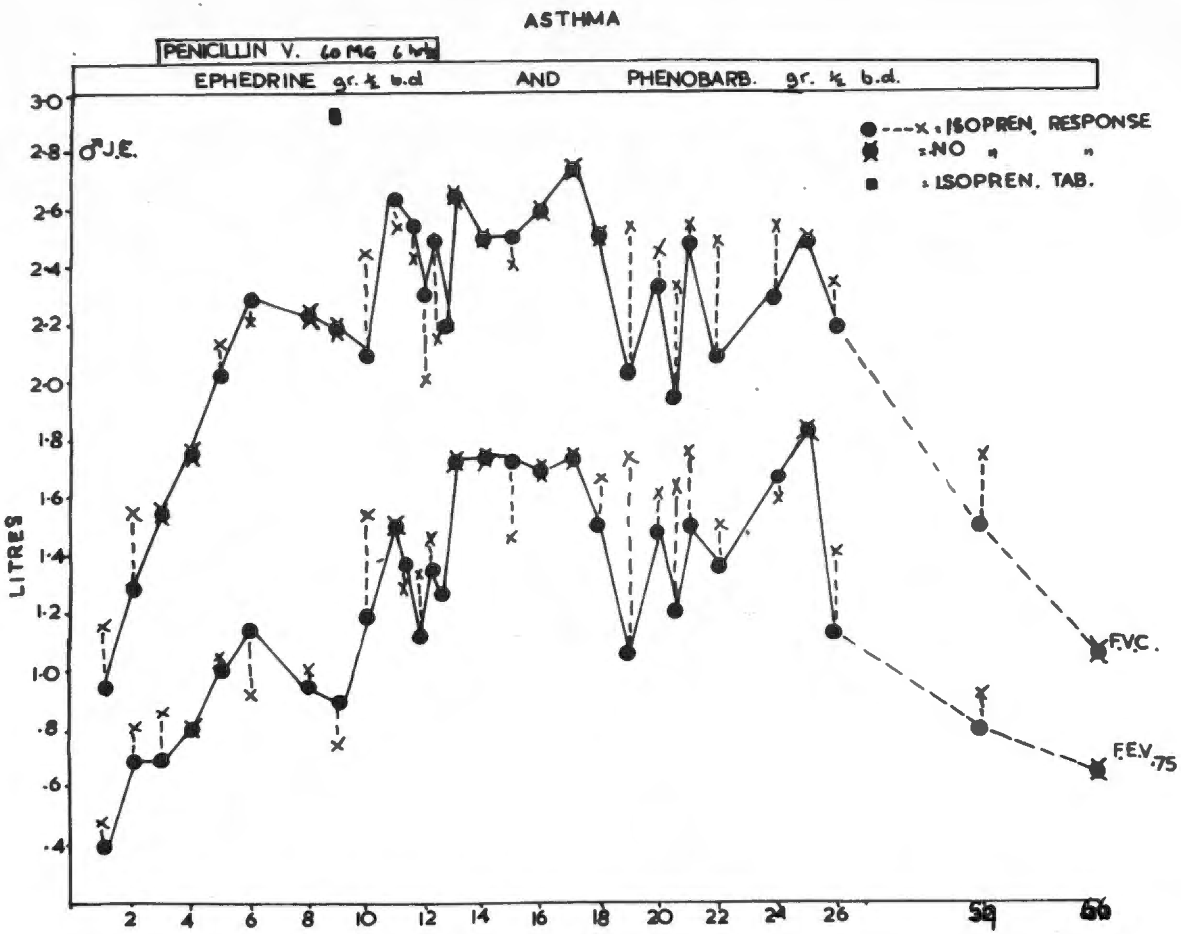
FIG. 33B



ASTHMA
¼ gr. b.d.
EPHEDRINE
PREDNISOLONE
EPHEDRINE
PREDNIS.
10 mg.
♀ J.T.
●---x = ISOPRENALINE RESPONSE
= NO " "
= ISOPREN. TABLET
LITRES
2·0
1·9
1·8
1·7
1·6
1·5
1·4
1·3
1·2
1·1
1·0
·9
·8
·7
·6
·5
·4
·3
·2
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
40
42
44
DAYS

FIG. 32C


ASTHMA
10 mg.
5 mg.
2½ mg.
10 mg.
PREDNISOLONE
PREDNIS.
♀ J.T. (cont.)
LITRES
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
·9
·8
·7
·6
·5
·4
·3
·2
46
48
50
52
54
56
58
60
62
64
84
89
95
DAYS
FIG. 33C



ASTHMA
PENICILLIN V. 60 MG 6 hrly
EPHEDRINE gr. ½ b.d AND PHENOBARB. gr. ½ b.d.
♂ J.E.
---x : ISOPREN. RESPONSE
: NO " "
: ISOPREN. TAB.
LITRES
3·0
2·8
2·6
2·4
2·2
2·0
1·8
1·6
1·4
1·2
1·0
·8
·6
·4
F.V.C.
F.E.V.·75
2
4
6
8
10
12
14
16
18
20
22
24
26
DAYS

FIG 33D

ASTHMA

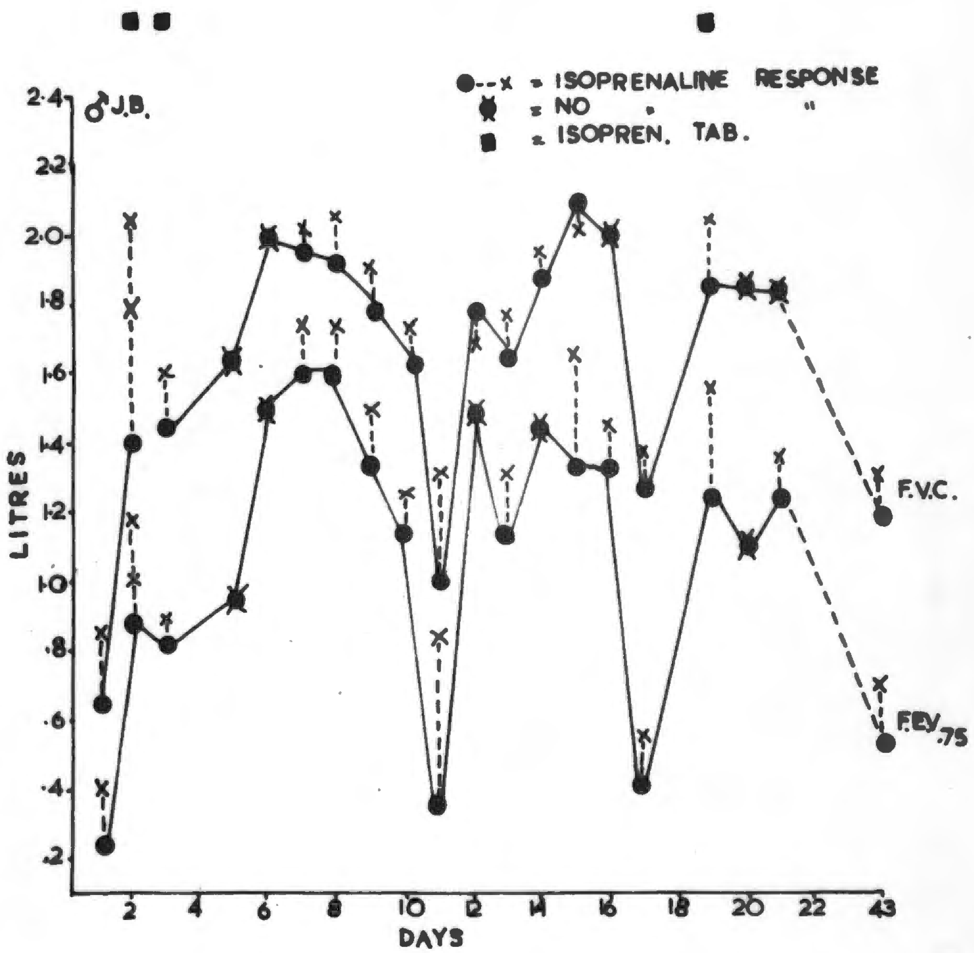


FIG 33E

E

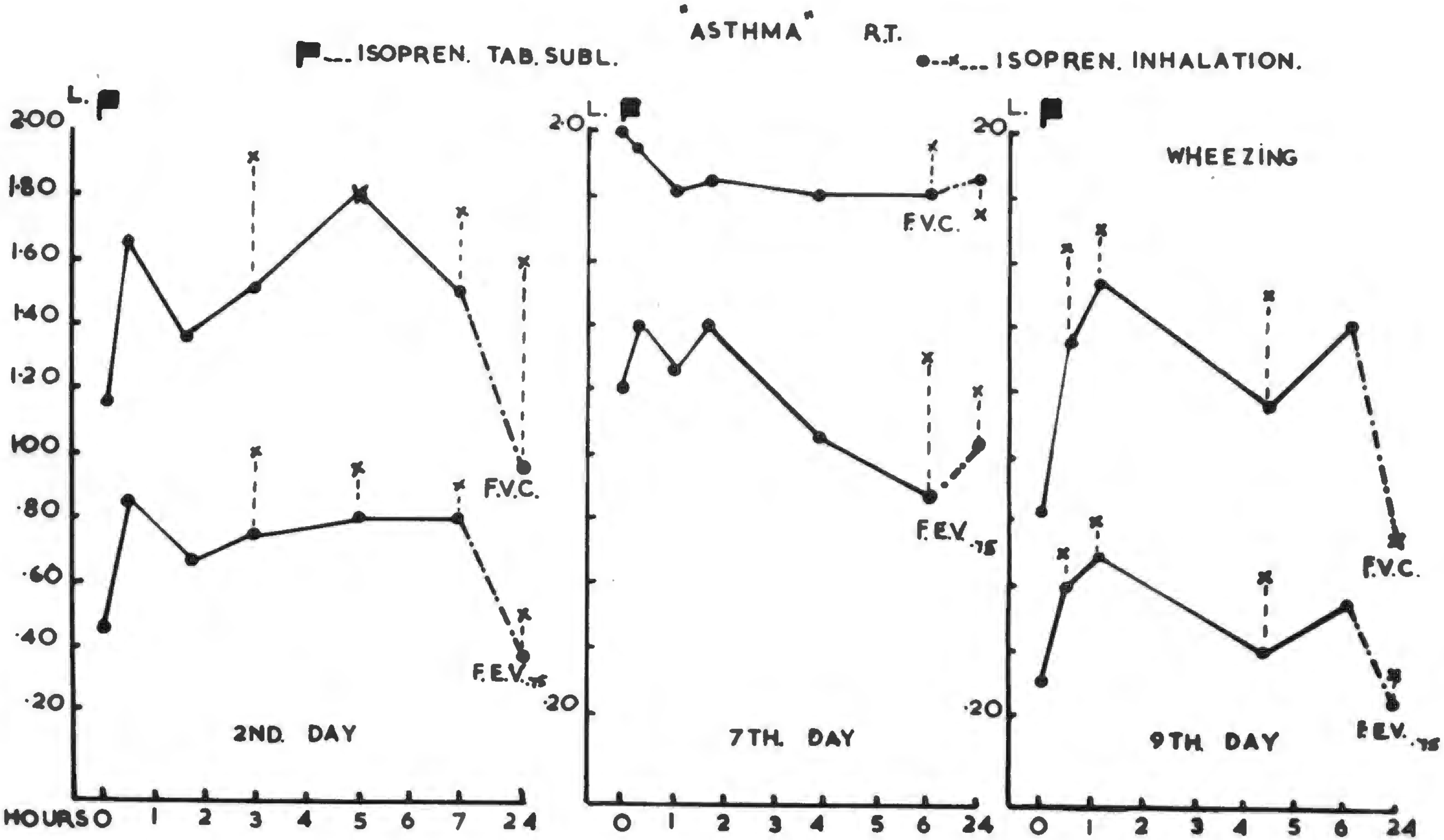

"ASTHMA" R.T.
ISOPREN. TAB. SUBL.
ISOPREN. INHALATION.
L.
200
1·80
1·60
1·40
1·20
1·00
·80
·60
·40
·20
F.V.C.
F.E.V.·75
2ND. DAY
HOURS 0 1 2 3 4 5 6 7 24
2·0
·20
7TH. DAY
0 1 2 3 4 5 6 24
WHEEZING
9TH DAY

FIG.34

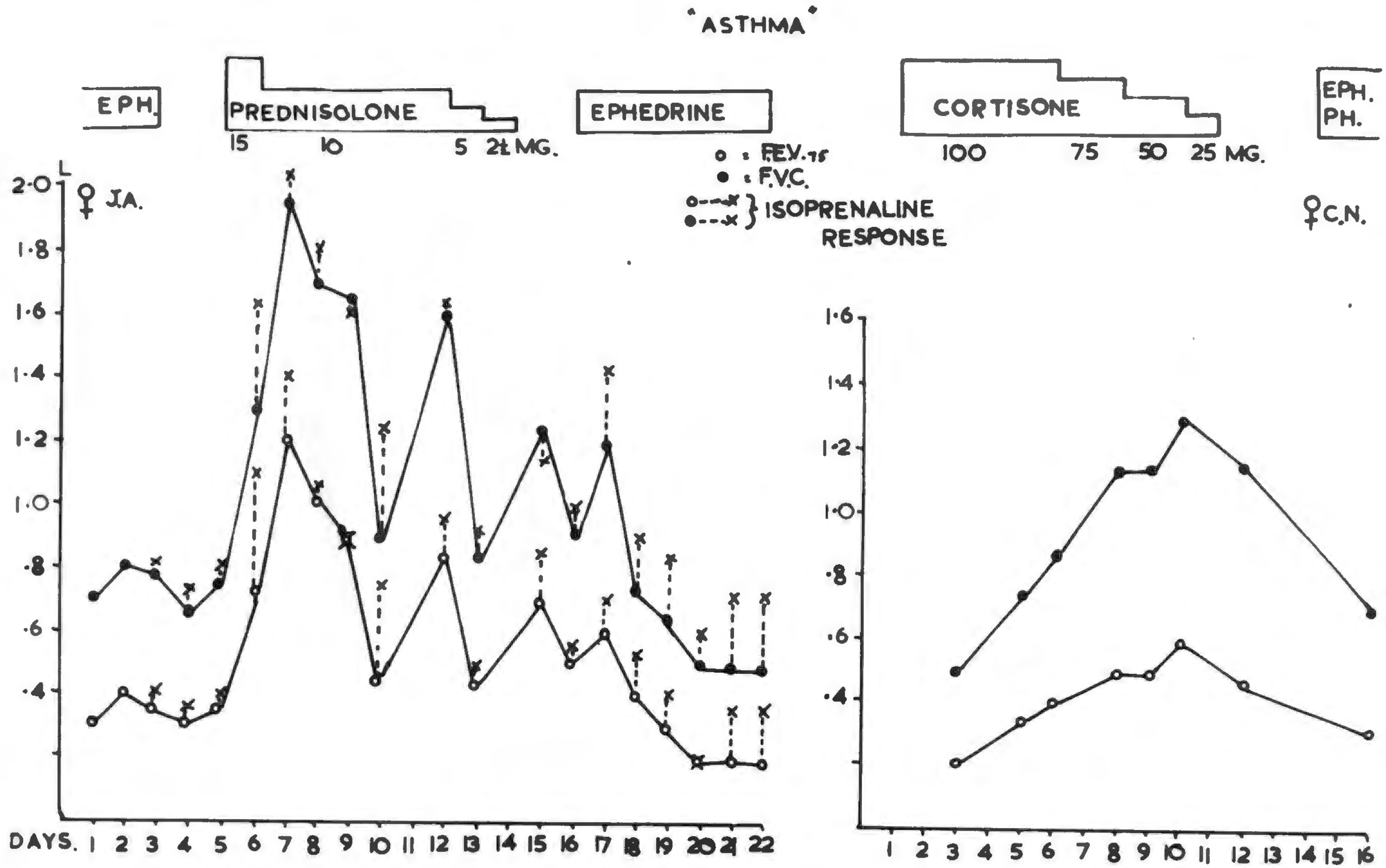

"ASTHMA"
EPH.
PREDNISOLONE
15 10 5 2½ MG.
EPHEDRINE
CORTISONE
100 75 50 25 MG.
EPH.
PH.
o : F.E.V.·75
● : F.V.C.
o--x ●--x } ISOPRENALINE RESPONSE
♀ J.A.
♀ C.N.
L
2·0
1·8
1·6
1·4
1·2
1·0
·8
·6
·4
DAYS. 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16

FIG. 34A

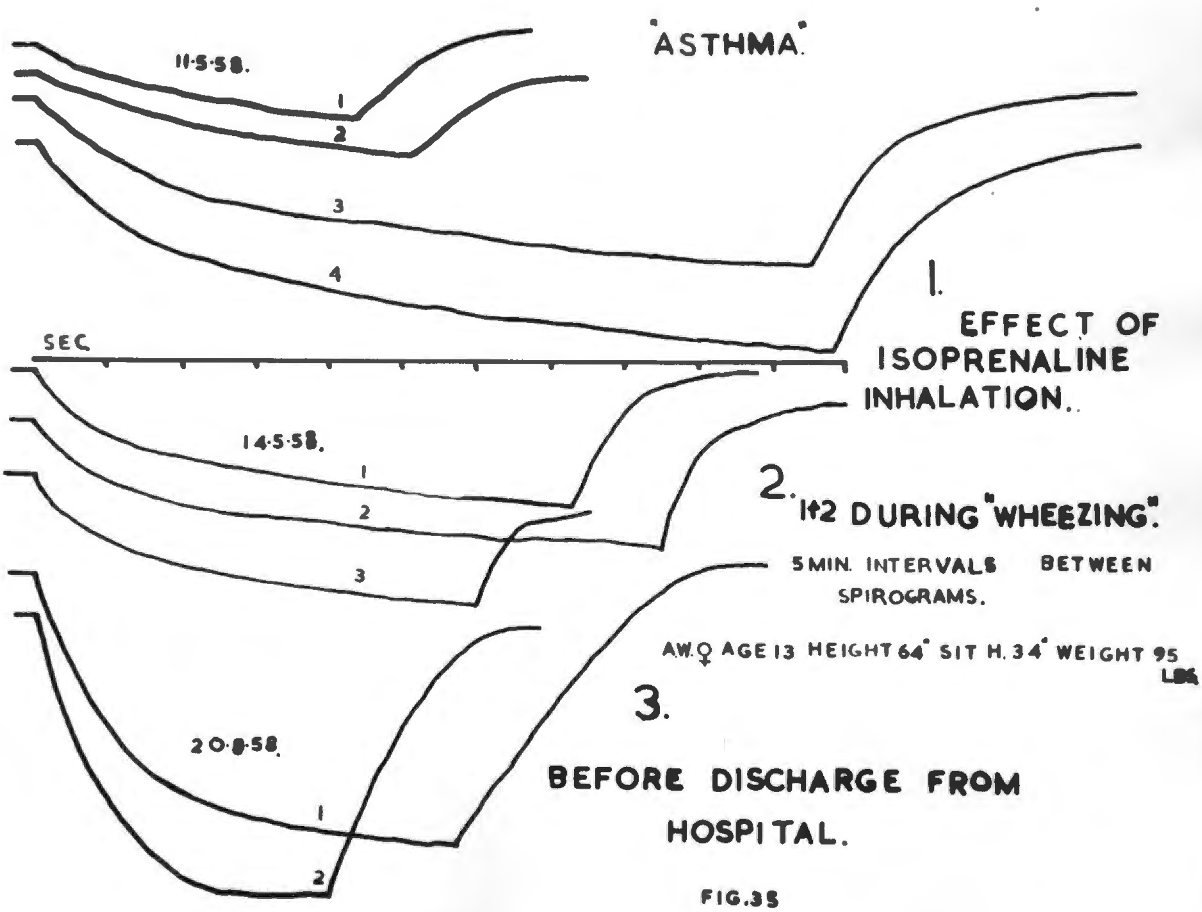

"ASTHMA"
11·5·58.
1
2
3
4
SEC.
1. EFFECT OF ISOPRENALINE INHALATION.
14·5·58.
1
2
3
2. 1+2 DURING "WHEEZING".
5 MIN. INTERVALS BETWEEN SPIROGRAMS.
A.W. ♀ AGE 13 HEIGHT 64" SIT H. 34" WEIGHT 95 LBS.
3.
20·8·58.
1
2
BEFORE DISCHARGE FROM HOSPITAL.

FIG. 35

KEY TO FIGS. 37 AND 38

▬	GROUP 1	ASTHMA
×	GROUP 2	ASTHMA
●	GROUP 3	ASTHMA
□	CONGENITAL HEART DISEASE	
⊗	MISCELLANEOUS GROUP	

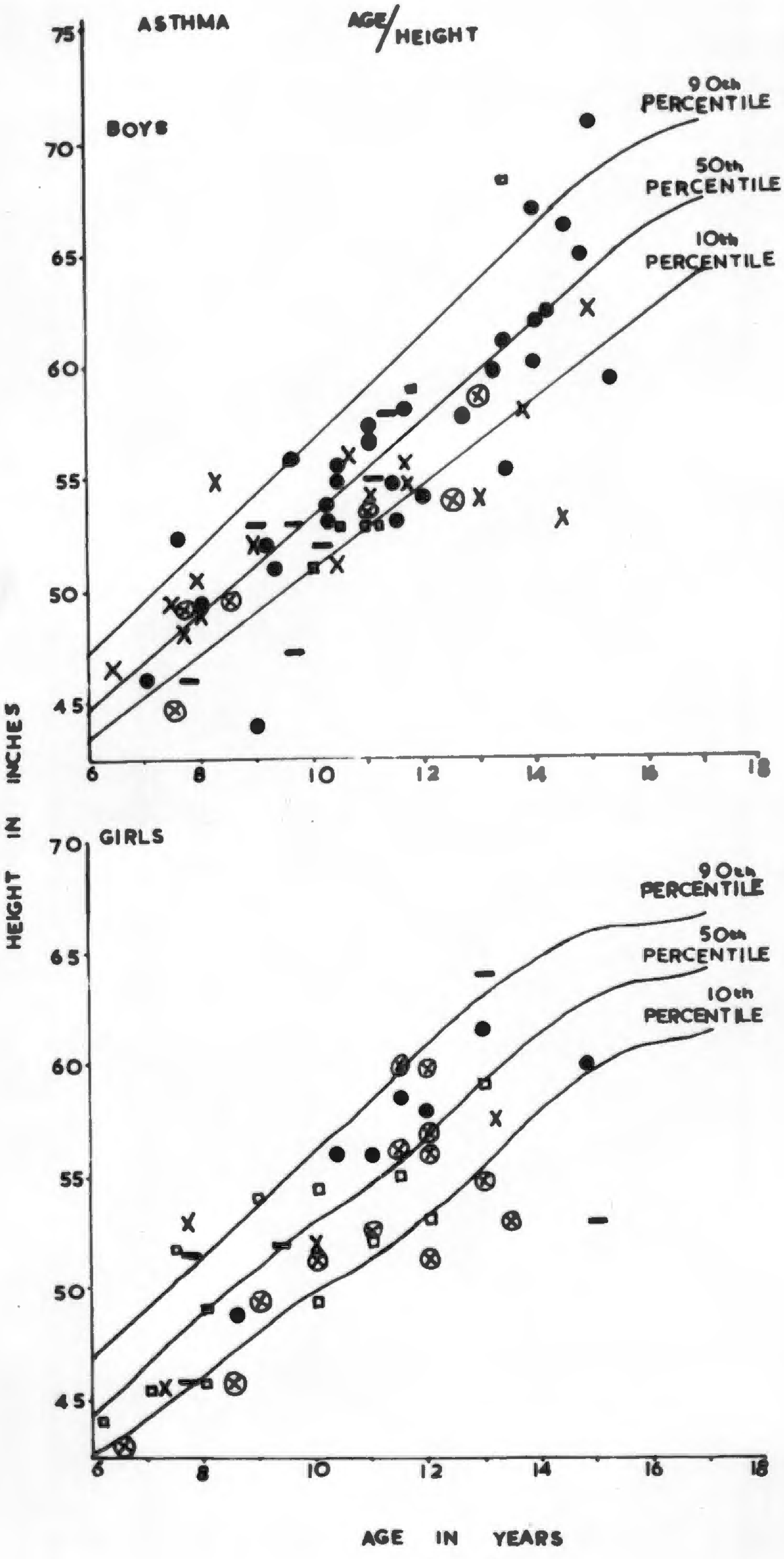

ASTHMA
AGE/HEIGHT
BOYS
GIRLS
HEIGHT IN INCHES
90th PERCENTILE
50th PERCENTILE
10th PERCENTILE
75
70
65
60
55
50
45
6
8
10
12
14
16
18
AGE IN YEARS

FIG. 37.

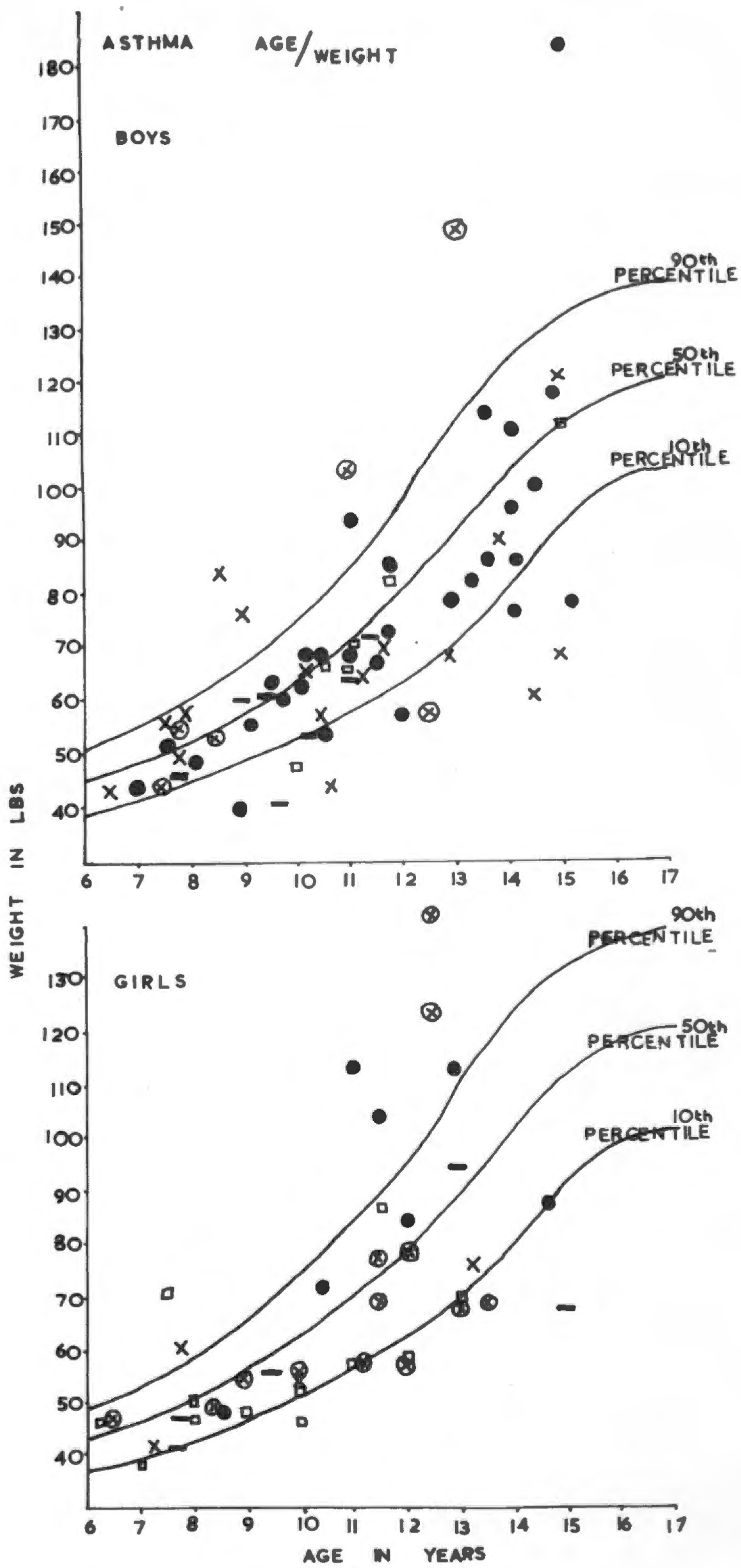

ASTHMA AGE/WEIGHT
BOYS
GIRLS
WEIGHT IN LBS
90th PERCENTILE
50th PERCENTILE
10th PERCENTILE
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
6 7 8 9 10 11 12 13 14 15 16 17
AGE IN YEARS

FIG. 38.

CONGENITAL HEART DISEASE.

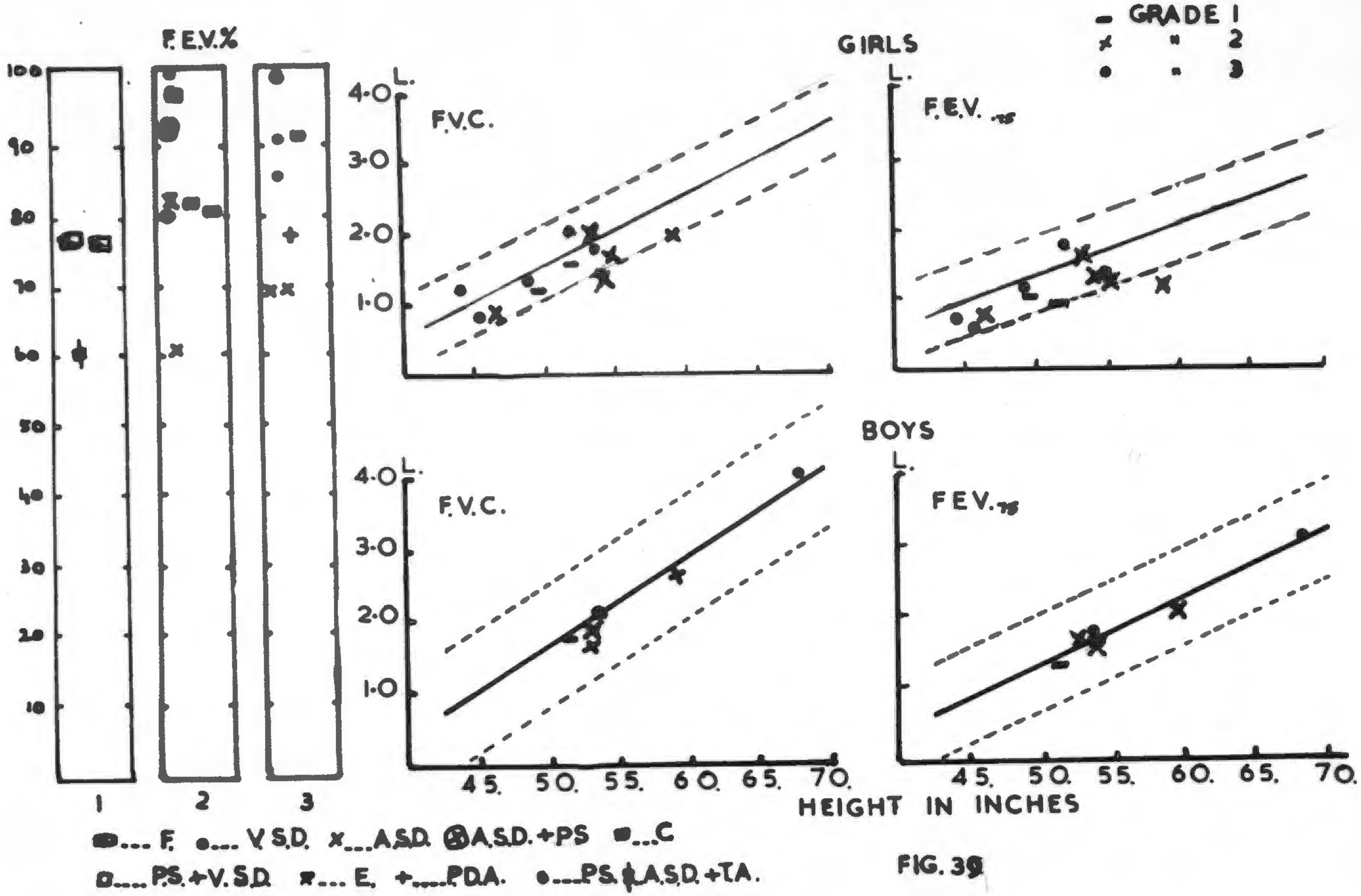


FIG. 39

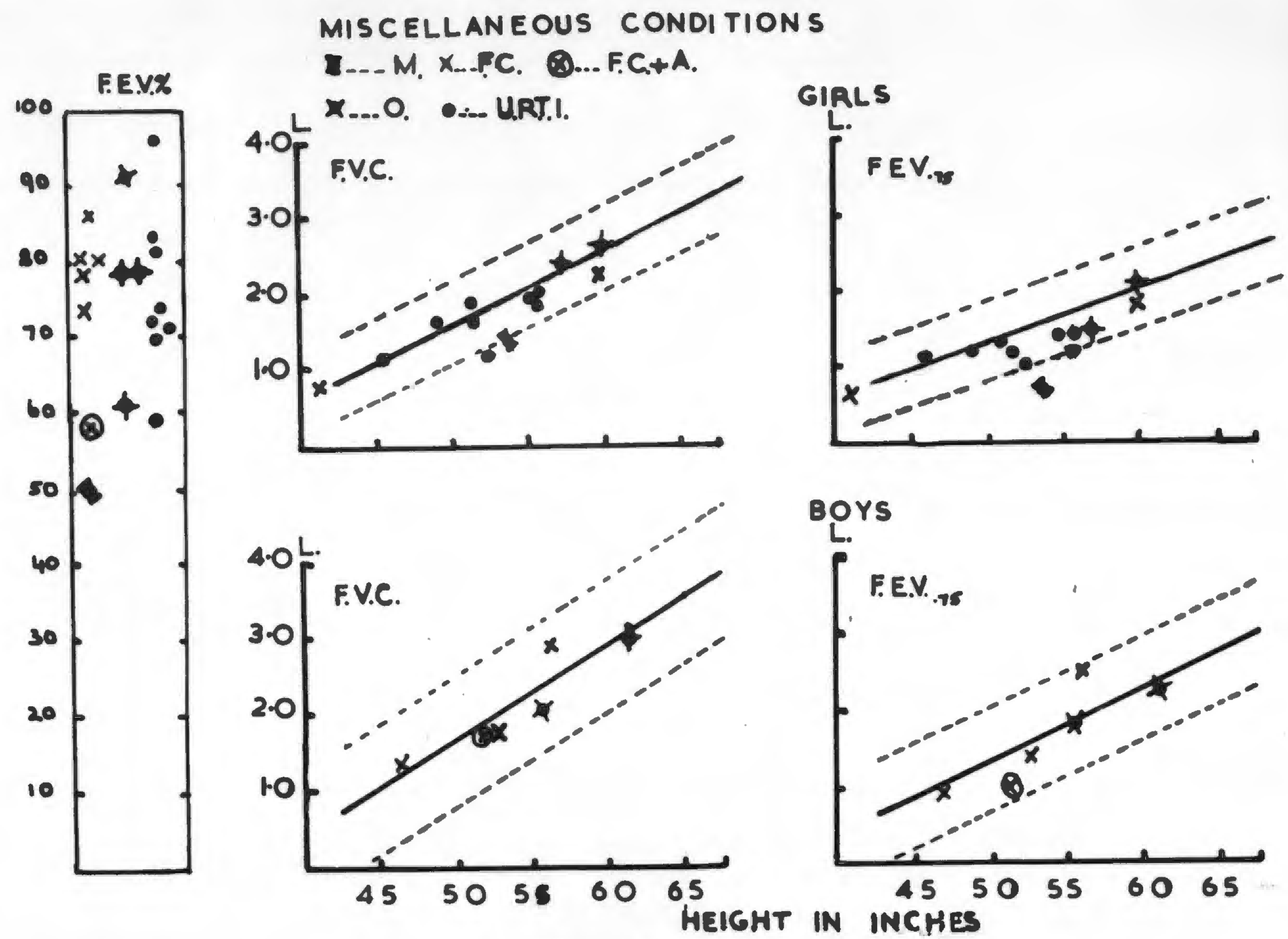

MISCELLANEOUS CONDITIONS
■--- M. x---F.C. ⊗--- F.C.+A.
✖--- O. ●--- U.R.T.I.
F.E.V.%
100
90
80
70
60
50
40
30
20
10
GIRLS
BOYS
L.
4·0
3·0
2·0
1·0
F.V.C.
F.E.V..75
45
50
55
60
65
HEIGHT IN INCHES

FIG. 40

PART 2

The second part of this thesis deals with a study which was carried out in:

A. A group of asthmatic children

B. A group of children suffering from congenital heart disease

C. A group of children suffering from miscellaneous conditions, namely "funnel chest", obesity, gross chest deformity and chronic respiratory tract infection.

These groups were selected for investigation because of the disturbed ventilatory function which may have resulted from their various conditions.

The study included both clinical and spirometric investigations, in order to explore the practical uses of the $F.E.V_{.75}$ and F.V.C. test, and to establish it as an aid to the usual methods of clinical assessment of ventilatory function.

CHAPTER 11

ASTHMA

A. MATERIAL

B. CLINICAL INVESTIGATION

(a) METHOD

(b) FINDINGS:

(i) Clinical Classification into Groups
(ii) Chest Deformity
(iii) Aetiological Factors
(iv) Discussion of Aetiological Factors.

In asthmatic children, the severity of the asthma is closely related to the impairment of ventilatory function of the lung. It is often difficult to assess the severity of this impairment on clinical grounds, and a test for ventilatory function, such as the $F.E.V_{.75}$ and F.V.C. test, can therefore be of much help.

The test was therefore carried out in 68 asthmatics and some of the findings, both clinical and spirometric, with emphasis on the latter, are discussed.

A. <u>MATERIAL</u>

When the investigation was planned for the asthmatic cases it was decided (1) to examine and test spirometrically, at random, patients who attended the Out-patient Department or special Asthma Clinic, (2) to examine and test, daily, asthmatic patients who were admitted to the ward and so follow the course of their disease by clinical and spirometric investigation, and (3) to examine and test a group of asthmatic boys who attended a weekly physiotherapy class over a period of five weeks, to study the effects of exercise on their respiratory function.

There was no selection of cases, except on the basis of age, and cases were seen and examined whenever convenient to myself, except those cases who were admitted to the ward, who were all seen every morning. The effects of therapy and management were investigated although, as these were always prescribed by the Consultant Paediatrician in charge of the case there was no uniformity of management. Treatment was in no way influenced by the spirometric findings and these investigations were used solely to explore the practical uses and possibilities of the test from the material obtained.

A total of 68 asthmatic children, 16 girls and 52 boys, aged between 7 and 15 years, were studied. The majority of these children had attended the Out-patient Department of the Royal Hospital for Sick Children, Bristol at regular intervals and complete notes were available of past attendances.

Ten of these 68 children were subsequently admitted to the wards because of the severity or resistant nature of their asthma. These children were studied in detail and frequent physical and spirometric investigations were carried out to determine the course of their asthma and pulmonary function.

A group of 7 boys were seen at weekly intervals for 3-5 weeks at the physiotherapy classes where breathing exercises were carried out. A clinical and spirometric examination was carried out on each child before and after each class. One of these boys (J.E.) had been an in-patient.

The remaining 51 children were seen only in the Out-patient Department. Nine of these were examined on two occasions and 42 were examined only once. All these children were seen by a Consultant Paediatrician or Assistant and by myself.

B. <u>CLINICAL INVESTIGATION</u> (a) <u>Method</u>:

The method of examining and testing these 68 children was the same throughout. A history was first taken with special reference to the frequency and severity of asthmatic attacks, the number of days absent from school because of asthmatic attacks, the frequency and amount of any anti-asthmatic medicants used, the presence of any associated symptoms such as cough, listlessness and anorexia. The general comments of the mother and child were noted. In addition the following data was recorded - the child's age and sex, the age at onset of "wheezing", the duration of asthma, the occurrence of any past or present eczema or hay-fever and the age at its onset, the presence of a family history of asthma, and the number of other children in the family.

A complete physical examination was then carried out with special reference to the respiratory system. A note was made of any chest deformity, such as Harrison's sulci, kyphosis of the thoracic vertebrae, prominence of the sternum, "pigeon-chest" deformity or "barrel shaped" chest. Evidence of obstructive emphysema was looked for and any adventitious sounds on auscultation noted.

The standing height, sitting height and weight were then measured in the same way as for normal children.

(b) Findings:

(i) Clinical Classification: The 68 cases were classified into three clinical groups, using the following criteria.

Group 1: Asthmatics with a history of wheezing continuing for days without relief from broncho-dilator drugs or other treatment. These cases usually gave an additional history of cough, listlessness and anorexia. Some of these children were admitted to the ward is status asthmaticus. On examination, all showed signs of severe obstructive emphysema, expiratory and/or inspiratory wheezing and diminished breath sounds. Of the 11 children in this group, 9 were admitted to the ward and 2 were treated as out-patients.

Group II: Asthmatics with a history of 2 to 3 attacks of wheezing per week but who were relatively well between attacks. In the majority of these cases the child had to be kept away from school during at least some of the attacks. On examination most of these had auscultatory evidence of expiratory difficulty such as wheezing and prolonged expiration. Other adventitious sounds, such as crepitations, were sometimes present, depending on the severity of the condition at the time of examination. Signs of obstructive emphysema such as "barrel-shaped" chest with hyper-resonance and diminished cardiac dullness were often present. Twenty of the 68 cases were classified into this group.

Group III: Asthmatics who were well at the time of examination with a history of absence of wheezing in the preceding three weeks. These children took part in all games at school with no apparent impairment of pulmonary function. Sixteen of the 37 children in this group had been free of symptoms for over 3 months, and 3 for more than 2 years. On examination there was very little to find, apart from evidence of past respiratory disease such as "pigeon-chest", "barrel-shaped" chest, Harrison's sulci, etc. On auscultation no adventitious sounds apart from an occasional rhonchus, and perhaps some prolongation of expiration, were heard. Auscultatory findings in nearly all these cases were reported as normal by the Consultant in charge of the Clinic.

Distribution of Cases

TOTAL 68	16 Girls	Group I	5
		Group II	4
		Group III	7
	52 Boys	Group I	6
		Group II	16
		Group III	30

(ii) Chest Deformity : Amongst the 68 children, chest deformity was noted in 4 (36%) of Group I cases, 11 (55%) of Group II cases, and 9 (24%) of Group III cases. This gives a total of 24 (35%) cases in the 68 asthmatics examined.

(iii) Aetiological Factors : Data on the average age, average age of onset and average duration of the asthma in the 68 children were as follows:-

TABLE XXIII

	Group I	Group II	Group III
		Y e a r s	
Average Age	10.16	10.22	11.7
Average Duration	6.91	7.02	8.5
Average Age of onset of wheezing	3.25	3.2	3.2

From the histories and findings of the 68 cases the aetiological factors present in the three groups were analysed. In Table XXIV the results obtained are expressed, firstly as a percentage of the number of cases in the group having a positive history or finding of the specific aetiological factor, and secondly as a percentage of the total number of cases examined.

TABLE XXIV

AETIOLOGICAL FACTORS

	Group I	Group II	Group III	Total for 3 Groups	
Family History Asthma	36% (4)	35% (7)	43% (16)	40%	27
Only Child	27% (3)	20% (4)	24% (9)	24%	16
Eczema	36% (4)	45% (9)	30% (11)	35%	24
Hayfever	54% (6)	45% (9)	18% (9)	34%	23
Colds	82% (9)	75% (15)	35% (13)	55%	37
Psychological Factors	91% (10)	70% (14)	27% (10)	50%	34
Combination of Factors	82% (9)	56% (13)	46% (17)	57%	39
No. of Cases in Group	11	20	37		68

Skin sensitivity tests against different allergens including cotton flock, house dust, horse dander, cat fur, dog hair, all pollens including those of grass, trees and moulds, were carried out and recorded in 45 of the 68 patients over a number of years. Those recorded as having a sensitivity of 2 + or more, were taken as being positive. These tests showed that in 25 of the 45 cases (53%) positive results against one or more allergen were recorded.

A history of hayfever was obtained in 23 of the 68 cases seen (34%) and a history of eczema, usually present within the first two years of life and preceding the asthma, was obtained in 24 of the 68 cases (35%).

A family history of asthma was given in 27 of the 68 cases (40%).

In 37 cases (55%) the attacks of wheezing were usually precipitated by colds.

Although more difficult to assess, psychological and emotional factors were considered to play a major part in 34 of the 68 cases (50%). Amongst the Group I cases psychological factors were thought to play a part in 10 out of the 11 children. Most of these cases were seen by the Psychiatric Social Worker or a Consultant Psychiatrist. The latter gave the following report, for instance, on the mother of C.N. (Fig. 34A):

"A pleasantly friendly mother but who has lost her 'sense of touch' and is afraid to do the wrong thing. C.N. showed no enthusiasm when her mother came to visit her in hospital except to look in the paper bags she had brought to find out what was there".

C.N. aged 7¼ years was admitted on 10 occasions to the Children's Hospital and was eventually transferred to a sanatorium inSwitzerland. The report of the Psychiatric Social Worker on the mother of J.B. (aged 11¼ years) was:

"The attitude of the mother is that of over-protection as she refuses to admit that J.B. is a normal child and so must treat him as an invalid which only exacerbates his condition".

The report of the Psychiatrist on J.T. (aged 9 years), and her mother reads:

"The social history is significant. Mother aged 44, only child. The early training was rigid. The mother is tense and nervous and says she gets 'butterflies and big moths' and does not sleep, if she has to do anything out of the ordinary. She feels she cannot afford to let the child disobey her and gets very upset when she is rude to her. The mother cannot tolerate the child's arguments and always has to have the last word. J.T. enjoys being seen and is inclined to be neat and tidy. So is her handwork. She does not like rough games - this contrasts with her quite ready aggressive expression here. The child is emotional but with too strong a control; she sets herself very high standards and cannot afford to fail. It seems likely that the home does not tolerate this girl's normal emotional expression".

The same patterns were present in most of the 10 cases, although the three cases quoted are probably gross examples.

In 39 of the 68 cases (57.3%) a combination of two or more aetiological factors played a part in precipitating an attack of wheezing. However, in a certain number of cases a single factor only could be found to precipitate the attacks (Table XXV).

TABLE XXV

SINGLE AETIOLOGICAL FACTORS

	GROUP I	GROUP II	GROUP III	TOTAL
COLDS	9% (1)	20% (4)	25% (9)	20.6% (14)
ALLERGY	(0)	15% (3)	30% (11)	20.6% (14)
PSYCHOLOGICAL FACTORS	9% (1)	(0)	(0)	1.5% (1)
NO. IN GROUP	11	20	37	68

(iv) Discussion of Aetiological Factors:

Since a large part of this work is concerned with asthma and volumetric measurements made in that condition, it is essential to make quite clear just what has been included under the somewhat nebulous limits of the term. Moreover, since there are various schools of thought - each convinced of a different aetiology - as to the basic cause of the asthmatic attack, it is necessary to review briefly the current trends in that direction. The influence of mind over matter, or vice versa cannot be ignored when an assessment which involves both is under consideration in an unphysiological state where the basic fault has not been infallibly demonstrated.

Bronchial asthma occurs in subjects with an over-excitable mucosa and musculature of the bronchial tree and the condition is dharacterized by recurrent cough and a wheezing type of dyspnoea in which the patient's main difficulty appears with expiration. It may manifest itself as an acute paroxysm which lasts from a few minutes to several hours or days, or it may become severe and persistent, in which case it is termed status asthmaticus. In other cases it may be present in a sub-clinical form.

The reaction is "non-specific" and appears to be a reaction to a wide variety of diseases and factors such as allergens, infections, and reflex physical and psychic stimuli that generally have no effect on normal subjects. Hippocrates first noted that asthmatic attacks could be brought on by emotional disturbances such as hostility and anger.

The role which these various factors play, and their relative importance, has for long been a subject of controversy amongst clinicians and pathologists and opinions are largely influenced by the orientation of the attending physician. The majority of clinicians tend to disregard the "non-specific" nature of this reaction and those who consider "allergy" to be the basic factor seek relentlessly for evidence of hypersensitivity to a foreign substance by skin testing against different known allergens. This tendency is well illustrated by an article from Chobot et al.(1951) in which they discussed the relationship of aetiological factors in asthma in 400 infants and children, whose asthma started before the age of three years, without making any mention of possible psychic factors. They came to the conclusion that chronic focal infection was one of the most important causes of asthma, followed by inhalation of allergens, with food playing a subordinate role to both. In contrast to this tendency, the psychiatrist is often able to discover only psychic stimuli in the history given by an asthmatic patient, as the basic aetiological factor.

In an attempt to put psychological, infective and allergic factors in their proper perspective Wittkower (1952) classified asthmatic patients into three groups; (a) asthmatics whose clinical manifestations can be sufficiently accounted for on an organic basis: (b) asthmatics about whom positive psychiatric evidence indicates that emotional states have led to physiological changes which are identical with those observed in purely allergic diseases: (c) asthmatics in whom evidence of both specific hypersensitivity and specific emotional states exist and in whom, owing to a clear correlation between emotional and clinical manifestations, it must be assumed that the emotional disturbances act as a catalyst to a dominant allergic predisposition. Dekker and Groen (1956) recorded, by measuring the V.C. in patients prone to asthma, the severity of asthmatic attacks induced firstly by nebulized allergens and secondly, by emotional stimuli selected from their histories. The clinical pictures induced by the different methods were indistinguishable.

Walker (1918) classified asthmatics into "intrinsic" and "extrinsic" groups. Rackemann (1947) also divided them into two groups, the first beginning before the age of 30 years ("extrinsic" or allergic) and the second beginning after the age of 40 years ("intrinsic" and generally demonstrating no allergic factors).

The patient with "extrinsic" asthma is now generally defined as one under 30 years of age who demonstrates specific allergic sensitivity by history, by environmental control tests, or by skin or serological tests. The attacks are often acute and seasonal in character with complete freedom from symptoms between attacks. The patient with "intrinsic" asthma is generally one over the age of 40 years. Specific allergens are usually not demonstrable and there is usually no family history of allergy. This patient is usually more sensitive to psychic and physical stimuli.

From the findings in this relatively small series, one must conclude that the classifying of asthmatic patients into "extrinsic" and "intrinsic" groups is largely artificial and the majority of cases examined at Bristol presented with features of both groups. Each individual's susceptibility, inherited predisposition and sensitivity to infection, physical and psychic factors appears to determine his course as an asthmatic.

CHAPTER 12

SPIROMETRIC INVESTIGATION: GENERAL OBSERVATIONS

A. METHOD

B. SPIROGRAMS

C. SPIROMETRIC MEASUREMENTS

(i) $F.E.V_{.75}$, F.V.C. and F.E.V.%

(ii) $F.V.C._T$

D. OCCULT BRONCHOSPASM

E. TRAPPING

F. CLINICAL APPLICATION OF THESE OBSERVATIONS

A. METHOD

The spirometric test was carried out with the patients standing, using the same technique as was used for normal children (p.48) with one difference. Three expiratory and inspiratory vital spirograms were obtained at ½-minute intervals.

This procedure was adopted because of the evidence that, in patients with asthma, during a forced expiration some of the narrower air passages are closed by the abrupt increase in the pressure applied to the lungs and gases are trapped beyond these in appreciable amounts. (Gandevia and Prime, 1957). This manifestation of "trapping" is well illustrated by the greater volume of the vital capacity when delivered slowly compared with that when delivered as quickly as possible (Franklin et al. 1955). (See "trapping" experiments and Fig. 9). After an interval of 10 minutes, the patient was given three inhalations of Isoprenaline Sulphate B.P. delivered through a MEDIHALER ISO propellant unit (Riker). The dose of isoprenaline sulphate delivered per spray is 0.075 mg.

Approximately five minutes later 3 more spirograms were obtained as before at ½-minute intervals.

The F.V.C. and $F.E.V_{.75}$ values were then measured from the three pre-inhalation and three post-inhalation spirograms. These values and the total time over which the F.V.C. was delivered were then recorded from the first and third curves of the pre- and post-inhalation spirograms.

B. THE FORCED EXPIRATORY AND THE FORCED INSPIRATORY SPIROGRAMS IN ASTHMATIC PATIENTS

In normal subjects the resistance to airflow during normal breathing is similar during inspiration and expiration. In asthma the resistance to airflow is increased during both phases. Aerosols of histamine and acetylcholine can be shown in asthma to produce two or three fold increases in this airflow resistance, while antispasmodics have the reverse effect (Gilson, 1957).

Andrews and Simmons (1959) showed that the increase in the functional residual capacity and residual volume that have been reported in adults and children (Lukas, 1951; Beale et al., 1952; Briscoe and McLemore, 1952 and Kraepelien et al., 1958) can occur as early as 6½ years of age and after a history of asthma as short as six months. This resistance to airflow in asthma is reflected in the shape of the spirograms obtained from these patients. When the shapes of the F.E.S. and F.I.S. in asthmatics (Figs. 35 and 30) are compared with those of normal subjects (Figs. 7 and 8) a number of observations can be made.

In the normal subject the curve of the F.E.S. initially drops steeply and is approximately a straight line. After a certain volume of air has been expelled, the curve deviates more and more from this almost straight line. The whole volume of the F.V.C. is always expelled in under 2.8 seconds (average 1.7 secs.). In asthmatics, depending on the severity of the disease, the initial drop in the curve becomes less steep, the shape being that of a shallow curve rather than an almost straight line. The F.E.S. in Fig. 30 illustrate this point. The first F.E.S. is that of a patient from Group I with severe asthma. It will be noted that it took the patient more than 5 seconds to deliver the small F.V.C. and that the amount of air the patient was able to expel in the first few seconds was very small. This is the amount of air which is of use to a person in ordinary ventilation and during hyperventilation. In patients in Group III, however, the F.E.S. shows a closer approximation to the normal, although the shape of the curve is still shallower than the normal and more than 3 seconds is necessary for the delivery of the F.V.C. The F.E.S. of patients in Group II fall between the shapes of those for Group I and Group III patients.

The F.I.S. in children varies with age and is a less reliable index of ventilatory function than the F.E.S. Only in the older child does it approximate to that of an adult and appear as a practically straight line. In asthmatics an alteration in the shape of the F.I.S. from the normal is seen. Although not so well defined as the alteration in the F.E.S. shape it is a similar alteration, the slope becoming less steep and the F.I.V.C. is breathed in over a longer period than normal (average normal = 1 sec.) indicating some degree of inspiratory obstruction.

So, by simply observing the spirograms in a given patient one is able to form some idea of the degree of impairment to ventilatory function. The shape of the spirogram in an asthmatic reflects the abnormality in the mechanical properties of the lungs in this disease. McIlroy and Marshall (1956) have shown that there are two main abnormalities - an increase in the resistance to the flow of air in and out of the lungs and an increase in the stiffness of the lungs. These changes are less marked after broncho-dilator drugs. The changes in the shape of the asthmatic spirogram following therapy with a broncho-dilator such as isoprenaline indicate the presence of reversible bronchospasm (Kennedy and Thursby-Pelham, 1956; Hume and Gandevia, 1957a) and gives one some immediate, though not absolute, indication of the severity of the condition and the likelihood of successful broncho-dilator therapy (Fig.30).

Throughout this present study a change in values was only regarded as significant if the increase after broncho-dilator therapy represented 10% or more of the initial value for the $F.E.V._{.75}$ and F.V.C. A further proviso has been made throughout, that the increase in the value must be at least 75 - 100 ml. because at low $F.E.V_{.75}$ levels (e.g. 250 ml.) an increase of, for instance, 50 ml. would represent a 20% increase. Furthermore, the measurement of 50 ml. or similar small amounts is difficult and unreliable.

When a group of asthmatics were given water to inhale (from a nebulizer) no significant change in the shape of the spirogram or in the $F.E.V_{.75}$ and F.V.C. values was noted (Table XXVI).

TABLE XXVI

EFFECT OF WATER AEROSOL INHALATION ON $F.E.V_{.75}$ AND F.V.C. VALUES

	Pre-Water Inhalation			Post-Water Inhalation		
	$F.E.V_{.75}$ In	F.V.C. Litres	F.E.V%	$F.E.V_{.75}$ In	F.V.C. Litres	F.E.V%
B.B.	1.175	2.025	58	1.150	2.025	57
D.B.	1.150	1.900	61	1.200	1.925	62
	0.175	0.600	29	0.300	0.750	40
C.N.	0.250	0.775	32	0.275	0.750	37
	0.275	0.750	37	0.250	0.700	36
	0.425	0.750	57	0.425	0.800	53
J.T.	0.400	0.750	53	0.375	0.800	47
	0.475	1.000	48	0.450	0.875	51
A.B.	0.975	1.800	54	0.900	1.650	55
	1.250	1.750	71	1.150	1.750	66
	1.300	2.500	52	1.200	2.100	57
J.E.	1.425	2.450	58	1.350	2.350	57
	1.750	2.500	70	1.650	2.500	66

C. SPIROMETRIC MEASUREMENTS

(i) F.E.V$_{.75}$, F.V.C. and F.E.V%

The values for the F.E.V$_{.75}$ and F.V.C. plotted against standing height and the F.E.V% values in the different groups are given for girls in Fig. 31 and for boys in Fig. 32. All these values are the volumes measured from the spirograms taken at the first attendance of each of the 68 children.

From Figs. 31 and 32 and the results in Table XXVII, the distribution of F.E.V$_{.75}$ values for boys and girls can be seen for the three groups.

TABLE XXVII

DISTRIBUTION OF F.E.V$_{.75}$ VALUES (FIGS. 31 AND 32).

GIRLS	GROUP I	GROUP II	GROUP III
Above Average Line and Within 2σ_z Range	0	0	1 (14%)
Below Average Line but Within 2σ_z Range	0	2 (50%)	5 (72%)
Below 2σ_z Range	5 (100%)	2 (50%)	1 (14%)

DISTRIBUTION OF $F.E.V_{.75}$ VALUES (FIGS. 31 AND 32)

BOYS	GROUP I	GROUP II	GROUP III
Above Average Line and Within $2\sigma_z$ Range	0	3 (19%)	6 (20%)
Below Average Line but Within $2\sigma_z$ Range	0	6 (37%)	14 (46.7%)
Below $2\sigma_z$ Range	6 (100%)	7 (44%)	10 (33.3%)

These values of the $F.E.V_{.75}$ for Group I and Group II fall within the range one would expect from their clinical condition and groupings. The three boys in Group II whose $F.E.V_{.75}$ values were above the average line are of some interest in that they demonstrate the difficulty of classifying asthmatics on clinical findings.

In R.W. aged 7½ years, asthma started at the age of 12 months. It was always worse in the summer and during the three months before being seen by me he had been wheezing almost every night. On examination his chest was hyper-resonant and on auscultation high pitched expiratory rhonchi were heard. His $F.E.V_{.75}$ showed an improvement of 16% following isoprenaline inhalation (Table XXVIII). Thus he was probably a child sensitive to one or other allergen prevalent in the summer and had he been seen in the winter would probably have been classified as Group III.

R.W. Spirometric Measurements

TABLE XXVIII

		Pre-I.P.	Post-I.P.
$F.E.V_{.75}$	=	1.250	1.425
F.V.C.	=	1.675	1.850
F.E.V%	=	74.6%	77%
$F.V.C_{T}$	=	2.4 secs	2.0 secs

In A.B., aged 9¼ years, asthma started at the age of 2 years. Since its onset he had had frequent intermittent attacks with short periods of relative freedom from symptoms between. When seen by me for the first time he was in one of relatively free phases having only one or two attacks each week of slight wheezing at night. On examination, an occasional expiratory rhonchus was heard on auscultation. The $F.E.V_{.75}$ showed no improvement following isoprenaline inhalation. However, he was later admitted to the ward during a phase of severe wheezing and Fig. 33A demonstrates the subsequent course of his asthma in hospital.

In I.B. aged 8 years, asthma started at the age of 2 years. He had a strong family history of asthma and hayfever in both his mother and father. When first seen by me he had 3 - 4 attacks of wheezing a week. On examination, a few expiratory rhonchi were present in both lung fields. No evidence of obstructive emphysema was found. The F.E.V $_{.75}$ value showed no improvement following isoprenaline inhalation. He was seen on two subsequent occasions and although having broncho-dilator therapy and breathing exercises, he showed no clinical improvement and the spirograms reflected this deterioration.

TABLE XXIX

I.B. Spirometric Measurements

	Pre-I.P	Post-I.P.	Pre-I.P	Post I.P.	Pre-I.P	Post I.P
F.E.V $_{.75}$	1.100	1.100	0.825	1.000	0.350	0.425
F.V.C.	1.600	1.650	1.375	1.650	0.675	0.850
F.E.V%	69%	67%	60%	60.5%	52%	50%
F.V.C $_T$	3.0 sec	2.8 sec	4.2 s.	2.9 s.	4.3 s.	3.6 s.
	2/9/58		9/9/58		16/9/58	

All Volumes in Litres

These 3 cases illustrate how variable is the clinical course of asthma and consequently the difficulties of classifying asthmatics into rigid groups. Furthermore, they show how a single reading of the $F.E.V_{.75}$ and F.V.C. is only of value in that it reflects the state of the bronchial tree at that particular time. However, the importance of these first readings in these cases is to show that, regardless of subsequent readings, these lungs have suffered no irreversible damage from the past severe asthmatic attacks and are essentially normal lungs. Although the patients fall clinically into a group with severe asthma no evidence of emphysema is present.

The results of the $F.E.V_{.75}$ for the Group III cases show that the scatter of values is below that of normal children but that the values are much better than those of the Group II cases. 14% of girls and 33% of boys in this Group III had $F.E.V_{.75}$ values below the $2\sigma_z$ range. These figures show that although these children clinically appeared to have relatively mild asthma the spirographic tests showed the presence of impaired ventilatory function which may be due to bronchospasm or emphysema.

Table XXX gives the distribution of values for the F.V.C. in the 3 different groups.

TABLE XXX

DISTRIBUTION OF F.V.C. VALUES (FIGS. 31 AND 32)

GIRLS	GROUP I	GROUP II	GROUP III
Above Average Line and Within $2\sigma_z$ Range	0	1 (25%)	3 (43%)
Below Average Line but Within $2\sigma_z$ Range	0	3 (75%)	4 (57%)
Below $2\sigma_z$ Range	5 (100%)	0	0
BOYS			
Above Average Line and Within $2\sigma_z$ Range	0	4 (25%)	15 (50%)
Below Average Line but within $2\sigma_z$ Range	2 (33.5%)	10 (62%)	15 (50%)
Below $2\sigma_z$ Range	4 (66.5%)	2 (13%)	0

These figures show that the F.V.C. values for Group III patients approximate the normal values. Those of Groups I and II are below the normal distribution, but the diminution in values is far less than that seen for the $F.E.V_{.75}$ values of these Groups.

The F.E.V% values for the 3 different Groups are also compared in Figs. 31 and 32. The values for girls show a close correlation with their clinical groupings, the values for Group III all except two cases being within the expected normal range. For the boys, 5 in Group I show levels within the range one would expect from their clinical condition, the exception being S.P. (Fig.33). whose F.E.V % on the first day was 77%. At this time there was no radiological evidence of collapse of the lungs and this value indicates a proportional fall in the F.E.V $_{.75}$ and F.V.C. values. The absolute values for the F.E.V $_{.75}$ and F.V.C. were very low. This illustrates the point that the F.E.V% as a single criterion, without knowledge of the absolute values for the F.E.V $_{.75}$ and F.V.C., can be misleading and of little value. It is therefore not per se a measurement of bronchial obstruction. For the boys in both Groups II and III the F.E.V% values fall within the same range, although they vary from the low value of 40% to values well within the normal range.

From these findings it becomes evident that, in general, the F.E.V $_{.75}$ value is diminished to a greater extent than the F.V.C. in patients with asthmatic disease. These findings are in agreement with those of other workers (Roy et al., 1955; Stewart, 1922) who noted that in children subject to the disease for many years there was no apparent reduction in the V.C.

(ii) $F.V.C._T$

The accuracy of measuring the time intervals over which the F.V.C. and F.I.V.C. are delivered is open to certain criticism as the determination of the exact end points of the expiratory and inspiratory spirograms may be very difficult. From a study of the Graphs (Figs. 7, 30, 35) it can be seen that this difficulty is increased with the perseverance of the child. Towards the end of the expiration he may be able to expel only a very small volume (less than 75 ml.) over one or even more seconds and, from the resulting curve, it is very difficult to assess the exact end point. This small volume of air at the end of expiration is of no practical use to the patient.

Despite this objection, the measurement of the $F.V.C_T$ is of practical value in helping the clinician to elucidate and interpret auscultatory findings in these patients. Breath and adventitious sounds depend on the movement of air in and out of the lungs. By comparing the opinions of different clinicians as to whether they considered expiration or inspiration in a given asthmatic child was prolonged, and by then comparing their findings with those from the spirogram it soon became evident that, in Group I cases, and to a lesser extent Group II cases, there was a close correlation between clinical observations and objective measurement. However, in Group III cases, prolonged expiration or inspiration (obstruction to airways) only became obvious from the spirogram (Table XXXI).

Furthermore from these investigations, it becomes evident that it is very difficult to ascertain by auscultation any response to isoprenaline inhalation, not only in these Group III cases but also in those of Group II. In the latter Group the auscultatory signs before and after isoprenaline inhalation showed no marked difference in the number or quality of sibilant rhonchi in the majority of cases. Even after considerable experience in comparing auscultatory and spirometric findings we were able to predict the isoprenaline response from our auscultatory findings in only a few cases. In these, the differences before and after isoprenaline were mainly in the pitch (higher pitch before isoprenaline) and in the duration of expiration (prolonged before isoprenaline). But in the majority of cases any response was only detected from the spirograms. The anthropometric measurements of the three patients (Fig. 30) from whom spirograms were obtained, and their spirometric values, are recorded in Table XXXI.

TABLE XXXI

	GROUP I		GROUP II		GROUP III	
	Pre-I.P.	Post-I.P.	Pre-I.P.	Post-I.P.	Pre-I.P.	Post-I.P.
$F.E.V._{.75}$	0.300	0.300	0.725	1.325	1.300	1.575
F.V.C.	0.950	0.950	1.250	1.925	1.975	2.050
F.E.V.%	31.6%	31.6%	58%	69%	65%	75.8%
Increase $F.E.V._{.75}$		-		82.8%		21%
Incfease F.V.C.		-		50.4%		2.5%
$F.V.C._T$	5.5 sec.	5.5	3.2 sec.	2.4	3.0 sec	2.0
Age	10.25 yrs		10 yrs		9.5 yrs.	
Weight	49 lbs		65 lbs		61 lbs	
Standing Height	53"		52"		53"	
Sitting Height	28"		27½"		26½"	

All Volumes in Litres

From this Table it can be seen that the measurement of the time intervals over which the F.V.C. and F.I.V.C. are delivered are of some help in assessing a return to "normality" in the asthmatic child. When the patient in Group III (Fig. 30) for instance, is assessed on the pre-isoprenaline $F.E.V_{.75}$ and F.V.C. values only, both these values are seen to fall within normal limits. However, the shape of the spirogram, the F.E.V.% lying on the lower limits of normality, and the abnormally long $F.V.C_T$ (3 seconds) make one suspect either occult bronchospasm or emphysema to be present. After isoprenaline there is not only an increase in the F.E.V $_{.75}$ and F.V.C. values, but the F.E.V% value and F.V.C$_T$ both come to lie within the normal range also. This suggests strongly that no permanent impairment or damage to lung function has resulted from the disease process.

On the other hand the F.V.C$_T$ may under certain circumstances become more prolonged with improvement in ventilatory function. The first group of spirograms taken on the 11/5/58 (Fig. 35) illustrates this point. Here, associated with a dramatic subjective improvement in the asthmatic symptoms, the increase in the F.E.V $_{.75}$ and F.V.C. values is 160% and 150% respectively over the pre-isoprenaline levels, although the F.V.C$_T$ has increased from 5 to 11 seconds and the F.E.V.% shown no change (31% to 30%). A possible explanation of these findings is discussed on p.156 - 161.

Although the F.V.C$_T$ by itself, without aligning it with the other measurements from the spirogram, is of little value, it is interesting to compare the F.V.C$_T$ values in the 3 Groups. These are given in Table XXXII.

TABLE XXXII

AVERAGE F.V.C.$_T$

	Pre-isoprenaline	Post-isoprenaline
GROUP I	6.2 sec.(4.6 - 10.6)	5.8 sec. (3.0 - 11.6)
GROUP II	3.65 sec.(1.7- 7.0)	3.5 sec. (1.5 - 7.0)
GROUP III	3.24 sec.(1.2- 6.3)	3.07 sec.(1.2 - 6.0)

The $F.V.C._T$ value must therefore always be considered along with the other spirometric measurements, such as the $F.E.V_{.75}$, F.V.C. and F.E.V%, and not alone. When assessing a spirogram these latter values are always more significant than the $F.V.C._T$ (p.).

D. OCCULT BRONCHOSPASM

A number of cases were seen in the Out-patient Department (Table XXXIII), where on examination one could find no clinical evidence to suggest the presence of bronchial obstruction and where the chest was reported to be clear by both the clinician in charge of the case and myself. These children, however, showed a spirometric response to isoprenaline inhalation of more than 10% in their F.E.V $_{.75}$ values and, in the majority of cases, in their F.V.C. values also. This indicated the presence of reversible bronchospasm. All these children were Group III cases with the exception of D.B. and J.G. D.B. was seen only on this one occasion. He gave a history of wheeziness at night but of being quite well during the day, and took part in all the games at school. Although his chest was clinically clear he was classified in Group II because of this history. J.G. when first seen also gave a history of wheeziness at night and although his chest was clinically clear he was also classified in Group II. He was seen on three subsequent occasions and on two of these occasions he showed clinical signs of bronchial obstruction.

TABLE XXXIII

OCCULT BRONCHOSPASM

Name	Age (yrs)	Sex	Clinical Group	(A) PRE-ISOPRENALINE INHALATION F.E.V .75 In Litres	(A) PRE-ISOPRENALINE INHALATION F.V.C. In Litres	F.E.V%	(B) POST-ISOPRENALINE INHALATION F.E.V. .75	(B) POST-ISOPRENALINE INHALATION F.V.C.	F.E.V%	Increase in FEV .75 and FVC values (B) expressed as % of (A) F.E.V .75 In litres	Increase in FEV .75 and FVC values (B) expressed as % of (A) F.V.C. In litres	Symptom-Free Period in Months
A.B.	9.25	M	III	1.150	1.750	66	1.400	2.075	67.5	22	18.5	>3
S.B.	13.25	M	III	2.500	2.950	85	2.750	3.250	85	10	10	>1
J.B.	14.00	M	III	1.400	3.300	42	2.500	3.600	69	78.5	9	>6
C.B.	12.00	M	III	0.900	1.675	54	1.050	1.850	57	17	10.5	>3
R.C.	10.25	M	III	0.900	2.000	45	1.125	2.200	51	25	10	>2
C.F.	8.5	F	III	0.950	1.700	56	1.150	1.850	62	21	8.8	>3
M.M.	14.5	M	III	1.300	2.925	44	2.250	3.200	70	73	9.4	>3
M.P.	9.75	M	III	0.775	2.050	38	1.150	2.375	48.5	48	16	>1
K.W.	7.5	M	III	0.650	1.050	62	0.750	1.000	75	15	-	>1
D.B.	10.75	M	II	1.150	1.900	61	1.475	2.300	64	28	21	Wheezing every night. Regular medication with bronchodilator drugs.
J.G.	14.5	M	II	0.800	1.500	53	0.900	1.750	51	12.5	16.6	

This finding of occult bronchospasm indicates that a number of asthmatics who may have long periods of freedom from symptoms and no clinical signs to suggest ventilatory impairment may in fact have considerable bronchospasm revealed only by spirometric examination.

Earlier published studies have also shown that in asthmatic patients during symptom-free periods ventilatory function may still be impaired (Bates, 1952; Beale et al., 1952; Gaensler, 1950b, Herschfus et al., 1953b). Lukas (1951) made a study of six symptom-free asthmatic children and showed that the pulmonary function could be improved by the administration of epinephrine hydrochloride subcutaneously, or vasonefrin from a nebulizer.

Apart from the work by Lukas, most of the studies on this subject have been done on adults until more recently Kraepelien et al. (1958) showed that, in asthmatic children during symptom-free periods, the functional residual capacity and the residual volume are increased. Kraepelien (1958) demonstrated a significant lowering of the residual volume and functional residual capacity after isoprenaline inhalation but some evidence of abnormality still remained. The explanation of this may be that isoprenaline had not entirely released the bronchial spasm but had only a partial effect. Or the explanation may be that the changes in the lung are caused both by bronchial obstruction and permanent parenchymal changes, such as are found in emphysema. It is, however, impossible from a single reading to tell which of these two is responsible. Only observation of serial readings can differentiate between them.

Airflow obstruction of even a minor degree may seriously reduce ventilatory capacity because resistance to flow increases in inverse proportion to the fourth or fifth power of the internal diameter of a tube (Gaensler et al., 1952). The question arises as to whether the presence of this occult bronchospasm is an indication for prolonged treatment with broncho-dilator drugs, even during symptom-free periods, as suggested by Kraepelien (1958).

From the present study of hospital cases during the course of asthma the response to isoprenaline inhalation appears to be so variable (Figs. 33 - 33E) that further serial studies are necessary before prolonged treatment can be advocated, especially in those children who have been free from attacks of wheezing for 3 months or more.

It is also quite possible that a patient, who may have been symptom-free for some time, may because of apprehension (performing the test for the first time, strange hospital atmosphere, etc.) develop mild bronchospasm which is relieved by isoprenaline, and so give a false indication of the state of the bronchi. That this is not always the case, however, can be seen from studying the graphs of hospital patients who in symptom-free periods still showed signs of occult bronchospasm (Figs. 33, 33A, 33B, 33C, 33D, 33E).

Abott et al. (1953) studied 294 patients (pre-senile age group) with emphysema and demonstrated unequivocal evidence of bronchospasm in 267 of them. They assumed that a combination of such spasm or hyper-irritability, plus oedema of the bronchial tree, provides a mechanism of partial or intermittent obstruction to air evacuation from the alveoli and that it may be an important factor in the production of emphysema.

Ryssing (1959) reviewed the status of 298 asthmatic children who were questioned in 1944. Information could be obtained concerning 281 out of 283 survivors. Out of the 120 cases who were free from attacks for more than one year in 1944, only 58 have since remained free of symptoms; 59 have experienced symptoms again; 2 have died, and 1 case could not be traced.

Further longitudinal studies must be carried out to ascertain whether any permanent damage to the lung has resulted from bronchospasm.

E. THE TRAPPING PHENOMENON

It is a well known fact that in asthmatics a slow expiration may produce a greater volume of exhaled air than a rapid one. This is even more marked in emphysematous subjects (Franklin et al., 1955; Scarrone et al., 1955). This phenomenon is often seen after a bout of coughing, and the spirograms in J.E. (Fig. 9) illustrate this "trapping". At the time, his spirogram (1) was in the normal range. He was asked to cough for approximately 2 minutes and then to repeat the spirogram. The spirogram (2) shows the reduction in the $F.E.V_{.75}$ and F.V.C. values by approximately half and the increase in the $F.V.C._T$ by 2.5 times. After 3 inhalations of isoprenaline he was asked to blow into the spirometer again immediately, and the resulting spirogram shows an improvement. A similar "trapping" was demonstrated by asking him to blow into the spirometer 3 times at intervals of ½-minute. The "trapping" was again shown, though to a lesser extent than that shown after coughing. He was then given 3 inhalations of isoprenaline and again asked to blow into the spirometer 3 times at ½-minute intervals.

Measurements taken from the first and third spirograms, before and after isoprenaline, showed that the isoprenaline not only reversed the initial trapping but also prevented further trapping. The whole test was subsequently repeated using the same procedure but with water in the nebulizer. Evidence of trapping was present in the first 3 spirograms and after water inhalation the 3 spirograms showed evidence of still further trapping. (Table XXXIV). "Trapping" is considered to be present if a reduction of 10% or more occurs in the F.E.V $_{.75}$ and F.V.C. values, when the third F.E.S. is compared with the first.

TABLE XXXIV

	F.E.V $_{.75}$		F.V.C.		F.E.V%		F.V.C. $_T$	
	I	III	I	III	I	III	I	III
Pre-Isopren	1.750	1.425	2.500	2.350	70	61	2.4	3.2
Post-Isopren	1.750	1.650	2.550	2.450	69	67	2.6	2.4
Pre-Water	1.700	1.400	2.500	2.300	67.5	61	2.6	3.4
Post-Water	1.500	1.300	2.350	2.250	65	58	3.4	3.8

All Volumes in Litres

Factors which may play a part in this phenomenon of "trapping" have been put forward. It takes pressure to cause air flow and the total force required to move a given volume of gas at a given rate must overcome elastic recoil and tissue, as well as airway resistance. The pressure required for quiet breathing in health is very small, but to surmount airway obstruction in disease it can, and often does, reach high positive and high negative levels. Taking into consideration the cross-sectional area of the body, the total force with which the abdominal contents may thrust against the lung bases in a patient with a serious expiratory obstruction and distressed breathing may exceed 100 lbs for every expiration. Pressures of this magnitude come into play because of a check-valve mechanism. This is seen for instance in patients with emphysema and asthma where some of the narrower airways are closed by the abrupt increase in pressures applied in the lung during a forced expiration (Franklin et al. 1955; Dayman, 1956).

Some degree of concentric expansion and narrowing of the bronchial system also occurs with inspiration and expiration. All intrathoracic airways are check-valves on expiration and intrathoracic expiratory obstruction can be rendered absolute if sufficient pressure be applied. The most important safeguard is adequate elastic parenchymal recoil to keep the bronchioles open during expiration (Dayman, 1951). Recoil becomes progressively depleted as a normal person exhales and becomes zero near the expiratory terminus of the Forced Vital Capacity. Loss of recoil from any cause enhances the tendency to expiratory check-valve closure permitting bronchiolar collapse. Lesions intrinsic to the airways themselves and directly encroaching on the airway lumena, such as swelling of the bronchiolar mucosa, also increase the tendency to check-valve collapse.

Larger airways are necessarily subjected to greater compression, being situated "downstream" with respect to the direction of expiratory flow, but the cartilage enables them to meet increasing compression. Endoscopic investigations have shown that, in spite of the protecting effect of the cartilage, pressure invaginates the posterior membrane and reduces the lumen to a crescent shaped slip. This mechanism has also been postulated as an important factor in obstruction during asthmatic attacks by Dekker and Groen (1957).

In all the 68 asthmatics examined in this series "trapping" was looked for. In 42 cases it was tested for once, in 9 cases on two occasions, in 7 cases between 3 and 5 times, and in the patients in the ward it was looked for daily.

If those cases examined on more than one occasion (and with "trapping" present in their spirogram with the largest F.E.V $_{.75}$ value) are added to those seen on only one occasion, "trapping" is seen to have occurred in 8 Group I cases, in 7 Group II cases and in 9 Group III cases.

Further analysis showed that, although the F.E.V $_{.75}$ levels in all the cases returned to pre-inhalation levels or above, isoprenaline gave protection in a fashion demonstrated above in J.E. in only 12 (50%) of the cases. One explanation of the unpredictable nature of "trapping" may be an excessive sensitivity to stimulation of the bronchi and bronchioli in these patients. To obtain some idea as to whether this, in fact, was an explanation, a family history of asthma or hayfever, a history of past or present eczema, or both of these, were carefully looked for. In the 24 cases showing "trapping", 5 cases gave a family history of asthma or hayfever; 4 cases gave a history of past or present eczema; 8 cases gave a family history or asthma or hayfever and a history of past or present eczema. That is, a total of 17 cases (71%) while the remaining 29% of cases gave no such histories. These percentages for the cases showing "trapping" were very similar to the percentages seen in the group of asthmatics

TABLE XXXV

"TRAPPING"

	I								II								III							
	F.E.V.75		F.V.C.		FEV.%		FVC.T		F.E.V.75		F.V.C.		FEV.%		FVCT		F.E.V.75		F.V.C.		FEV.%		FVCT	
F.E.S's	I	III	I	III	I	III	I	III	I	III	I	III	I	III	I	III	I	III	I	III	I	III	I	III
B.B. a	1.050	1.175	1.975	2.025	53	52	4.2	4.2	1.200	0.850	1.850	1.750	65	49	2.4	3	1.100	1.050	1.825	1.750	59	60	2.8	3.3
B.B. b	1.250	0.950	2.025	1.850	56	51	3.2	3.4	1.450	1.150	2.100	1.750	69	66	2.0	2.5	1.300	1.300	1.900	2.000	69	66	2.3	2.2
A.W. a	0.250	0.250	0.800	0.800	31	31	5.0	5.0	0.875	0.750	2.300	2.150	38	35	7.0	7.0	1.300	1.200	2.700	2.650	48	45	3.6	4.2
A.W. b	0.450	0.600	1.750	2.000	26	30	10.0	11.0	1.450	1.250	2.700	2.700	54	46	5.2	5.0	1.650	1.650	2.800	2.900	59	57	4.2	3.8
J.B. a	0.350	0.350	0.700	0.500	50	70	3.0	2.4	0.850	0.600	1.450	1.200	59	50	3.4	4.0	1.350	1.125	2.100	1.850	64	61	3.2	2.6
J.B. b	0.400	0.375	0.850	0.850	47	44	4.4	5.0	0.875	0.850	1.600	1.550	55	55	3.2	3.4	1.550	1.400	2.050	1.825	76	77	1.6	1.4
A.B. a	0.475	0.425	1.000	0.825	48	52	4.5	4.9	1.050	0.825	1.600	1.250	66	66	3.6	3.8	1.250	1.300	1.900	1.900	66	68	2.6	3.6
A.B. b	0.650	0.500	1.250	1.150	52	44	5.5	5.4	1.200	1.350	1.600	1.700	75	79	2.4	2.2	1.250	1.300	1.800	1.850	69	70	3.0	3.4
J.E. a	0.400	0.350	0.950	0.950	42	37	3.8	5.4	1.150	0.850	1.950	1.750	59	49	3.8	3.8	1.750	1.425	2.500	2.350	70	61	2.4	3.2
J.E. b	0.450	0.450	1.150	1.025	39	44	5.4	4.6	1.450	1.650	2.300	2.500	63	66	2.8	2.8	1.750	1.650	2.550	2.450	69	67	2.6	2.4
R.T. a	0.250	0.200	0.800	0.600	31	33	6.2	6.0	0.975	0.800	1.900	1.750	51	46	3.6	4.8	1.225	1.100	2.000	1.750	61	63	2.8	2.6
R.T. b	0.450	0.300	1.250	0.500	36	60	8.5	3.0	1.025	1.000	1.850	1.850	55	54	2.8	3.6	1.450	1.375	1.850	1.750	78	78	2.0	2.0

a = Pre-isoprenaline b = Post-isoprenaline inhalation.

I = F.E.S. obtained during an acute paroxysm of asthma.

II = Condition improved; intermittent wheezing; rhonchi ++++.

III = No wheezing or occasional mild attack; occasional rhonchus.

All volumes in litres.

(68 cases) as a whole, where 79% gave such histories and 21% did not. Therefore, speaking generally, these children who show "trapping" do not differ in their "allergic backgrounds" from cases which do not show the phenomenon.

"Trapping" does not seem to have any relationship to the initial level of F.E.V $_{.75}$ or F.V.C. values or to the phase of the asthma. These points are illustrated by Table XXXV. B.B. was seen on five weekly occasions at physiotherapy classes. During that period his weekly F.E.V $_{.75}$ and F.V.C. values showed the usual fluctuations seen in asthmatics. On two occasions "trapping" was present, with no relationship to the initial F.E.V $_{.75}$ and F.V.C. values. The other cases were in-patients who showed evidence of "trapping" in different phases of their asthma.

Why "trapping" should only occur in certain patients and why its presence or absence should vary so much in the same patient is difficult to understand on the basis of the factors discussed and no adequate explanation can be given.

F. <u>CLINICAL APPLICATION OF THESE OBSERVATIONS</u>

The impairment of ventilation during an asthmatic attack is due to bronchospasm, swelling of the mucous

TABLE XXXVA A.W. - SPIROMETRIC MEASUREMENTS

DATE:	11/5/1958		14/5/58		15/8/58		20/8/58		22/8/58	
	Pre-I.P.	Post-I.P.	Pre-I.P.	Post-I.P.	Pre-I.P.	Post-I.P.	Pre-I.P.	Post-I.P.	Pre-I.P.	Post-I.P.
F.E.V $_{.75}$	0.250	0.600	0.575	0.600	0.875	1.450	1.400	1.700	1.750	2.000
F.V.C.	0.800	2.000	1.250	1.475	2.300	2.700	2.500	3.000	3.100	3.000
F.E.V%	31%	30%	46%	41%	38%	54%	56%	56.5%	56.5%	66.6%
F.V.C $_T$	5 sec.	11 sec.	7.5 sec.	6 secs	7 sec.	2.5 sec.	5.8 sec.	2.8 sec.	2.5 sec.	2.7 sec.
Trapping	Neg.	Pos.	Pos.	Pos.	Pos.	Pos.	Pos.	Neg.	Neg.	Neg.
Increase F.E.V $_{.75}$		160%		4.4%		66%		21.4%		14.3%
Increase F.V.C.		150%		18%		17.5%		28%		0%

All Volumes in litres

membrane and increased secretions. The patient's $F.E.V_{.75}$ values will be lowered according to the severity of these 3 factors. A similar lowering of the $F.E.V_{.75}$ may, however, be seen in emphysema (defined as a pathological condition of the lung characterized by reduction or loss of elastic fibres, tearing of the alveolar septa, and a decrease in the pulmonary capillary bed).

If the $F.E.V_{.75}$ value is low in an asthmatic during a given phase of the disease, any subsequent serial improvement in this value would indicate the presence of reversible factors causing the ventilatory impairment. Should the $F.E.V_{.75}$ value reach a normal level the presence of emphysema and its irreversible changes can be ruled out. Similarly, if a lowered $F.E.V_{.75}$ value should show an improvement following an isoprenaline inhalation this would indicate the presence of reversible bronchospasm.

A.W., aged 13 (Fig. 35 and Table XXXVA) illustrates some of these points. Her history is one of repeated attacks of bronchitis with wheezing since she was 18 months old. A history of infantile eczema and hayfever was obtained. She was an only child and her home conditions were difficult (father aged 73 and mother 53). The mother was domineering and over-protective.

A.W. had no interests, no hobbies, and practically no friends. She was not interested in the Girl Guides Movement or any society. Since attending school most of her asthmatic attacks had been triggered by emotional upsets at school and in the home.

She was first seen by me in an acute asthmatic attack of a few hours' duration on the 11/5/58. There was marked difficulty with expiration. The chest was held in a position of inspiration, the accessory muscles of respiration were active, and all the signs of obstructive emphysema were present. There was only a slight audible wheeze and breath sounds were almost absent. A spirogram was obtained after this examination. She was then given 10 inhalations of isoprenaline from a Medihaler and the chest auscultated and spirograms obtained at 5-minute intervals. Between the taking of the 2nd and 3rd spirograms she volunteered that her breathing felt much easier but by now marked inspiratory and expiratory wheezing was audible. On auscultation numerous sibilant rhonchi were present and the inspiratory and expiratory breath sounds were prolonged. When the 4th spirogram was taken she was no longer wheezing and felt "quite free". Although much less marked, sibilant rhonchi and an expiratory wheeze were still heard. Ephedrine ½ gr. and phenobarb. ¼ gr. t.d.s. were then prescribed and she was allowed home.

The attack of wheezing recommenced that same evening and although she was not severely distressed the wheezing persisted until she was seen in the Out-patient Department three days later. On examination marked audible wheezing was present and she looked tired and distressed. Signs of emphysema were present and on auscultation numerous expiratory rhonchi and expiratory wheezes were heard. The same procedure was followed as on the previous occasion. Although she admitted some subjective improvement after the isoprenaline and the audible wheezing seemed less marked, the only changes in the spirograms were an increase of 18% in the F.V.C. and a shortening of the $F.V.C_T$ from 2.3 to 1.6 seconds. She was allowed home.

After a subsequent attack of short duration and a response to isoprenaline similar to that seen on 11/5/58 it was decided to admit her to hospital. She showed rapid improvement and no physical signs of obstruction to airflow were found after 6 days. However, after isoprenaline inhalation the spirogram showed a closer approximation to normal, indicating the presence of "occult bronchospasm". Further spirometric tests on the

22/8/58 showed further improvement with response to isoprenaline and no evidence of "trapping". (Table XXXVA). This patient was discharged from hospital before further investigations could be carried out but these would probably have shown a further improvement in the readings.

In this case, the comments by the patient, the auscultatory findings described, and the spirometric findings at different times during the course of the disease, show the difficulty in assessing the severity of asthma from any one of these findings alone. The auscultatory signs, which are difficult to express quantitatively, are increased when there is increased ventilation for any reason and decreased when flow of air falls. With subjective relief of symptoms and an increase in the $F.E.V_{.75}$ and F.V.C. values there may be no change in the auscultatory signs or they may even become increased.

This case also illustrates well the natural history of an asthmatic attack. Early in the attack obstruction to airflow is caused by bronchospasm. This may pass off or be partially or completely relieved by bronchodilator drugs at this stage (see spirogram on 11/5/58). If this should not happen, swelling of the mucous membranes takes place and increased secretions are formed. In asthmatics the increased secretion of mucus is produced by a dramatic change whereby nearly every columnar cell of the bronchi, small bronchi and bronchioli is turned into a goblet cell (Engel 1958). There is also a diffuse detachment of superficial ciliated epithelium (Houston et al., 1953; Thomson, 1945). As ciliary activity is by far the most important mechanism by which mucus is removed from the smaller bronchi, loss of ciliated epithelium seems to be the most probable explanation for the accumulation of mucus and bronchial obstruction. Once this stage is reached the asthma fails to repond to antispasmodics (see spirogram 14/5/58). If the attack is not relieved at this stage the excessive mucus may cause asphyxia and death by blocking the air passages (Earle, 1953).

CHAPTER 13

ASTHMATIC PATIENTS IN HOSPITAL

A. MATERIAL AND METHOD

B. DAILY SPIROMETRIC MEASUREMENTS

(i) $F.E.V_{.75}$ and F.V.C.
(ii) F.E.V.%

C. SPIROMETRIC RESPONSE TO ISOPRENALINE

(i) Inhalation

(ii) Sublingual - General
- Experimental

D. SPIROMETRIC RESPONSE TO STEROID THERAPY

E. FOLLOW-UP OF HOSPITAL PATIENTS

A. MATERIAL AND METHOD

Eight asthmatics (J.B., J.E., J.T.,R.T., C.N., P.P., S.P., A.W) admitted to the ward, either in status asthmaticus or with asthma of such severity that it warranted admission, were seen by me daily or at regular intervals. These cases were examined both clinically and spirometrically. The latter investigations were usually started the day following admission. By then, most of the children had improved and were able to co-operate. Two other asthmatics, A.B. (Fig. 33A) and F.W., (Fig. 33) were admitted to the ward because of the frequency of their attacks which were thought to be brought on by conditions at home. They were not acutely ill on admission and differed in this respect from the other cases.

All the children were co-operative and took a keen interest in their "blowing tests" and tried hard to better their own and the others' efforts, At first they were tested in groups of two or three but it appeared that the keen competition and perhaps the more rapid improvement of one or other child gave rise to jealousies and even attacks of bronchospasm. J.T. was particularly easily upset in this way. For this reason they were more often tested alone.

The same procedure for obtaining their spirograms was followed as was described for asthmatic out-patients. Where the child was too ill to stand up, the test was performed in the sitting position. Three spirograms were obtained at ½-minute intervals before and after isoprenaline inhalation from a Medihaler. On occasions, isoprenaline was given in the form of a 15 mg. laevo-isoprenaline bitartrate ("ISOLEVIN" - Wyeth) tablet sub-lingually. The tablets were used (i) therapeutically during an attack of wheezing, and (ii) for experimental purposes to study their bronchodilator effect and duration of action. In the experiments, laevo-isoprenaline bitartrate ("ISOLEVIN" - Wyeth : 1 ml. solution = 7.5 mg.) was administered from a nebulizer containing a dilution of 1 in 5, after the administration of the sublingual tablet, to see whether the response to the latter had been complete. (Fig. 34).

Days on which the sublingual form was given, either therapeutically or experimentally, have been noted on the Figs. 33 - 33E. There seemed to be very little difference in the response to isoprenaline sulphate (MEDIHALER - Riker) and laevo-isoprenaline bitartrate (ISOLEVIN - Wyeth). The findings of Dornhorst and Herxheimer (1958) suggest that the pharmaceutical separation of these isomers has no advantage to justify the cost entailed.

B. DAILY SPIROMETRIC MEASUREMENTS

(1) $F.E.V_{.75}$ and F.V.C.

All cases showed the usual response to treatment on admission and within two or three days they were symptom-free. Then they usually took an active interest in ward life.

The graphs show the corresponding spirometric improvement in the $F.E.V_{.75}$ and F.V.C. values from day to day (Figs. 33 - 33E). In Table XXXVI the anthropometric measurements and the expected normal values for the $F.E.V_{.75}$ and F.V.C. calculated from the regression

TABLE XXXVI

HOSPITAL ASTHMATIC CASES

(Figs. 33 - 33E)

Name	Sex	Age (yrs)	Standing Ht. (ins.)	Sitting Ht. (ins.)	Wt. lbs.	Calculated Expected Normal Values in Litres F.E.V$_{.75}$	F.V.C.
J.B.	M	11.5	58	30	72	2.022	2.654
A.B.	M	9.75	47.5	25.5	40	1.088	1.310
J.E.	M	11.5	55	28	64	1.755	2.270
C.N.	F	7.75	46	25	41	1.072	1.243
S.P.	M	9.5	53	26.5	61	1.577	2.014
P.P.	F	15	53	28	68	1.611	1.922
J.T.	F	9.5	52.5	27.5	56	1.573	1.874
R.T.	F	7.75	51.5	27.5	47	1.496	1.777
A.W.	F	13	64	34	95	2.458	2.989
J.W.	M	8.25	55	29	86.5	1.755	2.270
F.W.	M	10.25	52	27.5	65	1.488	1.886

All Volumes in Litres

BOYS: F.E.V$_{.75}$ $\sigma_z = 0.325$ F.V.C. : $\sigma_z = 0.439$

GIRLS: F.E.V$_{.75}$ $\sigma_z = 0.308$ F.V.C. : $\sigma_z = 0.345$

TABLE XXXVI. A

ASTHMATICS ADMITTED TO HOSPITAL BECAUSE OF THE SEVERITY OF ATTACKS

Name Sex	Day of Objective Improvement	Treatment over first 2 days	Comments
S.P. M	2	1. Isoprenaline 15 mg. sub-lingually on admission 2. Procaine Penicillin 500,000 U 3. Breathing Exercises	Short history of cold associated with attack of wheezing over approx. 36 hours
J.B. M	2	1. Isoprenaline inhalation 2. Breathing Exercises	Attacks of wheezing nightly. Antispasmodics used at home with no improvement. Wheezy on admission
A.W. M	2	1. Ephedrine gr. ½ t.d.s. 2. Isoprenaline 15 mg. sub-lingually on admission	Wheezy ++ at night. Better in day. Not in status asthmaticus on admission but wheeze audible
J.E. M	2	1. Phenobarb. gr.½ b.d. 2. Ephedrine gr. ½ b.d. 3. Penicillin V 60 mg. 6 hrly	Admitted with severe paroxysm of approx. 12 hours duration. Frequent night attacks
J.T. F	7	1. Taken off O.P. treatment of antispasmodics 2. Postural percussion and physiotherapy	Wheezing almost nightly "Tight" during day. Productive cough. No response to anti-spasmodics. Loss of weight - severe in last 6 months
R.T. F	5	1. 5 mg. isoprenaline sub-lingually on admission 2. Phenobarb.gr.½ tablet t.d.s. for 48 hours 3. Breathing exercises and percussion	Almost continual wheezing for 3 months. Fewer periods of freedom. Slight and transient response to antispas-modics.
P.P. F	3	1. Isoprenaline 7½ mg. sub-lingually 4 hrly x 5 2. Achromycin 250 mg. 6 hrly 3. Breathing exercises and percussion	Severe cold for past 3 days with wheezing getting progressively worse. Productive cough
C.N. F	5	1. O_2 for 36 hours 2. Isopren. 7½ mg. sublingually one dose 3. Subcut. adrenaline 1:1000 4. Ephedrine gr. ½ b.d. 5. Phenobarb. gr.½ t.d.s. 6. Penicillin V 60 mg. 6 hrly	Admitted in status asthmaticus. Spirometry commenced on 3rd day.

equations using standing height, are given. From a study of the graphs, the great variability in response to admission and/or treatment can be seen in the improvement in the F.E.V $_{.75}$ and F.V.C. values. These values also show the response to isoprenaline during different phases of the disease and the variations in daily ventilatory function.

As early as the second day of testing, four cases (S.P., J.B., A.W. and J.E.) showed a rise in their F.E.V $_{.75}$ and F.V.C. values, whereas the spirograms of four (P.P., C.N., R.T., and J.T.) only started to improve on the 4th, 5th, 5th and 7th days respectively. In spite of the low levels during this initial period of the F.E.V $_{.75}$ and F.V.C. values all these children except C.N. admitted subjective improvement. These responses seem to have very little correlation with the form of treatment used but rather with the duration and severity of the paroxysm of wheezing prior to admission (Table XXXVIA) Three cases (P.P., S.P., and A.W.) showed a steady improvement in their F.E.V $_{.75}$ and F.V.C. values until they were discharged from hospital. Of these, only S.P. reached expected normal levels for both his F.E.V $_{.75}$ and F.V.C. values before discharge. The other two were discharged home because of their marked clinical improvement and absence of signs of bronchial spasm. Their $F.E.V_{.75}$ values were still below the expected normal level.

Three cases (R.T., J.B. and J.E.) all improved until their $F.E.V_{.75}$ and F.V.C. values reached their expected normal levels but all three relapsed again and developed attacks of asthma while in hospital. The two cases (F.W. and A.B., Figs. 33, 33A) showed a similar variation while in hospital and the same pattern was observed in those boys who were seen weekly in the physiotherapy classes (see the findings in J.W., Fig.29). These $F.E.V_{.75}$ and F.V.C. readings indicate the changes in the ventilatory status from day to day. The interesting observation was made that these variations could usually only be demonstrated by spirometric tests and not by clinical examination or by observing the activities of the child in the ward. This variation in the ventilatory function during symptom-free periods has also been recorded by Herschfus et al. (1953b) who studied the fluctuations in the V.C. and the M.B.C. in 42 adults with chronic bronchial asthma during symptom-free periods.

One child (C.N.) was discharged home with not much improvement in her condition and was eventually transferred to a sanatorium in Switzerland. Another girl, J.T. (Fig. 33C) was resistant to therapy using conventional broncho-dilator drugs and was ultimately treated with Prednisolone. The spirometric response to Prednisolone is discussed later in this chapter.

(ii) Observations on the F.E.V.% values

The day to day variation in the F.E.V.% calculated from the corresponding F.E.V $_{.75}$ and F.V.C. values (Figs. 33 - 33 e) are given in Table XXXVIB. In four cases, S.P. (Fig. 33), J.E. (Fig. 33d), J.B. (Fig. 33e) and R.T. (Fig. 33), the F.E.V $_{.75}$ and F.V.C. values reached the expected normal levels for the particular child within 7 to 13 days of admission to hospital. When the F.E.V.% values for J.E., J.B. and R.T. are studied the levels are seen to have been low initially, and they remained fairly constant for the first few days. Only when the F.V.C. value had reached the normal range did the F.E.V.% increase further and approximate normal levels. These findings are in agreement with those of Thomson and Hugh-Jones (1958) for adults.

J.B. and R.T. each had a relapse while in hospital and both their F.E.V.% values dropped to very low levels.

In the course of an acute asthmatic paroxysm, or during clinical improvement, the F.E.V.% level may

TABLE XXXVIB

VALUES FOR F.E.V.%
(FIGS. 33- 33E)

DAY	F.E.V% C.N.	DAY	F.E.V% J.E.	DAY	F.E.V% J.T.	DAY	F.E.V% J.T. Contd	DAY	F.E.V% F.N.
1	25	1	42	1	44	37	40	1	43
2	36	2	54	2	53	38	40	2	65
3	33	3	45	3	68	39	30	3	71
4	44	4	46	4	40	40	57	5	56
6	41	5	49	5	44	41	50	7	64
7	32	6	50	6	43	42	44	9	60
8	37	8	42	7	44	43	43	10	66
9	34	9	41	8	42.5	45	42		
10	33	10	57	11	55	46	37		
11	24	11	57	12	50	48	45		
12	38	12	48	13	70	52	54.5		
13	36	13	66	14	58	53	51.5		
14	33	14	70	15	65	54	67		
15	31	15	70	17	43	56	64		
16	33	16	65	18	50	57	70		
17	41	17	63	19	44	58	48		
18	39	18	60	20	46	59	57		
19	37	19	52	21	47	60	48		
21	37	20	64	22	56	61	46		
22	46	21	60	23	62	63	44		
23	42	22	64	24	65	84	54		
24	46	24	72	25	55	89	63.5		
27	45	25	74	26	50	95	54		
28	27	26	52	28	55				
29	35	59	53	29	49				
41	45	66	62	31	56				
49	44			32	51				
56	47			33	50				
63	43			34	57				
70	47			35	45				
77	43			36	40				

TABLE XXXVIB

VALUES FOR F.E.V%
(FIGS. 33 - 33E)

DAY	F.E.V%	DAY	F.E.V%	DAY	F.E.V%	DAY	F.E.V%	DAY	F.E.V%
A.B.		P.P.		J.B.		R.T.		A.W.	
1	66	1	39.5	1	38	1	31	1	44
9	53	3	39	2	64	2	38	2	49
10	57	4	40	3	58	3	39	3	50
11	69	5	40	5	59	4	37	6	55
12	67	6	39.5	6	75	6	51	7	48
13	45	7	40	7	82	7	61.5	8	56
14	53	8	47.5	8	84	8	52.5		
15	62			9	75	9	32		
16	65			10	70	10	33		
17	70			11	35	12	35		
18	68			12	84	13	54		
19	65			13	70	14	45		
44	42.5			14	76	15	61		
				15	65	46	24		
				16	68				
				17	28				
				19	68				
				20	60				
				21	68				
				43	46				

DAY	F.E.V%
S.P.	
1	77
2	65
3	62.5
4	72.5
8	67
13	68.5
14	73

be within the normal range and remain constant while the $F.E.V_{.75}$ and F.V.C. values are only recovering to within normal limits. This type of response is seen for instance in S.P. (Fig. 33) and J.W. (Out-patient, Fig. 29). These readings must indicate a proportional rise or fall in both the $F.E.V_{.75}$ and F.V.C. values during improvement or relapse. Furthermore, in the patient C.N., the F.E.V.% level actually increased from 34 to 60 during an attack of wheezing and returned to 34 after the spasm had been relieved.

A tentative explanation of these findings can only be suggested with considerable reserve. In those cases where the F.V.C. reaches a normal level before the $F.E.V_{.75}$ it may be that this indicates the presence of patent but spastic bronchi and bronchioli. In those cases where there is a proportional increase of $F.E.V_{.75}$ and F.V.C. with a fixed F.E.V.% the rationale may be that once a bronchiole becomes patent at all it opens completely.

C. SPIROMETRIC RESPONSE TO ISOPRENALINE

(i) Inhalation

When the different graphs are studied, the response to isoprenaline inhalation is seen to be extremely variable and to differ from day to day in any given individual. If a response of more than 10% is obtained it is regarded as being significant in that it indicates the presence of bronchospasm.

When the graph of R.T. (Fig. 33) is compared with that of S.P. (Fig. 33) one of the advantages of the $F.E.V_{.75}$ and F.V.C. test immediately becomes evident. S.P. never showed any significant improvement in his $F.E.V._{.75}$ and F.V.C. values in response to isoprenaline except on the first day and again just before discharge from hospital. This lack of response to broncho-dilator drugs may indicate that therapy with these drugs will serve no useful purpose in this patient. On the other hand, R.T. showed a striking improvement in both $F.E.V_{.75}$ and F.V.C. values in response to isoprenaline throughout her stay in hospital. The question arises as to whether since the drug was so beneficial, she should have been actively treated with it as the chosen therapeutic agent. But when the graph (Fig. 33) and Table XXXVII are studied, the magnitude of the response to isoprenaline inhalation is shown to be extremely variable and quite independent of the pre-inhalation value for the $F.E.V._{.75}$. Where days with the same pre-inhalation $F.E.V._{.75}$ values are paired and the responses to inhalation are tabulated, it is clear that the effect of the drug taken in this one responsive individual was quantitatively unpredictable.

TABLE XXXVII

R.T.: RESPONSE TO ISOPRENALINE SPRAY

	1st Day		10th Day		3rd Day		4th Day	
	Pre- I.P.	Post- I.P.	Pre- I.P.	Post- I.P.	Pre- I.P.	Post- I.P.	Pre- I.P.	Post- I.P.
$F.E.V_{.75}$	0.250	0.450	0.250	0.375	0.375	0.550	0.350	0.450
F.V.C.	0.800	1.250	0.750	0.750	0.950	1.600	0.950	1.150
F.E.V.%	31%	36%	33%	50%	39%	34%	37%	39%
% Increase $F.E.V_{.75}$		80%		50%		47%		32%
% Increase F.V.C.		56%		0%		68%		21%

All volumes in litres

The same variability of reaction to isoprenaline inhalation was found in other children. These findings are not in agreement with those of Gandevia et al. (1957) who showed that in adults, as the pre-inhalation values of the $F.E.V_1$ rise from low levels associated with wheezing so does the response to isoprenaline, until it reaches a sharp peak of maximum response after which the response decreases.

(ii) Sublingual Tablet:

The response to isoprenaline given sublingually was also variable in any given patient. The graph of J.B. (Fig. 33 E) illustrates this when the response on the 2nd and 3rd days are compared (Table XXXVIIA)

TABLE XXXVII A

J.B. RESPONSE TO SUBLINGUAL ISOPRENALINE

	2nd Day		3rd Day	
	Pre-I.P.	Post-I.P.	Pre-I.P.	Post-I.P.
$F.E.V._{.75}$	0.900	1.175	0.850	0.875
F.V.C.	1.400	2.050	1.450	1.600
F.E.V.%	64%	57%	58%	55.5%
$F.E.V._{.75}$ % Increase		31%		10%
F.V.C. % Increase		46%		10%
All volumes in Litres				

From the graph of J.B. (Fig. 33E) it is interesting to note that the response to sublingual isoprenaline on the 2nd day resulted in the F.V.C. value reaching the expected normal level. Similar normal values for the F.V.C. were obtained on the 6th, 8th, 15th and 18th days but not on the intervening days.

As part of the investigation into the practical application of the spirometric test, the effect of laevo-isoprenaline bitartrate sublingually on the $F.E.V_{.75}$ and F.V.C. values and the duration of its effect were studied in 8 of the patients admitted to hospital.

A spirogram was obtained and the $F.E.V_{.75}$ and F.V.C. values measured and the patient was then given a sublingual tablet containing 15 mg. of laevo-isoprenaline bitartrate. Spirographic tracings were obtained after half an hour and at intervals over the next 6 hours. After some of the readings had been taken, inhalations of laevo-isoprenaline bitartrate were given and further spirograms obtained to see whether the response to the sublingual tablet had been complete. These inhalations may have had some influence on the duration of action of the sublingual tablet.

Fig. 34 shows a number of graphs obtained from R.T. during different phases of her asthma. In the 2nd day in hospital her condition was much improved and although clinical signs of asthma were present, she was not wheezing. On the 7th day there were no subjective or objective signs to suggest the presence of bronchial obstruction. On the 9th and 10th days audible wheezing was present. All these graphs show the effect of the broncho-dilator drug. It began within half an hour of taking the sublingual tablet and lasted for a variable time, seldom less than 6 hours on those days when she had wheezing. After the inhalation of isoprenaline the increase in $F.E.V_{.75}$ and F.V.C. values to levels above those obtained with the sublingual tablet indicate that the response to the latter was incomplete and that a considerable amount of bronchospasm was still present.

A further point of interest concerns the lack of correlation between the presence of audible wheezing and the initial $F.E.V_{.75}$ and F.V.C. values. Audible wheezing was present on the 9th and 10th days when the values were low but was not present on the 2nd day when the initial values were approximately the same. The graph also shows (2nd day) that the combined effect of the sublingual and inhaled broncho-dilator resulted in the F.V.C. value reaching the almost normal level of 1.900L. (highest F.V.C. recorded for this child = 2.000L.) The $F.E.V_{.75}$ increase was less marked and reached a value of only 1.000L. (highest $F.E.V_{.75}$ recorded for this child = 1.450L.).

The difficulty of comparing the responses to a broncho-dilator drug in the members of any group of asthmatics is, of course, considerable (Table XXXVIII). The phase of the disease, the duration not only of the disease itself but of the current attack, and all the manifold peculiarities of each individual - some of them unknown and many unassessable - combine to make comparisons

TABLE XXXVIII

RESPONSE TO SUBLINGUAL ISOPRENALINE.

Name	Day in Hospital	F.E.V.$_{75}$ ½ hr.	F.E.V.$_{75}$ 1 hr.	F.E.V.$_{75}$ 2 hrs.	F.E.V.$_{75}$ 6 hrs.	F.E.V.$_{75}$ 24 hrs.	F.V.C. ½ hr.	F.V.C. 1 hr.	F.V.C. 2 hrs.	F.V.C. 6 hrs.	F.V.C. 24 hrs.	
R.T.	2	89%	≠	44.5	77.5	-16.5	52	≠	17	17	-17	No symptoms or wheeze. Signs of obstructive emphysema. Phenobarb. gr. ½ t.d.s.
	7	16.5	-	16.5	-29	-16.5	-	-	-	-	-	Ambulant. No symptoms or signs. No treatment.
J.B.	2	19.5	31	31	-	-11	43	44	45	21.5	7.2	Slight wheeze. Obstructive emphysema ++. No treatment. Admission to hospital.
	18	12	19	-8	-	-	-	-	-	-	-	No symptoms. No treatment.
P.P.	1	-	-	-	-	-	-	12	-	-	-	Wheeze ++. Accessory muscles active. Isoprenaline 7½ mg. 6 hrly.
	4	-	44	66.5	≠	≠	26	39	100	-	-	No symptoms. Ambulant. No antispasmodics.
C.N.	9	-	-14	-	-28	-	-10	-25	-32	-35	-25	Well. Ambulant. Eph. gr. ½ b.d. Phen. gr. ½ t.d.s.
	27	50	25	25	-	-37	28.5	31.0	20	-	-31	Ambulant. Dyspnoea only on exertion. Phen. gr. ½ t.d.s. Aminophylline .2 Gm. t.d.s.
J.T.	4	25	25	44	25	-12	17.5	15	20	10	-20	No subjective symptoms at rest. No treatment.
	12	50	50	70	40	40	20	25	30	25	20	Well. Ambulant. Slight wheeze. Productive cough. Poor air entry. Expiratory wheeze. No treatment.
	15	-	-	21	-	-	-	-	-	-	-	No symptoms. Ephedrine gr. ½ b.d.
	17	-	-	-	-	-	-	-	-	-	-	No symptoms. Ephedrine gr. ½ b.d.
A.W.	1	34.4	69	71	-	37	4.4	17.5	15	-	4.4	Slight wheeze. Obstructive emphysema. Ephedrine gr. ½ t.d.s.
J.E.	9	-	-	35	106 (4 hrs.)	41	-	-	-	17	-	Ambulant. No symptoms. Phen. gr. ½ b.d. Ephedrine gr. ½ b.d.
A.B.	5	10.5	15.7	26.3	15.7	-16	-	-14	-	-	-22	Ambulant. No symptoms. No antispasmodic treatment.

- = Change < 10% and not significant. ≠ = No measurement.

unreliable. The variation in response, with the phase and severity of the disease, is illustrated by the two patients who were seen on the first day of admission to the ward. P.P. (Fig. 33A) had been wheezing for two or three days prior to admission and was suffering from a severe cold. Presumably the relative lack of response to isoprenaline was due to the fact that the bronchial obstruction was being caused by swelling and other inflammatory changes in the mucous membrane. Only when these factors were removed could isoprenaline relieve the spasm and result in the increase in the $F.E.V_{.75}$ of 66% and in the F.V.C. of 100% shown on the 4th day. A.W., (Fig. 33A) when admitted to the ward had no cold and only a slight wheeze. The obstruction to airflow was probably mainly due to bronchospasm and this was relieved immediately by isoprenaline, resulting in a significant increase in the $F.E.V_{.75}$ and F.V.C. values. The magnitude of the responses shown by R.T. (Fig. 33) on the 2nd day and J.B. (Fig.33E) also on the 2nd day can be explained in the same way (Table XXXVIII). The relative lack of response is J.T. is striking. From the graph (Fig.33C) it can be seen that she responded only to steroid therapy.

The unusual response shown by C.N. is difficult to explain. She was also resistant to all forms of therapy except steroids during her stay in hospital. The values obtained for the $F.E.V_{.75}$ and F.V.C. were often lower after the inhalation of isoprenaline, indicating an actual deterioration in her ventilatory state (Fig.33B). On the 22nd day, however, while on oral aminophylline she was given a sublingual tablet of laevo-isoprenaline bitartrate and an increase in the $F.E.V_{.75}$ and F.V.C. values followed. The question arises as to whether the aminophylline may have played a part in making the bronchi more sensitive to the action of isoprenaline (Fig.33B).

The relative lack of response in J.E. (Fig.33D) during the first few hours, with a subsequent response, may be explained by the fact that he developed palpitations and nausea fifteen minutes after the tablet had been placed under his tongue.

These observations, and those on the daily response to isoprenaline inhalation, serve to emphasize the problems of attempting to evaluate the therapeutic value of broncho-dilator drugs given over a period of days to a group of patients. Each patient must serve as his own control. But, in spite of the variability found in their reactions, it must be pointed out that all the patients did show a response of over 10% in the F.E.V$_{.75}$ and F.V.C. levels to isoprenaline given sublingually.

D. SPIROMETRIC RESPONSE TO STEROID THERAPY

From Fig. 34A and Fig. 33C the value of the F.E.V$_{.75}$ and F.V.C. test when following the progress on steroid therapy of patients with poor ventilatory function can be seen.

C.N. was admitted to hospital in status asthmaticus and unconscious. She was treated in the usual way with antispasmodics but her condition was so alarming that she was soon given cortisone. The response was dramatic and after the O_2 tent was removed on the 3rd day spirometric measurements were started. The F.E.V$_{.75}$ and F.V.C. values showed a progressive improvement and the F.V.C. reached the expected normal level on the 10th day. The cortisone was then stopped and gradual deterioration in the values followed. Clinically she was still very well. On the 14th day she had a mild attack of wheezing and was then given phenobarbitone gr. ½ t.d.s. and Ephedrine gr. ½ b.d. On the 16th day she was judged on clinical grounds to be well enough for discharge to a convalescent home. She was re-admitted to the ward in status asthmaticus 3 weeks later.

J.T. was in the ward with persistent attacks of bronchospasm for 20 days before it was decided to try the effect of steroids on her condition. During these 20 days she had shown some clinical improvement, after 6 days in hospital. The F.E.V$_{.75}$ values during this initial period varied between 20% and 30% and the F.V.C. values between 30% and 58% of the expected normal. She then showed a slow improvement, reaching a peak on the 12th day, with the post-isoprenaline inhalation F.E.V$_{.75}$ at 59% and the F.V.C. at 75% of the expected normal values. Gradual deterioration followed thereafter, so that by the time steroid therapy with prednisolone (see Fig 33C for dosage) was commenced, the values for the F.E.V$_{.75}$ and F.V.C. were 20 - 28% and 37 - 40% of the expected normal. Fig. 34A and Fig.33C show the initial dramatic response to steroid therapy and the deterioration which followed as the dose of steroid was reduced. Ultimately the recording fell lower than the pre-prednisolone levels. During this period, ephedrine gr. ½ b.d. was again prescribed. A second course of prednisolone was started but because of the previous experience, it was decided to keep her on a dosage of 10 mg. per day. The response was less striking than before and the spirometric measurements again began to deteriorate. Treatment was reinforced with first oxtriphylline 100 mg. t.d.s. (choledyl - Allen Hanbury) for four days then theophylline sodium glycinate 150 mg. t.d.s. (englate - Nicholas). The $F.E.V_{.75}$ and F.V.C. values showed improvement and reached 83% and 111% of the expected normal values. As soon as the dosage of the prednisolone was dropped below 10 mg. per day these levels diminished. Nevertheless she was discharged home on prednisolone 2½ mg. daily and theophylline sodium glycinate, 150 mg. t.d.s. (englate tab. ½. t.d.s.) but her $F.E.V_{.75}$ and F.V.C. values dropped to 17.5% and 32.0% of the expected normal. It was apparent that an increase in the dose of prednisolone was unavoidable. After a week on 10 mg. a day and englade tab. ½ t.d.s., the $F.E.V_{.75}$ and F.V.C. values were again approaching the expected normal levels.

From these limited studies, the possibility of using the test to determine not only the response to treatment, but also the minimum effective dose of the steroid and other drugs used, can be seen. It is interesting to note that Thursby-Pelham and Kennedy (1958) showed that 15 mg. of prednisolone and 75 mg. of cortisone produced a similar satisfactory effect.

On this dosage a peak response was generally observed after two or three weeks. When the dosage was reduced the response usually waned.

When prednisolone was given to J.T. for the first time the response was measured at intervals over the first 8 hours and at the end of 24 hours (TABLE XXXIX). When the tablets were given it was suggested to her that they would act within a few minutes and that she would soon feel better. She, in fact, volunteered the information that she felt much better and the small spirometric improvement in the first hour may be accounted for by the combined psychological effect of having new tablets and suggestion. The F.V.C. level showed a steady improvement in the first 6 hours and improved further over the next 24 hours. The F.E.V$_{75}$ level only started to improve at the end of 6 hours, and then showed a continued improvement. These findings are in agreement with those of Creip (1956) and Taub et al. (1956) that, on prednisolone therapy, relief from asthma has not been evident clinically until 6 - 72 hours after the onset of therapy. The improvement found in the F.V.C. supports the findings of Pinkerton and van Metre (1958) who studied the effect of prednisolone on the V.C. during the treatment of an

TABLE XXXIX

J.T: THE EFFECT OF PREDNISOLONE ON THE $F.E.V_{.75}$ AND F.V.C. VALUES

TIME	$F.E.V_{.75}$	F.V.C.	F.E.V%
0	0.375	0.750	50
10 mins.	0.425	0.900	47
20 mins.	0.375	0.900	42
40 mins.	0.375	0.950	39.5
1 hour	0.425	0.750	57
1½ hours	0.400	0.850	47
3 hours	0.500	0.900	55.5
4 hours	0.500	0.950	53
6 hours	0.450	1.000	45
8 hours	0.600	1.100	54.4
24 hours	0.725	1.300	56

All Volumes in Litres

attack of asthma and also showed this improvement beginning soon after the onset of therapy.

According to Thursby-Pelham and Kennedy (1958) the response to adrenaline is at first inhibited and later enhanced by either cortisone or prednisolone therapy. From the limited experience of this one case (J.T.) it is impossible to reach any conclusions to support or disagree with these findings. But when the improvement in $F.E.V_{.75}$ is expressed as a percentage of the initial level there is no marked difference between the pre-steroid response to isoprenaline and the post-steroid response.

E. FOLLOW-UP OF HOSPITAL PATIENTS

Five of the cases who were studied in the ward were seen subsequently in the Out-patient Department. Four (R.J., J.B., J.E. and A.B.) were seen one month after discharge and one (J.T.) three weeks after discharge.

When discharged from the ward, the $F.E.V_{.75}$ and F.V.C. values of all the children (except J.T.) were within their expected normal ranges. All were clinically well and active in the ward. All were sent home on anti-spasmodic drugs daily and in addition J.T. was on prednisolone 2½ mg. daily.

All returned to the Out-patient Department giving a history of wheezing every night. A.B. and J.B. began wheezing on their first night at home and J.B. subsequently stayed away from school for 2 weeks. J.T., when seen after 3 weeks at home, looked tired and was unable to take part in the physiotherapy class. All had signs of obstructive emphysema, prolonged expiration and expiratory rhonchi.

In Table XL the values for the $F.E.V_{.75}$ and F.V.C. taken on admission to hospital, the highest values reached in hospital, the values on discharge, and the values on attending Out-patient Department one month after discharge, are given. It may be seen that the low $F.E.V_{.75}$ and F.V.C. values correlate well with the clinical history and findings of deterioration since discharge from hospital. It is interesting to note that none of the children showed evidence of "trapping" (p.151). All showed evidence of reversible bronchospasm despite the antispasmodic drugs and phenobarbitone therapy.

TABLE XL

FOLLOW-UP OF HOSPITAL PATIENTS.

		One Month After Discharge								On admission to hospital		Highest value in hospital		On discharge from hospital	
		$F.E.V._{.75}$		F.V.C.		F.E.V.%		$F.V.C._T$		$FEV._{75}$	FVC	FEV_{75}	FVC	$FEV._{75}$	FVC
		I	III	I	III	I	III	I	III						
A.B.	a	0.400	0.425	0.925	1.000	43	42.4	5.3	5.0	1.100	1.650	1.300	2.000	1.150	1.800
	b	0.500	0.450	1.175	1.100	43	41	5.8	6.0	1.100	1.850	1.300	1.900	1.150	1.800
J.B.	a	0.500	0.500	1.100	1.100	45	45	4.4	4.0	0.250	0.650	1.600	1.950	1.250	1.850
	b	0.600	0.700	1.100	1.300	55	54	3.9	4.0	0.400	0.850	1.750	2.000	1.350	1.900
J.E.	a	0.800	0.800	1.500	1.400	53	57	3.9	3.9	0.400	0.950	1.850	2.550	1.250	2.200
	b	0.900	0.900	1.750	1.700	51	53	2.2	2.4	0.450	1.150	1.850	2.550	1.500	2.350
R.T.	a	0.275	0.275	1.175	0.825	23	33	5.6	5.0	0.250	0.800	1.225	2.000	1.100	1.850
	b	0.450	0.400	1.200	1.175	37	34	5.5	5.7	0.450	1.250	1.450	1.850	1.450	1.950
J.T.	a	0.250	0.250	0.650	0.650	38	38.5	5.0	5.2	0.450	0.975	1.200	1.950	0.500	1.150
	b	0.375	0.350	0.875	0.875	43	40	5.0	5.4	0.450	0.875	1.400	2.000	0.700	1.600

a = Pre-Isoprenaline b = Post-Isoprenaline inhalation.

I = 1st Spirogram and III = 3rd Spirogram taken on the same occasion.

All volumes in litres.

CHAPTER 14

THE EFFECT OF EXERCISE ON THE $F.E.V_{.75}$ AND F.V.C. VALUES

The value of breathing exercises in asthmatics is difficult to assess. Weiser (1950) noted that such exercises were favoured amongst the Chinese in 2500 B.C. and later in classical and mediaeval times. Donald (1953), Becklake et al. (1954), Sinclair (1955), Campbell and Friend (1955), McNeill and McKenzie (1955) all doubt the value of breathing exercises and the work of Wade (1954) throws considerable doubt on the ability of the individual to control diaphragmatic movement at all in the act of breathing. This diaphragmatic control is stressed by physiotherapists and is emphasized in the exercises recommended by the Asthma Research Council (1949)

On the other hand, Miller (1954) from his studies, concluded that training in diaphragmatic breathing resulted in an increased excursion with a striking increase in the tidal volume and a decrease in respiratory rate. This resulted in more effective alveolar ventilation being accomplished without significant increase in total ventilation.

All these studies were carried out in adult patients suffering from emphysema, asthma and bronchitis.

Dekker and Groen (1957) presented evidence that asthmatic wheezing is due to considerable narrowing of the cervical and thoracic trachea and of the main bronchi. This is due to the peculiar type of breathing seen in asthmatics causing a high intrathoracic pressure which is an important mechanism by which asthmatic attacks are brought about. They suggest that breathing exercises can alter this type of breathing and so prevent asthmatic attacks.

It was decided, therefore, to attend some of the physiotherapy classes held for asthmatic boys and plan an investigation for the assessment of the value of breathing exercises.

Many mothers refuse to let their asthmatic children take part in games and often restrain them from being too active, fearing that it might bring on an attack of wheezing. However, at the classes it soon became evident that most of the boys, regardless of what their mothers had told us about the severity of their wheezing, enjoyed themselves immensely, rushing about and "playing the fool" and often not carrying out the breathing exercises properly. It was interesting to note that even the more strenuous exercises did not seem to affect them adversely.

From these preliminary observations the difficulty of assessing the value of breathing exercises in children seemed to be formidable. It was therefore decided instead to measure objectively the effect of strenuous exercise on ventilatory function, using the F.E.V $_{.75}$ and F.V.C. test. The physiotherapist planned a series of exercises and games, lasting approximately 25 minutes, which kept the boys active and on the run for most of that time. When a new class was formed, the investigation was started.

The children were seen before each class. A history of the severity and number of attacks of wheezing over the preceding week was obtained and the repiratory system examined. The F.E.V $_{.75}$ and F.V.C. were then measured from spirograms obtained using the same technique as already described for asthmatics. The series of exercises was then carried out and the boys were observed and any signs of undue distress or cough were noted. At the end of 25 minutes the childrenw ere taken in turn and their spirograms again obtained. While one child was performing the test the other children went on with the particular game so that there was no interval or rest period between exercise and being tested.

The class consisted of 7 boys (B.B., J.W., J.G., J.E., I.B., and R.T.). Of these 4 attended 5 weekly classes, and 3 each attended on 3 occasions. All the boys belonged to Group II except J.E. who was a Group I case. All had clinical evidence of bronchospasm before the exercises on every occasion. Only J.E. had to stop the exercises because of excessive coughing and wheezing on one occasion (2nd week). A few boys developed an audible wheeze during some of the more strenuous games but this did not affect their performance in any way.

The values for $F.E.V_{.75}$ and F.V.C. before and after the exercises are given in Table XLI. The improvements in the $F.E.V_{.75}$ and F.V.C. values were estimated and expressed as percentages of the pre-exercise values and the mean for the period under observation worked out. These average percentage increases for the group were 19.2% for the $F.E.V_{.75}$ and 12.2% for the F.V.C. The values after the exercises were, in nearly every case, much higher than before but where the value was lower than the pre-exercise level it was never a large difference (50 - 75 ml.).

Except for the 2nd week, all the boys had

TABLE XLI

THE EFFECT OF EXERCISE ON THE $F.E.V._{75}$ AND F.V.C. VALUES.

	Grading	1 $F.E.V._{75}$	1 F.V.C.	2 $F.E.V._{75}$	2 F.V.C.	3 $F.E.V._{75}$	3 F.V.C.	4 $F.E.V._{75}$	4 F.V.C.	5 $F.E.V._{75}$	5 F.V.C.	Average increase expressed as a % in F.V.C. ($F.E.V._{75}$) after exercises: $F.E.V._{75}$	F.V.C.
B.B.	II A	0.825	1.800	1.200	1.850	1.000	1.650	1.100	1.825	1.175	2.025		
	B	1.150	2.000	1.450	2.100	1.175	1.700	1.400	2.000	1.250	2.025	21%	7.4%
J.W.	II A	0.900	1.100	1.250	1.900	1.250	1.900	1.350	2.075	0.750	1.075		
	B	0.975	1.200	1.350	2.100	1.500	2.200	1.500	2.000	0.900	1.100	13.4%	14.9%
R.T.	II A	0.600	1.000	0.800	1.200	0.475	0.950	0.600	0.875	0.725	1.150		
	B	0.850	1.400	1.150	1.775	0.550	0.950	0.550	0.975	0.850	1.150	21%	20%
J.G.	II A	0.750	1.450	0.600	1.300	0.850	1.500	0.825	1.275	0.800	1.500		
	B	1.050	1.850	0.700	1.350	0.975	1.600	0.900	1.400	0.950	1.600	17%	10.7%
J.E.K.	II A	1.400	2.050	1.050	1.900	1.475	2.175						
	B	1.600	2.150	1.575	1.875	1.675	2.350					20%	4.4%
J.E.	I A	0.975	1.900	0.650	1.250	1.475	2.175						
	B	1.550	2.350	0.600	1.100	1.675	2.350					21%	6.5%
I.B.	II A	1.100	1.600	0.825	1.375	0.350	0.675						
	B	1.200	1.700	1.050	1.500	0.500	1.000					21.3%	21.8%

All volumes in litres

A = Before } Exercises.
B = After }

isoprenaline inhalations as part of the pre-exercise assessment (as for other asthmatics) to determine whether reversible bronchospasm was present. It may be argued that some of the improvement in the F.E.V$_{.75}$ and F.V.C. values was due to the effect of the isoprenaline, but the improvement in the values in the 2nd week (see column 2 for values) was very much the same as for the other weeks.

Although the number of cases investigated is too small for a definite conclusion, these findings support the view that asthmatics in general should take part in physical training, athletics, games and sports at school. Their mothers should be encouraged not to restrict any of their activities or be too over-protective. Through activity they may be able to liberate themselves from tensions which may cause bronchospasm. In the same way, perhaps, when regarded as an indirect form of psychotherapy, breathing exercises may be of value.

CHAPTER 15.

A. CONGENITAL HEART DISEASE

B. MISCELLANEOUS CONDITIONS

A. CONGENITAL HEART DISEASE

The assessment of effort intolerance in patients with heart disease may be difficult, especially in those patients where the history and clinical examination suggest the presence of associated disease of the lungs such as chronic bronchitis and emphysema. It may be difficult to decide from the clinical findings alone, whether the disability is due mainly to the heart-disease or mainly to the lung-disease. Congestion of the pulmonary vascular bed in left sided heart failure causes a decrease in the V.C. (Peabody et al. 1917; Drinker et al., 1922; Christie and Meakins, 1934, and Mack et al. 1947). This reduction in the V.C. is reversible, either partially or wholly, after treatment of the congestive heart failure.

In adults the F.E.V. and F.V.C. test has been used in the assessment of heart disease (Stock and Kennedy, 1953; Frank et al., 1953; Michelson et al. 1955). Capel and Smart (1958) used the test to decide whether effort intolerance in such cases was due mainly to the heart-disease or mainly to the lung-disease.

The characteristic manner in which the speed of expiration is altered in heart disease, such as chronic congestive cardiac failure, was first noted by Cournand et al. (1939). The expiratory spirograms in patients with congestive heart failure show a rapid initial expiration with a marked and abrupt slowing which occurs as the terminal 100 - 200 ml. are delivered (Michelson et al., 1955; Capel and Smart, 1958). The F.E.V.% is therefore high. This configuration can be explained by assuming the presence of an unobstructed airway (Parker and Weiss, 1954) and a relatively non-elastic and rigid lung (Mead et al. 1953). The changes in the spirogram and the lowering of the F.E.V.% in pulmonary disease associated with obstruction of the airway, have already been discussed.

Eighteen children with congenital heart disease were examined and asked to perform the test. The $F.E.V_{.75}$, F.V.C. and F.E.V.% were recorded for the pre- and post-isoprenaline values.

Effort intolerance, judged by the presence or absence of dyspnoea on exertion, was evaluated and

TABLE XLIIA

CONGENITAL HEART DISEASE
(FIG. 39)

A.S.D. = Auricular Septal Defect
V.S.D. = Ventricular Septal Defect
F = Tetralogy of Fallot
P.S. = Pulmonary Stenosis
P.D.A. = Patent Ductus Arteriosus
C = Coarotation of the Aorta
E = Eisenmenger Syndrome
T.A. = Truncus Arteriosus

	Sex	Age (yrs)	Standing Ht. (ins)	Sitting Ht. (ins)	Wt. (lbs)	Diagnosis	Grading	F.E.V.$_{.75}$ (Litres)	F.V.C. (Litres)	F.E.V.%
1	F	13	59	30	70	A.S.D.	2	1.175	1.950	60
2	F	6	44	24	46	A.S.D.	3	0.775	1.125	69
3	F	7	45.5	26	38	A.S.D.	3	0.600	0.875	69
4	F	9	54	27	49	A.S.D. + P.S.	2	1.250	1.350	92
5	F	8	46	25	46	V.S.D.	2	0.800	0.825	96
6	F	8	49	27	50	V.S.D.	3	1.150	1.350	85
7	F	7.5	52	29	70	V.S.D.	3	1.850	2.050	90
8	M	11	53	28	66	V.S.D. + P.S.	2	1.600	1.650	97

<u>TABLE XLIA</u>

CONGENITAL HEART DISEASE
(FIG.39)

	Sex	Age (yrs)	Standing Ht.(ins)	Sitting Ht.(ins)	Wt.(lbs)	Diagnosis	Grading	F.E.V .75 (litres)	F.V.C. (Litres)	F.E.V.%
9	F	12	53.5	29.5	58	P.S.	2	1.575	2.000	80
10	F	10	54.5	28.5	52	P.S.	3	1.075	1.400	76.7
11	F	10	49	26	46	F	1	1.050	1.375	76
12	M	10	51.5	27.5	49	F	1	1.350	1.750	77
13	M	15	68	36	113	P.D.A.	3	3.150	4.050	76
14	M	11	53	28	70	C	3	1.650	1.850	90
15	M	10.5	53	29	68	C	2	1.650	2.050	80
16	M	11.75	59	31	83	C	2	2.100	2.550	82
17	F	11.5	55	29	86	E	2	1.275	1.550	82
18	F	11	52	28	56	A.S.D. + T.A.	1	0.900	1.525	59

classified as follows:

Grade 1: Dyspnoea on minimal exertion

Grade 2: Dyspnoea on walking or running on a level surface; inability to take part in any games at school.

Grade 3: No dyspnoea; able to take part in all games at school; no clinical evidence of any impairment to ventilatory function.

The diagnosis and gradings and the values for the $F.E.V_{.75}$, F.V.C. and F.E.V% are given in Table XLIA and Fig. 39. In Fig. 39, the values for the $F.E.V_{.75}$ and F.V.C. are compared with the normal levels expected for the standing heights. The values obtained for all the boys were well within the expected normal ranges.

The $F.E.V_{.75}$ values for 3 of the girls (cases 1, 10 and 18) were on the lower limits of normality. When their expected normal $F.E.V_{.75}$ and F.V.C. were calculated from the multiple correlation equation for girls and the lower limits of normality determined by subtracting $2\sigma_z$, the following results were obtained:

TABLE XLII

Case	Observed Values			Calculated Expected Normal Values	
	$F.E.V_{.75}$	F.V.C.	F.E.V.%	$F.E.V_{.75}$	F.V.C.
1	1.175	1.950	60	1.397	1.716
10	1.075	1.400	76.7	1.037	1.195
18	0.900	1.525	59	0.986	1.195

Volumes in Litres

Both the F.E.V $_{.75}$ and F.V.C. values in Case 10 fall within the normal range. The normal F.E.V.% may mean that these values are the absolute normal volumes, or that the F.E.V $_{.75}$ and F.V.C. have been reduced proportionately. In view of the absence of symptoms in this case, the former can be fegarded as correct. In Cases 1 and 18 the relatively low F.E.V.% values of 60% and 59% in the presence of below-normal F.E.V $_{.75}$ values and normal F.V.C. values indicate that some of the dyspnoea in these children was due to impairment of ventilatory function. There was no response to isoprenaline inhalation in either of these cases, which suggests the presence of irreversible pathology. At the time these two were investigated clinical and radiological examination of the respiratory system revealed no abnormal respiratory pathology. Both children had suffered repeated respiratory tract infections in the past. Therefore, the spirometric findings in these cases were the sole indication that some of the dyspnoea was due to lung damage resulting from previous respiratory disease.

The F.E.V $_{.75}$, F.V.C. and F.E.V.% values in all the other cases were well within the expected normal range. Their effort intolerance can be accounted for by the congenital heart disease. The small number of cases investigated and the lack of data on the assessment of the cardiovascular function, based on cardiac catheterisation, prevents one from drawing any definite conclusions from this study. The test, however, merits further investigation to determine its use and limitations in assessing the contribution of disease of the lung to effort intolerance when heart disease is also present in a child.

B. MISCELLANEOUS CONDITIONS

The $F.E.V_{.75}$, F.V.C. and F.E.V.% values were measured in a group of children, 13 girls and 6 boys, suffering from a variety of conditions which may affect respiratory function in one way or another. The test was performed using the procedure already described. All the children were then given isoprenaline inhalations and the test repeated. The effect of their various conditions on ventilatory function, as measured by the $F.E.V_{.75}$, F.V.C. and F.E.V.% values, was assessed.

Funnel Chest: (Fig. 40 and Table XLIII). Six children with a funnel chest deformity were tested. All these children were well at the time of examination and none of them complained of dyspnoea on exertion or of any symptoms referable to the respiratory system, except that one boy had a history of attacks of wheezing and bronchitis. These children attended the Out-patient

TABLE XLIII

(1)

FUNNEL CHEST DEFORMITY

	Sex	Age (yrs.)	Standing Ht. (ins.)	Sitting Ht. (ins.)	Wt. (lbs.)	F.E.V .75 (litres)	F.V.C. (litres)	F.E.V %	TYPE
1	F	11½	60	32	77	1.800	2.225	81	Severe
2	M	12½	56½	29	58	2.525	2.925	86	Moderate
3	M	7¾	52	27	55	1.000	1.750	57	Moderate
4	M	7½	47	26	44	1.000	1.300	77	Minor
5	M	8½	52½	26	53	1.400	1.700	82	Minor
6	F	6½	42	22	47	0.600	0.825	73	Minor

OBESITY

1	F	12	57	29½	123	1.500	2.450	61	
2	F	12	60	31½	144	2.100	2.700	78	
3	M	13	61½	32	147	2.325	3.000	78	
4	M	11	56	29	103	1.925	2.100	92	

GROSS CHEST DEFORMITY (MORQUIO'S DISEASE)

	F	13½	53½	25	69½	0.700	1.400	50	

TABLE XLIII

(ii)

CHRONIC RESPIRATORY TRACT INFECTION

	Sex	Age (yrs)	Standing Ht. (ins.)	Sitting Ht. (ins.)	Wt. (lbs.)	F.E.V .75 (litres)	F.V.C. (litres)	F.E.V %	TYPE
1	F	12	51½	29	57	1.350	1.875	72	
2	F	10	51½	29	55	1.450	1.750	83	
3	F	8½	46	26	49	1.050	1.100	96	
4	F	11	52½	28	57	1.025	1.250	82	Cong. Abn. Rll.Bronchus
5	F	9	49½	25½	55	1.175	1.650	71	
6	F	12	56	29	79	1.400	2.000	70	
7	F	13	55	29	69	1.400	1.950	72	
8	F	11½	56	29½	69	1.150	1.950	59	Bronchiectasis and wheezing

Department at yearly or six-monthly intervals for observation.

The deformity was considered to be severe in one of the girls and she showed the typical radiological changes (Evans, 1946; Master et al., 1949; Albrechtsen, 1954 and Myhre, 1955). The heart was displaced to the left and the left cardiac border was straightened with a prominent pulmonary conus, assuming the appearance normally seen in the right oblique view. In the lateral views the heart appeared flattened (cor planum). Her only complaint was the cosmetic disfigurement caused by her deformity. At the age of 11 she was keen on athletics, especially swimming, and the deformity was a cause of embarrassment to her.

Her spirograms on both occasions on which they were obtained showed $F.E.V._{.75}$, F.V.C. and F.E.V.% values within the expected normal range for her standing height.

TABLE XLIV

	Standing Height	$F.E.V_{.75}$ In Litres	F.V.C.	F.E.V.%
1.	60"	1.800	2.225	81
2.	60"	1.875	2.200	85
Expected normal for	60"	2.150	2.601	
$S.D. = 2\sigma_z$		0.616	0.690	

In two boys the deformity was considered to be moderately severe (Table XLIII). One of these was the boy who complained of occasional attacks of wheezing and bronchitis. The values for his $F.E.V_{.75}$ and F.V.C. were found to be within the lower limits of normality but his F.E.V.% values were definitely subnormal. After isoprenaline inhalation the $F.E.V_{.75}$ value showed no increase. Unfortunately this boy attended only on this one occasion and further serial readings, which would have elucidated the nature of his ventilatory defect were unobtainable.

The remaining two boys and one girl showed only minor deformities and the values for their $F.E.V_{.75}$ F.V.C. and F.E.V.% were all within their expected normal ranges.

These findings, for the F.V.C. values, are in agreement with those of Master and Stone, (1949) Brodkin et al. (1950), Ravitch (1951), Myhre (1955) and Fabricius et al. (1957) who found normal, or only slightly reduced values for the V.C. in most cases of funnel chest deformity. Myhre (1955) and Fabricius et al. (1957) noted that the M.B.C. was usually lower than normal in these cases. A review of the literature showed no reports on the measurement of the $F.E.V_{.75}$

or F.E.V_1 values in children with funnel chest deformities.

Obesity: The effects of obesity on ventilatory function, as measured by the F.E.$V_{.75}$ and F.V.C. test, were looked for in two boys and two girls. The weights of these children were more than 20% above the average normal for their age and height. The F.E.$V_{.75}$, F.V.C. and F.E.V.% values obtained were all within the expected normal range for their heights and no impairment of ventilatory function could be demonstrated (Fig. 40 and Table XLIII).

Gross Deformity of the Chest: The effects of severe chest deformity on ventilatory function were studied spirometrically in one girl, aged 13½ years, suffering from Morquios disease with gross deformity of chest and spine. She had no symptoms or signs referable to the respiratory or cardiovascular systems. The F.E.$V_{.75}$ F.V.C. and F.E.V.% values are given in Fig. 40 and Table XLIII). Both the F.E.$V_{.75}$ and F.V.C. values were low and outside the $2\sigma_z$ range. The F.E.V.% was below average, being only 50%. These values showed no significant changes after isoprenaline inhalation.

These findings suggest a disproportionate lowering of the F.E.V $_{.75}$ and F.V.C. values and the low F.E.V $_{.75}$ values suggest some impairment of ventilatory function. Chapman et al. (1939) investigated cases of pulmono-cardiac failure due to chest deformity and found that the V.C. in these cases became gradually reduced to half or less.

Chronic Upper Respiratory Tract Infection: The test was carried out on 8 girls all suffering from chronic respiratory infection. All gave histories of repeated attacks of bronchitis and sinusitis. Radiological evidence of collapse of one or more lung segments during past infections was obtained from the records of four of the cases. The values obtained for the F.E.V $_{.75}$, F.V.C. and F.E.V.% are recorded in Fig. 40 and Table XLIII).

Case 8 is of interest. Her history was one of repeated attacks of bronchitis, chronic sinusitis and wheeziness. Radiological examination showed the presence of bronchiectasis. The F.E.V $_{.75}$ value was rather low while the F.V.C. was well within the normal range. The F.E.V.% of 59% suggests the presence of bronchospasm or emphysema. The spirogram showed no improvement after isoprenaline inhalation, a finding which although not conclusive, suggests emphysema. Further serial readings taken before and after isoprenaline inhalation would have helped to differentiate between reversible and irreversible pathology.

Case 1 was also of interest. The history was one of recurrent respiratory tract infections. Over the few months prior to being examined she had developed attacks of tachypnoea unassociated with any wheezing, coughing, or other symptoms. Clinical examination revealed no abnormality. X-Ray of the chest showed no gross pathology, but the Radiologist suggested that there might be some radiological signs of emphysema. Spirometric examination showed normal $F.E.V_{.75}$, F.V.C. and F.E.V.% values and a diagnosis of hysterical hyperventilation was made with considerable confidence.

Case 4 had attended the Out-patient Department over a period of four years for recurrent attacks of bronchitis associated with wheezing. She also complained of dyspnoea on exertion. Bronchography showed a normal left bronchial system, but on the right side the lower lobe bronchus was abnormally narrow and poorly developed. The peripheral bronchi supplying the right basal segments were abnormal. These findings suggested a congenital failure of the right lower lobe to develop.

The spirometric findings of lowered $F.E.V_{.75}$

and F.V.C. values with a normal F.E.V.% presumably reflect this developmental failure with its subsequent impairment of ventilatory function.

CHAPTER 16

S U M M A R Y

A. ASTHMA :

1. Although the primary emphasis was on the spirometric investigation, its possible application to the problems of asthma was one of the chief reasons for the present investigation. A total of 68 asthmatic children (16 girls and 52 boys) aged 7 to 15 years were investigated spirometrically. Ten of these children were admitted to the ward and studied in detail. A group of 7 boys was examined at weekly intervals for a period of 3 to 5 weeks before and after physiotherapy classes. The remaining 51 children attended as Outpatients and the majority were seen on one occasion only. The children were all co-operative and showed a keen interest in the $F.E.V_{.75}$ and F.V.C. test. Even during severe paroxysmal attacks of wheezing they were able to perform the test satisfactorily.

2. The aetiological factors which play a part in causing asthmatic attacks were investigated. In the majority (57%) of cases a combination of allergic,

infective, and psychological factors was found to be responsible for precipitating paroxysms of wheezing. In the remainder the attacks were brought on by a single factor. In 20.6% of cases the precipitating factor was a "cold" and in 20.6% of cases it was an allergic factor. In only 1 case (1.5%) were psychological factors thought to be solely responsible for attacks. The particular precipitating cause did not appear to have any bearing on the spirometric tests.

3. The patients were classified into three clinical groups depending on the frequency of their asthmatic attacks and the clinical findings. The following aspects of the spirometric findings in the three clinical groups were studied:

(i) The shape of the F.E.S. and F.I.S. in the groups was compared to the normal. It was seen that in asthmatics, in proportion to the severity of the disease in the severe cases, the initial drop in the curve becomes progressively less steep, the shape being that of a shallow curve rather than an almost straight line. The time over which the F.V.C. is expelled is prolonged. A similar change is seen in the F.I.S. The changes in shape of the F.E.S. are, in general, well correlated with the clinical grouping. There are two points of importance here. First, the results are in keeping with time-honoured belief and indicate that these tests and the calculations made from them are in keeping with general experience. They are in no way obstruse. And secondly, the tracings obtained can be filed as a visual record of a disease which has hitherto not been assessable objectively with any material accuracy either during a single attack or over a period of months or years.

(ii) The change in the shape of the F.E.S. of an asthmatic child after exhibition of a broncho-dilator drug such as isoprenaline, indicates the presence of reversible bronchospasm. This change, to be regarded as significant, must result in an increase of at least 10% in the $F.E.V_{.75}$ and F.V.C. values and the absolute increase in these values must be 50 - 75 ml. or more in volume. This response to a broncho-dilator drug also gives an indication, although not absolute, of the likelihood of successful broncho-dilator therapy and of the benefit or futility of treatment of any particular individual with a particular drug. The advantage of such an objective assessment in clinical therapeutic trials of drugs with alleged broncho-dilator efficiency is obvious. This form of spirometry is, of course, not limited to the evaluation of drugs but is equally applicable to any of the multitudinous "cures" for asthma. If they have merit, the record will show it. This aspect of the test applies with special emphasis to the therapeutic regimes involving prolonged use of the adrenal steroids where the action of the drug is by no means limited to the bronchial tree but involves the widest possible systemic changes, the results of which are still not fully known. The least benefit that could follow would be a reasonably accurate objective assessment of the minimal effective dose which at present is based on intelligent guesswork or subjective report.

(iii) The values for the $F.E.V_{.75}$ and F.V.C. in both girls and boys for the cases in Groups I and II fell within the range one would expect from their more serious clinical condition, i.e. well below normal. The $F.E.V_{.75}$ values in many of the Group III cases were also below normal, indicating that although they appeared clinically to have relatively mild asthma, there was, in fact, quite considerable impairment of ventilatory function. The F.V.C. values for Goup III cases were approximately normal. These cases who appear to have relatively mild asthma, but have, in fact, considerable impairment of ventilatory function often give rise to diagnostic difficulty with consequent problems as to appropriate therapy. If the more general use of this simple test will make the accurate selection of the patient with an unrecognized asthmatic background easier, as it could, there would be at least some diminution in the very large numbers of apparently inexplicable "respiratory problem children" who are labelled as "subject to bronchitis" for no obvious reason.

(iv) The F.E.V.% values for all three groups of asthmatic girls and for the Group I asthmatic boys correlated well with the clinical findings. They were low and in the region of 40% in Group I cases for both boys and girls, higher in Group II, and practically normal for Group III girls. But for boys in Groups II and III the values varied from below 40% to above 80%. These findings, and those under (ii) indicate that, ingeneral, the $F.E.V_{.75}$ value in asthma is lowered to a greater extent than the F.V.C. value.

(v) The $F.V.C_T$ is prolonged in asthma. In the groups with more severe asthma (Groups I and II) there was a close correlation between clinical assessment and objective measurement. In the less severe cases (Group III), however, prolonged expiration only became evident on studying their spirograms. The comments made in (iii) above apply equally well here.

4. The $F.E.V_{.75}$ and to a lesser extent the F.V.C. are measures of ventilatory function at any given time, the former being the most useful single spirometric index of ventilatory assessment. A daily measurement of the $F.E.V_{.75}$ and F.V.C. values in the 10 asthmatic patients in hospital showed the value of the test in the objective assessment of improvement or deterioration in ventilatory function. In those patients who showed an improvement after admission and/or treatment and who appeared to be quite well the test revealed that their $F.E.V_{.75}$ and F.V.C. values were still low and varied greatly from day to day, reflecting the severity of their residual ventilatory impairment. This impairment could be

assessed only by spirometric tests and not clinically or by observing the child's activities in the ward. The lack of correlation between audible wheezing and the F.E.V $_{.75}$ and F.V.C. values was striking. The "threshold for wheezing" was extremely variable even from day to day in the same individual.

The impairment of ventilatory function, during an asthmatic attack is due to bronchospasm, swelling of the mucous membrane and increased secretion. The F.E.V. $_{.75}$ value is lowered in proportion to the severity of these factors and as the latter subside the spirogram will show improved ventilatory function. Chronic asthma may sooner or later produce irreversible pulmonary changes and treatment must aim at preventing this. Should the F.E.V $_{.75}$ value reach a normal level for that individual the presence of permanent lung damage such as emphysema can be ruled out. As the F.E.V $_{.75}$ in asthma is lowered to a greater extent than the F.V.C. there is also a lowering of the F.E.V.%. A low F.E.V.% therefore suggests that either the three reversible obstructing factors are still present or that the asthma is complicated by permanent parenchymal damage and the irreversible changes of emphysema. Serial readings of the F.E.V $_{.75}$ F.V.C. and F.E.V.% , or a response to isoprenaline inhalation with a return to normal values, can be used to differentiate between the two. The F.E.V%, however, as a single index of airway obstruction without knowledge of the absolute values for the $F.E.V_{.75}$ and F.V.C. is of little value. Where there is a proportionate lowering of the $F.E.V_{.75}$ and F.V.C. during an asthmatic attack, the F.E.V% may be within the normal range.

Nevertheless, the proper interpretation of the test can allow of an authoritative opinion as to the presence or absence of irreversible changes. This, in turn, allows of a rational prescription for the child as to his mode of life, choice of a future occupation and also a forecast to the parents of their probable commitments in the years ahead.

5. The $F.V.C_{T}$, although prolonged in asthmatics, is a less reliable index of ventilatory function than the $F.E.V_{.75}$, F.V.C. or F.E.V%. These latter values are always of more significance in the assessment of ventilatory function in asthmatics.

6. Asthmatics who have been free of symptoms for prolonged periods may still have impaired ventilatory function and occult bronchospasm as shown by an improvement of 10% or more in their $F.E.V_{.75}$ and F.V.C. values

following the inhalation of isoprenaline. Further longitudinal studies must be carried out to ascertain whether any permanent damage to the lung may result from this persisting sub-clinical bronchospasm. The acquisition of such knowledge is obviously important to the adolescent particularly if a faulty choice of a career or even of a domicile is to be avoided.

7. Four of the hospital in-patients who had $F.E.V_{.75}$ and F.V.C. values within the expected normal ranges when discharged from the ward were sent home on daily antispasmodic drugs and seen again one month later. One child who had $F.E.V_{.75}$ and F.V.C. levels still below normal when discharged from hospital was sent home on daily prednisolone and seen again three weeks later. All five children returned to the Out-patient Department giving a history of wheezing attacks at night and the low $F.E.V_{.75}$, F.V.C. and F.E.V% values which were recorded correlated well with the clinical history and findings of deterioration since discharge from hospital. The test can thus be used as a means of making a rapid check on the history, the efficacy of the treatment, and on the need for something more to be done, e.g. in investigation of possible allergic factors in the home, or in the psychological background.

It can serve, not necessarily as an index of defeat, but as a spur to further effort and appraisal.

8. Spirometric measurements carried out before and after a series of strenuous exercises by 7 asthmatic boys showed average increases of 19.2% for the $F.E.V_{.75}$ and 12.2% for the F.V.C. after the exercises. These findings support the view that asthmatic children, in general, should take part in physical training, athletics, games and sport at school and that their parents should be discouraged from restricting their activities and being over-protective. The advice is easy to give, but more than usually difficult to accept by the parents. It is much more likely to be taken if a recorded tracing can be demonstrated to them, especially if they have actually seen the test applied, as it can easily be, in their presence. The paradoxical nature of the advice to the "breathless" child to indulge in exercise becomes more rational when justified by the patient himself on an impersonal machine, with the doctor merely another interested onlooker.

B. NON-ASTHMATIC CONDITIONS

(i) CONGENITAL HEART DISEASE

The $F.E.V_{.75}$ and F.V.C. were recorded before and after isoprenaline inhalation in 18 children with congenital heart disease. Effort intolerance, judged by the presence or absence of dyspnoea on exertion was evaluated clinically and an attempt was made to determine, by using the $F.E.V_{.75}$ and F.V.C. test, the contribution of associated lung disease to the intolerance. In two cases the spirometric findings were the sole indication that some of the dyspnoea was due to lung damage resulting from previous respiratory disease. Effort intolerance in the other cases could be solely accounted for by the congenital heart disease. The test merits further investigation in children to determine its use and limitations in assessing the contribution of disease of the lung to effort intolerance when heart disease is also present

(ii) In 6 children with funnel chest deformity the values for the $F.E.V_{75}$, F.V.C. and F.E.V.% were found to fall within the expected normal ranges with the exception of those relating to one boy. This boy, who may have been a mild asthmatic, complained of occasional attacks of wheezing and bronchitis which probably accounted for his lowered spirometric values. This was a surprising result in some of the more severe cases of the condition. It would indicate that the child need not be handicapped or limited in his physical activities and although the cosmetic effect is alarming, it is apparently of minor functional importance in this age group.

(iii) No impairment of ventilatory function as measured by the $F.E.V_{.75}$ and F.V.C. test could be demonstrated in 4 obese children. These subjects are notoriously disinclined to vigorous movement, but from the angle of pulmonary ventilatory capacity they are normal, and objective demonstration of the fact can supply their medical advisers with adequate justification for refusing to count dyspnoea of pulmonary origin in their list of tribulations.

(iv) One girl with Morquio's disease and gross deformity of the chest and spine showed evidence of severe ventilatory impairment. Subjective, objective and mechanical indications were in complete accord.

(v) Of 8 girls with histories of repeated attacks of sinusitis and bronchitis, the majority showed no spirometric evidence of impaired ventilatory function. The test was of particular value in the case of one of these girls who had developed attacks of tachypnoea unassociated with any wheezing, coughing, or other symptoms or signs. Spirometric examination showed normal $F.E.V_{.75}$, F.V.C. and F.E.V% values, confirming the clinical diagnosis of hysterical hyperventilation.

Even in this group of non-asthmatic children (ii - v) the possible applications of the test are evident although perhaps in a smaller way than in the asthmatic group.

In the assessment of these asthmatic and non-asthmatic cases, the main disadvantage of the test becomes apparent, namely that the bounds ($\pm 2\sigma_z$) about the "most probable" spirometric value are large when calculated from the prediction formula. This means that although a value for the F.E.V $_{.75}$ or F.V.C. may be within these bounds it may be abnormal for the given individual. This difficulty may be partly overcome by considering together the F.E.V $_{.75}$, F.V.C. and F.E.V.% values in any case. If, for instance, the F.V.C. value is high and in the upper regions of the bounds about the "most probable" value, while the F.E.V $_{.75}$ is in the lower regions and the F.E.V.% is below normal this would suggest that the F.E.V $_{.75}$ for that child is abnormal. Any increase in the F.E.V $_{.75}$ after isoprenaline inhalation resulting in an increase in the F.E.V.% to normal levels may give an indication of the "normal" F.E.V. $_{.75}$ value for that individual. Often, only by taking serial readings can the normal $F.E.V_{.75}$ and F.V.C. values be determined in a patient.

The $F.E.V_{.75}$ and F.V.C. test can therefore be of considerable assistance to the clinician, both in the evaluation of disability and in the immediate and longitudinal assessment of pulmonary disease. The test, however, is only a measurement of overall mechanical lung function and persistently abnormal values may be an indication for the use of more complicated tests which measure the different components of ventilatory function.

It is not suggested that spirometry should be added to the routine tests applied to all children on admission to hospital, or to as many as possible in the Out-patient Department. It is, however, clear that in view of its simplicity, its acceptability by the children, and its usefulness in supplying recorded information in any condition in which pulmonary ventilation is under consideration, more widespread use might with advantage be made of it. The main difficulty is that it is not applicable to infants and young children under the age of about 6 years. At the moment that must be accepted as a regrettable fact and a challenge to further adaptation. It is to be regarded as an addition to, not a substitute for, the presently accepted standard methods of investigation by way of history, physical and radiological examination and its results have to be interpreted in conjunction with these established basic enquiries.

- FINIS -

"The matter of this communication is founded upon a vast number of facts - immutable truths, which are infinitely beyond my comprehension. The deductions, however, which I have ventured to draw therefrom, I wish to advance with modesty, because time, with its mutations, may so unfold science as to crush these deductions, and demonstrate them to be unsound.

Nevertheless, the facts themselves can never alter, nor deviate in their bearing on respiration - one of the most important functions of animal economy. "

John Hutchinson, Surgeon (1846).

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